

Edible Intelligence: The New Age of
Nutrition

Edited by

Dr. Manisha Maity



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-Dr. Manisha Maity

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Effect of *Allium sativum* (garlic) on fertility : a systematic review

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Abstract

Male fertility is significantly influenced by sperm quality, and disturbances in this process can lead to infertility, which has detrimental effects on many couples. *Allium sativum* (garlic) can improve women's fertility, hormonal balance, menstruation management and maintenance, inflammation prevention, and general wellness. It is a common remedy that may affect male fertility, according to research. According to some research, the antioxidants in garlic may improve testicular shape, testosterone levels, and spermatogenesis. Despite the strong evidence, certain studies indicate that garlic may affect testicular function, which calls for further clinical studies. In addition, the extensive pharmacological effects of garlic in both nutritional and medicinal benefits have been noted. According to previous studies, *Allium sativum*, a superfood, has been known to be beneficial for many therapeutic purposes and is often developed to cure various ailments. Using data from both historical traditional medicine and current scientific studies, this systematic review investigates the effects of *Allium sativum* on male fertility. Because of its antioxidant properties, garlic, as a medicinal plant, is also gaining support as an alternative treatment of infertility-a major problem affecting millions of people across the globe. Male infertility, most often tied to sperm quality and spermatogenesis, is a huge issue both financially and emotionally for couples. Countless options are laying for those, as natural alternatives to invasive treatments like hormone therapies and surgeries can be a hefty financial effort and

very unpleasant. Apart from its culinary uses, garlic has been considered beneficial for its alleged health benefits including cholesterol-lowering, liver protection, anti-cancer, and anti-diabetic properties. Contemporary treatments of garlic hit a fresh controversy over their positive, negative, or neutral effects on female fertility. Given the interesting properties of garlic, there is a need to carry out further work to gain a knowledge of its effects on reproductive health.

Keywords: *Allium sativum*, Menstruation, Inflammation, Spermatogenesis, Superfood, Infection, Infertility

Introduction

Allium sativum (garlic) is widely used around the world for its pungent flavour as a seasoning or condiment. From the history, it is known that garlic has been used for more than 7,000 years by humans. Originally the plant was native to central Asia (Renub, 2021), but it has long been used for consumption (raw or cooked) as seasoning in many other parts of the world such as the Mediterranean region, Africa, and Europe. It has specifically been used for its medicinal purposes in ancient Egypt (Singh et al, 2021). The garlic plant's bulb is the most used part of the plant. As mentioned, garlic or more specifically cloves is believed to have many medicinal properties- blood pressure (BP) regulation; lowering cholesterol and treatment for the common cold (Alam et al, 2016). Even Hippocrates, Galen, and Dioscorides all mention the use of garlic for many conditions, including parasites, respiratory problems, poor digestion, and low energy (Javed et al, 2021). *Allium sativum* is an edible tuber belonging to the family Liliaceae. It has been used since ancient times as a spice to enhance the sensory characteristics of food and as a household remedy for the treatment of a variety of ailments. Garlic has been studied for its medicinal and therapeutic effects in the treatment of various human diseases for a long time. It is associated with the consumption of garlic are attributed to the various sulfur compounds present in it such as allicin, ajoene, vinyl-dithiin, and other volatile organosulfur compounds which are all metabolized from alliin. Several research in the literature have shown evidence that the garlic exhibits antioxidant, antiviral, anti-microbial, anti-fungal, anti-hypertensive, anti-

anemic, anti-hyperlipidemic, anticarcinogenic, antiaggregant, and immunomodulatory properties. In this context, some studies shed doubt on garlic benefits especially on fertility. In fact, garlic has been used in oriental medicine to improve male sexual dysfunction since ancient times, and it has shown beneficial effects in the recovery of testicular functions. But other authors reported the spermicidal effect of garlic. Following these contradictory studies, this review focused on clarifying the current ambiguity regarding the effects of garlic on testicular functions.

Allium sativum

Allium sativum belongs to a family of Amaryllidaceae or the genus *Allium*. Its closest relatives in the onion genus include the onion, shallot, leek, rakkyo and chive (Javed et al, 2021). The bulbs are mainly composed of water (approximately 84.09%), organic matter (13.38%) and inorganic matter (1.53%). The leaves consist of more or less the same components with slightly different ratios (water 87.14%, organic matter 11.27% and inorganic matter 1.59%) (Puvaca, 2022; Ashfaq et al, 2021). The organic matter is mostly carbohydrates while the inorganic matter is compounds such as sulphur and iron. The large number of sulfur compounds contribute to the smell and taste of garlic. Allicin has been found to be the compound most responsible for the “hot” sensation of raw garlic (RG) (Khubber et al, 2020). Allicin, along with its decomposition products diallyl disulphide and diallyl trisulphide, are major contributors to the characteristic odour of garlic, while other allicin-derived compounds, such as vinyl dithiols and ajoene show beneficial in vitro biological activity (Javed et al, 2021). Despite having minimal amount of ions and other compounds, those that are present play a very important role in the composition and overall beneficial effects of garlic (Aggarwal et al, 2022).

Nutritional composition:

Garlic is a vegetable species that can be categorized as a food or a medicinal herb. It is a member of the Amaryllidaceae family or genus *Allium* that is cultivated all over the world. Various Nutritional composition of garlic per 100 g as per

United States Department of Agriculture (USDA) 2019 is given in Figure 1 (United States Department of Agriculture, 2022).

Raw Garlic nutritional composition chart per 100g	
	01 MAJOR CONSTITUENTS Water (59.6 g), Energy (623 kJ), Protein (6.56 g), Total fat (0.5 g), Ash (1.5 g), Carbohydrate (33.1 g), Total dietary fiber (2.1 g), Sugars (1 g)
	02 MINERALS Calcium (181 mg), Iron (3.7 mg), Magnesium (25 mg), Phosphorus (1153 mg), Potassium (401 mg), Sodium (17 mg), Zinc (1.16 mg), Copper (0.299 mg), Manganese (3.67 mg), Selenium (14.2 µg)
	03 VITAMINS Vitamin C (31.2 mg), Thiamin (0.2 mg), Riboflavin (0.11 mg), Niacin (0.7 mg), Pantothenic acid (0.596 mg), Vitamin B6 (1.24 mg), Total folate (3 µg), Total Choline (23.2 mg), Vitamin A (9 IU), Vitamin E (0.06 mg), Vitamin K (1.7 µg)
	04 FATTY ACIDS Total saturated fatty acids (0.089 g), Total monounsaturated fatty acids (0.011 mg), Total polyunsaturated fatty acids (0.249 g)
	05 AMINO ACIDS Tryptophan (0.096 g), Isoleucine (0.217 g), Leucine (0.508 g), Lysine (0.277 g), Methionine (0.076 g), Cysteine (0.065 g), Phenylalanine (0.0185 g), Tyrosine (0.081 g), Valine (0.291 g), Arginine (0.634 g), Histidine (0.113 g), Alanine (0.132 g), Aspartic acid (0.499 g), Glutamic acid (0.305 g), glycine (0.2 g), Proline (0.1 g), Serine (0.19g)

Figure 1: Nutritional Composition of *Allium sativum*

Bioactive components:

The fundamental classes of bioactive substances found in garlic are polysaccharides, phenolic compounds, saponins, and organosulfur compounds. According to reports, garlic bulb contains 36.1 mg kg⁻¹ FW of total flavonoids, 12.64–22.66 mg/1 g of polyphenolic compounds, and 9.92–40.41 mol Trolox/g of antioxidant activity, as measured by the DPPH technique. Other organosulfur compounds that contribute to the bioactive properties of garlic include diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), E-ajoene, Z-ajoene, S-allyl-cysteine (SAC), and S-allyl-cysteine sulfoxide (Alliin). Diallyl thiosulfinate will have the largest contribution.

Allium sativum and human health:

The molecule allicin is unstable and readily degrades. It is therefore recommended to eat raw or fresh garlic because it contains the highest amount of allicin. It is also believed that allicin is what gives garlic its potent smell. The higher the allicin content and related health advantages attributed to the bulb, the stronger the odor (Berginc et al, 2010; Kopec et al, 2020). This instability has prompted pharmaceutical

companies to create alliin, a stable precursor to allicin found in garlic supplements. The body will have a chance to have a good enough level of the beneficial metabolite with the extra benefit of the safer, more stable alternative because it is only released during digestion (Beato et al, 2011; Rouf et al, 2020). Over the years, garlic has been the subject of numerous studies aimed at enhancing human health and is thought to be a meal that can help avoid diseases. The health benefits of garlic infusion-based treatment have led to an upsurge in research on its advantages. In both plant and animal models, garlic has been shown to have anti-atherogenic effects and to reduce the amount of lipid or free fatty acids (Aggarwal et al, 2022). Because of this method, research on garlic substitutes has grown recently, and it has been demonstrated that they mirror the effects of garlic on the human body. Several studies have demonstrated that, under certain circumstances, allium compounds can either prevent cancer or lower a number of cancer risk factors (Sativi, 1999). Although some studies have discovered signs of benefits, others have concluded that it is largely unsuccessful (Ozma et al, 2022). Many of the negative consequences of garlic are yet unknown, despite reports that it has therapeutic qualities. Raw garlic as well as garlic oils and powders would work either as functional or therapeutic food. There are several evidences showing that garlic plays preventive and therapeutic roles in the enhancement of immunity, and its antioxidant properties help combat free radicals (Cheng et al, 2020; Sasaki et al, 2007). A balanced diet composed of functional foods prepared with garlic is beneficial for human health. Garlic can modify blood anticoagulant levels and boost the activity of various organs in the body mainly of respiratory and digestive systems (Lee et al, 2015). It is found that garlic alone puts forth strong positive impacts in management of hypertension (Hussein et al, 2017), diabetes (Mutlu-Ingok et al, 2022), immunity (Kumari et al, 2022), and blood lipid levels (Perez-Rubio et al, 2022) and could actually be of great help in medical-surgical interventions (Daharia et al, 2022).

Effects on reproductive system:

Infertility and particularly idiopathic infertility has been

growing up in the last century. Infertility is defined as failure to conceive following one year of unprotected coitus (Shojai et al, 2016). In 19-57% of the cases, the male is to blame, once infertility concerns arise in a couple (Onyiba, 2022). Thus followed a lot of investigations on male fertility and the male reproductive system. Garlic and its effect on the male reproductive system has caught considerable attention in the Andrology and reproductive field because whereas some researchers believe it to have a beneficial influence, others conclude it has a detrimental effect on the male reproductive system. The differences in views may perhaps arise from the way garlic is prepared and the amounts given.

Effects on female reproductive functions:

Scientific studies have suggested benefits of garlic for sexual health, fertility, and hormonal balance. Nowadays, women's ailments are among the most daunting medical problems that variously affect health and enforce a bunch of serious costs on communities (Renub, 2022). The female reproductive system is a complex set of organs by which reproduction occurs; it includes the ovaries, the fallopian tubes, the uterus, and the vagina, which support menstruation, ovulation, and the birthing process (Cheng et al, 2020). Maintenance of the reproductive system very highly affects the fertility and mental health of women. According to studies, garlic is potentially among the good things for the female reproductive system (Sasaki et al, 2020). According to reports, this plant, for instance, possesses antibacterial qualities that can both prevent and treat illnesses pertaining to the external genitalia (Lee et al, 2015). Garlic has been used in the treatment of infections caused by vaginal yeast for centuries. Especially its antifungal properties may help prevent or lessen the severity of the infections. Its anti-inflammatory properties can also help relieve some symptoms of endometriosis or pelvic inflammatory disease and/or the inflammation of reproductive organs (Ashfaq et al, 2021; Hussein et al, 2017). Studies are going on about the influence of garlic on hormone balance in women. Hormones play a great part in making the menstrual cycle and normal reproductive process (Mutlu-Ingok et al, 2022). Studies suggest that garlic might modulate

the levels of estrogen in the body, by which it might influence the female reproductive system (Wang et al, 2022; Imaizumi et al, 2022). Some findings indicate that the compounds in garlic possess properties structurally and functionally similar to estrogen, which aid in regulating the hormones. Other studies claim that garlic can help control the levels of various hormones in females, including estrogen. Various studies suggest that garlic may/does exert its influence on other hormones, such as progesterone and estrogen, but further research is needed to chart this influence (Kumari et al, 2022).

Anti-microbial properties and Antibiotic properties:

Allicin, found in the garlic bulb, serves as a powerful antibiotic that helps the organism to inhibit the growth and reproduction of bacteria. One milligram of allicin is equal to 15 standard units of penicillin. It inhibits the activity of both gram-negative bacteria like *Aeromonas hydrophila* (Paul et al, 2021), *Pseudomonas aeruginosa*, *E. coli*, and gram-positive bacteria like *Bacillus cereus*, *Streptococcus mutans*, *Staphylococcus epidermidis*, and methicillin-resistant *Staphylococcus aureus* (Girish et al, 2019), salmonella including *S. enterica* and *L. monocytogenes*. Other microbes like fungi and yeast are also inhibited. Broad-spectrum fungicidal activity of garlic extracts was found against *Candida* (Li et al, 2017; Abdallah, 2017), *Trichophyton* (Aala et al, 2014), *Aspergillus* (Abdallah, 2017), and *Rhodotorula* spp. (Al-Bader, 2019). Garlic extract acts antifungal and prevents the growth of *Meyerozyma guillionii* and *Rhodotorula mucilaginosa* (Pârvu et al, 2019). In addition, garlic oil can be used for external applications for the treatment of ringworm, warts, and skin parasites (Papu et al, 2014). Allicin deactivates Streptolysin O (SLO), a very potent cytolytic toxin of about all group. Treatment of SLO with Allicin completely neutralized the haemolytic activity of the bacteria. Garlic extracts have been shown to be antihypertensive in nature. It has been used in treating many diseases, including venereal, tuberculosis, skin lesions, and lung infections.

Anti-tumor properties:

The anti-cancer activity of garlic has been reported to be

emphatic, especially against tumors of the digestive tract. In a review of studies done on human populations, garlic decreased the incidence of esophageal, gastric, and colon cancer (Wang et al, 2022). Several bioactive compounds in garlic, including DATS, allicin, DADS, diallyl sulfide, and allyl mercaptan possess anti-cancer properties (Imaizumi et al, 2022).

Anti-hypertensive properties:

The beneficial effects of garlic as an antihypertensive agent would be due to organosulfur compounds which stimulate factors that relax endothelium and lower blood pressure (Piragine et al, 2022). The extracts of garlic, tested in aqueous form on coronavirus-infected embryonic eggs, could well be used to inhibit or lessen the spread of viruses.

Conclusion

Allium sativum has been proven in numerous studies to have antimicrobial, cardioprotective, antihypertensive, and hypocholesterolemic properties. According to some research, it may also reduce the risk of cancer. A vital component in ready-to-eat snack meals, garlic is an aromatic herbaceous plant that improves the product's flavor, therapeutic effectiveness, and shelf life. Garlic is also a good source of organosulfur and flavonoid chemicals, which can help avoid reproductive abnormalities and are effective in treating a variety of other health issues. To support the claims that garlic can be used to treat and prevent a variety of illnesses, more conventional tests and clinical research are required.

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Millets and Their Nutraceutical Properties: A review

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Abstract

Millets, a diverse group of small-seeded cereals, have gained global attention for their exceptional nutritional and nutraceutical potential. Once regarded as coarse grains, millets are now considered “smart foods” due to their rich content of dietary fiber, antioxidants, vitamins, minerals, and phytochemicals. These grains exhibit resilience in harsh climates, making them sustainable and economically viable crops for food security. Millets possess significant nutraceutical properties that help manage and prevent chronic diseases such as diabetes, cardiovascular disorders, obesity, and certain cancers. This review explores the classification of millets, their nutritional profile, bioactive compounds, health benefits, and potential applications in nutraceutical and functional food industries. The increasing evidence supporting the health-promoting roles of millets positions them as critical components in the fight against malnutrition and non-communicable diseases. Future strategies should focus on improving millet-based product development, consumer awareness, and integrating millets into mainstream dietary systems.

Introduction

Millets are ancient grains cultivated for thousands of years, particularly in Asia and Africa. They include a variety of small-seeded cereals such as pearl millet (*Pennisetum glaucum*), finger millet (*Eleusine coracana*), foxtail millet (*Setaria italica*), proso millet (*Panicum miliaceum*), and others. Millets were historically sidelined in favor of more popular cereals like

rice and wheat but are now regaining popularity due to their superior health benefits and adaptability to climate change.

The increasing burden of lifestyle-related diseases such as type 2 diabetes, obesity, and cardiovascular disease has necessitated a re-evaluation of dietary patterns. Nutraceuticals—foods or parts of food that provide medical or health benefits—play a pivotal role in health promotion and disease prevention. Millets, being rich in fiber, polyphenols, flavonoids, and other functional compounds, qualify as potent nutraceuticals. This paper reviews the various nutraceutical attributes of millets and their implications for public health and nutrition.

2. Classification and Types of Millets

Millets are generally categorized into major millets and minor millets based on their grain size and significance in agriculture.

2.1 Major Millets

- Pearl Millet (*Pennisetum glaucum*): Most widely grown; rich in iron and zinc.
- Finger Millet (*Eleusine coracana*): High in calcium and dietary fiber.
- Foxtail Millet (*Setaria italica*): Known for low glycemic index and antioxidant properties.

2.2 Minor Millets

- Proso Millet (*Panicum miliaceum*)
- Barnyard Millet (*Echinochloa frumentacea*)
- Kodo Millet (*Paspalum scrobiculatum*)
- Little Millet (*Panicum sumatrense*)

These varieties are traditionally cultivated in dryland areas and are known for their drought tolerance and low input requirements.

3. Nutritional Composition of Millets

Millets offer a unique and dense nutritional profile compared to mainstream cereals:

Nutrient	Millets (avg.)	Rice	Wheat
Protein (%)	7-12	6.8	11.8
Fat (%)	1.5-5.0	0.5	1.5
Dietary Fiber (%)	8-12	0.2	1.2
Calcium (mg/100g)	20-350	10	30
Iron (mg/100g)	2-10	0.7	3.5

- **Macronutrients:** Millets are a good source of protein, with finger millet particularly high in essential amino acids like methionine.
- **Micronutrients:** Rich in iron, zinc, phosphorus, magnesium, and especially calcium.
- **Fiber:** High in both soluble and insoluble fiber, supporting digestive health and glycemic control.
- **Antioxidants and Phytochemicals:** Contain phenolic acids, flavonoids, tannins, and lignans with therapeutic properties.

4. Bioactive Compounds in Millets

Millets are a natural source of a variety of bioactive compounds, which contribute to their functional and nutraceutical potential:

4.1 Polyphenols

These are powerful antioxidants that reduce oxidative stress and inflammation. Finger millet is notably high in polyphenols, especially in the outer seed layers.

4.2 Flavonoids

Found in various millets, these compounds possess anti-inflammatory, anti-cancer, and anti-diabetic properties.

4.3 Phytosterols

Present in millets like pearl millet, phytosterols help lower cholesterol levels and improve heart health.

4.4 Tannins

Though sometimes considered anti-nutritional, tannins have antioxidant effects and potential anti-carcinogenic properties when consumed in moderation.

5. Health Benefits of Millets

The consumption of millets is associated with numerous health benefits:

5.1 Anti-Diabetic Effects

Millets have a low glycemic index (GI), slowing glucose absorption. This helps in controlling blood sugar levels in diabetic patients. Studies show that regular millet consumption can reduce fasting blood glucose and improve insulin sensitivity.

5.2 Cardiovascular Health

The presence of magnesium, potassium, and antioxidants contributes to blood pressure regulation and lipid profile improvement. Millet fibers and phytosterols lower LDL cholesterol levels and improve heart health.

5.3 Anti-Cancer Properties

Phenolic compounds in millets possess anti-carcinogenic activity by inhibiting free radicals and modulating cell proliferation.

5.4 Anti-Obesity and Weight Management

High dietary fiber promotes satiety and reduces calorie intake. Millets help manage weight through better metabolic control and reduced fat accumulation.

5.5 Gastrointestinal Health

The prebiotic properties of millet fibers support gut microbiota diversity and help prevent constipation and other GI disorders.

5.6 Bone Health

Finger millet is extremely high in calcium (up to 344 mg/100g), supporting bone mineralization and reducing the risk of osteoporosis

6. Processing and Bioavailability

Despite their nutritional richness, millets also contain anti-nutritional factors like phytates, tannins, and enzyme

inhibitors. Traditional processing techniques enhance their bioavailability:

- Soaking and Germination: Increases nutrient absorption and decreases anti-nutrients.
- Fermentation: Improves amino acid profiles and introduces beneficial microbes.
- Malting: Enhances enzymatic activity and digestibility.
- Decortication: Removes outer husks, reducing tannin content.

These processes not only improve nutritional quality but also enhance palatability and functional use in food products.

7. Industrial and Nutraceutical Applications

Millets are increasingly being used in the development of functional foods, health supplements, and ready-to-eat (RTE) products:

- Millet-based Breakfast Cereals and Snacks
- Gluten-Free Bakery Products
- Health Bars and Nutraceutical Powders
- Fermented Beverages and Probiotic Foods

These applications are expanding due to consumer demand for gluten-free, high-fiber, and organic foods.

8. Challenges and Future Perspectives

While millets have many advantages, several challenges hinder their widespread acceptance:

- Limited Consumer Awareness
- Inferior Taste Profile (compared to rice/wheat)
- Lack of Processing Infrastructure
- Anti-Nutritional Factors

To overcome these, strategies should include:

- Promoting millet-based foods through public health campaigns.

- Government incentives for millet farming and processing.
- Advancing food technology to improve taste and shelf life.
- Encouraging millet integration into school meals and public nutrition programs.

Conclusion

Millets, once marginalized as poor man's crops, are now recognized for their immense nutraceutical and ecological value. Their unique composition of dietary fiber, resistant starch, bioactive compounds, and micronutrients makes them potent tools in combating non-communicable diseases and promoting sustainable agriculture. With increasing interest in functional foods, millets are poised to play a pivotal role in future health and nutrition strategies. Embracing millets as a regular part of the diet, alongside modern processing and product development, can pave the way for a healthier global population and more resilient food systems.

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Anaemia Prevalence and its Associated Variables among Tribal Population in India: A Review

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Abstract

Anaemia is a widespread health issue that is extremely common in both industrialized and developing nations. It is alarming to notice that anaemia exists in countries that are developing at all stages of life. Despite a variety of causes, tribal populations are highly susceptible to anaemia along with in comparison to urban centers, anemia is more common in rural regions. The key causes of anaemia in tribal people consist of low socioeconomic status, inadequate education, poor health and nutrition, and a lack of knowledge of nutrition. Several studies indicate anaemia is prominent among tribal people at every stage of life. Anaemia is more likely among elderly tribal people, even though it is more common in children, pregnant women, and women of reproductive age. According to studies, anaemia in tribal people is caused by a diet lacking in iron, vitamin C, folic acid, vitamin B12, and protein. Anaemia among tribal people can also be caused by environmental factors, such as infections like schistosomiasis,

hookworm, and other parasites that can cause excessive loss or competition for hematological resources. Anemia is a significant social issue in addition to a medical issue since it lowers earning potential and productivity at work.

Keywords: Tribal People; Anaemia; Nutritious Diet; Poverty.

Introduction

According to the census conducted in 2011, 10.43 crore people in the entire nation are tribal, making up 8.6% of the overall population. Of them, 89.97% reside in countryside and 10.03% in urban centers (Dolai *et al.*, 2021). The Indian Constitution was the first document to use the term “scheduled tribes. “Such tribes or tribal communities or parts of or groups within such tribes or tribal communities as are deemed under Article 342 to be Scheduled Tribes for the purposes of this constitution” according to Article 366 (25) defines scheduled tribes (Stiller *et al.*, 2020). The word “Adivasis,” which refers to a broad range of ethnic and tribal groups regarded as India’s original population, is frequently used to refer to these tribal people (Stiller *et al.*, 2020). There is a substantial disparity in the proportion of cases between Union Territories and States when it comes to the incidence rate of anaemia in India. The bulk of the tribal people lives in the country’s hilly and forested areas. 705 Scheduled tribes and 75 Particularly Vulnerable Tribal Groups (PVTGs) are recognized by the Indian Constitution. These tribes are dispersed in one Union Territory (UT) in India and eighteen states. The Scheduled Tribe comprises 52547215 females and 51998501 males. It has been proved that indigenous people are more prone to anaemia compare to general people (Sau *et al.*, 2022).

Anemia is extensively widespread in India and attack on all gender and age group (Sahu *et al.*, 2007). The six fundamental phases of the human life span are fetal, children, infants, adolescent, adult, and geriatric. In each of these phases, people experience daily, gradual, and ongoing changes (Devoto *et al.*, 2009). It may have been caused by a variety of circumstances. Patients with long-term inflammatory, infectious, or malignant illnesses such carcinoma, rheumatoid arthritis, kidney dysfunction, and cardiac failure are frequently

affected by anemia. Infections, genetic predispositions without chronic conditions, and vitamin deficiency are common causes of anemia(Khambalia *et al.*, 2011). As a result, anemia is significantly influenced by illnesses linked to water management, hygienic drinking water and sanitation. Anaemia was accelerated by lack of food, poverty, and low levels of bioavailable iron, especially in the post-weaning phase(Yu *et al.*, 2019).

Red blood cells include the metalloporphyrin hemoglobin (Hb), which is a bilateral gas exchanger that carries carbon dioxide from tissues to the lungs and oxygen from the lungs to the tissues. The World Health Organization (WHO) defines anemia as a condition whereby a person's ability to carry oxygen is inadequate compared to the demands of their body for proper physiology(DeMaeyer *et al.*, 1989). Every nation's development benefits from having healthy citizens. The healthcare system needs to make an attempt to reduce medical problems among tribal members and lower their susceptibility to falling back as a group(Rohisha *et al.*, 2019). A vital indication of poor health state, iron deficiency anemia is largely caused by inadequate nutrition. The increasing need for iron during growth and puberty in children and adolescents sets them at risk for iron deficiency anemia(Kamath *et al.*, 2013).According to Joshi (2011), the overall incidence of anemia reached 95.3%, especially in a group that includes tribal women (Joshi 2011). According to Jai Prabhakar and Gangadhar's 2009 study, 77.1% of the study sample had this condition(Prabhakar and Gangadhar 2009). According to De et al. (2006), the overall incidence of anemia was 53.7% in the state of Arunachal Pradesh, 57.45% in the state of Tripura and 59.82% in Assam indigenous groups (De *et al.*, 2006).

