Phytopharmaceutical millets: nutraceutical potential and health benefits of bioactive compounds


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Abstract
Millets, small-seeded cereal grains, are being recognized as sources of phytopharmaceuticals, bioactive compounds derived from plants with significant therapeutic benefits. These phytochemicals, including polyphenols, flavonoids, phenolic acids, saponins, tannins, terpenes, alkaloids, sterols, and glycosides, contribute to the unique health-promoting profile of millets. These compounds address chronic health concerns like diabetes, cardiovascular disorders, and cancer. Millet-derived phytopharmaceuticals, such as polyphenols, reduce oxidative stress, while saponins and sterols manage cholesterol levels, supporting cardiovascular health. With the global demand for natural and functional foods increasing, millets are emerging as sustainable, plant-based solutions to lifestyle diseases. This aligns with regulatory shifts in India, where phytopharmaceuticals are being recognized as equivalent to synthetic drugs. Incorporating millets into daily diets can provide a natural, cost-effective approach to disease prevention and management, contributing to personal and public health.

Keywords: Millets, Phytopharmaceuticals, Functional foods, Disease prevention

1. Introduction
Phytopharmaceuticals, derived from plants, are bioactive compounds that possess medicinal properties and offer significant therapeutic benefits. They have gained increasing attention due to their ability to act as natural remedies for a wide range of diseases, with minimal side effects compared to conventional pharmaceuticals. Millets, a group of small-seeded grasses, have been cultivated for thousands of years and are widely consumed in many regions, particularly in Africa and Asia (India). Indian farmer grows several species (Figure 1) such as pearl millet (*Pennisetum glaucum*), finger millet (*Eleusine coracana)*, foxtail millet (*Setaria italica*), and sorghum (*Sorghum bicolor*) (1). These ancient grains have recently gained attention not only for their resilience in harsh environmental conditions but also for their significant phytochemical value in public health. Theses mall-seeded grains are rich in a variety of phytochemicals such as Phenolic acids, Flavonoids, Tannins, Phytosterols, and Saponins. These compounds contribute to the health-promoting properties of millets.These bioactive compounds exhibit antioxidant, anti-inflammatory, anti-diabetic, and cardioprotective properties, making millets a potential dietary intervention for lifestyle-related diseases (1,2). As consumers and researchers alike focus on the role of diet in promoting health and preventing chronic diseases, millets have emerged as an important food crop due to their rich composition of bioactive compounds and essential nutrients (3).

Millets are an excellent source of nourishment. Millets are becoming increasingly popular both in India and around the world because of their potential to provide food security, environmental sustainability, and nutritional value. As part of wider measures to address global issues including malnutrition, climate change, and sustainable agriculture, both Indian and international programs are attempting to increase the production, consumption, and knowledge of millets. In order to promote the production and consumption of millets and to increase awareness of their significance as a food crop, the Food and Agricultural Organisation of the United Nations (FAO) launched the IYOM 2023 worldwide campaign. Millet awareness and consumption have increased in recent years as individuals have begun to pursue a healthier lifestyle. In 2018, India suggested 2023 as the International Year of Millets. The UN Food and Agriculture Organisation accepted it, and the United Nations General Assembly declared 2023 to be the 'International Year of Millets'. This was approved by a United Nations resolution (4).