Maternal and neonatal mortality are mostly caused by anemia, and long-term anemia can result in additional organ damage such congestive heart failure. Anemia is a significant social issue in addition to a medical issue since it lowers earning potential and productivity at work. It's a vicious cycle where anemia causes poverty and poverty contributes to anemia. In comparison to urban centers, anemia is more common in

rural regions. In marginalized populations, including tribal populations, the frequency is still rising (Ismail *et al.*, 2017). A higher frequency of anemia among these tribal people may be caused by a number of reasons, including insecurity, low socioeconomic status, malnutrition, lack of education, undesirable cultural practices, lack knowledge of the disease, insufficient geographic connection, and a lack of medical personnel and activities. Because of corruption or a lack of understanding these disadvantaged groups gain the least from government initiatives (Ismail *et al.*, 2017; Panchal *et al.*, 2022; Stiller *et al.*, 2020).

Three main mechanisms can be explored to clarify the pathophysiology of anemia: the loss of blood, enhanced red blood cell breakdown, and decreased red blood cell synthesis. The main causes of chronic blood loss that results in anemia are bleeding disorders and helminthic infections. Red blood cell entrapment from diseases like malaria or structural defects in red blood cells like sickle cell anemia or thalassemia both results in an increase in red blood cell death (Chaparro and Suchdev 2019). Insufficient synthesis of red blood cells can be attributed to various factors such as elevated demand during pregnancy, ongoing infections, carcinomas, and prolonged inflammation that interfere with bone marrow function, or insufficient dietary intake or poor absorption of iron, vitamin A, folate, vitamin B12, or protein, which are crucial components for red blood cell formation (Ghosal *et al.*, 2023; Stauder *et al.*, 2018). Balgir (2006) documented that severe, moderate and mild anaemia were 0.6 to 2.3%, 7.4 to 13.6% and 30.7 to 48.2% respectively in tribal population in Orissa. It was also noted that female was more affected compared to male in anaemia.

1. Methodology

This review work focused on the overall anemia prevalence rate of tribal population in different parts of India. The strategy of this review discovers appropriate research on papers that have been published in India's different states on this topic. The electronic International Journal of Science searches the data on published literary works. The search terms were broad and general at first when it came to anemia, but they were

later filtered based on the purposes of the study. The following keywords were applied to find applicable published articles: micronutrients, WHO and UNICEF, India NFHS, state-by-state tribal, particularly susceptible tribal communities, their occurrence, variables, distribution, and incidence of anaemia.

Prevalence of anaemia in different stage of life in tribal population

Previous studies recorded that tribal people in all stage of life are affected by anaemia. Socio-demographic variables and nutritional deficiencies are main cause of anaemia in tribal population. In the present study, we discussed about anaemia among tribal population in different stage of life.

Children

A serious public health issue, anemia is excessively prevalent in countries that are developing across the globe. Additionally, anemia affects over 40% of children who are under five worldwide (Singh *et al.*, 2023). It has been estimated that 33% of school-age children worldwide experience anemia (Rani and Bandrapalli 2017). Several variables, including socioeconomic status, ecological, biological, and nutritional ones, have been linked to anemia in tribal children, as per studies. This anemia can then cause fetal mortality, poor cognitive function, delayed motor development, and a delay in completing school (Panchal *et al.*, 2022). The World Health Organization (WHO) reports that 1.62 billion individuals worldwide suffer from anemia, with 293 million preschoolers considered to have the highest prevalence of the disease (47.4%); a total of 89 million among those children are Indian. Tribe children are an especially vulnerable group because of a lack of development in society, higher lack of education, restrictive customs, minimal food and health protection, poor living conditions, and an elevated level of malnutrition (Kapoor and Dhall 2016). Hookworm infestation and malaria may cause anaemia among tribal children widely (Sahu *et al.*, 2007).

National Family Health Survey (NFHS-5) reported that the prevalence of any anemia (Hb<11 g/dl) in children aged 6-59 months in India was 67.1% (NFHS-5 2021). Panchalet al., (2022) conducted a cross-sectional study among 300 tribal children

age group of 6 months to 5 years in Santrampur village, Gujarat and of them 87.7% were anemic (Panchal *et al.*, 2022). Dolai *et al.*, (2021) conducted a cross-sectional study among 1010 tribal children age group of 5-13 years and showed that 46.34% of children were anemic overall. Out of all the children that were anemic, 47.65%, 51.93%, and 0.42% (n=2) reported mild, moderate, and severe anemia, accordingly (Dolai *et al.*, 2021). According to Prabhakar *et al.* (2016), children from the Soliga tribe in Karnataka had an overall incidence of anemia of 91.4% (Prabhakar and Gangadhar 2016). According to Sahu *et al.* (2007), 94% of children under the age of five in Orissa were found to be anemic, and 8.8% of them were classified as severely anemic. Nearly every child in the 5-14 age range was anemic; of these, 5.4% were extremely anemic and 59.4% were mildly anemic (Sahu *et al.*, 2007).

Women

According to the World Health Organization (WHO), adult anemia is defined as having hemoglobin (Hb) levels that are below 13.0 g/dl for men and less than 12.0 g/dl for non-pregnant females (Cappellini and Motta). Women during reproductive age of 15-49 years are more prone to anaemia due to their unique physiology such as menstruation, pregnancy, blood loss during childbirth compared to men. Anaemia in women of reproductive age affects the physical condition of the offspring as well as the mother. In populations devastated by anemia, this is one of the main causes of poverty and poor health throughout generations (Ghosal *et al.*, 2023; Tang *et al.*, 2022). Iron deficiency anaemia is extremely common during pregnancy. Anemia in pregnant women might result in premature babies along with a low weight at birth. Tribals are India's most disadvantaged ethnic population, and the actual prevalence and distribution of diseases among them is rarely published (Dwivedi *et al.*, 2023). According to the Demographic and Health Survey (DHS) report from 2005-06, India has a greater than normal incidence of anemia in women and children compared to other South East Asian countries. Anemia is a major cause of maternal mortality, with low hemoglobin concentration being the primary cause in most cases worldwide (Sau *et al.*, 2022). In Rajasthan's

district Sirohi, 85.7% of tribal women had anaemia, with an average hemoglobin measurement of 9.21 ± 1.3 g/dL across three indigenous-dominated blocks: Pindwara, Abu Road, and Sheoganj (Dwivedi *et al.*, 2023). According to Sharma and Ninama (2015) from the southern Rajasthan district of Banswara, there was a 90% total incidence of anemia, with 3.33 percent of women having a severe, 53.33 % having a moderate, and 33.33 % having mild anemia. Merely 10% of women do not have anemia (Sharma and Ninama 2015). Prevalence of anaemia among tribal women was 55.5% in Paschim Medinipur district of West Bengal, India (Choudhury *et al.*, 2014). Correa *et al.* (2017) also found that the overall incidence of anemia was 92.4%, with severe anemia observed in 6.9% of the tribal women participants (Corrêa *et al.*, 2017). In a study of the Trivandrum area of Kerala, it was also found that the prevalence of anemia among ethnic pregnant women accessing basic healthcare was 53.33%. The overall incidence of mild, moderate, and severe anemia had been 26.66%, 25%, and 1.66%, correspondingly (Ponny *et al.*, 2021). The prevalence of anemia among the tribal pregnant women attending primary health care in Trivandrum during the study tenure was 53.33%. The prevalence of mild, moderate and severe anemia was observed as 26.66%, 25% and 1.66% respectively (Ponny *et al.*, 2021). Kamath also documented that 55.9% of tribal women suffered from anaemia in Udupi Taluk, Karnataka (Kamath *et al.*, 2013).

Adolescence girls

Adolescence is the stage of life among childhood and adulthood. It is a distinct period of human development and a critical time for setting up conditions for optimal health. During a growth spurt, the rate of growth is very high. Adolescent health has received international attention during the last decade (Rao *et al.*, 2003). Adolescent girls are more susceptible to the sickness, and the adolescent group is especially exposed to dietary challenges in developing nations. Studies revealed that the most significant nutritional issue in emerging nations was adolescent anemia. When compared to other developing countries, India appears to have a greater prevalence of anemia among adolescent girls (Chandrakumari *et al.*, 2019).

Adolescent anemia has a negative impact on growth and development, infection resistance, cognitive growth, and efficiency at work. Adolescents with chronic malnutrition are more likely to experience undernourishment throughout adulthood and pregnancy, which increases the risk of low birthweight babies—a vicious cycle (Ragini Kulkarni *et al.*, 2019).

Mahanta *et al.*, (2014) was conducted a community based intervention study on tribal adolescent girls in Dibrugarh District, Assam and revealed prevalence of anaemia was 96.3% with median serum ferritin, 22.9 ng/ml (Mahanta *et al.*, 2014). Ragini Kulkarni *et al.*, (2019) also conducted a community-based cross-sectional study among 240 unmarried tribal adolescent girls in Palghar district of Maharashtra and 81.6% exhibited mild anaemia (Ragini Kulkarni *et al.*, 2019).

Elderly life

The aging process impairs and burdens the elderly, leading to an overall decline in their state of health. Even though they are physically incapacitated, the elderly are a valuable resource for any nation (Soren *et al.*, 2022). As the elderly are a significant group of people with several physical and mental health issues, their social and physical wellness has become a difficult challenge in India. Age-related alterations in bone marrow, limited absorption, and other altered metabolism result in inadequate hematopoietic blood cell formation and subsequent loss in hemoglobin, making elderly populations more prone to anaemia (Daniel *et al.*, 2023). Kerketta *et al.*, (2009) showed that 70% of males and 76.7% of females were severe anaemia among tribal of Langia Saora (LS) in Orissa. Geriatric anemia can have multiple causes, including nutritional, psychological issues or pathological factors (Kerketta *et al.*, 2009). Prevalence of anaemia among tribal elderly people was 66.7% in residents of Kannavam, Kannur, North Kerala (Ismail *et al.*, 2017).

Discussion

Perumal (2014) noticed that increasing marital age is a crucial preventive measure against anemia for rural pregnant women in India (Perumal 2014). Extensive awareness efforts

and educational initiatives by government departments and social groups may have had an impact on the indigenous community, reducing the frequency of teen marriages and pregnancies significantly (Bantebya *et al.*, 2014). Several studies have revealed that the frequency of anemia in tribal communities varies from 51% to 91.4% in different parts of India (Dolai *et al.*, 2021; Prabhakar Sc and mysore rajagopal 2017).

Although many elements are required for the synthesis of red blood cells and hemoglobin, iron deficiency is a prevalent cause of nutritional anaemia around the world. Folate deficiency, particularly in pregnant women, is a significant cause of anaemia. A lack of vitamin B12 can cause severe anaemia known as pernicious anaemia. Protein deficit may contribute to anemia in children suffering from severe protein energy malnutrition (Ifeanyi 2018). Intestinal infection by parasites is a major issue for children in rural or disadvantaged circumstances, leading to anaemia and inadequate nourishment. In children, intestinal parasite infections, particularly helminthiasis, can produce a variety of unfavorable health effects, including anemia (Yanola *et al.*, 2018). According to Chakma *et al.*, (2000), 50% of children in Madhya Pradesh having parasitic infections, with hookworms (16.3%) and lumbricoides (18.5%) being the most frequent (Chakma *et al.*, 2000). Anemia and other nutritional deficiencies have been found to be more common among indigenous societies, according to several studies (Leite *et al.*, 2013; Stiller *et al.*, 2020).

Nutritional deficiencies, genetic haemoglobin abnormalities, and infectious disease-related anaemia are more common in low- and middle-income nations (Panchal *et al.*, 2022). When the prevalence of anemia was studied according to age, it was found that the prevalence of anemia in above 10 years of age in adolescent girls was higher than that in boys. This may be connected to the physiological alterations that occur in boys throughout adolescence (the increase in testosterone) and the blood loss that occurs in females during menarche (Dolai *et al.*, 2021).

Anemia is a disease that can be eliminated by dietary changes, improvements in socioeconomic status, etc (Kamath *et al.*, 2013). The dietary approach has the potential for being an effective tool in preventing anemia prevalence. An essential water-soluble molecule that increases non-heme iron absorption by 20–25% is vitamin C (Sau *et al.*, 2022). A whole day's worth of food is cooked just once in many tribal households, resulting in two meals that can be as much as twelve hours apart. Additionally, it was found that nearly 93.7% of children who were consuming meals with low iron bioavailability, or 5–10%. This may happen because to reasons like availability, ignorance, and poverty (Sahu *et al.*, 2007). In these conditions, it is challenging to achieve the requirements for folic acid, iron, and ascorbic acid without supplementing with a high-quality source of these nutrients (Meshram *et al.*, 2012; Sau *et al.*, 2022). Iron, Folic acid and vitamin-C rich food must be included in the daily diet. Table 1 is iron containing food with decreasing order.

Table 1; Iron containing foodstuff with decreasing order (ICMR, 2017)

	Foodstuff	Scientific name	Iron (mg/100g edible portion)
1	Goat spleen	Capra aegagrus	51.41±17.21
2	Turmeric powder	Curcuma domestica	46.08±1.83
3	Beef spleen	Bostaurus	31.68±4.50
4	Pork spleen	Susscrofa	27.21±6.43
5	Pork liver	Susscrofa	20.74±7.24
6	Cumin seed	Cuminumcyminum	20.58±4.24
7	Coriander seeds	Coriandrumsativum	17.64±6.74
8	Asafoetida	Ferula assafoetida	15.68±4.51
9	Gingelly seeds black	Sesamumindicum	13.9±1.60
10	Mustard seeds	Brassica juncea	13.49±3.95
11	Pepper, black	Piper nigrum	11.91±3.48
12	Poultry chicken liver	Gallus gallus	9.92
13	Cloves	Syzygiumaromaticum	9.41
14	Amaranth seed black	Amaranthuscruentus	9.33

15	Tamarind, pulp	Tamarindusindicus	9.16±1.71
16	Horse gram Whole	Dolicusbiflorus	8.76±1.16
17	Curry leaves	Murray koenigii	8.67±0.09
18	Mint leaves	Menthaspicata	8.56±3.21
19	Soyabean brown	Glycine max	8.29±0.51
20	Lentil whole brown	Lens culinaris	7.57±0.67
21	Raisin dried black	Vistisvinifera	6.81±0.91
22	Bengal gram whole	Cicerarietinum	6.78±0.75
23	Bengal gram, dal	Cicerarietinum	6.08±0.27
24	Coriander leaves	Coriandrumsativum	5.30±1.55
25	Egg, poultry yolk boiled	Gallus gallus	4.92±0.33
26	Ragi	Eleusinecoracana	4.62±0.36
27	Puffed rice	Oryza sativa	4.55±1.03
28	Rice flakes	Oryza sativa	4.46±0.81
29	Wheat flour atta	Triticumaestivum	4.10±0.67

Conclusion

A high prevalence of anaemia among tribal population in different stage of life was observed. A lot of factors was impact on prevalence of anaemia among tribal population in various stage of life. These factors are lack of development in society, lack of education, restrictive customs, minimal food and health protection, poor living conditions, and an elevated level of malnutrition and poor health throughout generations. Successful approaches for preventing anemia include food supplements, health services, sanitary development, as well as nutrition and health programmes. Community health professionals, experts in nutrition, nurses, and policymakers may find this review most useful as a teaching tool and guide.

Data Availability

The information included in this systematic review is based on previously published research and databases that have been referenced. Upon reasonable request, the associated author provides the processed data.

Ethical Approval

Since the study's conclusions had already been known, the

authors of the systematic review did not require ethical approval.

Conflicts of Interest

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A comprehensive review on plant-derived anti-cancer compounds

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Abstract

Cancer is one of the biggest health concerns for the human kind and require intervention strategies. Plant-derived bioactive compounds have received spotlight in cancer research since they have been reported for therapeutic potential. Plant based diet contains various phytochemicals which are safe for prevention and treatment of cancer as compared with conventional treatment methods. Studies have revealed the various such sources like dietary fibre and biologically active polysaccharides from mushrooms, lycopene from tomatoes, resveratrol from berries, curcumin from turmeric, which have been shown anti-cancer effects. This study provides information on various plants and their bioactive compounds with potential to cure different types of cancer. The study also highlighted the potential of those components in the drug and food product development. Furthermore, there is an extensive scope for the domain of applications and toxicological studies evaluating the anti-cancer components found in plant sources.

Keywords: Plant-derived bioactives; Anti-cancer; Plant-based diets; Health; Nutraceuticals.

Introduction

The development of anticancer drugs is a highly intricate and technologically advanced area in which numerous aspects such as molecular biotechnology, genomics, proteomics,

and biopharmaceuticals are currently creating significant waves and making substantial advancements in the field of cancer treatment. In the last decade alone, we have witnessed the remarkable approval of a total of 34 distinct cancer drugs; notably, many of these innovative drugs have been derived from natural products found in our environment. For countless millennia, humans have relied on various types of plants as a vital source of medicinal compounds. It is important to acknowledge that while there are a vast number of different chemicals present in plants, the specific compounds that exert definite and beneficial physiological effects in humans are relatively sparse and limited. Out of the small selection of effective plant-derived anticancer agents, three notable ones, which include etoposide, teniposide, and paclitaxel, are currently utilized in clinical settings for treating cancer patients. Various traditional medicine systems across the globe use plant extracts extensively for the treatment of a wide range of diseases and disorders. In many distinct cultures, there is a longstanding practice of using medicinal plants as a first line of treatment for numerous diseases, along with the alleviation of symptoms associated with disease processes, including those related to cancer and other chronic conditions. A striking statistic reveals that over 60% of the current anticancer drugs are derived, either directly or indirectly, from natural sources, underscoring the significance of our natural environment in the development of therapeutic agents. Despite this, many failures in drug development are attributed to a loss of interest in these natural products due to various challenges, including their complex molecular structures, unsatisfactory clinical responses observed upon continual usage, and more specifically, the imminent threat of increased tumor resistance that poses significant complications. Nonetheless, most of the current drugs available on the market are characterized as water-soluble; therefore, the strategic introduction of lipophilic groups should ideally enhance the overall effectiveness of these therapeutic agents by increasing their residence time within the tumor environment, ultimately prolonging their cytotoxic effects and improving patient outcomes in the fight against cancer (Dehelean et al., 2021; Garcia-Oliveira et al., 2021; Huang et al., 2021).

2. Historical Perspective of Plant-Derived Compounds in Cancer Treatment

Cancer is the most fatal of all human diseases. Acute leukemia, lymphoma, breast cancer, brain cancer, and adrenal carcinoma are the most common cancers affecting children in the United States. Current methods of treating cancer, including surgery, radiotherapy, and chemotherapy, are not completely effective. Early detection of the disease often leads to successful treatment. However, delayed diagnosis creates a usually incurable state in the patient. Nearly half of the drugs used for cancer treatment are derived from natural sources. The limitations in current cancer treatments have led to a stress in the search for natural antitumor agents. The prospects of the use of natural products, particularly those derived from plants, have increased in recent years.

Historical Perspective of Plant-Derived Compounds in Cancer Treatment: In ancient times, the physicians treating diseases used herbs as agents. The most significant progress in civilization took place when humankind found that herbs alleviated many health problems. The writings of the Ebers Papyrus report 700 different remedies, including the use of 22 species of biologically active plants. The antitumor effect of many natural products can be verified by different ancient civilizations. For the aboriginal people in different countries, the wealth of natural botanical medicine was a primary living resource. A comprehensive survey comparing modern allopathic medicine with traditional medicine indicates that traditional medicine was effective in alleviating diseases like tumors, abscesses, or tumors in breast cancer and esophagus cancer. The traditional narratives of folklore medicine contain a great deal of herbal remedies for various diseases, including cancer treatment (Huang et al., 2021; Dehelean et al.2021; Ma et al., 2021).

3. Mechanisms of Action of Plant-Derived Anti-Cancer Compounds

Natural phytochemicals, which comprise mainly phenolic compounds and terpenoids, represent potential anti-cancer agents and are beneficial for cancer prevention and therapy. Both in vitro and in vivo studies have shown that these

compounds possess the capacity to prevent a variety of malignancies through the induction of cell cycle arrest and apoptosis. Over the past 10 years, active research has revealed numerous intracellular targets of phytochemicals. Many of these compounds modulate the signaling that determines cell fate in a manner that results in the death of cancer cells but not that of normal cells. We present an extensive overview of and categorize the information on the anti-cancer pharmacology of numerous phytochemicals that have been identified in diverse food sources and medicinal plants and that have been shown to be capable of inhibiting tumorigenesis. In particular, we elaborate, in numerous instances, upon the molecular and cellular targets of the phytochemicals, with special regard for the mechanisms through which they exercise signaling in the regulation of key metabolic enzymes, protein kinases, transcription factors, oncogenes, and tumor-suppressor proteins in cancer cells, as well as for their capacity to target the surrounding tumor microenvironment.

Phytochemicals have been employed for many years in traditional medicine and have stimulated the development of modern therapeutic methods for the prevention and treatment of cancer. One of the major difficulties with plant-derived phytochemicals is that many of the mechanisms of action by which phytochemicals suppress carcinogenesis have remained elusive. Therefore, understanding the mechanisms through which natural phytochemicals modulate gene expression and the signaling molecules involved in cell cycle and apoptosis, as well as specific protein targets, is crucial both for verifying their capacity to prevent the occurrence of tumors and for the optimization of future cancer chemoprevention strategies. We present and discuss the major natural phytochemicals in a varied number of plant-based diets and medicinals that have been employed for preventing tumors, focusing not only on the compounds responsible for the bioactivity but also on the connection between cancer and anti-cancer agents, on the performance of these natural anti-cancer agents, their suppressing processes, and means of action on the different cellular and molecular targets with their potential role in cancer prevention, and on the levels of evidence for their bioactivity (George et al., 2021; Paudel et al., 2023; Ahmed et al., 2022).

3.1 Apoptosis Induction

The pro-apoptotic effects of natural compounds contained in foods have largely been linked to their anti-cancer properties. The use of nutritional therapy to modulate apoptosis both in the initial stages of tumor formation, as well as in the intermediate phases of tumor development, is thought to represent new fields for cancer prevention and treatment. Apoptosis induction is mainly directed by the mitochondrial and death receptor pathways and is regulated through the ratio of pro-apoptotic to anti-apoptotic Bcl-2 family proteins. Plant-derived natural compounds have been shown to promote apoptosis through direct perturbation of the mitochondria or the death receptor itself, thereby inducing cytochrome c release or lowering the mitochondrial membrane potential (Ng et al., 2022; Rizvi et al., 2021).

Following the decrease of mitochondrial membrane potential or cytochrome c release, the apoptosome complex is assembled, leading to caspase-9 autoprocessing and activation of the downstream apoptotic cascade of caspases. Activation of caspase-8 is also a crucial step in apoptosis. Plant-derived phytochemicals can activate these pathways, as well as activate lysosomal enzymes that contribute to lysosomal membrane permeabilization, which in turn can initiate a caspase-independent apoptotic process. Activation of lysosomal cathepsins has been shown to contribute to the release of the apoptosis-inducing factor. Small amounts of apoptosis-inducing factor are normally located in the mitochondrial inter-membrane space, yet upon mitochondrial outer membrane permeabilization and due to its large size, it is normally retained in the inter-membrane space and not released into the cytosol. Any perturbation of this critical balance can lead to apoptosis induction but also necrosis since it stimulates apoptotic pathways. (Rahman et al. 2021) (Khan et al., 2022) (Olędzka & Czerwińska, 2023)

3.2 Cell Cycle Arrest

Several natural compounds derived from plants have been observed to regulate cell cycle arrest in cancer cells. Induction of cell cycle arrest has been considered an interesting strategy

in the eradication of cancer cells. The cell cycle includes four different stages: G1 phase, S phase, G2 phase, and M phase. Numerous studies have reported that cell cycle arrest at the G2/M phase leads to high rates of apoptosis in cancer cells. In the G2 phase, the undivided cancer cells will proceed directly to mitotic events, leading to an ascending mitotic catastrophe. Curcumin shifts the cell cycle distribution of the prostate cancer cell line LNCaP toward the G2/M phase through the downregulation and activation of transcription factor E2F-1, cyclin D, cyclin E, and Cdk2. Quercetin, a dietary polyphenol contained in a variety of fruits and vegetables, has been reported to induce G2/M arrest through the increase of the cyclin kinase inhibitors p21 and p27 in human pancreatic cancer cells. Gallic acid, another dietary polyphenol found in plants, promotes G2/M phase arrest through the upregulation of p21 and p27 protein expression and the reduction of the translocation of cyclin B1 in HCT116 human colon cancer cells. Formononetin and its derivatives, which contain chrysin and biochanin A, have been reported to induce G2/M phase arrest in liver cancer cells. Cell cycle arrest has provided a way to reverse the carcinogenic events and the eradication of cancer cells. In cancer, the cell cycle is not synchronized, leading to an arrest, generally in the G0/G1 or G2/M phase. Cell cycle arrest leads to cell apoptosis or senescence. Some plant-derived compounds can cause disturbance in the cell cycle in cancer cells. Cytotoxic drugs have been found to inhibit the expansion of cancer cells by causing an arrest at the G0/G1, S, and G2/M phases. Some plant-derived compounds have proven their potential for cell cycle arrest. This review will summarize some representative plant-derived anti-cancer compounds and reveal their mechanisms to regulate the cell cycle distribution in cancer. (Wang, 2021; Pani et al.2022; Qi et al., 2021)

3.3 Anti-Angiogenic Effects

An effective regulation of angiogenesis could promise the development of new drugs for cancer treatment. Endostatin, overexpressed in endothelial cells, is translated and cleaved by metalloproteinase, mediates anti-angiogenesis, and is used for cancer therapy. A study reported that the tissue

microenvironment, namely paracrine fibroblast hepatocyte growth factor, has a role in inducing the transformation of endostatin. Recent studies have found that terpenoid is still an excellent candidate for anti-angiogenesis drug development. A compound found that 4'-acetoxy-resveratrol, a resveratrol derivative, inhibited tumor growth in a mouse ovarian cancer model by reducing tumor angiogenesis. Although the exact anti-angiogenesis mechanisms of 4'-acetoxy-resveratrol require further research, this study indicated that 4'-acetoxy-resveratrol inhibits HUVEC migration and suppresses HGF-stimulated *in vitro* tubular formation. (Salla et al.2024; Wang et al.2024)

In the context of progress on the biological justification and successful examples of natural compounds, such as vincristine and camptothecins, the importance of inhibiting tumor angiogenic ability, cancer adjuvant chemotherapy, anti-angiogenesis drug development, and endothelial cell cytology focusing on natural compounds, flavonoids, phenolics, terpenoids, polyynes, and some other plant-derived natural compounds are attracting research on tumor angiogenesis to explore their potential development prospects in the field. Among the compounds, a multi-target natural product is a potent and non-toxic anti-angiogenesis agent that manifests activity in both *in vitro* and *in vivo* animal models. In another example, theaflavins are polymethylated and polyhydroxylated catechins that are present in black tea and inhibit eukaryotic peptide chain initiation by binding to the ribosomal subunit. Additionally, the activation of AMP-activated protein kinase and its downregulation of VEGF and hypoxia-related signaling contribute to its anti-angiogenic effects. (Kciuk et al.2023; Thiruvengadam & Kim, 2023)

4. Clinical Studies and Evidence-Based Research

Aloe-emodin was evaluated for its cytotoxic effects in a liver carcinoma cell line and showed that hardness was influenced by its long-term use; tolerance suggested its possible use in the treatment of breast and colorectal carcinomas. Resveratrol in conjunction with red clover was used in 62 women who had a family history of breast cancer, discussing their safety and concluding that this randomized, double-blind, placebo-

controlled trial using resveratrol in high-risk women showed no safety issues, which is certainly important for future clinical research. Another phytoestrogen is genistein, which was studied and showed that when used alone, either in hormone-dependent, hormone-independent, or hormone-positive cells, it inhibited cell growth by 60%, 40%, and 90%, respectively. These results may be interesting in the future development of new breast cancer treatments. (Sharifi-Rad et al., 2021; Rendón et al., 2022)

5. Future Directions and Potential Applications

Phytochemicals derived from edible plants have been reported to exert medicinal effects against cancer through various pharmacological activities, such as inducing cell cycle arrest, activating apoptosis, modulating pathways and inflammatory activity, and inhibiting invasion and metastasis. Herein, we will provide a comprehensive review on cell-line and mouse model studies of a variety of edible plant-derived anti-cancer compounds. The bioavailability, bio-efficacy, and molecular targets of these compounds in relation to their inhibition of cancer initiation, growth, migration, and invasion are also discussed. There are various mechanisms by which dietary compounds inhibit cancer cell growth, including preventing initiation by modulating a pro-oxidative imbalance; increasing apoptosis and suppressing the natural release of tumor suppressive genes; inhibiting migration and invasion by suppressing cytokine signaling and promoting extracellular matrix control; and decreasing angiogenesis by decreasing tube formation and secretion of VEGF. These powerful mechanisms have led to a growing interest in nutraceuticals and new possibilities regarding their use in drug combination strategies or in the design and synthesis of related compounds. Our review offers additional investigation guidelines and proposes ultimate goals to further develop these compounds into anti-cancer therapeutic drugs. (de Carvalho & Conte-Junior, 2021; Macharia et al.2022; Regassa et al.2022)

Conclusion

Increasing levels of cancer incidence have forced the pursuit of unconventional medicines and the examination of traditional plants. Nature, especially plants, has embraced a significant role in treating several diseases, including cancer. The discovery or invention of new drugs is not necessary since many conventional products play a vital role. This review highlights anti-cancer medicinal plants and some of the most common bioactive compounds produced by these plants. However, cancer treatments depend on the medicinal plants for their metabolites with significant levels of protection that can satisfy medication safety and effectiveness demands. The physiochemical, pharmacological, and absorption-distribution-metabolism-excretion-toxicology predicted properties and molecular docking data are analyzed by performing an *in silico* scientific investigation, promising the anti-cancer compounds from naturally derived metabolites.

The plant-derived metabolic profiles could be seen as an important resource for continued drug discovery and development. The continually increasing capacity of computational biology methodologies resolves the unsatisfactory biosynthetic efficiency and bioactivity distribution of existing bioactive metabolites from plants. In conclusion, natural medicines have a vital role in the treatment of cancer, and many metabolic compounds that have demonstrated a capacity for cancer therapy are packed in these natural products. Given the above information and investigations, we can confirm that plants may be a main source of bioactive anti-cancer compounds for chemoprevention and chemotherapy and could promote further investigations of plant-based medicinal anti-cancer compounds, even though some compounds may be harmful when consumed in high levels or cause toxic effects to immune systems or organs.

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Traditional Fruits of Odisha: Nutritional Value and Functional Properties

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Abstract:

This review highlights the nutritional and functional properties of traditional fruits native to Odisha, India. Odisha's rich biodiversity provides a variety of fruits with significant health benefits, including antioxidants, vitamins, and bioactive compounds. Key fruits such as Bael (*Aegle marmelos*), Jamun (*Syzygiumcumini*), and Wood Apple (*Limoniaacidissima*) offer unique therapeutic potential, traditionally utilized in managing conditions like diabetes, inflammation, and digestive health. This paper explores the nutritional composition, phytochemical properties, and potential health applications of Odisha's traditional fruits, drawing attention to their functional role in promoting health and preventing diseases.

Keywords: fruits, health benefits, nutrition, functional properties, *Syzygiumcumini*, *Aegle marmelos*, *Limoniaacidissima*

Introduction

Odisha, located on the eastern coast of India, has a rich diversity of native fruits that have been consumed for centuries due to their nutritional value and medicinal benefits. Many of these fruits are high in essential nutrients, antioxidants, and phytochemicals, providing both dietary value and therapeutic effects (Behera et al., 2017). With a growing

interest in functional foods, understanding the properties of these fruits has become essential for promoting health and preserving cultural food practices. This review examines the nutritional profiles and health benefits of Odisha’s traditional fruits.

1.2 Nutritional Composition of Traditional Fruits

1.2.1 Bael (*Aegle marmelos*): Known for its high vitamin C content, bael is also rich in dietary fibre and minerals like calcium and phosphorus. Its pulp contains significant levels of phenolic compounds, which provide antioxidant activity (Swain et al., 2018). Studies indicate that bael’s fibre and nutrients support digestive health, making it a valuable addition to traditional diets (Patra et al., 2020).

1.2.2 Jamun (*Syzygiumcumini*): Jamun is widely recognized for its anti-diabetic properties, containing compounds like jamboline, which assist in controlling blood sugar levels (Sharma & Pant, 2017). It is also rich in iron, vitamin A, and flavonoids, which help improve vision and bolster immune health (Tripathy et al., 2019).

1.2.3 Wood Apple (*Limoniaacidissima*): The wood apple is high in vitamin C, calcium, and potassium, known for its anti-inflammatory and antimicrobial properties. The fruit has been used traditionally for treating gastrointestinal issues and is high in antioxidants that support cellular health (Mishra et al., 2018).

1.2.4 Custard Apple (*Annona squamosa*): Custard apple is rich in energy, carbohydrates, and dietary fibre, which aid digestion. The fruit also contains vitamin B6, which plays a role in mental health and reducing stress levels (Behera et al., 2017).

Table: Nutritional Composition of Traditional Fruits of Odisha from Previous Studies

Fruit	Nutritional Components	Key Nutritional Highlights	Reference
Bael (<i>Aegle marmelos</i>)	High in dietary fibre, vitamin C, calcium, phosphorus, potassium	Rich in antioxidants and bioactive compounds	Swain et al. (2018)

Jamun (<i>Syzygiumcumini</i>)	Iron, vitamin A, calcium, magnesium, phosphorus, flavonoids	Known for its high iron and vitamin A content; anti-diabetic	Sharma & Pant (2017)
Wood Apple (<i>Limoniaacidissima</i>)	Vitamin C, calcium, phosphorus, fibre, tannins, flavonoids	High vitamin C content; excellent for digestion	Mishra et al. (2018)
Custard Apple (<i>Annona squamosa</i>)	High in carbohydrates, dietary fibre, vitamin B6, potassium	Rich in energy, vitamins, and essential minerals	Behera et al. (2017)
Kendu (<i>Diospyros melanoxylon</i>)	Vitamin C, tannins, phenolic compounds, fibre, iron	High tannin and iron content; used traditionally for its health benefits	Patra et al. (2020)
Jackfruit (<i>Artocarpus heterophyllus</i>)	Carbohydrates, vitamin C, potassium, fibre, protein	High energy, fibre, and antioxidant properties	Dash & Dash (2019)

1.3 Functional Properties and Health Benefits

1.1.1 Antioxidant Properties: Many traditional fruits of Odisha, like bael and wood apple, contain high levels of antioxidants, which play a crucial role in reducing oxidative stress, lowering inflammation, and preventing chronic diseases such as heart disease and cancer (Swain et al., 2018).

1.1.2 Antidiabetic Effects: Fruits like jamun are commonly used in traditional medicine for their antidiabetic properties. Jamboline, a bioactive compound in jamun, helps to regulate blood sugar and enhance insulin sensitivity, making it beneficial for diabetes management (Sharma & Pant, 2017).

1.1.3 Anti-Inflammatory and Antimicrobial Benefits: Wood apple, due to its bioactive compounds, exhibits both anti-inflammatory and antimicrobial properties, helping to prevent infections and support immune health. These properties make it beneficial in traditional medicine for treating infections and promoting wound healing (Mishra et al., 2018).

1.1.4 Digestive Health: High-fibre fruits like bael and custard apple contribute to digestive health by improving gut motility and acting as prebiotics, supporting beneficial

gut bacteria. This aids in nutrient absorption, alleviates constipation, and improves overall gastrointestinal function (Patra et al., 2020).

Table: 2 Functional properties and health benefits of the traditional fruits of Odisha.

Fruit Species	Local Name (Odia)	Functional Properties	Health Benefits	References
<i>Carissa carandas</i>	Karanda Koli	Contains antioxidants, vitamins, and minerals.	Exhibits anticancer, antidiabetic, anthelmintic, and adaptogenic activities.	Ahuja et al., 2024
<i>Citrus medica</i>	Limbu	Rich in vitamin C and antioxidants.	Acts as an analgesic, antioxidant, anticancer, and possesses antiulcer properties.	Patra& Basak (2020)
<i>Ficus auriculata</i>	Raja Dimiri	High in antioxidants and possesses antimicrobial properties.	Offers antimicrobial and antifungal activities.	Jenipher et al. (2025)
<i>Limoniaacidissima</i>	Kaitha	Contains bioactive compounds with medicinal properties.	Functions as an antidiabetic, anticancer agent, and aids in wound healing and hepatoprotection.	Amardeepa& Vijayakumar (2025)
<i>Phyllanthus emblica</i>	Aonla	Extremely rich in vitamin C and antioxidants.	Provides astringent, laxative, antipyretic, analgesic, and diuretic effects.	Tiwana et al. (2025)

<i>Sonneratiacaseolaris</i>	Orua	Contains essential nutrients and bioactive compounds.	Used as vegetables, acts as anthelmintic, relieves cough, and serves as an antiseptic.	Aznawi et al. (2025)
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Future Research and Applications

While traditional fruits of Odisha have been shown to have beneficial properties, further research is necessary to explore their bioactive compounds, dosage, and mechanisms of action in health and disease prevention. Developing functional food products using these fruits could promote local biodiversity and enhance community health.

1.5 Conclusion

The traditional fruits of Odisha possess rich nutritional and functional properties, making them valuable for both diet and health. Emphasizing their consumption and integrating them into modern food systems could provide health benefits while preserving cultural heritage. Ongoing research and awareness are essential to realize the full potential of these fruits in promoting health and preventing disease.

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A Comprehensive Review on Analyzing the Effectiveness of Different Leaves in Food Packaging: A Sustainable Alternative to Plastics

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Abstract

This work is aimed at reviewing the effectiveness of different leaves and their potential applications in the field of food packaging. In the realm of technological advancement, every material, whether it is in a developed stage or at an early stage of manipulative configuration, is under scrutiny to its maximum potential to be utilized as a resource for humans in a more profitable, affordable, and eco-friendly manner. Particularly in the case of the packaging requirements that are significantly inclined towards plastics, it is crucial to comprehend a plastic-less environment, as plastics are considered a pet feedstock, which indeed takes several decades to break down. Although in most of the packaging requirements, plastic, a very big resource, plastic waste impacts several environments, including air, the aquatic environment, soil, non-microorganisms, soil microorganisms, insects, and even humans, leading to complete damage.

Several parameters related to economic, physical, chemical, and mechanical flow, ductility, and stiffness have been discussed together with advanced applications of nano-fibers and mixed fiber reinforced polymer matrices. This study deliberates the role of leaves and leaf-derived fibers as good reinforcements in polymer composite matrices for advanced packaging requirements. In this context, the packaging

requirements that are significantly inclined towards plastics make human life more beautiful and facilitate the transportation of foodstuffs. However, the million tons of facilities producing plastic waste affect the environment in a critical way. Furthermore, the obliteration of this waste plastic is essential as it decomposes very slowly and can also bind chemical pollutants as well as toxins, cause diseases, and ultimately lead to human death. Therefore, a feasible and eco-friendly resource has to be generated that substitutes plastic waste entirely.

Keywords: Biodegradable packaging, plastics, pollution, plant leaves.

Introduction

Due to the increasing scale of pollution caused by plastics, the research and development of biodegradable and environmentally-friendly materials have been affected worldwide. Food packaging itself is an item carried by the product, but it is also expected to provide proper protection to the commodity. Therefore, the need to balance an environmentally friendly product with enough mechanical strength and other protective properties required by use is the main purpose of this study. In the packaging system, materials, and processing technologies are essential. Inert, low-cost, lightweight polymers, such as polyethylene, polystyrene, polypropylene, polyethylene terephthalate, and polymethyl methacrylate are commonly used in the packaging and other sectors. However, it is difficult to manage these plastics after use. The discharge and decomposition of these plastics contaminate natural resources and the environment. Since 1950, humans have produced about 8.3 billion metric tons of plastic waste. Due to the global production of plastics and lack of recycling processing, approximately 79% has been accumulated in landfills and the environment, resulting in various problems and damage. Plastics come into the food chain through animals, water sources, and other items after pollution of the marine ecosystem. Thus, researchers and scientists are compelled to turn their attention toward finding biodegradable and environmentally friendly alternatives such as leaves, bark, nutshell, soil, almond, and many

more that degrade within days or weeks and do not create toxic pollution in nature. Food packaging is defenseless against possible external damage, such as mechanical or environmental threats. So, it is necessary to use multiple materials together with different barrier properties to protect the compressed food industry (Koketso Ncube et al., 2020).

1.1. Background and Rationale

Plastic as the most common material used in the food packaging industry is a serious cause of environmental pollution. The aim of this study is to find if leaves can be used effectively in place of plastic as poly bags, poly covers, etc. for food packaging and to determine how effective these are compared to plastic. A comprehensive, systematic review of the literature is conducted to understand the effectiveness of utilizing different leaves in food packaging. The topic is discussed in a multidisciplinary frame, and historical materials, cultural heritage, scientific methods, market demands and trends, waste management, and contributions to standardization are reviewed simultaneously.

The use of plastics, an environmentally harmful product, significantly increased during the COVID-19 pandemic. Promoting environmentally friendly, low-cost, and sustainable use of resources for the packaging industry is crucial. Leaves as natural materials are a sustainable, abundant, and biodegradable alternative source for food packaging instead of plastic. Over 50 countries use different leaves for food wrapping, and the business is worth over a billion dollars. It seems so important to revive this ancient tradition.

The use of leaves for wrapping food goes back to ancient times, and mutual transitions exist on the subject between 7.000-year-old Chinese and South African traditions. More than 300 different edible leaf-based meals could be found worldwide. There is an important relationship between plant- and tradition-specific food, such as a curry made of mutton-mint or okra-lemongrass kept in banana leaves. Local soil, water content, plant, cultivation, geographic, and social conditions directly affect the taste, preparation, and

method of the food. Additionally, 50% of traditional post-cook food waste is easily decomposed in 2 to 4 weeks without environmental pollution.

1.2. Research Aim and Objectives

The research aims to study and analyze the effectiveness of packaging leaves in comparison with conventional petroleum-based plastic for food packaging efficiency. Furthermore, to attain the central objective, it is important to analyze a variety of leaf mechanical properties, barrier performance, and biodegradability (Agarwal et al., 2022). Packaging is essential because it provides security, containment, information, physical and chemical safety to food, and finally to satisfy commercial values. Nevertheless, the employment of conventional petroleum-based packaging has raised environmental problems. Therefore, it is important to analyze the effectiveness of bio-based or natural leaves for packaging material in order to reduce or replace conventional petroleum-based packaging. The table below lists parameters for appropriate packaging material performance. Real amounts and measurable ranges are given from the guidelines of suppliers.

For research purposes data will be collected from suppliers or wholesalers of leaf packaging. Since most of the leaf packaging is produced locally, suppliers are identified and will be contacted for more information. As a competitive initiative, data accumulation for petroleum-based plastic packaging is comparable locally. The reason is that, the growth and production of leaves and petroleum-based plastics are different. However, as a result of utilization, there is a competition for consumption and industry development. Statistical methods or tests will then be used between the means. Successful leaf packaging should also meet the needs about running out time before a category or group of leaves can be packaged. This research focuses primarily on mechanical packaging leaves, (either acceptance or not), and the barrier to petroleum-based plastic packaging (it should also be involved, but as discretion). For mechanical aspects, researchers will study further awareness of types of leaves that have overall sturdiness, are easily folded and unfolded, etc. (Parra, 2008). For packaging, statistical tools will be used.

2. Literature Review

Food packaging is currently the largest segment of the plastic packaging market, with fresh food products accounting for the highest share. However, plastics are neither good in terms of health nor environmental protection. The most commonly used plastics significantly compromise the environment and health. On the one hand, the plastic production process and waste incineration lead to toxic emissions, release of greenhouse gases, and generally negative implications for the environment. Mainly, because these are usually prepared from petrochemical sources, may consist of hazardous substances. On the other hand, poor plastic waste management causes the soil, plants, and small animals take up all these toxic substances from the environment and transfer them to the human body through the food chain. This directly threatens human health. In addition, it causes the death of many aquatic and terrestrial species. As stated above, plastics are non-biodegradable and deteriorate over time, presenting another significant risk to health because they break down into very small particles due to the effects of UV rays, and are released to the soil, water, and air, which affects natural life in a negative way. Particles smaller than 2.5 microns can pass into the cells of living things and cause serious damages like cancer (Koketso Ncube et al., 2020).

Sustainability is an increasingly important factor for developing new materials, especially in packaging. It is questionable how long the packaging industry based on non-biodegradable and harmful-to-nature plastics can maintain its dominance. For this reason, it is necessary to try to find new alternative materials that are effectively used in packaging, have a lower impact on nature and health, and have specific advantages in terms of economic sustainability. There are many different alternative material options that can replace plastics. It will not be possible to acquire the desired properties of a plastic material from a single alternative material. Because of this, composite materials consisting of several different ingredients have begun to be produced, and there have been very successful developments so far. One of them is edible films and coatings prepared from biodegradable

materials such as proteins, polysaccharides, lipids, and their combinations. With the increasing importance of sustainability today, many different natural materials, such as leaves, are explored as alternatives to plastic (M. S. Cruz et al., 2022). Since dried leaves are natural biodegradable products, when compared to plastics, they have better degradability into the environment and can be considered as an alternative to plastics in an important field such as food packaging.

2.1. Current Challenges in Plastic Packaging

Plastic materials are an integral part of modern day-to-day life, especially in packaging applications like food packaging. Various forms of plastic materials have been employed in packaging industries, which tend to be non-biodegradable in nature. The impact of such materials on the ecosystem has become devastating due to their slow rates of disintegration, resulting in accumulation of waste at unprecedented rates. There is a compelling breadth of research concerning the impact of plastic materials on the ecosystem. Yet another issue of concern is the leaching of harmful chemicals from plastic materials to the drink or food stuffs, especially at high temperatures. Almost all plastic materials release bisphenol A or phthalates, out of which a portion of the leaching compounds are considered as toxic to the drink or food stuffs (Koketso Ncube et al., 2020). All these issues have led to the search for alternative materials that can replace the conventional plastic materials in food packaging applications.

Plastic food packaging: a disaster: A significant amount of the plastic waste generated comes in the form of food packaging. A broad variety of the packaging materials used for traditional food packaging are non-degradable and are based on synthetic plastic polymers. Environmental concerns, land contamination, waste related issues, and protection from pollution are some substantial problems related to the use of these non-degradable plastic materials. The disposal of the plastic wastes is a crucial concern due to the shelf life of the wastes, which may not be in a position to degrade over many dozens of years. Many species of animals die due to ingesting various types of plastic wastes (M. S. Cruz et al., 2022). Likewise, numerous considerations damage the municipal

and industrial effluents due to the flow of the plastic wastes. Burning plastic waste generates highly toxic and carcinogenic fumes. Wastes consisted by plastics if discarded constitute approximately 25–35% of the litter. Integrated efforts should be put forth to resolve the utilization of environment vulnerable materials like synthetic polymer based packaging materials. This will create awareness and guide the people to make due use of the eco-friendly sustainable materials like biodegradable based packaging materials. And since, formation matter is conspicuous; numerous biodegradable matter forming sources are discussed. The comprehensive information related to biodegradable based food packaging materials is encapsulated here. The only long term option to all these problems is to minimize plastic packaging usage or to look for some eco-friendly alternatives, out of which replacement of plastic materials with biodegradable is considered as a more promising one.

3. Types of Leaves Used in Food Packaging

Packaging presents a major environmental challenge, with plastic as the chief agent of concern. This has led to a renewed search for alternative materials, especially from the standpoint of sustainability. In this context, wide interest is being shown in using natural leaves for packaging foods since ancient time. This section outlines various types of leaves used to package foods. Various leaves offer aesthetic properties to provide a vehicle for cultural coding of the contents, which may be particularly significant when the leaves used are symbolic or culturally charged in a special way. Three main leaves can be readily used in food packaging are discussed, viz. areca nut leaf, plantain leaf, and sal leaves.

The use of leaves for packaging fresh meat and fish contributes to odor absorption and preservation. Plantain is not used in this process in the traditional Tamil diet. Leaves used in the refrigerated foods market may change rapidly in their home country context, due to the direct consequence of the phenomenon of globalization (Agarwal et al., 2022). The use of plantain leaves for wrapping varies according to different regional and culinary practices emergent in India's changing socio-economic context. There have been wide changes in the

availability of plantain leaves in the wake of the development of the supermarket economy in India, cut leaves in general no longer being locally processed; this has dramatically changed traditional food production and consumption practices in south India.

3.1. Banana Leaves

Food packaging is an essential aspect of food safety that consists of various methods of storing and preserving food. Traditionally, food is wrapped in various materials such as banana leaves or corn husks and the contained food is then warmed or baked. Modern packaging is typically made of plastic, paper, or other materials. In more recent times, food packages have been provided with a center seam having a folding edge flaps at opposite sides of the seam, respectively attached to the seam sides. The edge flaps are retained closed partly by adhesive and partly by tucking the edge flap bound by adhesive inside the other edge flap. The edge flaps are detached from their closed state by separating the side seams by handling a flexible band through openings located in each edge flap. Such a package can serve as an alternative to paper packaging, as engaging would prevent it from opening and exposing the food during transportation.

Banana is one of the top 5 most consumed fruits globally. Bananas are eaten all over the globe by people from various cultures. Banana plants are also cultivated in nearly all countries. Thus, a great deal of banana leaves is potentially available for packaging. It would make it possible to develop multiple wrapping variants that are specific to several Asian and African nations, and customized to their traditions. A container for food packaging has a transparent envelope housing a piece of a butter flake, where the corresponding sizes of the transparent envelope and the piece of a butter flake are optimized so, when said packaging is exposed to transmittable light, the piece of the butter flake contained in the transparent envelope looks like a real piece of a butter flake. Such a container for food packaging makes it possible to preserve the fresh look of the piece of a butter flake, which is likely to lure the attention of a larger consumer audience (Ai et al., 2021). With a goal towards substituting

plastic food packaging, using the transparent envelope may include materials that allow free transmission of UV light but simultaneously secure the piece of the butter flake.

3.2. Palm Leaves

Palm leaves are traditionally being used around the globe for wrapping or making plates to cater food. Palm leaves are available in varieties like coconut or palmyra leaf, areca nut leaf and palm leaf, and offers a wide range of application (Gigante et al., 2023). The simplistic and artisanal process to manufacture varied utility items has dated back centuries in different parts of the world. These leaves are processed traditionally and it involves sun drying, washing with water and wiping out the dust with a clean cloth. The natural wax coating (cuticle) present on the dried leaves after wiping prevents damage due to heat and moisture. This cleaned leaf is placed in the press/mould and is heated by gas stoves, for a while, which makes the plate is ready for marketing. However, the process to make plates/containers differs in their indigenous traditional methods.

Palm leaves are durable with high stiffness, can hold weight for a longer time, resists moisture up to 2–8 h and can withstand heat at a temperature ranging between 120 and 180 °C. This shows that applications are broader and they are also used in different parts of world especially in India, Sri Lanka, Indonesia, Malaysia, Thailand, Vietnam, Cambodia... and other parts like Canada, UK, Australia and New Zealand. Considering both ancient cultural and recent applications, designer/bio-plastic technology can be tailored in such a way for above mentioned long back cultural application, this would have assured that dryer leaves are suitable for modifying with designer/bio-plastic technology dominated by poly-caprolactone. The drying machines can underline the development of a new range of sustainable technology for simple, clean and sustainable innovation to eliminate traditional kerosene heater. The proposed processing machine will definitely be having a quality improvement supplying higher value in the end product compare. As palm leaves are abundantly available, these are much cheaper but it is of innovative one, can create employment, improve income,

can earn foreign currency to the developing economy. On the other hand, a lab scale testing machine can be designed and developed for the other leaves on pilot scale.

3.3. Lotus Leaves

3. Results And Discussion

3.3. Lotus Leaves

Reusable bags or disposable food packaging can be produced using lotus leaves instead of plastics. In India and Southeast Asia, this style of packaging has become very popular. The advanced analyses found that the leaves of the lotus plant are hydrophobic and have antimicrobial properties. In food packaging, leaves from regionally available plants such as ruellia, teak, hemp, and lotus have been proposed as environmentally acceptable alternatives to non-biodegradable polymers. These plants are also widely used in local Indian medicine. The lotus leaf, in particular, has a long hydrophobic surface microstructure with a high contact angle and possesses a natural hydrophobicity.

Lotus plants occupy a significant place in the traditions and culture of both Eastern and Western civilizations, and the natural scum on the leaves of the lotus plant gives the leaves hydrophobic properties, which also has an antimicrobial effect (Dai et al., 2023). An elegant umbrella is made of natural leaf material, which is chemically resistant to water and dirt and has the potential to act as a wiper for internal health protection. When people look at the lotus leaf, they wonder about the environmentally amazing and sustainable chemistry that creates a robust rough surface. It could also serve as inspiration for products. Food preservation: People throughout history also use leaves as plates, cups, and baking dishes. Today, some high-end restaurants still serve food directly on a bed of hay or a banana leaf rather than a plate. Wine from medieval Sweden was made using fruit juices and a few units of spruce resin. China was the first recorded drinking vessels made out of various materials, such as bronze, pottery, stones, trees, animal horns, and hooves. The use of human-made cups dates back to the Neolithic era, and the oldest at the time was thought to be a ceramic pottery

cup. The Drinking Cup of God, an archeological artifact, was discovered in the tomb of King Dennis Hymn (Romão et al., 2022).