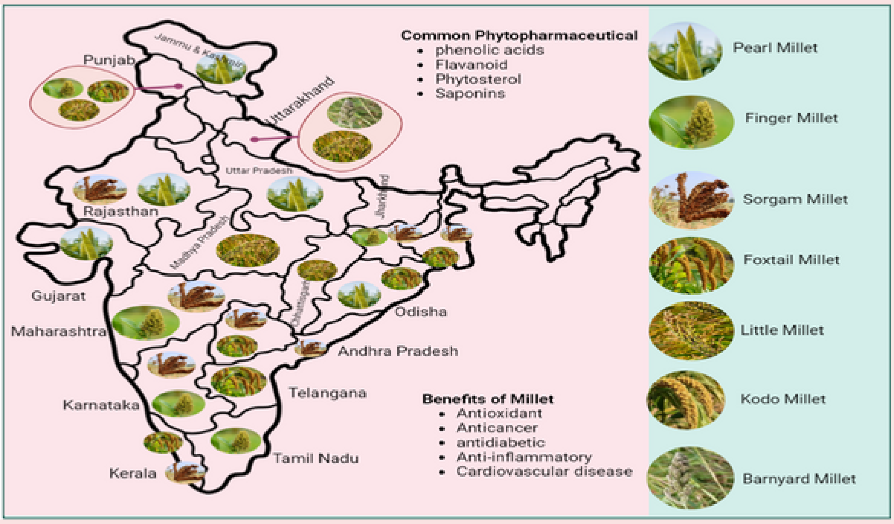


Figure 1. Geographical distribution of different species of millets in India.

The aim of this review is to explore the phytopharmaceutical potential of millets by focusing on their bioactive compounds and health benefits. Given the increasing prevalence of lifestyle diseases such as diabetes and cardiovascular disorders, understanding how millet-derived phytopharmaceuticals can mitigate these conditions is of growing importance (4).

2. Phytopharmaceuticals in millets

2.1. Polyphenols

Polyphenols are intermediates in metabolic pathways that function as defense and signaling molecules, contributing to essential biological processes. In millets, phenolic acids and, flavonoids are the primary polyphenol groups. These compounds contribute to the significant antioxidant properties of millets in both dietary and biological contexts. The seed coat of millets is especially rich in dietary fiber and polyphenols. Research suggests that millet consumption may reduce free radical induced stress in the hippocampus and downregulate genes such as γ-secretase, tau, and amyloid precursor protein, which are associated with Alzheimer's disease. Millet-derived polyphenols also show anti-diabetic properties, displaying specific hypoglycemic effects. Furthermore, bound polyphenols from millet bran, including p-Coumaric acid (p-CA) and Ferulic acid (FA), demonstrate anticancer activity. These compounds enhance the sensitivity of drug-resistant colorectal cancer (CRC) cell lines to oxaliplatin (OXA), a chemotherapy drug for CRC. Additionally, foxtail millet polyphenols induce apoptosis, inhibiting colorectal cancer progression in mice. Millet-bound polyphenols also exhibit immunomodulatory and antifungal properties (11).

Table 1. Phytopharmaceuticals in Indian grown millets

Millets	Phytopharmaceuticals	Nutritional Aspect	Ref
Sorghum bicolour L. (Sorghum)	Salicylic, protocatechuic, caffeic, sinapic, ferulic acids, p-coumaric acid), phenolic acids (gentisic, cinnamic; flavonoes (luteolin, tricin, and apigenin); flavonones (eriodictyol and naringenin)	Anti-oxidant Capacity	(5)
		Fat, carbohydrate, protein, calcium and iron	
		Essential Amino Acids	
Eleusine coracana L. (Finger Millet)	Phenolic acids (gallic, vanillic, querticin, caffeic, FA, p-CA): flavonoids (Catechin equivalent)	Protein Content, phenolic content copper, iron, manganese, zinc	(6)
		Iron, zinc, calcium, essential amino acids	
		Vitamin C	
Pennisetum glaucum L. (Pearl Millet)	3- Deoxynthocyanidin; Phenolic acids (gallic, vanillic, Chlorogenic acid, Sinapic acid, Ferulic acids, p- coumaric acid)	Phenol, soluble protein, amylase glucose, calcium, zinc, iron	(7)
		Lysine, Methionine	
		Protein and Starch Digestibility	
Setaria italica L. (Foxtail Millet)	Phenols (apigenin, N'- Caffeoyl-N'-Feruloylspermidine, Di-p-coumaroyl Spermidine, N,N',N''- diferuloyl spermidine- Dihexoside); Carotenoids (xanthophyll, Zeaxanthin)	Protein, Copper, Iron, Manganese	(8)
		Phenolic Acids, Flavonoids	
Paspalum scorbiculatum L. (Kodo Millet)	Phenolic acids (Stigmasterol, Campesterol, N-(5- hydroxy-pentyl) arachidonoylamide, Pregnenolone)	Protein, amino acids availability and starch digestibility	(9)
		Anti-oxidants, proteins, fats, carbohydrates	
Panicum sumatrense Roth. (Little Millet)	Flavonoids (6-C- Glucosyl-8-C-arabinosyl apigenin); Phenol (Sinapic acid, p-coumarylpentose, synapaldehyde, kaempferol)	Copper, iron, protein content, manganese, zinc, phenolic content	(10)
		Starch digestibility and protein	
		Flavonoids, and Phenolic Acids	