And the shape is close to a beer bottle; it seems that alcohol is very important for sacrifice. Tea is the most popular drink besides water. Tea culture originated in China and then spread to Japan, England, Costa Rica, and other areas, and was specially developed by humans from consuming it to growing it. There is a certain Tealab language system. Japan has the world's first Tea Set, which includes tea jars, pots, cups, towel cloth, and chopsticks. At that time, a nozawa was used. As a drinking vessel for tea, nozawa is made of pottery and has a treelike bark. Insert the wooden edges of the paper tree into the cronies, and the hollow edges around corn grow out over time. With the stamen of the isthmus plaited together, the beverage tree was actually rejected as parchment paper.

4. Mechanical and Barrier Properties of Leaf Packaging

The strength and durability of packaging materials are very important because a package should be able to withstand various handling and storage conditions. Leaf materials have been shown to have good mechanical properties that are in the range of commercially available paperboard products. The mechanical properties of leaf packages were measured and their strengths and stabilities were determined. The extent of strength and durability also strongly depends on the type of leaves and the type of manufacturing processes. Greater bio-composite strength also relies on the pattern of interlacing of the components in smaller scale. Leaf packaging materials with good mechanical properties are a promising alternative to thermoplastics due to their biodegradability and sustainability (Syafiq et al., 2020). They also need to have good barrier properties. Leaf materials have been found to have good resistance to moisture and gases which can be of advantage in prolonging food freshness. Barrier properties of leaf packages against oxygen, water, and water vapor were also tested and the values obtained were compared with commercially available polyethylene packages (Trottfeld et al., 2023). This study showed that the values of oxygen and water vapor transmission rates of some bio-composite

packages were better than some of the leaves and were in the range of commercially available polyethylene packages.

To assess the suitability of leaves in food packaging applications, studies need to be conducted to look at the current frontier of bio-based materials has helped promote the use of leaves as packaging materials. To this end, an accurate understanding of the mechanical and barrier properties of leaves is essential. Existing comparative studies indicate the effectiveness of leaf packaging, though it is paramount to delineate a broader knowledge. Antarctica provides a relevant benchmark to evaluate the performance of leaves. The purpose of this article is to review the research and developments of leaves for packaging, focusing on the mechanical and barrier properties. Given the nature of packaging, the review constitutes a range of leaves that are indispensable to a comprehensive evaluation.

4.1. Strength and Durability

The most prominent advantage of a packaging material that is strength and durability. The packaging material should have attractive and robust appearance. As an object that has to store, organize, and transport something, the packaging's load should be considered. A packaging should be compacted, hardly break, and not easily bent (Wang et al., 2022). Especially for safety packaging, it is always considered to choose a robust packaging that has been displayed with many large-lettered warnings.

A competent and convincing packaging study should have been able to display a strain analysis topic. Over loaded packaging could reveal the inherent properties of strength of the packaging itself. Quasi-static stress analysis must indicate the loadings that cause failure, or yield, in the packaging, the degradations in strength, or, in a failure analysis, the locations at which failure initiates, and aspects of the packaging that prevent catastrophic failure. Compression is the most wanted case to store objects. In numerous cases, the packaging is piled on top of one another after being loaded with objects, which increases the loading of the underlying covers. In these instances, an analysis in which a load is applied at a horizontal

surface in contact with the packaging is all the more helpful, but another possible analysis is an analysis in which an object in the shape of a wedge rests on the packaging material. So, the contact surface area and numerical static analysis for the packaging's form of leaves would be highlighted in this study. Folding processes are popularly tempting due to the ease of manufacturing (Syafiq et al., 2020). Cloth and bag-like packaging are impossible to manufacture without folding, and inherently have a reduced strength at their creases. Conversely, blown containers can store a larger amount of the object, and their round shape has a high strength until catastrophic failure occurs. It's required to find a way to laminate the existing packaging to increase its strength or design a new way of ways packaging for leaves that can store objects more effectively. Interwoven leaves and palm leaves are difficult to tear along the weave, greatly increasing the effective tensile strength of the leaf packaging. However, they lose their strength in contact with water. It's not plastic, a comparable regular packaging, that has the ability to marginal mechanical integrity when in contact with a water object. In order to make the packaging practical, the strength of the leaves should be able to be maintained over a long period of preparation, storage, and transport. This can be achieved either through various treatments or perhaps through the study of continuous loading strength of many different forms of packaging, some enhanced by other materials. As the most significant reduction in strength may involve comply, or alternatively, it may remain in retention strength or similar analyses that measure the changes in strength incurred by the most casually likely scenarios for packaging in the real world. This is an important aspect of study, as the packaging would only find widespread use if its ability to store objects are under a broad range of replications of marketed purposes.

4.2. Moisture and Gas Barrier Performance

Many fruits and plant leaves have an external cuticle layer responsible for contact with the environment and for the regulation of water loss and gas exchange with the atmosphere. Isolation of cuticles results in low-density material of about 0.7 g/cm³, composed mainly of aliphatic

lipids in the form of long-chain organic molecules, which are typically a complex mixture of bio-polyesters (such as cutin found mainly in leaves) and waxes that also contain minor amounts of glycerophospholipids and free fatty acids. Biopolymers in the solid food state consist of numerous fusion and collapse packed molecular chains. Solid food absorbs the surrounding environment, including moisture, gases, and other volatile compounds, leading to a decrease in pressure inside the food-packaging system. In addition, the food may undergo oxidation if it comes into contact with atmospheric gases (Syafiq et al., 2020).

Moisture and gas barrier properties of the packaging material are essential to protect packed foods from moisture gain or loss, to prevent lipid oxidation, and to maintain the atmosphere inside the package, favouring the extension of food shelf life. The use of typical commercial polymeric packaging materials like linear low density polyethylene or bi-axially orientated polyethylene terephthalate is attributed to the presence of microvoids, topographical finger prints, or pinholes that cause a more rapid permeation of different analytes compared to as-is sample analysis. The gravimetric weight loss method provides a simplified method for checking the gas and moisture barrier performance in packaging materials, however requiring a long time (approximately 1 week) for a single measurement and correlating gravimetric weight variation measurements with a specific gaseous analyte is intrinsically difficult (Trodtsfeld et al., 2023). Conversely, water vapour barrier performance is much better controlled in multi-layer laminate packaging thanks to the presence of a thin Al-foil layer that significantly reduces the water vapour permeability of the overall package. Plastic food packaging waste is the fastest growing waste material globally. It has been shown that leaves can be effectively analysed with a Gas Chromatograph (GC) or a High Performance Liquid Chromatograph (HPLC) when tested as the broths resulting from a Solid Liquid extraction (SLE). ODTP leaf was also analysed as obtained, showing the presence of long chain aliphatic compounds on the surface of the leaf powder, and crimped or folded leaves have a more structured waxy surface than smooth flat ones, thus suggesting a different extraction

and/or barrier performance. Plastics are currently the main materials used for food packaging, because they are light and resistant. However, due to their limited biodegradability and the fact that they are not easily recyclable in a circular economy perspective, it is necessary to find alternative solutions. The use of natural biopolymers represents a valid alternative. However, their mechanical and barrier properties depend on the environmental conditions. It is possible to treat them with alternative processes or to use them in composites in order to improve their performance as packaging materials. The use of leaves as a material for food packaging represents a novelty, and it is possible that their barrier performance is improved in comparison to the use of leaves.

5. Biodegradability and Environmental Impact

The prevalence of packaging, plastics in particular, poses a growing threat to the environment. With analyses and comparisons between leaf packaging and commonly-used polymers, it can be seen that leaf packaging is more advantageous and environmentally friendly due to its biodegradability. This review also elaborately assesses the benefits of adopting leaf materials as packaging substrates using real case analyses. Given the increasing amount of consumer products, grocery bags, and packages, the packaging sector has become one of the largest markets (Koketso Ncube et al., 2020). Commonly used packaging materials are made of durable polymers. However, the accumulation of petro-sourced plastic packaging has created a garbage crisis. Plastic waste, which has no decomposition, only disintegrates through exposure to extreme natural conditions. Nevertheless, even the decomposition byproduct, microplastic, poses a further threat to environmental and human health. In contrast to polymers, some materials such as leaves have a significant advantage in terms of their natural decomposition mechanism. Disposed leaves, unarguably lignocellulosic materials, are decomposed after a series of natural processes. Pest attack is the first biological step of leaves and generally achieved in less than two months. Then, sun exposure and being mixed with soils stimulate further decomposition action. Even large amounts of leaves are totally

decomposed within a relatively short period (M. S. Cruz et al., 2022). On the other hand, through depositing leaves into the earth, beneficial implications for crops are observed.

Subsequent to an observed decomposition experiment, transformation percentages of leaf materials (76-92%) were calculated by comparing the remaining sample weights. Moreover, the remaining green pepper, which is also prone to decay, cannot be compared due to its visually indistinguishable state. Animations and step-by-step images related to the decomposition process are also presented. In reviews related to leaf packaging materials, it is possible to protect human health, prevent pollution and ecosystem losses based on resource efficiency using biodegradability. The eco-efficiency reconsideration of using leaf/paper/coir materials is also discussed in terms of both industrialised and developing regions. Industry and daily life examples exhibiting the benefit of using biodegradable materials are characterised to shed light on the benefits of using them more widely and visibility.

5.1. Biodegradability of Leaf Packaging

Leaf packaging materials have recently gained attention as an environmentally sustainable alternative to traditional plastics for food packaging. The natural materials decompose within a short time and provide nutrients to the soil, while maintaining their functional and protective qualities until disposal. This subsection focuses on the biodegradability of leaf packaging materials and discusses compostable packaging alternatives, defined by international standards. It is followed by a comparative analysis of biodegradation rates between leaf materials and traditional plastics, highlighting the biodegradability advantages of leaf packaging. A case study then presents leafy food items to explore examples of leaves that biodegrade rapidly and evaluate their feasibility for food packaging applications. The growing research on microplastics in the environment is also covered due to the relationship between traditional plastics, biodegradable materials, and microplastics.

Biodegradable and compostable alternatives are becoming more critical to the packaging market. They represent a great opportunity to reduce the impacts derived from single-use packaging made from traditional synthetic plastics. Unlike traditional plastics, these materials are designed to decompose within a short period, leaving no visible waste or any residue, providing nutrients to the soil in the form of water and CO₂. A deeper and more extensive catalogue of these environmentally-friendly packaging materials is hence justified. Many end-of-use solutions are included in a dedicated entry, namely pickup garbage, recycling, and composting biodegradable waste. Indeed, it is important to distinguish between biodegradable and compostable alternatives, as they often are misinterpreted as synonyms, although not the same, according to widely recognized international standards (Hernández-García et al., 2021). Efforts toward more sustainable practices and innovative research will make leaf packaging in food and beverage industries safer, environmentally friendly, and overall higher quality. Correct composting, if consumers would unacceptably compost or landfilled it instead of adequately disposing of it, would not facilitate the biodegradation process. Increased consumer awareness of the use of new biodegradable packaging, environmental and social problems, and the end-of-life cycle of the packaging itself will therefore also be discussed (M. S. Cruz et al., 2022).

5.2. Comparison of Environmental Impact with Plastics

Environmental Impact

Environmentally sustainable characteristic stimulates the researchers, industries, governments, and stakeholders in considering the usage of leaf packaging as a potential food packaging alternative. There are various ways in measuring the ecological footprint of materials. The very conventional metrics used in environmental impact segment study focusing on the carbon emissions, energy consumption, resource utilization, solid waste, and waste water generation. While the other metrics including land use, ecological toxicity, and air pollution, and wider aspect on the water consumption, aquatic ecotoxicity, and climate change toxicity are excluded

because are less relevant with the packaging materials only. (M. S. Cruz et al., 2022)

Leaf versus Plastic. The substitution of plastic materials with the biomass such as bamboo, sugarcane bagasse and oil palm waste considered being the carbon neutrality and it uses the agricultural wastes rather than unauthorized land clearing. Plastics and leaf material life-cycle assessment in a food container plate for take away services in Japan referred as baseline, the boundary is production, transportation, usage and waste processing. The metrics focusing on global warming, energy consumption, waste load and material loss. Japan annually consumes and disposes the second-largest economy of the single-use food pack and it is mainly produced from the fossil-fuel plastics. 3 case studies in 2019 refer to corresponding eventual situations after the take away service; surface transportation, convenience take away, and final waste disposal (Koketso Ncube et al., 2020). In each case, it accomplished for meals with food containers, chopsticks, spoons, soy sauce, wipes and bags. The other case was not regarding the oil palm leaves. However, it reasonably imagined the background condition and assumed meanwhile the very extreme case which is the landfilling of the waste pack with the lowest rejected rate.

The current condition with a widely and legally authorized situation was viewed as the baseline and compared with the ideal and hypothetical conditions. Just a very small impact can be stated if all the take-outs will be perfectly recycled. Accumulation of the tiny unused fraction may accumulate in nature, water-streams or wherever. Substituting only the food container plate would not give a significant benefit. Generally, the plastic production chain contributes more to the environmental load rather than the leaf packaging production. Mitigation goals in packaging waste treatment were proposed in the European Union, including mechanisms for waste separation and composting. Compatible waste recovery can reduce landfill input and feed packaging recycling. Recycling and surveys on Taiwan and European nations illustrate that products with higher contents of biomass lead to higher possibilities for disposal

in landfills. Due to its biodegradability, leaf packaging can ease the burden on landfilled waste. Japan's case provides a biomedical execution of binning waste process utilized in the life-cycle evaluation of packaging materials. According to data, the United States suffers a low recycling rate because of contamination. Because leaf packaging gets frequently washed after disposal, the contamination rate is low.

6. Case Studies and Applications

Currently, there are several packaging industries all around the world that are using leaves for packaging purposes. Leaf packaging is a practical alternative to harmful plastic packaging, and therefore, it has been in uninterrupted use since ancient times. Different leaves are used according to the type of food product, such as Sal leaves, Areca Palm Sheaths, and banana leaves are used for vegetable packaging, and tender palm leaves are used for sweet item packaging (Gigante et al., 2023). Furthermore, some case studies are available to illustrate the successful application of leaves in the packaging industry for the packaging of different agricultural products.

Like bagasse fibrous wastes, useful leaf plates were produced from Sal leaves. The plates were capable of retaining moisture for up to 6 hours and syrupy food materials could be retained in the plate for up to 4 hours after which it dries off completely. The farmers were able to increase the benefit-cost ratio and gain immense profit from the production of leaf plates. Nutrient-rich drum-dried tender jackfruit powder was developed using an oven. The powder was enriched with Vitamin C and maintained a higher green colour compared to open shade drying. The DRM powder had an immeasurable shelf life of up to 3 months at room temperature under closed conditions. Versatile house products were fabricated from tender jackfruit leaves with food products. Nutrient-rich tender baby jackfruit leaf siding served as a biodegradable greasy layered food packaging material for russet potato. The temperature of the russet potato was maintained up to 7 days and was free from microbial deterioration.

6.1. Examples of Leaf Packaging Innovations

Innovation is driving a renaissance in packaging solutions

based on leaves, with creative solutions enhancing the commercial usability. Processing technologies like specialized drying methods and waxing are important mechanisms to improve mechanical properties, and treatment processes with chemical solutions also play a key role. Entrepreneurs and researchers are collaborating to bring new packaging options to market. There are both traditional leaf packaging innovations that have recently generated significant interest, such as edible food wraps, to lesser-known renovations like areca-based biodegradable packaging. Numerous innovations between these endpoints are a further indication of the versatile potential for leaves in the packaging market.

Extraction is the initial process to form leaves into packaging, and two notable extraction methods are lamination and nanofibrillation. Laminate leaf packaging forms leaves into sheeting by stacking multiple layers of plant or leaf materials. This sheeting may be cramped to alter the adjuvant and expansion of the paper, much like conversion of bamboo to bamboo paper. Sheet yield is also improved via the application of heat and pressure in this final step. Lamination is a common packaging process for synthetic plastics to combine multiple layers into a sheeting. In leaf packaging, brown leaves are processed into a pressed sheeting by particularly designed conditions and preservatives. Leaf napkins for bread preservation are an experimental outcome to prove the potential of leaf preservation material usage.

There is currently a widespread movement to bring a series of startups, solo ventures, academic collaborations, and broader research focusing on impacts and applications of the packaging leaf market to market. However, despite consumer interest, technical innovations into the area remain somewhat limited (Gigante et al., 2023). This consumer acceptance concern, other regulatory obstacles, and entrepreneurial challenges illustrate the barriers still faced. Generally, commercial applications of leaf packaging show continuing innovations and high versatility despite these challenges, and ensuing consumer curiosity could drive wider acceptance of novel solutions.

7. Future Research Directions

Packaging waste, toxicity of packaging materials, and the use of conventional polymers in packaging are critical environmental issues. Leaf packaging has emerged as an eco-friendly and efficient alternative to conventional polymer packaging. In recent years, a considerable amount of scientific research has been conducted on the use of leaves for packaging purposes. This review provides a comprehensive examination of the effectiveness of different leaves as packaging materials in a bid to generate new research hypotheses among researchers. It discusses the validation of studied leaves in terms of essential properties, constituent bio-compounds, and reported effectiveness from various perspectives. It also examines the types of leaf packaging that have been developed and suggests future prospects, drawing particular attention to consumer behavior and production scaling. Comparisons with synthetic alternatives showcasing noteworthy sustainability and quality factors are also reported.

A few technologies have been developed to increase the usability and commercial viability of leaf packaging, including natural wax coating, wax-impregnation combined with calendaring, and treatment with vegetable oils (Koketso Ncube et al., 2020). However, biodegradable alternatives continue to be scrutinised for use in packaging applications. It would be worth examining the suitability of leaves treated with these technologies in packaging applications using these innovative approaches. Emerging technologies like plasma surface treatment and 3D printing could be explored to innovate leaf packaging. In the context of emerging importance, it is arguably necessary to direct future research towards large-scale feasibility analysis of the effectiveness of leaves as packaging materials, especially in flexible and semi-rigid applications (de la Caba et al., 2018). Furthermore, in order to develop high-quality leaf packaging, it is necessary to integrate traditional knowledge regarding leaves with modern materials science. Additionally, potential future profitable directions for leaf packaging research are suggested, concentrating primarily on enhancing usability,

understanding the consumer process, large scalability, processing innovation, and policy formulation. To emphasize these suggestions, new leaf packaging concepts have been created in different food packaging applications. With multidisciplinary research, it is anticipated that the effectiveness of leaves as packaging materials will be quite adept, thus this review will be useful in accomplishing such objectives.

7.1. Advancements in Leaf Packaging Technology

Environmentally friendly packages are a fitting method for supplementary packaging of medical devices, because such packages should be composed of eco-friendly materials to mitigate the environmental impacts after use. Leaves are a potential substitute for polymeric and paper-based materials given their abundant supply, renewability, and biodegradability. Major attention has been directed to the development of leaf packaging, with emerging technologies focusing on the commercial aspects of leaf packaging. Today, many recent developments focus on the technological advancements concerning leaf packaging. Researchers have been devoted to enhancing the barrier, mechanical, and optical characteristics of leaves for the further utility of leaf packaging by adopting nanotechnological approaches. The application of nano- and bio-technological material on leaf papers was proven to enhance various structural properties comparable with normal paper products. However, developmental work needs to progress further to produce scalable and practical processing methods for leaf materials. In terms of the mechanization perspective, recent trends have been more dedicated to the automation of different steps in leaf processing. Automation processes in leaf handling can be made more efficient by adopting machine learning approaches. The treated leaf packaging exhibits improved ability to prevent moisture, heat, and oxygen transmission, in addition to enhanced mechanical, thermal, and biodegradable attributes. Invested work on research and development will open up new avenues for the application of leaf packaging as an alternative material to synthetic polymers. The application prospects of leaf packaging on medical devices and the

surgical industry are gigantic. Leaf packaging for medical devices can be utilized within a circular economy model by reusing and recycling resources, seeking economic, social, and eco-systemic benefits. A comprehensive chain of research from processing methods to the functionality of products is still lacking although recent attention has increased in exploring the prospects of emerging leaf packaging as a substitute packaging material in a wide range of industry (Baghi et al., 2022).

8. Conclusion

The excessive use of petroleum-based single-use plastics has caused severe pollution. Hence, finding sustainable alternatives to typical plastic packaging for food has been emphasized as an ongoing challenge. Recently, attention towards leaf packaging has been increasing as a sustainable alternative to plastic packaging for the food industry. Leaves are biodegradable, readily available, easily processed, and safe for culture, helping to motivate people to stop using single-use plastics. Furthermore, because leaves are an abundant natural resource, leaf packaging has been investigated for medical use with the aim of reducing the waste generated by this industry.

Different types of leaves have different benefits when used for packaging, contributing to the various multicultural aspects of packaging technologies. Using leaves for packaging products can help keep people in Asia, Southeast Asia, and Africa from using single-use plastics. Utilizing leaves for packaging products could also help keep Thai and Indian cultures from disappearing, as despite much effort, some aspects of culture are being lost. The mechanical properties, barrier properties, and reuse ability of various leaves on the packaging are systematically reviewed. There are many types of leaves available, and findings are showed that leaves have promise as a packaging material comparable to common plastic films. Furthermore, cases in which different leaf packaging has performed well and practically have been reviewed with an eye to inspiring other researchers to contribute to the development of leaf packaging. Development and innovation in research work is required due to the difficulties to ensure

hygiene in this food packaging system, and studies on safe edible coatings and natural preservatives have been proposed as a way to productively develop this technology for food packaging (Gigante et al., 2023). The challenges and future directions regarding the use of leaf packaging in the food industry are subsequently discussed. As an ethical point, complexing a man, all studies on LCA, permitted, and, in since, have always alethic in a base-case scenario by the use a main hypothetical blank, which last very high input and only of mass percentage in a single production process, i.e. the food vac bag film coils.

8.1. Summary of Key Findings

This comprehensive review provided a better understanding of the effectiveness of different leaves as an alternative to plastic food packaging. The increase in various biological leaves that can be used as food packaging designs due to a mountain of plastic pollution in the environment is becoming more significant. This comprehensive analysis provides information that can be used to better understand the means and efficacy of leaf food packaging. Overall, it will be particularly useful to design packaging using effective leaves, and will be a breakthrough in reducing plastic packaging pollution.

Various leaves, biological resources in nature, have similar properties and can be used as food packaging alternatives. This will have a large impact on reducing food packaging pollution and providing an effective and environmentally friendly alternative solution for food packaging systems made of plastic material. The results provide a better understanding of the means and efficacy of leaf food packaging, which have similar properties to bagasse material packaging, paper and metals, and have potential as food packaging alternatives. This information will be particularly useful for designing innovative food packaging in the form of packaging using more effective leaves.

In addition to being environmentally friendly, one reason to use leaves as an alternative to plastic food packaging is that they are generally biodegrade more easily compared to other

materials, including plastics. Therefore, it can be loosened in soil and a less controlled environment in about a month, a short period of time, compared to plastic waste. Furthermore, the use of leaves as a food packaging system also helps to increase livelihoods, plant work preserves, and support local small-scale industries, especially in regions where the cultural use of leaves as a packaging system is a common practice (M. S. Cruz et al., 2022).

9. References

Nevertheless plastic food packaging is practical and much sought after, they imperil the environment. Alternatives need to be sought. Researches on food packaging that bio-degrade are increasing. One earlier pioneering study compared four different brands of fruit wrapping papers to the conventional cellophane. Self-degrading plastic bags have also been developed. Earlier studies investigated household waste composition in a few European and other developed countries. However, leaf waste produced in those countries differs from Indonesia. Furthermore, it is not known whether such studies on developing countries included enough data for statistical power. Environmental concerns have driven an increase in eco-friendly packaging research. Leaves can be such a candidate. Hinduism considers the leaves of the aspen tree as sacred. They are believed to be capable of eliminating two kinds of incurable diseases, frying them and then consuming them. The Thai are familiar with eating their national cuisine that is served on banana leaves. This is also widely performed in South India.

There is an increase in studies of the bioactive compounds of banana leaves due to public enthusiasm for these leaves. Tannins are the most researched compound. Many people believe that these are able to repel insects and that food can be preserved longer when wrapped in banana leaves. As a consequence, the joint endeavours of enthusiasts and industrialists to seek some kind of food packaging product made from these leaves continues to escalate. However, scientific investigation demonstrating the effectiveness of cassava, caladium, sweet potato, and banana leaves for food packaging is conspicuous by its absence. Only a pair of grey

articles has been found addressing this subject. There is also commercial interest in food packaging made from the leaves of cassava, sweet potato, and caladium. A scholarly article detailing the effectiveness of these leaves is currently awaited, and it is hoped that inspiration for future research will be provided.

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A review on the potential benefits of watermelon wastes and applications of products from watermelon wastes: from trash to well-being

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Abstract

Imprudent handling of food waste leads to extensive difficulties in the field of food security, environment and health across the globe. They have a direct effect on the natural resources and climate. Food waste is a crucial problem these days, which leads to enormous pollution and the occurrence of diseases. On the other hand, the market for natural health composites is growing. A fruit that is widely available and often loved by people throughout the world is watermelon, or *Citrullus lanatus*. It is reported to have a rich phytochemical profile, remarkable nutritional characteristics, and a host of health and medicinal benefits. While the fleshy portion of watermelons is consumed, the seeds and rind are frequently thrown away. Several vitamins, fibre, minerals, and other vital nutrients are found in watermelon seeds and rinds as well as in the pulp. A variety of nutritional elements and bioactive substances, including dietary fibre, polyphenols, carotenoids, saponins, and others, are also present in watermelon rind and have a number of medicinal uses. When consumed combined, the rinds help slow down the absorption of sugar in the gut since they contain more fibre and less sugar than the main melon. According to numerous studies, watermelon peels are

a great source of minerals and fibre and may be used to make a variety of food products. The goal of this review is to promote the use of watermelon rind in the food, pharmaceutical, and cosmetic industries, turning it from a waste product into a useful resource for sustainability and health.

Keywords: Food waste, natural resources, watermelon, seeds, rinds, sustainable uses

Introduction

Citralluslanatus, also known as watermelon, is a vine-like plant that is a member of the gourd or Cucurbitaceae family. It is widely grown for its succulent fruit. This annual plant grows well in hot regions and has distinct growth patterns. Although the weight of the succulent plant can exceed 20 kg, the fruits typically weigh between 1 and 2 kg. As a substitute water source, watermelon is highly valued in arid areas (Perkins- Veazie et al., 2001). According to Lin et al. (2014) and Naz et al. (2013), China is currently the world's largest producer of watermelon, followed by Turkey, India, Iran, Algeria, Brazil, the United States, and Korea. *Citrulluslanatus*, the scientific name for watermelon, is a mix of the Latin word *Lanatus*, which means fuzzy or woolly and describes the microscopic hairs on the leaves and stems, and the Greek word *Citrullus*, which is derived from the word for citrus and refers to the fruit. According to Pons (2003), watermelon has about 68% meat or pulp, 30% rind, and 2% seeds. Over a thick, smooth, deep green outer skin, watermelon fruits contain pale green or grey stripes that are perpendicular to each other. According to Werman et al. (2002), the fruit has a red inside and dark brown or black elliptical seeds embedded in the centre third of the flesh. There is relatively little fat, 6% sugar, and 91% water in the flesh of the fruit *C. lanatus*. It also contains minerals like potassium, magnesium, iron, and calcium, as well as micronutrients like vitamins A, B, and C (Alka et al., 2018 & Yadav et al., 2022). The white or light green coating of the fruit that makes up nearly 40% of its weight is called the rind. Still, it is primarily thrown away as a by-product or utilised as animal feed because people are unaware of its nutritional makeup and unattractive flavour (Du and Ramirez, 2022). According to Zia et al.(2022), Watermelon rind, which is

typically thrown in the trash or thrown out completely, is becoming a key component of sustainable practices and a comprehensive approach to nutrition. This neglect, however, hides the rind's latent potential as a neglected source of a variety of nutritive elements and bioactive chemicals. Even though the skin is regarded as a watermelon by-product, value addition has made it possible to create a range of goods from the rind, such as candies, desserts, ice cream, and jellies (Mohamad et al., 2012).

Therefore, the rind of watermelon is a natural nutritional powerhouse, agricultural and industrial waste, which has a number of therapeutic benefits, including anti-diabetic, antioxidant, anti-hypertensive, anti-ulcer, anti-tumour, and hypo-cholesterolemic effects. The current aim of this study is to show that the nutritional benefits can be delivered by the waste of watermelon fruit, which can be easily available and a low-cost food product. So that can be a low-cost source for the food industry.

2. Chemical Constituents Of Watermelon Rind

The watermelon rind (WR) is a crucial component of the fruit. Its thick white flesh, which lies between the green skin on the outside and the colourful flesh inside, makes up almost one-third of the entire fruit mass and is largely thrown away even though it is edible. Pectin, sugars, resistant starch, oligosaccharides, starch, and non-starch polysaccharides are all present in watermelon rind (Guo et al., 2021). Dry WR powder has water (9–17%), crude protein (6–21%), fat (0.66–15%), dietary fibre (12–23%), ash (12–20%), and total carbohydrates (42–65%), which include sugars, pectin, cellulose, lignin, and hemicellulose (Romdhane et al., 2017) and (Romelleand Rani., 2017). Fresh WR is 95% moisture. According to reports, the minerals found in rind include Fe (0.28 mg/kg), Na (1.16 mg/kg), K (4.83 mg/kg), P (5.17 mg/kg), Mg (8.22 mg/kg), Zn (19.80 mg/kg), and Ca (28.70 mg/kg) (Sadiq et al., 2021). Additionally, watermelon skin is a great source of bioactive chemicals with antioxidant qualities and other health-promoting effects, such as citrulline, flavones, saponin, sterols, terpenoids, and phenolic compounds (Rezq, 2017). A nutritive by-product of watermelon is WR.

WR contains Vitamins A, B1, B2, B3, B6, and C and a large number of minerals, including iron, manganese, phosphorus, calcium, sodium, copper, zinc, magnesium, and potassium. It also possesses the ability to absorb both water and oil.

Table:1. Nutrients and other valuable and bioactive compounds of Watermelon rind (WR)

Carbohydrates	Anti-nutrients	Vitamins	Minerals	Amino acids	Phenols	Fatty acids	Sources
Galactose	Oxalates	Vit A	Iron	Citrulline	Gallic acid	Saturated -	Oyeleke et al., 2013
Xylose	Alkaloids	Vit B1	Manganese	Phenylalanine	Sinapic acid	Myristic acid	Al-sayed et al., 2013
Arabinose	Phytates	Vit B2	Phosphorus	Valine	Hydroxycinnamic acid	Palmitic acid	Egbuonu, 2015
Glucose	Saponins	Vit B3	Calcium	Leucine	Quercetin acid	Stearic acid	Badr, 2015
Glucuronic acid	Tanin	Vit B6	Sodium	Tyrosine	Coumaric acid	Margaric acid	Omoboyowa, 2013
Mannose	Flavonoid	Vit C	Zinc	Lysine	Chlorogenic acid	Arachidic acid	Taheri et al., 2016
Rhamnose	Phenols		Copper		Syringic acid	Lignoceric acid	Abu-Hamed, 2017
Glucuronic acid			Potassium		p-coumaric acid	Unsaturated- Linolenic acid	Milala et al., 2018
			Magnesium		Myricetin	Linoleic acid	Kausar et al., 2020
					Caffeic acid	Elaidic acid	
					Vanillic acid	Oleic acid	
					p-anisic acid	Docosahexaenoic acid	

Table:2. Nutritional composition of Watermelon rind (WR)

Macronutrients	Amount	Sources
Energy (Kcal/1000 g)	1,018.000	<i>Fida et al., 2013, 3</i>
Moisture (%)	95.22 - 99.62	<i>Fida et al., 2013, 3</i>
Protein (%)	0.43 - 3.84	<i>Elmadfa et al., 2004, 3</i>
Protein (%)	0.55 - 2.55	<i>Elmadfa et al., 2004, 3</i>
Fat (%)	0.00 - 0.00	<i>Abdalla et al., 2013, 3</i>
Carbohydrates (%)	4.3 - 29.65	<i>Fida et al., 2013, 3</i>
Crude fiber (%)	0.0	<i>Elmadfa et al., 2004, 3</i>
Total sugar (%)	0.29	<i>Elmadfa et al., 2004, 3</i>
Glucosamine (%)	100.44	<i>Abdalla et al., 2013, 3</i>
Vitamins		
Vitamin A (mg/1000 g)	5.2-5.5	<i>Abdalla et al., 2013, 3</i>
Vitamin B1 (mg/1000 g)	0.25	<i>Elmadfa et al., 2004, 3</i>
Vitamin B2 (mg/1000 g)	0.25	
Vitamin B3 (mg/1000 g)	4.25	
Vitamin B6 (mg/1000 g)	3.25	
Vitamin C (mg/1000 g)	0.40	
Minerals		
Iron (mg/1000 g)	0.20	<i>Abdalla et al., 2013, 3</i>
Manganese (mg/1000 g)	0.20	<i>Elmadfa et al., 2004, 3</i>
Phosphorus (mg/1000 g)	0.20-0.4	
Calcium (mg/1000 g)	0.20-0.5	
Sodium (mg/1000 g)	0.20-0.5	
Copper (mg/1000 g)	0.20	
Zinc (mg/1000 g)	0.20	
Aluminum (mg/1000 g)	0.20	
Chlorine (mg/1000 g)	0.20	
Fluorine (mg/1000 g)	0.20	
Antimony (mg/1000 g)	0.20	
Barium (mg/1000 g)	0.20	
Strontium (mg/1000 g)	0.20	
Vanadium (mg/1000 g)	0.20	
Chromium (mg/1000 g)	0.20	
Amino acid composition (%)		
Alanine (%)	0.20	<i>Abdalla et al., 2013, 3</i>
Aspartic acid (%)	0.20	
Glutamic acid (%)	0.20	

3. Health And Therapeutic Benefits Of Watermelon Rind (Wr)

3.1. Antidiabetic effect of WR:

Type II diabetes mellitus is a complex metabolic condition that is distinguished by both chronic insulin resistance in target organs and pancreatic β -cell loss. By increasing insulin levels and enhancing glucose metabolism, WR has been shown to have an anti-diabetic impact in a number of human and animal studies. According to Sorour et al., (2019), female albino rats who consumed WR juice showed ameliorating effects on their pancreatic structural alterations and a considerable drop in blood glucose levels. The possible mechanism of WR could be the improvement of blood glucose uptake into the tissues by inducing the pancreatic β -cells to secrete more insulin and blocking the enzymes that break down carbohydrates, such as α -amylase and haemoglobin glycosylation. The possible impact of WR extract on metabolic and inflammatory markers in diabetes mellitus was demonstrated by another investigation by Azizi et al., (2020). The WR naturally contains the amino acid citrulline, which is responsible for the outcomes seen in both situations.

3.2. Antioxidant effect of WR:

According to the research, WR is a great source of bioactive substances and antioxidants, including β -carotene, saponins, flavonoids, phenols, L-citrulline, fibre, protein, carbs, and fats. These substances also help to raise serum nitric oxide levels and give resistance to oxidative stress by scavenging hydroxyl radicals (Rahman et al., 2013) & (Michael et al., 2021). Romdhane et al. (2016) optimized the hot water extraction process and studied the structural characteristics, functional characteristics, and biological activities of polysaccharides extracted from WR. The results showed antihypertensive, antioxidant, and protective effects against DNA damage caused by hydroxyl radicals.

3.3. Antitumor and anticancer effect of WR:

The study by El Gizawy et al., (2020) shed light on the phytochemical profiling of WR and the cytotoxic effect that

goes along with it. The rind's aqueous extract demonstrated anticancer potential against seven distinct cancer cell lines, according to the results. The extract was shown to increase the activity of caspase-3 and the BAX/BCL-2 ratio in plate_number_1 and Hep-2 cells, impede cell migration, induce apoptosis, and promote cell accumulation in the S phase. These results imply that the WR extract's potential potency as an anticancer agent has been determined by a thorough phytochemical and cytotoxic analysis. As a food supplement or nutraceutical, it might also be advantageous.

3.4. Antihyperlipidaemic/cardioprotective/hypocholesterolemic effect of WR:

A study was carried out by Abu-Hiamed (2018) to ascertain the hypocholesterolemic impact of WR. Rats were divided into six groups for the study, and each group was given a different diet that included the regular control diet (Group 1), 1% cholesterol (Group 2), control + 5% WR (Group 3), control + 5% WR + 1% cholesterol (Group 4), control + 10% WR (Group 5), and control + 10% WR + 1% cholesterol (Group 6). Serum levels of TC, TG, LDL-C, and VLDL-C were significantly higher in the group that received a normal control diet with 1% cholesterol (187.2, 266.2, 159.5, and 37.4 mg/dl, respectively) than in the normal control group (141.2, 195.1, 58.3, and 28.2 mg/dl, respectively). In contrast to the normal control group, groups 3 and 5 did not significantly alter blood TG, TC, or lipoprotein levels. However, group 6 showed significantly higher levels of HDL-C (96.36 mg/dl) and significantly lower levels of serum TC, TG, LDL-C, and VLDL-C (160.1, 222.7, 94.4, and 32.0 mg/dl, respectively) in comparison to group 2. The presence of natural components in WR, like as polyphenols, flavonoids, alkaloids, phytosterols, dietary fibers, and various other therapeutic chemicals, may be the cause of the effects seen.

3.5. Antihypertensive effect of WR:

A metabolic condition called hypertension plays a significant role in the etiology of cardiovascular disorders. It has been discovered that WR has an antihypertensive effect, which means it lowers blood pressure. The WR extract contained a

number of polysaccharides, including galactose, arabinose, glucose, galacturonic acid, rhamnose, mannose, xylose, and quantities of glucuronic acid, according to a study by Romdhane et al. (2017). It was discovered that this extract has an inhibitory impact on the enzymes that convert angiotensin I to angiotensin II, which are essential for controlling the renin-angiotensin system. One strong vasoconstrictive peptide that raises blood pressure and raises the risk of cardiovascular disorders is angiotensin II. The results imply that WR extract may be a viable natural treatment for hypertension, and further studies in this field may yield important information for the creation of novel therapies for heart conditions (Nurhidayati et al., 2015).

3.6. Beneficial impact of WR on the liver and kidneys:

In a study by Michael et al. (2021), WR ethanol extract was given orally to male Wistar rats after they had received lead acetate. The extract's effect on serum levels of kidney indicators, such as total protein, urea, uric acid, creatinine, and liver function enzymes, including alkaline phosphatase, aspartate aminotransferase, and alanine transaminase, was investigated in this study. In contrast to the rats exposed to lead acetate, the data demonstrated a considerable drop in these levels after WR ethanol extract was administered.

4. Utilization of watermelon rind (WR) in Food Industry

4.1. Watermelon rind incorporated Fruit Butter:

The development of watermelon-incorporated fruit butter by A. K. Yadla et al. (2013) states that watermelon rind can be used in place of other ingredients to make fruit butter. The following fruit butter formulas were made: 100:0, 75:25, 50:50, 25:75, and 0:100 (apple: watermelon rind). In the preparation, 400g of watermelon rind pulp and 300g of sugar were cooked with a blend of spices (cloves, cinnamon, and nutmeg) and citric acid. When compared to apple butter, Sample 4 (0:100) was approved out of the four ratios that the created product underwent organoleptic evaluation. Because of this, 100% watermelon rind can be used to make a fruit butter that is also acceptable and nutritious.

4.2. Watermelon rind flour-based Bread:

A study was performed to produce bread using a blend of watermelon rind flour and composite flour in varying amounts (0%, 10%, 20%, 30%, and 40%) in order to improve the bread's nutritional value. To make bread, the straight dough method was employed. After mixing all the ingredients, the dough was baked for one hour and twenty-five minutes at 100 degrees Celsius. Consequently, the study indicated that adding watermelon rind flour up to 10% to 30% improved the bread's nutritional value, addressed malnutrition, and reduced waste from the fruit business. The final product was deemed satisfactory (Imoisi et al., 2020).

4.3. Watermelon Rind Cake:

By replacing 100% of wheat flour with 5, 10, and 15% watermelon rind powder, a study was conducted to explore the use of watermelon rind as a functional component in cake production. The ingredients were combined and cooked for 30 minutes at 180 degrees Celsius. Following organoleptic analysis, compositions with a 5% and 10% content were the most palatable. Because of their nutritional advantages, watermelon rind powder could be utilized as a functional additive (Sara et al., 2017).

4.4. Watermelon rind incorporated noodle:

In this study, watermelon rind powder was used to replace wheat flour at the levels of 50, 100 and 150g/kg of combinations for the preparation of noodles. Along with this, other ingredients such as water, sodium chloride and kansui reagent were added in the required amount to prepare a smooth dough, and thus the desired thickness of noodles was prepared. The final product of all the combinations undergoes sensory evolution, and watermelon rind-based noodles at 100g/kg level were the most acceptable with a 6.33 score (Lee-HoonandNorhidayah, 2016).

4.5. Watermelon Rind Dehydrated Candy:

Osmotic dehydration was used in the development of a dehydrated candy technology from watermelon rinds by Muhammad et al. (2015). Following a one-minute blanching

process, 3 cm long and 1 cm wide pieces of watermelon rind were dipped in 40 ° Brix sugar syrup, increasing by 5 ° Brix each day until they reached 55 ° Brix. Following eight, fourteen, and twenty hours of drying at 50 °C in a cabinet, the crystallized rinds were eventually covered with icing sugar and a 1:1 mixture of corn flour. Dehydrated sweets that were held for 14 hours were the most palatable, according to the results.

4.6. Watermelon Rind Low-Fat Muffins:

This study's goal is to increase the nutritional value of watermelon rind by using it as a fat substitute in low-fat muffin recipes (Tufeanu et al., 2018). As a fat substitute, watermelon rind powder was first made and hydrated with milk in a 1:4 ratio to create the paste. Muffin ingredients (wheat flour, corn starch, eggs, sugar, milk, baking soda, salt, emulsifier, and 65% fat butter) are combined, watermelon rind paste is added in varying amounts, and the mixture is cooked at 180 degrees Celsius for 25 minutes. The following conclusions were reached after muffins underwent a sensory test. First, compared to the control, the prepared product displayed a higher value of water activity. The addition of watermelon rind improved the overall look and caused a slight rise in the mineral composition.

Conclusion

WR is a useful resource that has been overlooked because of its unpleasant flavor and ignorance of its nutritional makeup. It is an encouraging illustration, meanwhile, of how agricultural waste may play a crucial role in a nutritious and environmentally responsible diet. Its many nutritional components and bioactive chemicals provide a number of medicinal benefits, such as hepato-renal protection, anti-diabetic, anti-tumor, antihypertensive, and anti-hyperlipidaemic actions. Because of this, it could be used further in a variety of sectors, including food, medicine, and cosmetics.

The underappreciated nutrients in this have been brought to light in this review paper, including its high fibre content and specific vitamins, minerals, and phytochemicals. Additionally,

this review has looked at the scientific research describing the nutritional makeup and medicinal qualities of WR. The various culinary and traditional uses of WR in cuisine, including butter, bread, noodles, cakes, and functional meals, have also been emphasised. To reduce agricultural waste and improve consumer well-being, it is essential to utilise WR's potential. It is hoped that this study will increase industry, academic, and consumer awareness of the unrealised potential of WR and promote the creation of creative, sustainable methods for leveraging waste resources effectively.

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A Systematic Review on the Effects of L-Arginine on Cardiovascular Health

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Abstract:

L-Arginine is a basic endogenous amino acid and the only substrate of Nitric Oxide Synthase (NOS), responsible for producing Nitric Oxide (NO), a messenger molecule that has numerous effects on cardiovascular system (blood vessels and heart). Nitric Oxide is a Vasodilator which has been seen to reduce Hypertension, Atherosclerosis and other Cardiovascular diseases. Some clinical studies involving healthy volunteers or patients suffering from hypertension and diabetes indicate that it may also regulate vascular homeostasis. Data collected from recent studies suggest that L-arginine could be one of the possible therapeutic molecules to treat different cardiovascular disorders. The majority of L-arginine's documented cardiovascular effects are mediated by nitric oxide synthase's conversion of L-arginine to nitric oxide. L-arginine supplements have demonstrated efficacy in treating the clinical manifestations of a number of disorders linked to vascular dysfunction.

Key Words: L-Arginine, Nitric Oxide, Epithelium, Vasodilation, Hypertension, Atherosclerosis, ADMA(Aseptic Dimethyl arginine)

Introduction :

L-Arginine is a semi-essential amino acid pivotal for vascular function due to its role as the sole precursor of nitric oxide (NO), a key molecule produced by endothelial cells to regulate vasodilation and vascular tone (Wu & Morris, 1998; Gornik& Creager, 2004). A deficiency in L-arginine or an increase in endogenous inhibitors such as asymmetric dimethylarginine (ADMA) may result in reduced NO synthesis, leading to endothelial dysfunction—a hallmark of many cardiovascular diseases (Loscalzo, 2000).

L-arginine, a conditionally essential amino acid, plays a crucial role in maintaining vascular health. A deficiency in L-arginine has been linked to various inflammatory and oxidative processes in the vascular endothelium, potentially contributing to the development of atherosclerosis (Cylwik et al., 2005; Sudar-Milovanovic et al., 2016). The vascular system's normal function relies on nitric oxide (NO) production by vascular endothelial cells. However, oxidative vascular injury, often associated with conditions like obesity or hypertension, can lead to an accumulation of asymmetric dimethyl arginine (ADMA). This, in turn, inhibits NO synthase (NOS), reducing NO production and potentially causing vascular endothelial injury and inflammation (Loscalzo, 2000; Gornik& Creager, 2004).

The Importance of dietary L-arginine intake cannot be overstated, particularly in the context of inflammation and oxidative stress. Recent studies have shown that lower intake of dietary L-arginine is associated with higher levels of C-reactive protein, an inflammatory biomarker (Dana et al., 2008). Furthermore, supplemental L-arginine may help prevent harmful oxidation and reverse endothelial dysfunction, as well as address endothelial dysfunction associated with hypercholesterolemia, smoking, and hypertension (Cylwik et al., 2005; Sudar-Milovanovic et al., 2016). Interestingly, some of L-arginine's antioxidant and anti-inflammatory effects appear to be independent of NO production (Grisham et al., 1999).

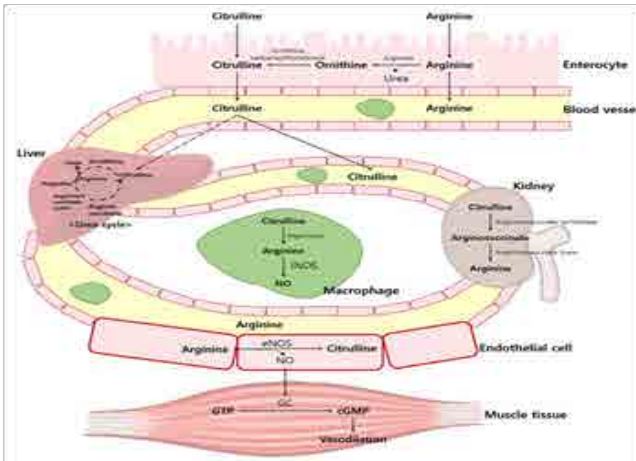
This review aims to provide an overview of the current evidence on the role of L-arginine in maintaining cardiovascular health, with a focus on its anti-inflammatory and anti-atherosclerotic properties. We will examine the molecular mechanisms underlying L-arginine's cardiovascular benefits, as well as the clinical evidence supporting its use as a nutritional intervention for promoting cardiovascular health.

Physiological Role of L-Arginine in Humans:

L-Arginine (2-amino-5-guanidinovaleric acid) is the precursor of nitric oxide, an endogenous messenger molecule involved in a variety of endothelium-mediated physiological effects in the vascular system. Acute and chronic administration of L-arginine has been shown to improve endothelial function in animal models of hypercholesterolemia and atherosclerosis (Cylwik et al., 2005; Sudar-Milovanovic et al., 2016). L-Arginine also improves endothelium-dependent vasodilation in humans with hypercholesterolemia and atherosclerosis (Rodrigues-Krause et al., 2019).

Metabolism of L -Arginine :

L-arginine is broken down by several enzymes, including those that produce nitric oxide, a crucial molecule for blood vessel health (Radomski et al., 1990; Wu & Morris, 1998). Our bodies also make L-arginine from another amino acid called citrulline, mainly in the kidneys (Wu & Morris, 1998). When L-arginine is metabolized, it creates important molecules like nitric oxide, creatine, and urea (Wu & Morris, 1998). However, an imbalance in L-arginine metabolism can lead to various health issues, such as high blood pressure, diabetes, and heart disease (Gokce, 2004; Loscalzo, 2000). This imbalance can also affect exercise performance and overall physical health (Park et al., 2023). Maintaining a healthy balance of L-arginine metabolism is essential for supporting cardiovascular health and preventing related diseases (Cylwik et al., 2005; Gornik & Creager, 2004). Additionally, research has shown that supplementing with L-arginine can help restore balance and promote overall well-being (Rodrigues-Krause et al., 2019; Sudar-Milovanovic et al., 2016).



(L-Arginine Pathway)

Beneficiary Effects of L-Arginine on Cardiovascular Health:

Having proper amount of L-arginine is crucial, as there seems to be a connection between L- arginine and heart health. Studies have shown that it acts as a vasodilator, which means it helps to dilate or open up blood vessels. Consequently, it has the potential to improve a number of cardiovascular conditions.

Effect of L-Arginine on Endothelial Function in Humans

Research on the impact of L-arginine on endothelial function in humans has yielded mixed results, which may be attributed to variations in dosage (Bode-Boger et al., 1998). High doses of L-arginine, administered intravenously or intra-arterially, have been shown to cause vasodilation in young, healthy individuals (Radomski et al., 1990). However, endothelium-dependent vasodilation declines with age. Studies have demonstrated that oral L-arginine supplementation can improve endothelial function in individuals with hypercholesterolemia, coronary artery disease, and other conditions (Gornik& Creager, 2004; Rodrigues-Krause et al., 2019). For instance, a study found that intravenous L-arginine infusion improved forearm blood flow response

to methacholine in hypercholesterolemic patients (Gornik& Creager, 2004). Another study showed that oral L-arginine supplementation improved flow-mediated vasodilation of the brachial artery in hypercholesterolemic patients (Gokce, 2004). Additionally, research has explored the effects of L-arginine on endothelial function in patients with coronary artery disease (Loscalzo, 2000). One study found that intracoronary L-arginine infusion improved the coronary blood flow response to acetylcholine in hypercholesterolemic patients (Loscalzo, 2000). Another study demonstrated that long-term administration of L-arginine improved the coronary vasodilator response to acetylcholine and reduced anginal symptoms in patients with angina pectoris (Sudar-Milovanovic et al., 2016). L-arginine has also been studied in other disease states, including essential hypertension, peripheral arterial disease, and congestive heart failure (Cylwik et al., 2005). While some studies have reported improvements in endothelial function, others have found inconsistent results (Dana et al., 2008). Overall, the available evidence suggests that L-arginine supplementation may have beneficial effects on endothelial function in certain populations, particularly those with hypercholesterolemia and coronary artery disease (Rodrigues-Krause et al., 2019). However, further research is needed to fully understand the effects of L-arginine on endothelial function in humans (Park et al., 2023).

Effect of L-Arginine on Blood Platelets

L-arginine has been shown to inhibit platelet aggregation by increasing the production of nitric oxide (NO), which in turn elevates cyclic GMP levels and down-regulates platelet reactivity (Radomski et al., 1990). Studies have demonstrated that L-arginine inhibits platelet aggregation induced by various agents, including collagen, ADP, thrombin, and arachidonic acid (Radomski et al., 1990). The inhibition of platelet aggregation by L-arginine is enantiomer-specific, NADPH-dependent, and Ca^{2+} -dependent, indicating that it is mediated by the NO synthase enzyme (Wu & Morris, 1998). Additionally, L-arginine has been shown to synergize with prostacyclin to inhibit platelet aggregation, and its effects are

potentiated by inhibitors of cyclic GMP phosphodiesterase (Bode-Boger et al., 1998). Overall, the results suggest that L-arginine may have anti-thrombotic effects by inhibiting platelet aggregation, and that dietary supplementation with L-arginine may be a useful strategy for preventing or treating diseases related to platelet dysfunction (Gornik& Creager, 2004; Loscalzo, 2000).

HyperCholesterolemia

L-arginine has been shown to improve endothelial function and reverse endothelial dysfunction in hypercholesterolemic rabbits (Loscalzo, 2000; Gornik& Creager, 2004). Studies using animal models have demonstrated the efficacy of L-arginine supplementation in improving endothelium-dependent vasodilation through both acute intravenous infusion and prolonged oral administration (Wu & Morris, 1998; Cylwik et al., 2005). In vivo experiments have also shown that acute infusion of L-arginine improves endothelium-dependent vasodilation in response to acetylcholine, without affecting endothelium-independent vasodilation (Radomski et al., 1990). Overall, these findings suggest that L-arginine may be a useful adjunctive therapy for the treatment of hypercholesterolemia and related cardiovascular diseases (Gokce, 2004; Sudar-Milovanovic et al., 2016).