Sorghum **Finger Millet** **Pearl Millet**



Foxtail Millet **Kodo Millet** **Little Millet**

Figure 2. Assorted millets verities available in India (Source: Google images accessed on 11.11.2024)

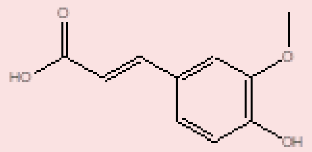
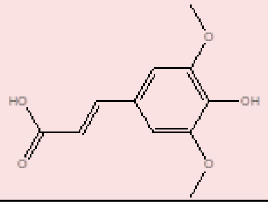
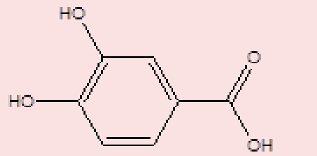
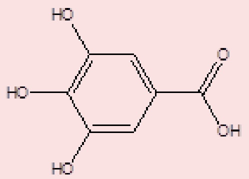
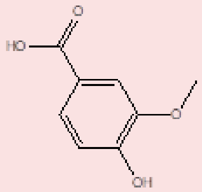
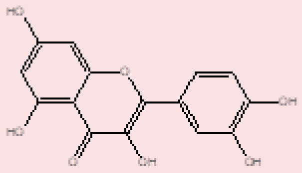
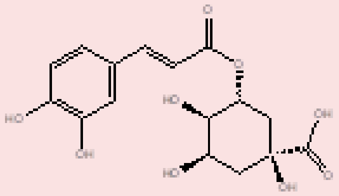
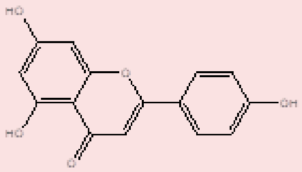
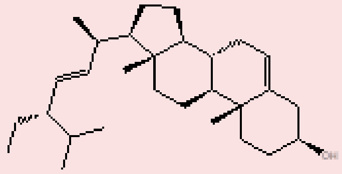
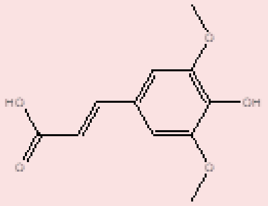
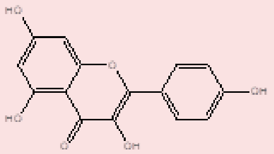
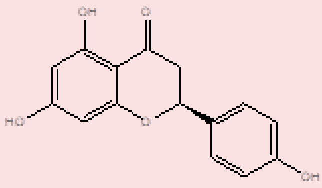
2.2.Phenolic acids

Millets, phytochemicals, and their Phenolic acids in millets originate from hydroxybenzoic acid and hydroxycinnamic acid, with content varying by millet species. The primary bound phenolic acids are derivatives of cinnamic acid, such as coumaric and caffeic acids, while free, unbound forms are typically derivatives of gallic acid, including syringic and vanillic acids. Notably, bound phenolic acids possess significant antioxidant and therapeutic properties, which are beneficial in promoting gut microbiota health and supporting overall gut function (12).

2.3 Flavonoids

Flavonoids are the primary class of polyphenols in millets, contributing valuable preservation qualities that support a balanced diet. Millet flavonoids are potent antioxidants, surpassing elements like zinc, selenium, and certain vitamins in antioxidant strength. Bhat et al. (2021) reported that millet flavonoids exhibit numerous health benefits, including anticancer, diuretic, antihypertensive, analgesic, hypolipidemic, and anti-inflammatory effects. Their Antihypertensive and Antiarrhythmic effects include the relaxation of smooth muscle in the heart, alongside LDL cholesterol oxidation prevention. Flavonoids also contribute to cholesterol reduction and inhibit platelet aggregation, while modulating the body’s response to pathogens and helping to control allergens (13).