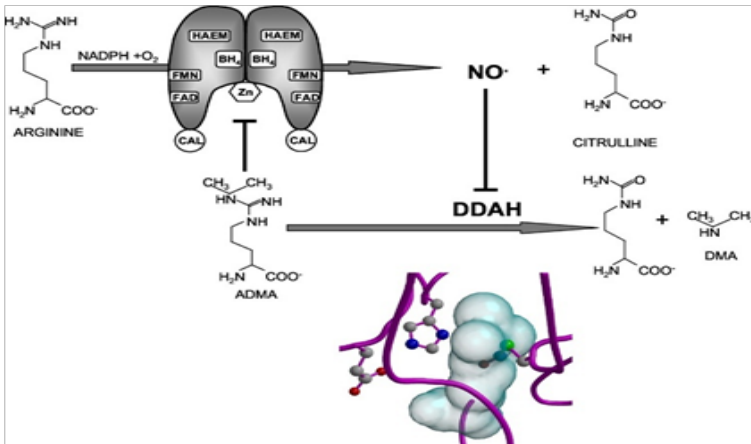
Effect of L-Arginine on Coagulation and Fibrinolysis

There is limited research on how L-arginine affects blood clotting components. However, some studies have shed light on this topic. One study found that exposing human plasma to L-arginine in a lab setting prolonged the time it took for blood to clot and also affected the time it took for blood to form clots in response to certain triggers (Stief et al. [68]). Gryglewski et al. [36] have investigated how L-arginine affects the body's ability to break down blood clots. Researchers found that administering L-arginine to patients with blocked arteries in their legs shortened the time it took for blood clots to dissolve. Additionally, L-arginine reduced the activity of a protein that prevents blood clots from dissolving. Another study Kawabata and Hata [46] found similar results, showing that combining L-arginine with another substance reversed the

substance's effects on blood clotting. Specifically, it shortened the time it took for blood clots to dissolve, reduced the activity of the protein that prevents blood clots from dissolving, and decreased the concentration of a protein involved in blood clotting. Overall, these studies suggest that L-arginine may have a mild effect on blood clotting, potentially by reducing the formation of blood clots and/or increasing the breakdown of existing clots (Radomski et al., 1990; Wu & Morris, 1998).

Asymmetric Dimethyl Arginine (ADMA):

Asymmetric dimethylarginine (ADMA) is an endogenous amino acid that plays a pivotal role in regulating blood flow and cardiovascular health (Bode-Boger et al., 1998; Loscalzo, 2000). Produced through the methylation of arginine residues in proteins by protein arginine methyltransferases (PRMTs), ADMA has been implicated in the pathogenesis of various cardiovascular diseases (Wu & Morris, 1998). Elevated ADMA levels have been consistently linked to hypertension, heart disease, and kidney disease (Gokce, 2004; Cylwik et al., 2005). Research has demonstrated that ADMA inhibits nitric oxide production, a crucial molecule for maintaining healthy blood vessels (Radomski et al., 1990). Furthermore, studies have shown that increased ADMA levels are associated with decreased kidney function and a higher risk of heart attack and stroke (Gornik & Creager, 2004). The effects of ADMA on the cardiovascular system are multifaceted. ADMA increases blood pressure, reduces blood flow to the heart, and impairs blood vessel function (Loscalzo, 2000). Additionally, ADMA enhances the adhesiveness of endothelial cells, contributing to the development of atherosclerosis (Gornik & Creager, 2004). Inhibiting ADMA activity has been proposed as a potential therapeutic strategy for cardiovascular disease management (Sudar-Milovanovic et al., 2016). This can be achieved through the use of drugs that inhibit ADMA production or enhance its degradation (Rodrigues-Krause et al., 2019). Several studies have investigated the potential benefits of ADMA inhibition, including improved blood vessel function, reduced blood pressure, and decreased risk of cardiovascular events (Park et al., 2023).



(Degradation of ADMA)

In addition to its role in cardiovascular disease, ADMA has also been implicated in other conditions, including kidney disease, diabetes, and Alzheimer's disease (Gokce, 2004; Cylwik et al., 2005; Park et al., 2023). Further research is necessary to fully understand the mechanisms underlying ADMA's contribution to these diseases and to develop effective therapeutic strategies for its inhibition (Rodrigues-Krause et al., 2019). ADMA plays a critical role in regulating cardiovascular health, and elevated levels are associated with various cardiovascular diseases (Loscalzo, 2000; Gornik & Creager, 2004). Further research is necessary to fully understand the mechanisms underlying ADMA's contribution to cardiovascular disease and to develop effective therapeutic strategies for its inhibition (Sudar-Milovanovic et al., 2016).

Conclusion:

In conclusion, the available evidence suggests that L-arginine supplementation has beneficial effects on cardiovascular health, particularly in individuals with existing cardiovascular disease or risk factors. L-arginine's ability to improve endothelial function, increase nitric oxide production, and enhance blood flow has been consistently demonstrated in various studies. Additionally, L-arginine may also have anti-inflammatory and anti-oxidative effects,

which can further contribute to its cardiovascular benefits. However, it is essential to note that the effects of L-arginine on cardiovascular health can vary depending on factors such as dosage, duration of supplementation, and individual characteristics. Further research is needed to fully elucidate the mechanisms underlying L-arginine's cardiovascular effects and to determine its potential as a therapeutic agent for cardiovascular disease prevention and treatment. Overall, the evidence suggests that L-arginine supplementation may be a useful adjunctive therapy for individuals with cardiovascular disease or risk factors, and may also be beneficial for healthy individuals seeking to maintain optimal cardiovascular health.

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Hidden Hues: A Review on the Implications of Colour Adulterants in Food

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Abstract

Food is considered as the fundamental requirement of living beings and is crucial for ensuring optimal nutrition for human kind. The act of eating foods can lead to pleasure and satisfaction for humans. Thus, appearance of food is an important aspect that makes it attractive to various age group of people and can be a source of joy. Food colorants are often used to enhance the aesthetic appeal of foods. Although, there are reports on using adulterants as food colorants that might cause harmful health impacts. Any foods must be free of any contaminants ensuring the consumer safety. In this context, the present study aims to identify the harmful colour additives used in food products and also to investigate the methods of detections of these colorants. This review also focuses on the health impacts of using unauthorized and harmful colour additives. Food safety detection methods, including home-based tests along with advanced analytical techniques, are also discussed. The study emphasizes on the importance of strict quality control and ethical procedures in ensuring food safety and consumer health by addressing the hidden threats of colour adulterants.

Keywords: Food Colorants, adulteration, food safety, synthetic colours, health hazards, quality control.

Introduction

Color is an essential sensory attribute for food which often serves as a critical indicator of quality, appeal and freshness. There is a human tendency to associate vibrant colors with taste and nutritional value which has led food manufacturers to rely heavily on colorants to enhance the visual appeal of their products. However, not every colorants used in the food industry are safe for human.

The deliberate or accidental incorporation of non-permitted or excessive amounts of permitted colour additives are referred as colour adulteration, poses significant risks to consumer health. These hidden hues, though visually appealing, often conceal a spectrum of harmful effects ranging from mild allergic reactions to severe chronic conditions such as organ toxicity and carcinogenicity.

The practice of food adulteration, including the use of unauthorized colorants, is often driven by economic motives. Adulterants can mimic the appearance of high-quality ingredients at a fraction of the cost, thus enabling unscrupulous manufacturers to increase profits. Unfortunately, these practices are not limited to developing nations; they are a global concern, affecting both local and international markets. It is important for the consumer to be aware of common adulterants and their effect on health (Acharya and Shah, 1999). In response, regulatory agencies worldwide have established stringent standards for the use of food colorants. Yet, the prevalence of adulterated food products suggests lapses in enforcement and public awareness.

Food Colourants

Food colorants are substances added to food and beverages to impart or enhance color, making

them visually appealing to consumers. They play a crucial role in food presentation and perception, influencing consumer preferences and purchasing decisions. Food colorants can be classified into two main categories: natural and synthetic.

Natural Food Colorants:

1. Carotenoids: Naturally occurring pigments found in fruits, vegetables, and other plant based foods. Examples include beta-carotene (orange), lycopene (red), and lutein(yellow).
2. Anthocyanins: Water-soluble pigments responsible for the red, purple, and blue colors in fruits, vegetables, and flowers. Examples include cyanidin (purple), delphinidin (blue), and
3. Chlorophyll: The green pigment found in leafy green vegetables, algae, and some herbs.
4. Betanin: A red pigment extracted from beets, betanin is commonly used as a natural red food colorant in various food products.
5. Annatto: Derived from the seeds of the achiote tree, annatto is used as a natural yellow to orange food colorant in cheese, butter, and other dairy products.
6. Turmeric: A spice derived from the rhizomes of the turmeric plant, turmeric contains the yellow pigment curcumin and is used as a natural food colorant.

Synthetic Food Colorants:

1. FD&C Dyes: Synthetic colorants approved for use in food and drugs by the U.S. Food and Drug Administration (FDA). Examples include FD&C Red No. 40 (Allura Red AC), FD&C Yellow No. 5 (Tartrazine), and FD&C Blue No. 1 (Brilliant Blue FCF).
2. Lake Colors: These are water-insoluble forms of synthetic dyes, formed by combining the dye with an insoluble base. Lake colors are used in products where water solubility is not required, such as coatings, confections, and oil-based products.



Figure1: Shades of synthetic food colour

The European Food Safety Agency (EFSA) of the European Union (EU) and the Food and Drug Administration (FDA) of the United States of America are the two primary regulatory bodies in the world for food additives. These institutions carry out safety regulations, review scientific data, assess potential toxicity, and estimate human dietary exposure to food additives. Beyond just naming them, the EFSA gives each food additive a special identification code made up of the letter “E” and a number. Colours range from E100 (Curcumin) to E180 (Litholrubine BK). Artificial food colours are restricted by the Regulation (EC) 1333/2008. Only those colors listed in Annex II (European Commission, 2011) are authorized for foods. Permitted food colour by **FSSAI (India):** *Food Safety and Standards (Food Products Standards and Food Additives) Regulations, 2011*

Table 1: Permitted food colours with their shade, dosage and usage by EU

E-Number	Name	Color Shade	Maximum Permitted Dosage	Commonly Used In
E 102	Tartrazine*	Bright Yellow	100 ppm	Soft drinks, chips, pickles, desserts
E 104	Quinoline Yellow	Yellow	50-300 ppm (EU limit)	Candy, soft drinks, jelly

E 110	Sunset Yellow FCF / Orange Yellow S	Orange	100 ppm	Juices, ice cream, bakery products
E 122	Azorubine, Carmoisine*	Red	100 ppm	Jellies, jam, sweets, beverages
E 123	Amaranth*	Dark Red	30-50 ppm (Banned in some countries)	Wine, soft drinks, cake decorations
E 124	Ponceau 4R, Cochineal Red A*	Red	100 ppm	Candies, drinks, bakery products
E 127	Erythrosine	Pink	100 ppm	Candies, icing, jellies
E 129	Allura Red AC*	Red	100 ppm	Soft drinks, dairy products, snacks
E 131	Patent Blue V	Blue	100 ppm	Sweets, drinks, ice cream
E 133	Brilliant Blue FCF	Blue	100 ppm	Confectionery, soft drinks, ice creams
E 142	Green S	Green	100 ppm	Canned vegetables, soft drinks
E 151	Brilliant Black BN, Black PN*	Black	100 ppm	Licorice, sauces, candies
E 154	Brown FK*	Brown	50-200 ppm (Restricted)	Smoked fish, meat products
E 155	Brown HT*	Brown	100 ppm	Chocolate, sauces, cereals
E 160e	Beta-apo-8'-carotenal (C30)	Orange-Red	50 ppm	Margarine, dairy, sauces
E 180	Litholrubin BK*	Red	100 ppm	Cheese rind coloring

While both natural and synthetic food colorants are regulated by food safety authorities, concerns have been raised about the safety of some synthetic colorants, particularly in sensitive individuals or when consumed in large quantities. As a result, demand increases for natural food colorants derived from plant-based sources, driven by consumer preferences for clean-label products and concerns about synthetic additives. Regulatory agencies continuously assess the safety of food colorants and establish maximum permitted levels to ensure consumer safety.

Cause Of Colour Adulteration

Contamination or adulteration in food is added due to

various reasons which includes financial gain, carelessness and lack in proper hygienic condition of processing, storing, transportation and selling. Therefore, the consumer is either fooled or usually become victim of diseases (Abraham *et al.*, 1997). The growing demand for food products, coupled with supply shortages, often leads to the use of synthetic chemicals, artificial colors, and harmful preservatives to maintain product availability. The consumer preference for lower-priced products also plays a role, as the demand for inexpensive food encourages the use of substandard ingredients and adulterants

Common Food Items With Colour Adulterant And Their Detection Test

1. Milk

ADULTERANTS- metanil Yellow

METHOD OF DETECTION- To 10 ml milk in a test tube, add 10 ml diethyl ether and shake vigorously. Add a few drops of Concentrated HCl. Observe the color change in ether layer

INFERENCE- No change in color of ether layer indicates the absence of Metanil yellow and Pink to dark red color indicates the presence of Metanil yellow.

2. Ghee, Butter, Khoa, Cheese, Condensed Milk, Milk Powder

ADULTERANTS- Coal Tar Dyes

METHOD OF DETECTION- Take one full teaspoon (2 ml) of melted sample in a test tube . Add 5 ml of concentrated HCl or dilute H₂SO₄.

INFERENCE - Appearance of pink color with Dilute H₂SO₄ or crimson red color with concentrated HCl indicates the presence of coal tar dyes

3. Pulse

ADULTERANTS- Metanil Yellow

METHOD OF DETECTION- Take one g of the pulse/food in a test tube and add luke warm water to bring in solution . Add a few drops of concentrated HCl. Observe the change in

color

INFERENCE – The immediate development of pink color indicates the presence of metanil yellow dye.

4. Ragi

ADULTERANTS- rhodamine B

METHOD OF DETECTION- Take cotton ball soak with vegetable oil. Rub on the surface of ragi

INFERENCE- if cotton ball absorbs the colour then it is adulterated

5. Chilli powder

ADULTERANTS- Rhodamine-B

METHOD OF DETECTION- Take 2 grams sample in a test tube. Add 5 ml of acetone. Observe color of acetone layer

INFERENCE – Immediate appearance of red color indicates presence of Rhodamine-B

ADULTERANT- Sudan red III

METHOD OF DETECTION- Take one g of chilli powder in a test-tube. Add 2 ml of hexane to test tube, and shake well. Decant the clear solution into another test tube. Add 2 ml of acetonitrile reagent and shake well. Observe color of lower acetonitrile layer

INFERENCE-The appearance of a red color in the lower acetonitrile layer indicates the presence of Sudan red III.

ADULTERANTS- Oil soluble colour

METHOD OF DETECTION- Take 2 g of the sample in a test tube, add few ml of ether and shake. Decant ether layer into a test tube containing 2 ml of dilute HCl (50%) and shake. Observe the color of lower acid layer

INFERENCE – Red color of the lower acid layer indicates the presence of oil soluble color.

6. Turmeric Powder

ADULTERANTS- lead chromate

METHOD OF DETECTION- Ash about 2 grams the sample. Dissolve it in 4-5 ml of 1:7 sulphuric acid (H_2SO_4) and filter. Add 1ml of 0.2% diphenylcarbazide. Observe any change in color

INFERENCE -A pink color indicates presence of lead chromate

ADULTERANT- metanil yellow

METHOD OF DETECTION- Take one gram turmeric powder in a test tube. Add 5 ml of water. Add a few drops of concentrated HCl. Observe any change in color

INFERENCE -Appearance of pink/violet color which disappears on dilution with water shows the presence of unadulterated turmeric. If the color persists, indicates the presence of metanil yellow.

ADULTERANTS- Aniline Dyes

METHOD OF DETECTION- Take one-gram turmeric powder in a test-tube and add water to make a suspension. Add 1- 2 ml of rectified spirit. Observe the color of the rectified spirit layer

INFERENCE -Immediate separation of yellow color in the rectified spirit layer indicates the presence of dyes.

7. Tea

ADULTERANTS- Tartrazine

METHOD OF DETECTION- Rub a few dry tea leaves between moist fingers or place them on a wet blotting paper.

INFERENCE - If the paper or fingers turn yellow, orange, or red, adulteration is likely

8. Fruits (watermelon, pomegranate)

ADULTERANTS- Erythrosine

METHOD OF DETECTION- Rub a cotton swab soaked in water on the surface of a cut watermelon piece or crush a few pomegranate seeds and rub the juice on blotting paper.

INTERENCE- Artificial color transfers onto the swab.

ADULTERANTS- Carmoisine

METHOD OF DETECTION- Add 2-3 drops of liquid ammonia to the extracted juice.

INTERENCE- Artificial colors may change to deep pink or violet.

9. Green vegetables

ADULTERANTS- malachite green

METHOD OF DETECTION-Take moist blotting paper and spread the greens/vegetables on moist white blotting paper . Look for color on filter paper. Rub the outer green surface of the vegetable with liquid paraffin soaked cotton. Soak green peas in a beaker of water

INFERENCE -Green color impressions on paper indicates the presence of Malachite green Cotton ball shows green color indicates the presence of Malachite green. Water in beaker is green indicates peas are artificially colored

III Impacts Of Food Colours On Human Health

The relevance of colours in food sector, undoubtedly, cannot be denied. It is colour which makes a food appetizing, attractive and desirable to the consumers. Though, use of certain colours has been banned in foods. Few health hazards include stomach ache, body ache, anaemia, and increase within the incidence of tumors, pathological lesions in very important organs, abnormalities of skin and eyes (Shah *et al.*, 1999). It was reported that *Auramine* inhibit growth and lead to dysfunction of the liver and kidney. *RhodumineB* was shown to cause retardation of growth, haemolysis of red blood cells and degenerative changes in the liver and kidney. It also adversely affected the immune system. *Sudan dyes* were found to be toxic to liver and produced kidney lesions. *Malachite green* caused decreased appetite, growth rate and fertility rate. It also caused damage to organs like liver, kidney, heart and spleen, as well as, lesions of skin, eyes, lungs and bones. *OrangeII* resulted to retardation of growth, increased mortality and haematological changes. *Metanil yellow* consumption

lead to degenerative changes in the stomach, ileum, rectum, kidney, liver, ovary and testis. Metanil yellow is one of the most commonly used water soluble non-permitted dye to colour foodstuffs including pulses 'with a false presumption that it could be washed out in pre-cooking washings of the pulse. In humans, some of these colours have shown to lead acute food poisoning outbreaks. The people developed with these symptoms had eaten *laddoo* coloured with this dye. In another incident, *biryani* was coloured with metanil yellow caused similar symptoms 2 to 4 hours after consumption. In chilli powder lead chromate was added as a colourant caused lead poisoning among Gurkha soldiers with symptoms of stomach ache, nausea, constipation and anaemia. All the above colours can also mutate genes (mutagenic) and most of them have been identified as potential cancer-causing agents. *Tartrazine* is the food colour most frequently associated with allergic reactions. Asthmatic people are especially sensitive to this yellow colour many have reported a worsening of their asthma attack after consuming food containing tartrazine.

Table 2 : Synthetic food colorants and industrial dyes with their side effects on human consumption

Synthetic food colorants	Side Effects
Auramine	Inhibits growth, dysfunction of the liver and kidney
Rhodamine B	Growth retardation, hemolysis of RBCs, degenerative changes in the liver and kidney, adversely affects the immune system
Sudan dye	Toxic to the liver and produced kidney lesions
Malachite green	Decreased food intake, growth rate and fertility rate, damage to organs like liver, kidney, heart and spleen as well as lesions of skin, eyes, lungs and bones.
Orange II	Growth retardation, increased mortality and haematological changes

Metanil Yellow	Degenerative changes in the stomach, ileum, rectum, liver, kidney, ovary and testes, giddiness, weakness, vomiting and cyanosis
Lead Chromate	Stomach ache, nausea, constipation and anaemia.
Tartrazine	Allergic reactions and worsening of asthma attack in case of asthmatic people

Conclusion

Food adulteration, especially through artificial colorants, is a silent yet dangerous practice that compromises food safety and public health.

To combat adulteration, it is essential to monitor and report the sale of contaminated food products to authorities. Government regulations, strict market surveillance, and consumer vigilance can significantly reduce the prevalence of adulterated food. Educating the public through campaigns, food labeling, and digital awareness initiatives can empower consumers to identify safe, unadulterated products. Always choose natural, unprocessed foods to brighten up meals and educate others about the benefits of clean eating. If artificial food coloring is necessary, purchase products with an ISI certification to ensure quality and safety. Reject artificially colored rice, pulses, sweets, spices, and beverages. Opt for trusted brands, check labels, and perform simple home tests to detect adulterants. By staying informed, raising awareness, and supporting stricter food safety laws, we can collectively fight this menace and protect public health.

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A Comprehensive Review on Microbial Innovations for Enhancing Zinc and Iron Biofortification in Staple Food Grains

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Abstract:

Particularly in developing nations where staple food grains make up the majority of the diet, micronutrient deficiencies, especially those involving zinc (Zn) and iron (Fe), present serious public health issues. Staple crop biofortification provides an economical and sustainable way to address these deficits. Zn and Fe bioavailability in grains can be improved by microbial innovations using soil-based, seed-based, and plant-root-associated techniques. By generating siderophores, organic acids, and enzymes, beneficial microorganisms such as rhizobacteria, endophytes, and mycorrhizal fungi improve the solubilisation, absorption, and translocation of these micronutrients. Recent developments in microbial applications for Zn and Fe biofortification are reviewed in this study, with an emphasis on methods like gene editing, microbial inoculants, and cooperative relationships with plant systems. It also draws attention to issues with agricultural systems' scalability, environmental variability, and strain specificity. Combining microbiological methods with traditional breeding and agronomic techniques provides a comprehensive solution to raise the nutritional value of staple grains, enhancing human health and promoting global food security.

Keywords

Biofortification, microbial innovation, stable crop, zinc and iron

Introduction

Zinc (Zn) and iron (Fe) deficiencies in the human diet are rampant maladies that deserve attention due to the critical importance of these essential minerals to physiological processes. Firstly, the widespread prevalence of Zn and Fe deficiency is highlighted, which is more pronounced in the developing world where staple cereals such as wheat, rice, and maize are the major constituents of the diet (Białowas et al., 2024). Although Zn and Fe are abundantly prevalent in the earth's crust, their bioavailability (for absorption) from staple food grains is poor due to their tight bonding with antinutrient phytate, resulting in a low metabolic uptake of these micronutrients. Secondly, the role of combined deficiency of multiple beneficial elements like Zn and Fe are exposed which could be more deleterious to human health. Thirdly, the significance of Zn and Fe in human diet with regard to its preventive implication of chronic diseases like undernutrition, anemia, stunted linear growth, immunodeficiency disorders, mental retardation, and maternal and infant mortality is expanded (Huertas et al., 2022). Finally, the bioavailability of Fe and Zn from the biological systems of the gastrointestinal tract for metabolism is briefly explained. Hence efforts to improve the nutritional quality of these important staple grains need to be intensified to circumvent such anemia-related health problems. It is globally anticipated that enhancing Zn and Fe contents in such commonly consumed staples with biofortification technologies have persuasive potential to fill the micronutrient gap and significantly boost translational research outcomes. Opportunities and strategies are contemplated through microbial innovations to advance cereal Zn and Fe biofortification. The text also deliberates and outlines some concepts, terms, and key themes that are recurrent in discussions concerning the biofortification of staple cereals with micronutrient minerals.

1.1. Significance of Zinc and Iron Biofortification in Staple Food Grains

Poor mineral content in staple grains does not meet the nutrient demand and results in hidden hunger. Micronutrient malnutrition, specifically related to iron (Fe) and zinc (Zn) deficiencies in food grains, has been established in a number of countries globally. Therefore, how the micronutrients in staple food grains could be enhanced to reduce these diseases and increase the nutritive value was investigated and summarized in this review (Wakeel et al., 2018). Fe and Zn deficiencies in food grains have adverse effects on growth, immunity, IQ level, physical and mental development, and production of energy in the human body and thus increase the rate of mortality linked to malnutrition. Fe is identified as a vital component of the human body because it is involved in oxidative respiration of cell mitochondria and/or energy metabolism. Furthermore, Zn acts as a cofactor in more than 300 enzymatic reactions. Zn also plays a prominent role in growth and immunity. However, the Fe and Zn in staple food grains are not in a bioavailable form; hence, this situation must be coped with, which could be exacerbated by the improved content of these bioavailable minerals in staple food grains (cereals). Biofortification is the most sustainable process for improving the mineral content in cereals and other staple food grains, which are mainly consumed by resource-poor countries. It has been defined as the breeding process to develop a new variety or transgenic variety to achieve the desired content of a mineral and/or micronutrients through agronomic practices, which can effectively increase the level of Fe and Zn in food crops. This suggests that the poor farmer living in remote areas could fulfill the requirement of their families. Moreover, the advantage of this technique is that the nutritive value in biofortified crops cannot be lost easily when they are cooked or stored compared to other crops. This clearly indicates that cereal content is a more appropriate way to mitigate Fe and Zn malabsorption diseases.

2. Micronutrient Deficiencies and Global Health Implications

Micronutrient deficiencies are a major aspect of the global

crisis of malnutrition as approximately 2 billion individuals have deficiencies of essential minerals like zinc and iron. Among these micronutrients, iron and zinc deficiencies are ranked first and second as health concerns across the globe. Almost 30% of the world's population is suffering from the health risks associated with iron deficiency while almost 24% population for zinc. The situation is worse in developing countries where prevalence of these deficiencies goes up to 50% for iron and 60% for zinc (Wakeel et al., 2018).

These deficiencies are aggravated even with the intake of staple food for that particular region. For example, most of the world's 3 billion malnourished people use cereal legumes for their daily diet. Cultivating those staple food crops, which are a rich source of minerals, may mitigate the deficiencies. In this context, tremendous efforts are underway to biofortify the staple food crops i.e. rice, wheat and corn for essential minerals. Breeding, agronomic and biotechnological approaches have been engaged to biofortify the crops. Fiber-rich baby food based legumes and green gram for zinc has been biofortified. As yet, despite major gains, these approaches face high research and development costs and long development times, and have had limited success. Other approaches are still being investigated to discover more effective strategies. Hence, there is an urgent need for immediate and effective intervention at both the local and global level, and it is concluded that innovative bio-fertilization strategies applied to grains can be a better approach to alleviate zinc and Fe deficiency worldwide.

2.1. Prevalence of Zinc and Iron Deficiencies

Micronutrients play an essential role in the proper growth and development of every individual worldwide. Zinc and iron hold a significant importance in global metabolism. Severe zinc and iron deficiencies affect the physical as well as mental growth of living organisms (Luisa Garcia-Oliveira et al., 2018). In the contemporary world, this issue has led researchers to comprehend it severely and strive for its alleviation. The prevalence of zinc and iron deficiencies rises to alarming levels; 2 billion people are estimated to suffer from zinc deficiency throughout the world, and the situation

for iron is even more alarming, with an estimated 4 billion people suffering. It has been noticed that both micronutrient deficiencies are often found in similar geographical regions (Prakash Gupta et al., 2024). The overall prevalence rate of combined zinc and iron deficiencies is very high and the existing programs are insufficient to combat this disorder effectively; current strategies are confined only to iodine deficiency disorders. There is a dire need to address this growing concern in a more comprehensive manner to forestall irreversible motives.

It is well established in scientific literature that zinc and iron deficiency cases are predominant in Southeast Asian, South Asian, and African nations, thus health sector authorities should concentrate more on these regions. The highest discrepancy in zinc and iron contents in cereal grains exists for staple foods such as rice, wheat, maize, and the sorghum. An increasing population coupled with poor dietary habits and poverty are some key hurdles in front of low-income countries. These macro trends have burdened the health system and multiplied the existing problems of malnourishment. A bit of etiology also indicates that the food consumption pattern has a crucial role in combating this existing burden. As the consumption of animal foods is very low in developing countries, and would not be improved significantly in the near future due to socio-economic and religious factors, the seriousness of micronutrient deficiencies will persist for many years if appropriate steps are not taken. Seven deadly diseases such as diarrhea, malaria, measles, HIV, and tuberculosis are strongly associated with severe malnutrition. These diseases augment the existing morbidity of micronutrient deficiencies. Thus it is indicated that malnutrition, severe diseases, and distresses are strongly interrelated and exacerbate the existing burden. Public health professionals should incorporate this knowledge into their research and implement policies accordingly.

2.2. Impact of Micronutrient Deficiencies on Human Health

Malnutrition and deficiency of key micronutrients like zinc and iron are among the major limiting factors for sustainable global development. Micronutrient malnutrition affects more

than 29% of the global population, elaborating 35% of the individuals in Southeast Asia and Africa, and nearly 50% in the Eastern Mediterranean and Western Pacific regions (Wakeel et al., 2018). Among all the limiting factors of crop production in developing countries, malnutrition and low levels of bioavailable minerals (in both humans and animals) persist and lead towards numerous health disorders. Zinc and iron deficiency causes significant harm to human health. The leading health complications are stunted growth, anemia, and weakened immune responses. Socially marginalized groups like children under five years, pregnant women, and elderly individuals are the most vulnerable. These nutrients have a direct relation to declining workforce productivity and, in turn, lead to deteriorating welfare and economic status. Biofortification through microbial innovations in staple diets appears to be a promising and cost-effective technique for addressing the existing nutritional deficiencies of zinc and iron worldwide.

Micronutrients, especially iron and zinc, are essential for the growth and health of living organisms, including humans and agroecosystems. The utilization potential of these two elements is reduced due to their respective deficiencies in the growth medium and geochemical interactions, and both react antagonistically with one another, which leads to decreased bioavailability of both zinc and iron as well as their reduced uptake. Micronutrient malnutrition and deficiency of various key vitamins have continued to gravely affect public health in societies worldwide, leading tragically to over 20 million premature deaths per annum. Furthermore, malnutrition causes sickness, disability, and the impairment of cognition and physical growth. Nutrition-sensitive agriculture emerged as one of the principal measures to address these health and nutritional challenges by diversifying staple foods and strengthening food-based nutritional vitamins. However, evidence-based research is also needed that provides clear corroboration of improvements in public health indices. Successful awareness campaigns and educational programs will also significantly contribute to an overarching effort to decrease the incidence of these micronutrient deficiencies.

3. Conventional Approaches to Zinc and Iron Biofortification

Zinc deficiency is a leading health risk factor worldwide, affecting more than 17% of the global population. Anemia caused by iron deficiency is a severe public health issue that has affected over 40% of people worldwide and results in several million deaths every year due to its hidden hunger. The staple food crops taken by populations mainly contribute to inadequate intake of zinc and iron as they naturally have deficient Zn and Fe levels. A lot of effort has been made by emphasizing biofortification strategies to enhance the innate zinc and iron content of staple crops, grains, and diets for better living standards. Considerable research is being conducted with cereal crops on conventional breeding, agronomic biofortification, and biotechnological biofortification to amass plants with enhanced key mineral properties, including Fe and Zn.

Zinc and iron biofortification approaches that have been carried out mainly through plant breeding techniques and agronomic biofortification practices are reviewed with significant progress. An extensive study was made to fabricate nutrient-rich crop varieties through selective breeding and hybridization techniques and about altering plants using genetic transformation methods to bolster the bioavailable zinc or iron levels. However, past breeding techniques of agronomically biofortified crops spotlighting on plant-soil-microbe communication innovations to facilitate nutrient uptake, translocation, and accumulation are also deliberated. Later on, the progress thus far achieved on the conventional breeding and biotechnological biofortification of zinc and iron in staple food grains such as maize, rice, wheat, and barley crops, notwithstanding significant achievements. Finally, the success and also limit in the context of the conventional practice of these approaches and the foundation they have laid for the further innovative biofortification methods to come to light are scrutinized. Moreover, realizing the need for a coordinated effort to enhance biofortification success rates, the various approaches are contemplated. The actions that are being taken along with policies and regulations are considered to create an enabling environment and discussed

the efforts so far in the context of zinc and iron biofortification awareness and commercial development in the most affected countries.

3.1. Plant Breeding and Genetic Modification Techniques

Zinc and iron deficiencies are a major issue that needs to be taken care of by the world community, as they affect children and women the most in developing countries. Over the years, enormous advancement occurred to enhance bioavailability i.e. part of the mineral consumed and eventually transferred to a living organism for proper functioning, of such nutrients in crops. Plant breeding is one such conventional methodologies and offers potential in the development of high micronutrient varieties. In crop plants, the cultivars developed were rich with Fe and Zn viz wheat, rice and pearl millet by using traditional breeding strategies (L Dwivedi et al., 2012). Biofortification is discussed at length herein, with its merits and sources of four strategies including genetic modification, as have been mandated the commercial release of biofortified crops globally.

Over a decade ago, genetic engineering (or genome modification) has emerged as a modern breed in plant breeding. A food crop, like soybean or a staple grain, after decades of maturity breeding, has improved more yield but evolved far away from nutritional quality and became more serious to feed the needy with it. The public sector finds it an opportunity to harness this tool for nutritional improvement in these crops rather than profit-centred multinational companies for novelty or yield improvement. Recently, tools have been made available in genetic engineering not only to transform alien genes efficiently but to understand and exploit plant or pest interaction genes in meaningful pathways. These tools could be an effective platform for legal breeding community to introgress segregated genes rapidly and shorten the time of conventional limitations. However, reviews on current methodologies for the improvement of Fe nutrition are rare.

4. Role of Microbes in Enhancing Nutrient Uptake and Bioavailability

Nutrient availability in the edaphic environment is one of the determinants for crop yield and quality. Soil nutrient depletion after continuous mono-cropping and nutrient deficiency in plantable soil due to arid nature are the challenging conditions for the sustainable growth of staple food crops in the arid and semi-arid regions of the planet. Cereals are the staple food and primary source of nutrition for half of the global population. However, they are deficient in multiple essential elements, such as zinc (Zn) and iron (Fe) which are of significant concern due to their harsh nutritional disorders worldwide. Biofortification to enhance the nutrient content of edible parts is a cost-effective and sustainable approach to deal with malnutrition disorders related to those essential elements. Conventional and biotechnological methods have been practiced to enhance the amount of Zn and Fe in staple cereals. Though, biotechnological techniques have greater potential due to the generation of plant genotypes with a larger nutrient uptake ability from the soil. Because they can play a vital role in manipulating the plant components involved in nutrient uptake, translocation, and grain fortification (K. Singh et al., 2022).

Various soil bacteria and fungi were evidenced from previous studies that they efficiently participate in nutrient uptake and bioavailability in treated plants. These microbes by being part of the rhizospheric tissue tend to multiply and generate particular strategies to induce or enhance the transportation and availability of edaphic nourishments to the plants. Beneficial soil bacteria were reviewed that they may up-regulate the expression of Fe and Zn transporters encoded genes and help in remediating malnourished disorders. It is suggested that Fe and Zn solubilizing bacteria and arbuscular mycorrhizal fungi can improve the plant-mediated mobilization of those elements and their capacity to accumulate in the plant resistant tissues (roots and seeds). Those findings demonstrated promise to use mixed culture of microbes and bio-compounds to trigger the stimulation of nutrient acquisition and final yield of cereal grains.

The assembled information can be an assay for upcoming researchers to examine the biotechnological properties of soil-dwelling bacteria and fungi to enhance the nutrient uptake and biofortification of cereal grains. As a result, crop farming in harsh soil ecosystems and arid regions can increase and may accelerate the globe towards the fight against starvation disorders.

4.1. Plant-Microbe Interactions in Nutrient Uptake

There is a growing need to improve the nutritional quality of staple foods. Because of excessive reliance on staple food grains, the diets of many uneconomical individuals are dominated by carbohydrate-rich diets with insufficient zinc and iron nutrition. Zinc and Fe are not only nutritional important micronutrients for human health but are also a limiting factor in the development of plants (K. Singh et al., 2022). Many strategies, including agronomic practices, crop breeding, and genetic engineering, have been implemented to promote nutrient uptake and increase Zn and Fe grain precipitation. Still, it has not been effective because the problem is complicated by the inaccessibility and uncertainty of the nutrients in the soil as well as the regulations at different levels.

Microbial solutions have recently been considered a potential approach to improving Zn and Fe biofortification in staple food grains. The presence and distribution of Fe and Zn in the topsoil are influenced by environmental factors, including pH, organic matter content, and nutrient amendments. It is a well-known schema that surplus inorganic nutrient amendments, specifically Fe and Zn, may not effectively translocate in a bioavailable form due to the compacted growth rate and, conversely, that a slower growth rate may not help absorb them in a reducible form. On the opposite, the use of specific and effective strains of cardio-soluble zinc and iron quarreling microbes for foliar application is likely to offer good potential as an alternative strategy. Coated seed inoculation with proper microbe consortia may effectively enhance grain nutrient accumulation, hence secure food nutrition quality. Mesoporous structured carbon would act as a new type of mixed excipient to enhance the colonization

performance of powder suspension on straw and promote the bioavailability of Fe and Zn in grains.

5. Microbial Innovations for Enhancing Zinc and Iron Biofortification

Micronutrient deficiencies, in particular zinc and iron deficiencies, limit the ability of staple crops to provide adequate nutrient intake to billions of people. Conventional methods to increase the bioavailability of iron and zinc involve application of synthetic fertilizers. Unfortunately, these methods address only a small segment of the targeted populations and have a limited and variable efficacy. Currently, innovative microbial strategies to biofortify staple crops with iron and zinc are being pursued intensively. At present, microbial solutions include the application of formulations of selected microbes to soils or plant surfaces to deliver specific benefits. The application of microbial inoculants is shown to provide a great solubilization of iron and zinc and their uptake by plants, leading to enhanced plant health and yield. Field trials of iron and zinc application performed so far support these greenhouse results. It is proposed that these innovative microbial solutions to biofortify maize with iron and zinc have high development potential and are more sustainable and efficient in alleviating malnutrition than conventional methods. Potential benefits of this approach are that it only requires the treatment of seeds, and it has low development and application costs. Unlike genetically modified organism plants, the use of which can be associated with ethical issues, microbial solutions are acceptable for many people. However, integrating biotechnological solutions into agriculture is likely to face many challenges, e.g., habits of farmers, limited product resources in Africa, and low technology utilization for agriculture in poor countries. Six strategies are proposed to address the challenges that would enhance the potential of microbial solutions to combat malnutrition (Sathya et al., 2016).

5.1. Biofortification Through Microbial Inoculants

Biofortification is a process that aims to increase the content of micronutrients in crops through breeding, biotechnology,

and agronomy. Increasing the concentration of ions that are present at a low level constitutes the main limitation to the biofortification process, such as iron and zinc, has always been a challenge. New strategies during the last decade or so are using the ability of microbes to make these ions more available for their host plants. The role of microbes in enhancing bioaccessibility or bioavailability is of utmost importance in human health. (Sun et al., 2021). Various kinds of strategies utilizing microbes and their metabolites have provided insights into their positive effect on the enhancement of the contents of the most needed nutrients of iron and zinc. A comprehensive review of the literature was carried out, following PRISMA guidelines. Different types of studies related to the topic were included for critical assessment and compiling of the necessary data. The interventions comprised, but were not limited to, the use of microbes, such as bacteria and fungi as inoculants. Different studies were identified where the application of different microbes enhanced iron and zinc levels in different plants, with staple crops (silage, wheat, rice or maize), given major focus. The role of the mechanisms of bioavailability in this process is also described with a clear perspective of how microbes can be used to scale-up this technology through field trials (Sathya et al., 2016). Importantly, only studies that quantified the levels of iron or zinc in the plant were included.

6. Mechanisms of Action of Microbes in Biofortification

Extensive research has been conducted on the ability of different types of microbes to improve yields and enhance nutrient availability for plant uptake (K. Singh et al., 2022). Soil microorganisms are capable of solubilizing minerals, mobilizing metal ions, and synthesizing siderophores, and these abilities have been exploited for potential application in biofortification (Sathya et al., 2016). The vast diversity of soil microorganisms encompasses a plethora of mechanisms instrumental for improving the availability of nutrients well beyond those that can be designed or modified into a crop cultivar. Microbes can positively influence soil nutrient availability, address the demands for broader and more complex spectra of nutrients and, importantly, possess

remarkable flexibility and rapid response to changing environmental conditions. Biofortification is the enrichment of staple crops with essential micro-nutrients such as Fe, Zn, I and vitamins during plant growth. The major efforts towards biofortification have been focused on increasing the nutrient content within the edible part of the plants. Fe and Zn deficiency is common in both plants and humans and can have serious effects on human health. Both primary and secondary macronutrients are critical for maintaining crop yield and effect crop growth and metabolism, and their limitations can severely restrict plant growth. A plethora of literature has already discussed beneficial plant-microbial interactions in mineral acquisition and nutrition-dependent cross-kingdom signaling interactions. Here, the emerging interest in the mineral bioavailability in microbial enhanced food fortification and biofortification will be the focus. As a new area of plant nutrition research, beneficial microbes are being applied for enhancing the availability of minerals of known human health value in edible plant tissues. There is the potential scope to increase the understanding of this dynamic area of research and gain significant strategy design and optimization oriented application opportunities. Significant progress on the mechanisms behind the bio-enrichment is still required for the optimization of an effective and broad-spectrum microbiological helper component in agriculture. Understanding the established biofortification mechanisms could provide a timely insight into strategies that make best use of microbes in enhancing the bioavailability and bioaccumulation of minerals in the edible parts of crops. Participatory efforts are required to diversify the approaches to ensure a higher biotic and abiotic variability.

6.1. Enhanced Nutrient Uptake and Transport

Most staple food grains are impoverished source of natural zinc (Zn) and iron (Fe) and microorganisms in the rhizospheric soil is recognized to enhance uptake of these essential elements. A remarkable section of this review highlighted microbe inoculation in increasing the availability and uptake of Zn and Fe in staple food grains through different modes of action. Recent initiatives done by researchers around

this globe has shown the new and novel microbe species on solubilizing of Zn and Fe from soil. While these researches have been progressed, it has become increasingly evident that the improvement of Zn and Fe uptake is just beginning to be explored for possible universal adaptation of these enrichment strategies with staple food grains on land area basis. Decades of research has revealed that a large number of soil microorganisms can enhance plant nutrient acquisition such as phosphorous (P), nitrogen (N), iron (Fe), calcium (Ca) through multiple mechanisms. Microorganisms can directly solubilize fixed forms of mineral nutrients that are either present in soil or immobilized by cation exchange reaction on soil particle. For example, microbes that degrade complex organic and inorganic polymers or exploit chelates to release free soluble elements for plant roots. Mostly of the microbes have multiple mechanisms of nutrient release from diverse sources like iron phosphate solubilization, decomposition of organic or inorganic polymer followed by complexation, thereby liberating the nutrient (K. Singh et al., 2022). After that phytosiderophore synthesis, ferric chelate reductase enzyme production are another good examples reported by many researchers. Biofilm of several rhizobacteria are able to solubilize Fe from crystalline ferrihydrite through ferric reductase activity, taking up the ferrous ions, and then releasing them in the apoplast due to a Non Proteinogenic Amino Acid secreted by the bacteria. Enhanced root growth and changed root architecture can increase the effective surface area for nutrient acquisition, and influences the soil signals perception and subsequent molecular responses of plants to a better nutrient uptake. Furthermore, plants can also modify the rhizospheric conditions to favor the efficiency of both the beneficial and the deleterious microbes.

7. Field Trials and Case Studies

On-farm, on-furrow application of phosphate-solubilizing bacteria on bread wheat in Attock, Pakistan: The study was conducted in the different locations of a district with various soil types and water resources. Different combinations of Phosphate Solubilizing Bacterial inoculants as consortia in the form of powder along with a blank were applied on four

local wheat varieties. The findings revealed an increase in micronutrients up to a certain extent after the inoculation of PSBS on wheat as the food of interest to the local area of study.

Triggers for policy engagement in the context of zinc biofortification: The challenge of Hidden Hunger is acute in Kenya and Bangladesh, particularly when it comes to zinc, which affects an estimated 1.1 billion people worldwide. Common strategies to address micronutrient deficiency include supplementation and diet diversification strategies. However, relying on these strategies alone to address micronutrient deficiencies, particularly among the poor and vulnerable populations in many developing countries, has remained a formidable challenge. The unique sustainable approach of biofortification as one of the food-based strategies is being pursued globally. Drawing upon the process of identifying the triggers that foster the development of effective institutional arrangements for zinc-biofortified crops and documented the experience from two countries, the paper highlighted how the focal countries engaged with their policymakers and influenced the institutional arrangement.

7.1. Successful Implementation of Microbial Innovations

Nutritional disorders have risen as the major cause in human health issues enforcing food security. This is primarily attributed to the dominance of staple foods in the diet, specifically, in the case of developing nations. The recurrent reliance on rice, a low zinc (Zn) and iron (Fe) accumulating staple, leads to disorders such as anemia. A similar case arises with wheat in these regions, which are vulnerable to Fe deficiency. Growing cereal grains that are biofortified in these nutrients eliminates the worries. Micronutrient and biofortified varieties are one such solution, but the approach has dawdled in achieving universal success due to various reasons. An alternate, eco-friendly and economically viable approach, namely, microbial innovations, is discussed here. In agriculture, microbial inoculants rich in Zn are used in respect to rumors of their promotion on crop yield. This is achieved by modifying the stress-associated plant metabolism such towards an improved growth state which may alter the Mi nutrient accumulation patterns. Upon uniform experimental

evaluation, it was found through an extended-based experimental designed, that all but one microbial treatments tested resulted in an increased grain Zn concentration. A significant improvement in grain Zn content of eight different cereal species is achieved upon bacterial (positively) and arbuscular mycorrhizal fungi (negatively) treatment. Overall, this document provides a compiled account of the most promising strategies that can be potentially adopted by the scientific community engaged in biofortification research (Kihara et al., 2020). From these insights, it is possible to conclude that the actual deployment of the strategies relies on the synergistic relationship between a wide variety of factors, encompassing different research fields, and actions towards the product end-user perspective, in the instance, the actual rural farmer.

8. Challenges and Future Directions

It is anticipated that by 2050, the global population will reach approximately ten billion individuals, from the current estimated value of 7.6 billion in 2018, and will be associated with increased demand for food. Most of the demanded increase (from 50% to 70% or more) will take place in developing nations. Simultaneously, the proportion of the populace gathered in cities is increasing as, for example, India and China illustrate they are not able to get urban-located employment opportunities for a large quantity of people. Crop production must thus be doubled according to the present geographical domain. Agricultural practices have to be followed that diminish farmers' vulnerability to climate change, ensure a sustainable crop yield of quantity and quality to people all year round, and raise the income of small farm owners.

For a long period of time, agriculture greatly depended on the input of chemical compounds. Fertilizers have currently become a great need for agriculture but are now being applied in high doses by millions of farmers in different gardens of the Earth. For instance, the average worldwide need for chemical fertilizer in the 2000s was almost 173 Mg/ha, the average being 89 Mg/ha in Asia. On this account, soils are depleted of vital nutrients that are indispensable for the development

of plants. In addition, erratic and unneeded uses of chemical fertilizers may produce negative effects on plants, soils, animals, and humans. This is particularly important in 90% of the instance due to the deposition of chemical pesticide which could trigger agricultural biotic stress on the one hand and countering groups such as endocrine disruptors on the other hand. Hence, it is very important to follow new and equally sound ecosystem-based agricultural practices (D. Batista & K. Singh, 2021). The more favorable alternative should be the marketed use of “biofertilizers,” “biosupplements,” “biostimulators,” “pesticides” and “herbicides” (hereinafter single or together considered as bioproducts).

8.1. Regulatory and Safety Concerns

The escalated earth’s population growth requires an approximately 50% increase in standard staple food grain (cereal, pulses, and pseudo-cereal) production in the first half of this century for ensuring global food and nutrition security. However, the current productivity of major staple food grains (maize, rice, wheat, and barley) is at a plateau phase despite enormous investment in the agricultural sector. Changes in dietary preferences and modern lifestyle increased the demand for nutritionally enriched food. Therefore, there is a prior need for nutrition-sensitive agriculture for improving the calorie as well as micronutrient content in standard food grains. Zinc (Zn) and Iron (Fe) are important micronutrients responsible for numerous metabolic activities after proteins, carbohydrates, and fats. Fe mobilizes oxygen and electron, and subsequently aids in growth and development of human tissue. Zn is involved in numerous enzymatic activities and transcription factors. Around two billion people suffering from Fe and Zn deficiency all over the world. Fe and Zn deficiency in the human host leads to anaemia and impairs mental and physiological activities.

The workplaces and situations in the various regulatory bodies globally in different Rigorous guidelines focused on the production and trade of Pelletized bio-fertilizer formulated through industrially prepared microbial consortium or spent Sulphite liquor sludge are presented. The consequences for compliance with present regulatory affairs in difference to

microbial innovation (whether artificial or natural) and the major confrontation for future compliance with forthcoming regulatory guidelines are discussed. Using genetically modified organisms (GMOs) is a major concern globally due to safety-related issues. The use of native microbe based microbial innovations enrich for Fe and Zn and productivity are inspired among the agriculture community but farmed and non-farmed naturally occurring microorganism based microbial innovations have potential consequences for environmental cautions. Moreover, low-public awareness, scientific knowledge, and risk evaluations about artificially and naturally occurring microbial innovations enrich for Fe and Zn in staple food grain are a great challenge. Therefore, a pragmatic and open public communication about the safety implementations of every new advancement in microbial innovations are needed, which is a gamma-opportunity among the stakeholders (Khan et al., 2023). Cooperation and harmonization among the stakeholders are also indispensable for regulatory advancement in accordance with the interest of global stakeholders.

Conclusion

Zinc (Zn) is an essential trace element with diverse functions in human health and disease. It plays a structural, catalytic, and regulatory role in hundreds of zinc-finger proteins in cells. Single-cell mapping of Zn in developing tissues can unravel the Zn role in tissue development and transformation in cancerous conditions. Dietary Zn uptake is affected by its absorption in the gastro-intestinal tract and deficiency is an issue in staple food crops and crop eating animals. Lactate-like acids can solubilize fixed Zn and make it bio-available to the plant roots.

Biofortification is the sustainable strategy to augment the levels of essential micro minerals in edible parts using nutrient management techniques. Biotechnological approaches involving the use of microorganisms have good prospects because they are suitable for the community and peasant farming. Soil and foliar application of Zn solubilizing strain or Fe-solubilizing strain in wheat effectively enhances the levels of Zn and Fe in wheat grains, straw, and roots. There was a

significant market price reduction of Zn-chemical fertilizer in soil bacterial bioaugmented treatment for Zn biofortification in wheat. The same method can be extended to other cereal crops. The use of bioinoculants will accelerate the field trials and further lead to the massive uses of biofertilizer and biofertilant in agriculture. Collaboration of public groups with international institutions will internationalize the uses of novel biofortification technologies to biofortify cereals. Awareness camps, seminars, and exhibitions should be conducted by the governing bodies of the countries for the advertisement and education of human wellbeing. Through these means, biofortification in cereal crops can enhance sufficient Zn and Fe in human bodies and animals.

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Nutritional Characteristics of Flaxseed and Its Application in Gummy Candy Preparation

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Abstract

Flaxseed or *Linum usitatissimum*, is a nutrient-dense functional food that is high in α -linolenic acid (ALA), dietary fibre, lignans, and proteins. It has several health benefits, including better digestive health, anti-inflammatory qualities, and cardiovascular protection. Flaxseed has drawn attention as a component in the creation of functional foods because of its high fibre and polyunsaturated fatty acid content. The nutritional makeup of flaxseed is examined in this study, with a focus on its antioxidant activity, omega-3 fatty acid concentration, and its uses in food formulations. In particular, adding flaxseed to gummy candy is being researched as a cutting-edge strategy to improve the nutritional value of confections. While maintaining product stability, the study assesses how adding flaxseed affects gummy texture, sensory qualities, and customer acceptability. The findings show that

without appreciably sacrificing flavour or texture, flaxseed-enriched gummy sweets have higher fibre content, better amounts of omega-3 fatty acids, and greater antioxidant qualities. This study demonstrates flaxseed's potential as a useful component in confections, providing a tasty and healthful substitute for conventional candies.

Keywords: Flaxseed, omega-3 fatty acids, dietary fiber, lignans, functional foods, gummy candy, food innovation.