Table 2. Chemical structures of some of the phytoconstituents present in millets

		
Ferulic acid	Sinapic acid	Protocatechuic acid
		
Gallic acid	Vanillic acid	Quercetin
		
Chlorogenic acid	Apigenin	Stigmasterol
		
Sinapic acid	Kaempferol	Naringenin

2.4. Alkaloids

Alkaloids, found in millets, enhance plant condition and provide health benefits. However, alkaloids can also have genotoxic, mutagenic, carcinogenic, fetotoxic, and teratogenic effects. In foxtail millet, alkaloids have demonstrated anti-hyperglycemic and hypolipidemic effects in diabetic rat models. (14).

2.5. Terpenes

Phytosterols are produced through biosynthetic pathways, with isopentenyl pyrophosphate as a key building block for terpenoids. Terpenes, the chemical compounds responsible for the distinct aroma and flavor of millets, are primarily found in essential oils and enhance the nutraceutical qualities of the plant. These include linalool, geraniol, myrcene, and limonene. Terpenes contribute to both the sensory characteristics and health benefits of millets. Traditionally, terpenes have been valued for their roles in medicinal systems, with further potential as antineoplastic, antibacterial, and pharmacognostic agents (14).

2.6.Saponins

Saponins are known for their ability to create a soapy lather when mixed with water and have been linked to reductions in blood cholesterol levels upon ingestion. In millets, this phytochemical is primarily found in the seed coat or outer grain layers. Finger and pearl millets are particularly rich in saponins, with pearl millet having the highest content. Compared to cereals and grasses, millets generally contain more saponins. Saponins exhibit valuable physicochemical and biological properties, making them beneficial in the food industry as emulsifying agents that improve bread porosity and aerate culinary items. Medicinally, saponins offer a variety of benefits, including anti-inflammatory, anticancer, antioxidant, and cholesterol-lowering effects (15).

2.7. Tannins

Millets comprise up to 0.61% of polyphenolic chemical substances called tannins. Millets' antioxidant capabilities, which lower aging and improve metabolic processes, are attributed to their tannins. Cultivars of millet with increased tannin content have better antioxidant qualities. It appears that different millet species have differing contents. Processing millets to increase their bio-accessibility and reduce their tannin content can lessen their anti-nutritional properties (16).

2.8. Sterols

Millet sterols, present as naturally occurring phytosterols, are secondary metabolites and essential components of plant cell membranes. Some commonly found sterols in millets include Episterol, 24-Methyllathosterol, Brassicasterol, Avenasterol, 24-Ethyllathosterol, 24-Methylenecholesterol, Isofucosterol, Fucosterol, 24-Methyl-5α-Cholest-24-en-3β-ol, and 24-Ethyldesmosterol. These sterols are typically found in millet seeds and are known for their cardiovascular benefits due to their structural similarity to cholesterol. By competing with cholesterol for absorption in the intestines, millet sterols effectively reduce cholesterol levels in circulation. As a result, regular millet consumption supports a balanced diet, promoting overall health and well-being. Fortifying millet products by increasing sterol content can enhance their nutritional value (17).

2.9. Glycosides

Glycosides in millets are compounds formed by sugar molecules linked to other functional groups. Key glycosides, include Kaempferol glucoside, Catechin/epicatechin glucoside, and Glucosyl orientin. Millets also contain esterified sterol glycosides and sterol glycosides, which are classified as millet glycolipids. These glycosides, as phenolic compounds in millet grains, contribute to reducing the risk of chronic diseases and enhance the antioxidant and anti-inflammatory properties of millets. Additionally, millet malts contain higher levels of free sugars and non-starchy water-soluble polysaccharides compared to unprocessed millets (18).

3. Conclusion

Millets have significant phytopharmaceutical potential, promoting health and preventing diseases. Their diverse phytopharmaceuticals, including polyphenols, flavonoids, alkaloids, terpenes, saponins, tannins, sterols, and glycosides, offer a sustainable and accessible solution to chronic health issues. As research continues, millets can be incorporated into functional foods and nutraceuticals, promoting healthier dietary choices and effective health management. This holistic approach to healthcare aligns with the growing preference for natural, sustainable solutions in modern society.

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