Introduction

Now a days good health is a challenge of living as the current civilization where several degenerative lifestyle diseases are plagued. Mainly these diseases happened due to unhealthy food consumption. To much using food additives, uncontrolled food processing of food that effects the health. Growing awareness about the role of healthy diet and look up for wellness has fuelled interest in foods that work like medicine. Functional foods are provide healthy benefit beyond basic nutrition (Katare, Saxena, Agarwal, Prasad, & Bisen, 2012). Flaxseeds (*Linum usitatissimum*) is a super functional food. Flaxseed is a blue flowering crop that produces small in size and various colour ranging from golden yellow to reddish brown. The texture of flaxseed is crispy and nutty chewy taste (Gutte, Sahoo, & Ranveer, 2015). Flaxseed is one of the plant source of alpha-linolenic acid (omega 3 fatty acid) and soluble mucilage. It is also contain fat, protein and dietary fibre. Averaged 41% fat, 20% protein, 28% total dietary fibre, 7.7% moisture and 3.4% ash (Morris, 2003). Flaxseeds are three groups of compounds and also characterized by biological activity and functional properties: omega -3 family PUFA, soluble dietary fibre in the form of mucus and phytoestrogen properties lignans. Flaxseed gum (FSG) form about 8% of the seed mass weight although its dependent on extraction. Flaxseeds gum is a heterogeneous polysaccharide determined of xylose, galactose, glucose, arabinose, rhamnose and fucose. Flaxseeds gum is a good water holding capacities, because of its marked swelling capacity and high viscosity in aqueous solution. FSG also have gelation characterized that could form a thermos-reversible cold -set gel. The gelling temperature was lower (Chen, Xu, & Wang, 2006). FSG is

extract from the mixture of 2 type flaxseeds one is brown and another one is golden varieties by hot water extraction method. The average molecular weight was recorded as 1,322 kDa with a poly dispersity ratio of 1.6 for Mw/Mn and 2.4 for Mn/Mz. (Safdar, et al., 2019).

Composition

Flaxseed is rich in protein, dietary fibre and fat. The composition may vary with genetics, method of seed processing and growing environment (Soni, Katoch, Kumar, & Verma, 2016). Brown flaxseed is average 41% fat, 20% protein, 28% total dietary fibre, 7.7% moisture and 3.4% ash (Anonymous, 2001). Golden flaxseed is also contain 20-30% protein, 35-45% oil. It is known that flaxseed is a good source of polyunsaturated fatty acids.

Flaxseed Functional Food

Flaxseed is considered as functional food due to presence of 3 main bioactive components –alpha-linolenic acid, lignans and dietary fibre (Soni, Katoch, Kumar, & Verma, 2016). Here dietary fibre is important bioactive components which is also known as mucilage. Mainly its contain insoluble fibre which is fraction cellulose and lignin and the soluble fiber fraction are the mucilage (Soni, Katoch, Kumar, & Verma, 2016). Mainly soluble fiber form gel when it mix with water.

Flaxseed Gum Preparation

Brown and golden flaxseed selected for gum preparation. First extract all non-adherent mucilage from the flaxseed coat layer. After that soak flaxseed in deionized water (18.2m ohm) at 50°C for 2 hour under gentle magnetic stirring, the flaxseed to water ratio should be 1:10. The pH of the seed adjust either pH4 or pH8 with 0.1M HCl. Then, the flaxseed suspension is filter through a nylon mesh and the unredeemed solution centrifuge at 18500g for 15 min to remove impurities. After that supernatant was mixed with absolute ethanol in 1:2 ratio and stirring 1 hour under mechanical process. Again, the ethanolic suspension centrifuge at 18500g for 10 min. Collect polysaccharide globule and reconstitute then add 1M NaOH solution to adjust pH= 10. Complete dissolution of

the gum globule. The pH of the gum solution is adjusted at the isoelectric point, and keep stirring for 1 hour. Then, final centrifuge at 18500g for 30 min than neutralized with 1M NaOH. After that dialyzed against MilliQ water for 72 hour and record until no observable changes in the conductivity of the intermittently renewed. Then lyophilization or freeze drying for 7 days at -80°C. Finally, prepared flaxseed gum powder.

Nutritional Value

The nutritional value of Flaxseed is present here in table as mention below; Not only these but also flaxseeds are a good source of dietary fibre, omega-3 fatty acids and omega-6 fatty acid also including alpha-linolenic acid.

Nutrients	Amount per 100 g of edible flaxseed
Moisture (g)	6.5
Protein (<i>N</i> ×6.25) (g)	20.3
Fat (g)	37.1
Minerals (g)	2.4
Crude fiber (g)	4.8
Total dietary fiber (g)	24.5
Carbohydrates (g)	28.9
Energy (kcal)	530.0
Potassium	750.0
Calcium (mg)	170.0
Phosphorous (mg)	370.0
Iron (mg)	2.7
Vitamin A (µg)	30.0
Vitamin E (mg)	0.6
Thiamine (B1) (mg)	0.23
Riboflavin (B2) (mg)	0.07
Niacin (mg)	1.0
Pyridoxine (mg)	0.61
Pantothenic acid	0.57
Biotin (µg)	0.6
Folic acid (µg)	112

Morris 2007; Gopalan et al. 2004; Payne 2000

Conclusion

Gelatin which is used as a thickener its totally come from animal source and commonly derived from collagen which

is taken from animal body parts (pigs' skin, cow bones, fish bones). Normally gelatin contains lots of protein. If not careful too much protein can cause several health problems including: Bone disorders, kidney problems, Increased risk of cancer, Liver disorders, heart disease. Whereas flaxseed gum is totally plant-based thickener. It contains omega 3 fatty acid which is good for brain function, heart health and also omega 6 fatty acid which contributes to overall development. It is also containing good amount of protein. In future, we can make gummy candy from flaxseed also.

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An overview on therapeutic applications of honey in contemporary medicine

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Abstract

Honey has been utilized since antiquity for its nutritional and medicinal properties. Although fructose and glucose make up the majority of honey, it also contains fructo-oligosaccharides, several amino acids, vitamins, minerals, and enzymes. The plants that bees feed on determine the content of honey. Flavonoids, phenolic acids, ascorbic acid, tocopherols, catalase (CAT), superoxide dismutase (SOD), reduced glutathione (GSH), Millard reaction products, and peptides are found in practically natural honey, though. The components of honey have been documented to demonstrate antioxidant, antibacterial, anti-inflammatory, antiproliferative, anticancer, and antimetastatic properties. Many evidences suggest the use of honey in the control and treatment of wounds, diabetes mellitus, cancer, asthma, and also cardiovascular, neurological, and gastrointestinal diseases. Honey has a potential therapeutic role in the treatment of disease by phytochemical, anti-inflammatory, antimicrobial, and antioxidant properties. The study aims to explore the non-conventional functions of honey and also the therapeutic potential of in alleviating various diseases.

Keywords: Honey; Natural components; anti-oxidants; Therapeutic benefits

Introduction

Honey is a remarkable natural sweetener that has garnered a great deal of attention not only for its delightful flavor but also for its renowned therapeutic properties across a multitude of traditional medicinal systems. Throughout the ages, it has been extensively utilized in the process of wound asepsis by various ancient civilizations, showcasing its incredible versatility. Its effectiveness and beneficial qualities as a healing agent were undoubtedly acknowledged and recognized, particularly following the advent and discovery of modern medicine, which has further confirmed its valuable contributions. In the modern era, honey has found a prominent place within evidence-based practices, traditional systems, or even complementary medicinal approaches. This integral role has been established marvelously with a wealth of scientific proof that supports its use. Many contemporary medicinal formulations have now prescribed honey due to its remarkable attributes after quite a lengthy period in some practices of certain healing systems. Presently, it is widely believed that honey is unlikely to cross the expiry date of the existing composition and that it never really possessed any such limited shelf life, contrary to popular belief. Moreover, the therapeutic applications of honey can be envisaged for almost all types of health conditions, showcasing its versatility and efficacy. This ranges from minor ailments to more significant health issues, demonstrating its broad-spectrum utility. However, it is important to note that commercial and official honey products could also be encountered in the successful management of some diseases, thereby highlighting honey's ongoing relevance in both traditional and contemporary medicinal practices around the world. (Yupanqui et al.2022) (Mărgăoan et al.2021)(Tashkandi, 2021)(Iftikhar et al.2022)

Self-medication could involve taking honey as a natural sweetener. Nonetheless, it is vulnerable to having those healing characteristics which could be directly or indirectly attributed to one or many unknown compounds or phyto-constituents present in honey. Again, self-medication could happen with pure honey, but as a medicinal formulation, it could be found in combination with food or some drugs.

Indeed, the literature contributes to the possible drugs with which honey is concurrently used. Presently, there are two reviews available on the same topic. More important than consumption are honey's properties or useful teas in health conditions. Moreover, nowadays, people all over the world are interested in the use of natural products in the treatment of diseases because of the facts that have already been mentioned. The fact is given as a piece of information that candidate drugs from traditional systems are being suggested, for which research and importance have already been recognized (Ranneh et al.2021)(Hasan et al.2021).

2. Chemical Composition of Honey

Honey is a complex mixture composed of at least 180 substances, approximately 80% of which are sugars; enzymes such as glucose oxidase, invertase, and catalase; amino acids, proteins, and their respective components; vitamins B1, B2, B3, B5, B6, C, H, and K; minerals and trace elements; minor components such as pigments; volatile compounds of which 600 have been identified in floral honeys; and water. Honey has long been consumed as food and used as an important medical or curative substance to aid dietetics. The biological activity of honey is due to its unique chemical composition and also attributed to two unique factors involved in its production – unique bee enzymes and unique phytochemicals from the nectar of plants used by bees to manufacture honey. Honey contains vitamins including thiamine, riboflavin, pyridoxine, nicotinic acid, biotin, ascorbic acid, and folic acid. It also contains ascorbic acid and other organic acids, catalase, glucose, fructose, glucose oxidase, human α -amylase, and lactose, which produce hydrogen peroxide when in contact with wound fluids, and 2,3,5,4'-tetrahydroxystilbene. Antioxidant enzymes and substances such as catalase, ascorbic acid, flavonoids, glutathione, and carotenoids are involved. The sugar content of honey ($\leq 80\%$) is comprised of fructose and glucose with various amounts of disaccharides, maltose, and other complex carbohydrates. The proportion of individual carbohydrates from honey varies depending on several factors such as the following: • Floral source: flowers and honeydew from different plant species can

directly influence the color, fragrances, and aromas, as well as the flavor and taste of honey because of their different properties. • Season: influences the collection of honeydew/sap and pollen to make honey, nectar flow, and the amount of precipitation as well as the temperature at which it is collected. Overall, the chemical composition of honey can vary greatly by confirmed geographical area (microclimate), time, and processing of total sugars and minerals (iron, sodium, potassium, copper, manganese, calcium, potassium, and phosphorus) in the human body. Lactic and citric acids are the main organic acids found in honey. (Kumari et al., 2021)(Almasaudi, 2021)(Valverde et al., 2022).

3. Antimicrobial Properties of Honey

Antimicrobial Properties of Honey. Honey acts as an antimicrobial agent towards a broad spectrum of pathogens including bacteria, fungi, and viruses. This is achieved through a variety of mechanisms including honey's osmotic effects, production of hydrogen peroxide, and antioxidants. In testing, it has demonstrated effectiveness against both non-resistant and antibiotic-resistant strains of bacteria, particularly in combating wound infections. By doing so, honey is not only establishing its role in contemporary medicine but also its position as an alternative microbial agent. (Yupanqui et al.2022)(Brudzynski, 2021)(Luca et al., 2024)

Bacteria. Today's increasing resistance to antibiotic treatments is a significant healthcare threat. Identified as MRSA in 1999, MRSA was globally disseminated and resistant to an array of antibiotics by 2005. Reports show MRSA is also changing, converting strains that were traditionally associated with hospital-acquired infections to strains that cause skin and soft-tissue infections in healthy people outside the hospital environment. Fortunately, some natural treatments are unaffected by resistance mechanisms; some honeys are one such example. (Akram et al., 2023)

Fungi and Viruses. Partly due to similarities in the behavior of fungi and bacteria, honey's antifungal properties are well researched. There are many different types of fungi that cause

a variety of infections; these range from superficial, mucosal, and systemic infections. Therefore, effective treatment can be difficult; however, honey has been identified as effective against a range of fungi associated with these infections. Viruses are another significant threat to public health, and honey has also demonstrated potential as an antiviral agent. Currently, drug options are limited, with only a small number of active pharmaceuticals available for patients. Further, these are only suitable for a few types of viral infections and are not suitable for widespread use. In this sense, honey is making its case for utilization. Overall, honey has the potential to be a useful component in contemporary medicine. With its unique component profile and broad-spectrum antimicrobial properties, it has potential for use in a range of fields including wound care, where it has demonstrated particular effectiveness. (de et al.2021)(Miller et al., 2021)(van et al.2021)

3.1 Against Bacteria

Among the most valuable properties of honey, of importance in the therapeutic context, is its antibacterial nature. It is well documented that it is effective against Gram-positive bacteria and Gram-negative bacteria. That is why honey is finding applications chiefly in the treatment of wounds and infections. Good results were obtained when heather honey was topically applied to mild-to-moderate superficial and partial-thickness burns in children. A beneficial influence of heather honey on recalcitrant infected post-surgical wounds following radical debridement after osteosynthesis was also reported. In order to explore the mechanisms associated with such activity, many researchers have also investigated the antimicrobial properties of honey and its inhibitory spectrum against various microorganisms. (Aljaghwan et al.2021) (Stavropoulou et al.2022)

Evidence of the high efficacy and a broader spectrum of bactericidal activity of honey preparations has been presented in comprehensive reviews, concentrating on multiple studies of the susceptibility of pathogens to most commercially available medicinal honeys. Moreover, the lack of bacterial resistance to honey is of great interest regarding the widespread use of topical medicinal agents based on honey

since antibiotic resistance is a severe and widespread problem among patients undergoing conventional antimicrobial therapies. Clinical trials are being conducted with various honey preparations that are used to treat, among others, burn patients, especially children. By standardizing the methods for collecting and processing therapeutic honeys, it will be possible to ensure that such honeys have optimal antibacterial activity and can be safe as antimicrobial agents. (Almasaudi, 2021)(Hossain et al.2022)

3.2 Against Fungi

Candida species are the most common fungal organisms that cause infection in humans. To target these pathogens, honey uses many mechanisms, such as inhibition of germ tube formation, damage to the cell wall, suppression of ergosterol biosynthesis, and the ability to produce reactive oxygen species. The minimum inhibitory concentration of honey that can inhibit the growth of *Candida* depended on its species and varied from 2.5% up to 75% from study to study. This indicates the necessity to standardize the experimental methods. In vitro studies frequently describe the synergistic effects of honey and standard antifungal drugs. In some clinical cases, where infection was caused by fungi resistant to traditional therapy, the addition of honey in the treatment protocol restored the success of therapy. Most of these cases concerned topically delivered honey, but some described complementary oral delivery of honey in immunocompromised patients. These results are crucial to consider and indicate honey as a natural remedy for physicians of many specializations, suggesting that the therapeutic use of honey can be proposed not only in classical medicine but also in dental, dermatological, and veterinary fields for the treatment of many mycoses, particularly candidiasis, frequently induced post-surgically. (van et al.2021)(de et al.2021)

Negative effects of pharmaceutical antifungal drugs on the human microbiota indicate the emergence of studies on naturally-based agents; honey seems to be a good candidate, particularly in chronic infection treatment. Consistent results of mutual enhancement in antifungal action by both honey and antifungal drugs suggest that comprehensive studies

using animal models or double-blind, prospective clinical trials are necessary to plan new therapy protocols. Because studies have proven the low MIC value of honey against many *Candida* species, in vitro and in vivo confirmations can be proposed before detailed tests. The only issue is the genetic and phenotypic differences of *Candida* species. The isolated human candidal species were different in susceptibility to hydrolysable tannins affecting wound healing in a dose-dependent manner. However, honey can be very useful and probably the optimal remedy in common drug delivery chaotic directions; it is also useful prophylactically, if used in a moderate dose as a sweetener, to protect mucosa and subsequently to prevent some candidiasis through its antimicrobial properties. (Yupanqui et al.2022)(Tashkandi, 2021)

3.3 Against Viruses

Honey has broad-spectrum antiviral properties. It has activity against a number of viruses, including those that cause upper respiratory infections, such as influenza virus, respiratory syncytial virus, human parainfluenza viruses, rhinovirus, and adenovirus. Two different mechanisms of action against influenza A virus may be suggested for honey: damage to virus structural proteins and inhibition of virus mRNA synthesis. The potential of honey to help with currently circulating viral diseases has not yet been demonstrated, but it has been suggested that sources of antioxidants and phenolic compounds present in honey might enhance immune responses against viral infections that lead to respiratory tract inflammation and catarrh, particularly in alleviating symptoms due to secondary bacterial infections. Medicinal honey is recommended as a last-resort treatment option for cough for the management of upper respiratory symptoms. However, there are no standardized cultivation and clinical studies on honey. (Asma et al.2022)(Sekar et al.2023)

Honey significantly decreases lower respiratory tract symptoms caused by rhinovirus, though whether it affects rhinovirus replication is unclear. Store-bought or genuine Manuka honey composition with the associated level of activity should be considered for future antiviral intervention

studies. Honey may offer the potential to reduce rhinovirus symptom duration. Honey is a good supplement to decrease symptoms of acute cough when already known, and there are several previous studies that have been done. Nevertheless, there are no studies on the use of Indonesian honey against influenza. So, new directions come up with new hope for a breakthrough in this research direction by studying the inhibitory power of honey directly, especially honey in the region of Indonesia against the influenza virus. Several clinical trials indicate that the use of honey can present antiviral activity in various types of viruses, but from many viruses, in Indonesia, clinical trials can be found only in dengue fever. In one clinical trial on the oral honey consumption process, a decrease in the number of the dengue virus was experienced. Most of these trials have focused on the effect of honey as an antiviral synergistic activity with other antiviral drugs. The use of honey is expected to accelerate the healing process and provide protection and immunity to the body. In a new publication of a review, bee honey showed inhibition of 11 viruses through the virus entry phase, 20 viruses in which the replication is inhibited, and 20 viruses in the release of the virus. (Abuelgasim et al., 2021)(Arentz et al.2021)

4. Wound Healing Properties of Honey

Honey is a sweet substance produced by bees and has been used for centuries as a traditional medicine to treat various diseases and injuries. Currently, many studies are underway that have proven its efficiency as an alternative for the treatment of wounds and many other diseases. In this work, we present the state of the art with therapeutic properties of honey according to its potential applications in contemporary medicine. Wound healing properties of honey. Honey has been used for centuries in the treatment of wounds and to encourage tissue regeneration and reduce inflammatory changes, thereby promoting rapid scarring. However, this mechanism was not well understood until late in the 19th century. It was determined that honey, when diluted, has an inhibitory effect on several pathogenic organisms. This observation correlated with the increased use of this product in clinical settings such as surgical wounds, ulcers, and burns.

Many studies have confirmed that honey increases the rate of wound healing. Its pharmacological properties are related to its chemical composition, which contains sugars, amino acids, proteins, vitamins, and, above all, key components such as nitrogen, hydrogen peroxide, and polyphenols: flavonoids, phenolic acids, and enzymes. The process of wound healing and regeneration plays an essential role at the molecular level; for example, nitric oxide levels are increased, and the balance between matrix metalloproteinases and tissue inhibitors is regulated. Honey maintains moisture and prevents the growth and colonization of bacteria and other pathogenic microorganisms. (Boukraâ, 2023)(Yupanqui et al.2022)

5. Clinical Applications of Honey in Medicine

Honey has been found to be a valuable alternative and complementary medicine for diseases such as respiratory conditions: bronchial asthma, chronic cough, cystic fibrosis, and bronchitis, as well as gastrointestinal disorders: indigestion, diarrhea, Crohn's disease, ulcerative colitis, constipation, and GERD. It also has value in managing chronic and long-term conditions; though research in the area is scarce and needs more studies to cover a variety of clinical fields of medicine. In this chapter, many clinical trials and reports on healing wounds and burns with honey are underway around the world. Much of this work is a combined research effort between conventional medical practice and holistic practice. Researchers argue that the expectation is to show the effectiveness of honey beyond just healing wounds; it is about holistically healing a person as a whole.

Use of Honey in Managing Respiratory Conditions: A typical application of honey in clinical practice is addressing various respiratory conditions, including bronchial asthma, chronic cough, cystic fibrosis, and bronchitis. Many clinical trials and case reports have been recorded in this area.

Use of Honey in Managing Gastrointestinal Disorders and Conditions: Honey is used clinically to address various conditions and disorders, including indigestion, inflammation, chronic inflammation, Crohn's disease, ulcerative colitis, constipation, GERD, gastric pain, and other problems.

Use of Honey in Managing Skin and Dermatological Conditions: Honey is used

clinically in a few instances involving skin diseases. These conditions include herpes complications, lip lesions, and skin moisturizers. Several clinical cases in eczema and psoriasis are also reported. There are other clinical applications in oral care with honey, managing diarrhea, and using honey prior to general anesthetic therapy. (Aw et al.2021)(Jaber et al.2021) (Tashkandi, 2021)(Ízol, 2023)

5.1 Respiratory Conditions

5.1.1. Chronic Cough

Honey can be used to treat cough. Clinical studies have shown that a single dose or a two-day administration of honey can enhance the health of patients who suffer from chronic cough and could not find any relief from medications. Being safe, honey can be used in the entire population. Honey reduced the severity of cough, the frequency of cough, and the discomfort associated with it. Therefore, it has been suggested as a potential substitute for industrial HCl (either used alone or in combination with other medications). The natural anti-inflammatory and emollient properties, which are attributed to the presence of flavonoids and antioxidants in honey, make it very suitable for the treatment of irritation in the respiratory tract. Almost all honey types are recommended in the treatment of cough, whether dark or light, though it has been suggested that honey with a darker color possesses more qualities. (Poursaleh et al.2022)(Sadr et al.2023)

Contrary to the well-known syrups sold as OTC medications for cough, honey has a sweet taste and, because of its better viscoelasticity, it sticks to the throat for a long time and prevents the tickling sensation in the throat. The daily consumption of honey can also prevent throat infections. A daily intake can have a productive result in patients suffering from cough diseases, even allergic rhinitis. Uncontrolled drug users with allergic rhinitis and cough stated that receiving honey in water gave them relief and improved various parameters like frequency of cough, intensity, and quality of sleep. This is popularly called the “honey remedy.” Other respiratory ailments that can be treated by honey, besides chronic bronchitis, include chronic bronchitis and laryngospasm in infants. (Ahmed et al.2023)

5.2 Gastrointestinal Disorders

It is well documented that honey has important therapeutic effects on gastrointestinal complaints such as gastritis and peptic ulcers, as well as other gastrointestinal disorders such as diarrhea and irritable bowel syndrome. Multiple mechanism research has mainly focused on hydroxymethylfurfural, phenolic compounds, and flavonoids in honey, as well as the synergistic effect of honey with other natural products related to inflammation. Multiple studies investigating the influence of promoting a healthy gut used honey as a positive-tasting prebiotic. This review presents a summary of the latest literature, explaining the role of the dosage forms of honey most commonly used for GI disorders, including the respected clinical advantages and long-standing beliefs about honey in promoting gut health. The antioxidant profile of honey is discussed alongside reported evidence of a direct free radical scavenging effect in clinical studies related to GI complaints. (Gośliński et al.2024)(Kim et al., 2024)

The active constituents of honey and randomized clinical research support the effects, with meta-analysis verifying that honey enhances the eradication rate and reduces the signs of *H. pylori* infection-related symptoms; however, treatment with a high intake of natural honey was seen to remarkably alleviate and strengthen ulcer symptoms. Children have also shown benefits from honey in one study; the intake of lyophilized bee pollen was shown to reduce symptoms after seven weeks, whereas a different type of lyophilized bee pollen was monitored to reduce erosion areas and the occurrence of psoriatic plaques after twelve weeks. It has been revealed to regulate stomach acid secretion and detoxify reactive oxygen species, regulate GI motility, and inhibit potential pathogen growth should gastric pH be raised, but also to nourish the GI lining and promote recovery. Furthermore, honey is reported to be absorbed slowly into the bloodstream and used directly by the body, providing a safe and effective remedy for those who suffer from digestive problems. (Cardos et al., 2021)

5.3 Dermatological Conditions

Honey has been reported as a natural moisturizer that can

help manage various skin problems. It has 20% water content, low pH, and contains amino acids, B vitamins, and other nutrients that help to regenerate the skin. Besides, honey also has antibacterial and anti-inflammatory properties. Because of its beneficial properties, honey has been used to heal some skin problems, like acne and eczema. Acne is a common skin condition characterized by the presence of comedones, papules, pustules, and nodules that can affect the face, chest, and back. Eczema is one of the most common chronic relapsing inflammatory skin diseases, characterized by pruritus, redness, and various skin lesions. (Almasaudi, 2021)(El-Seedi et al.2022)

Clinical studies of honey in dermatology are very limited and not widely conducted. However, in vitro and in vivo studies have shown the promising effects of honey as an adjunct therapy in dermatology. Honey has been used for skincare formulations to improve its properties and make it user-friendly. In formulating a product with honey, the parameters that must be considered are the concentration of honey, derivation, and a proper preservation system against bacteria and fungi. There is increasing evidence that honey is effective in reducing wound inflammation and enhancing the healing of wounds. Even though many clinicians believe that honey is a natural product and does not require patch testing to establish that patients are not allergic, it is better for dermatologists to perform a total allergy test with a skin patch test using honey before routine use. Moreover, it is more practical not just to think of the individual components of honey as having biological activity, but to be aware of the performance of honey as a whole. In conclusion, the application of honey is a modality that has proven to be an attractive dressing for treating wounds. It also has many uses in dermatology. Honey has been used successfully in patients suffering from a variety of wounds and skin diseases. (Tashkandi, 2021)(Ahmed et al., 2022)

6. Conclusion and future directions

In conclusion, this comprehensive review supports the notion that honey can be an effective complementary or, in some cases, alternative strategy for managing a plethora of

health conditions in modern medicine. Of particular note is that honey encompasses antioxidant, anti-inflammatory, antibacterial, and anticancer effects, possesses important immunomodulatory properties, expedites tissue repair, and can be used as a wound dressing to accelerate healing in an array of wound types, including burns. We have received further evidence that manuka honey is the most extensively studied honey type with established antimicrobial and immunomodulatory benefits for use in wound healing and reducing infections, but we have also suggested exploring the medical attributes of various honey types, not just manuka honey. For the majority of other health conditions, due to the dearth of RCTs, evidence is mostly drawn from in vitro, animal, or small clinical studies that suggest outcomes with the use of honey are promising. Our recommendation is to conduct larger, well-designed clinical trials to produce higher-quality evidence and provide clarity in the application of honey for such conditions.

We suggest conducting studies on the effects of different honey types and their consistency. In this respect, our advice is that the development of a standardized protocol for honey harvest, processing, storage, and application in health care is necessary to ensure that the honey contains the same beneficial and bioactive qualities in every batch produced. Researchers, apiarists, and clinicians should collaborate in the latest research findings to determine the most appropriate honey for various therapeutic applications and related health issues as a way of exploring new uses and benefits of honey as a future-generation product in the realm of modern medicine. Additionally, it is significant for further research to establish whether honey can be used for preventive medicine or optimally complemented with existing medication as a general health promotion agent. Furthermore, there is value in future research to instruct health professionals about the medical applications of honey.

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