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Bioactive compounds and therapeuticproperties of millet bran

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ABSTRACT

Millet bran is a by-product obtained during the processing of millet and is packed with a variety of nutrients. It is made up of the outer layer, seed coat, aleurone layer, a small part of the embryo, and the endosperm [1]. It makes up about 6–8% of millet's total weight [2]. This by-product is typically thrown away during the milling and refining of cereal grains due to its appearance, taste, and ability to extend shelf life [3]. It contains bioactive elements such as fibers, lipids, proteins, and minerals [4]. Additionally, millet bran is higher in vitamins B, C, and E compared to the kernels [5,6]. Moreover, millet bran is a good source of phytochemicals, including flavonoids, polyphenols, phytosterols, dietary fiber, and other bioactive substances [4]. Beyond its high fiber content, millet bran is also a rich source of essential oils. The fat content of the millet small bran had unsaturated fatty acids, linoleic acid, linolenic acid, arachidonic acid, and other essential fatty acids unsaturated fatty acids[7]. The millet bran must be exploited for its health benefits. Many research findings revealed the therapeutic potential of millet bran.This review discusses the phytochemical potential of millet bran and provides valuable insights into these compounds and their possible therapeutic properties in disease management.

Keywords: *millet bran; bioactive compounds; phenolic compounds; dietary fiber; peptides; therapeutic properties*

1. Introduction

The bran part of millet is a relatively inexpensive and widely available by-product of millet processing. However, despite its high nutritional value, millet bran is often overlooked and even discarded [8]. Currently, millet bran is primarily used in animal feed, with its abundant nutrients and bioactive components not being fully utilized, and its use rate is low [9]. Millet bran contains some bio-active functional molecules, such as polyphenols, protein, and polypeptides which possess antioxidant, antibacterial, and anti-hyperglycemic activity. [10].Research has shown that minerals like calcium and phosphorus, along with antinutrients, are concentrated in the bran fraction of pearl millet [11]. The seed coat or bran of finger millet, another by-product of traditional milling, contains beneficial elements such as dietary fiber, minerals, and protein [12]. Foxtail millet bran, another by-product of conventional milling, also includes nutritional components like dietary fiber, vitamins, fat, and protein [8]. This review was thus aimed to provide an overview of information related to the bioactive compounds and therapeutic properties of the millet bran isolated from various millets.

2.Bioactive compounds inmillet bran

2.1. Phenolic compounds

Polyphenols encompass a broad category of plant-based chemicals, primarily classified into flavonoids and nonflavonoids.

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These compounds have been proven to display a wide range of biological functions and possible health advantages both in vivo and in vitro. Studies on polyphenols from food sources have demonstrated their ability to greatly reduce various symptoms of metabolic syndrome, including central obesity, hypertension, dyslipidemia, and high blood sugar [13]. Compounds rich in polyphenols have multiple positive effects due to their antioxidant and anti-inflammatory activities [14]. Millet bran fiber contains mainly phenolic acids, which are mostly bound to arabinoxylans of the cell wall [15]. Similarly, it was reported that the phenolic compounds are primarily located in the outermost parts, hence the bran fractions of millet obtained as milling by-products could serve as a natural source of antioxidants and as an added value component in the production of functional food ingredients and enriched products [16].

2.1.1. Finger millet bran

It was observed that the finger millet seed coat contained various kinds of phenolic compounds, including phenolic acids, flavonoids, polymeric tannins, and anthocyanins [12]. Based on the findings of a study it can be concluded that the finger millet seed coat is a rich source of polyphenols possessed with major phenolic acids such as diadzene, gallic, coumaric, syringic and vanillic acids [17]. It was reported that the phenolics identified in the finger millet seed coat were the benzoic acid derivatives such as gallic, protocatechuic, p-hydroxybenzoic, vanillic, and ferulic acids, as well as cinnamic acid derivatives like syringic, trans-cinnamic, and p-coumaric acids [18]. Additionally, a flavonoid known as quercetin was identified. It was noted that the major bound phenolic acids such as ferulic, caffeic, coumaric, and vanillic acids were determined in the water unextractable portion from finger millet bran [19].

2.1.2. Foxtail millet bran

Phenolics are mainly found in the husk and outer bran layers of the foxtail millet kernel [20]. Bran from foxtail millet, which is a by-product of processing this grain, contains a high amount of phytochemicals. Specifically, polyphenols, a type of phytochemical, show a diverse array of pharmacological and medicinal properties [21]. It was found that the foxtail millet contains a high concentration of polyphenols, and these polyphenols are particularly concentrated in the bran of foxtail millet. The polyphenols present in the inner shell of foxtail millet bran include ferulic acid and p-coumaric acid [22]. Bound polyphenols of inner shell (BPIS) from foxtail millet bran was mainly phenolic acids by LC-MS/MS identification[23]. The primary components of the deep eutectic solvent foxtail millet bran extract were primarily fifteen types of phenolic substances [24].

2.2. Dietary fiber

Millet bran is a promising substance for supplying fiber from the diet because of its high fiber content [2,8,25]. Hydroxycinnamic acid bound arabinoxylans extracted from brans of five Indian millet varieties [26]. It was found that the crude fiber content of barnyard millet is higher than that of other cereals [27]. It was revealed that soluble dietary fiber from foxtail millet bran had strong Į-amylase inhibition, delaying the hydrolysis of starch to oligosaccharides [28]. A study revealed that foxtail millet bran is a good source of dietary fiber [8]. Foxtail millet bran-based dietary fiber has great potential to be used as a functional ingredient in food products. All the physicochemical features and functional properties of dietary fiber from foxtail millet bran suggested that it had a cholesterol-lowering effect in vitro and therefore could be beneficial for the management of lifestyle diseases [8].The study results indicated that the pearl millet bran can act as rich source of dietary fiber with health-enhancing properties and can be utilized as a potential food component in preparation of functional food products [29].

2.3. Peptides

Bioactive peptides represent a category of biological molecules that are typically embedded within the structure of their parent proteins and become functional following the cleavage of these proteins. [30]. Antioxidant peptides identified in food proteins receive more interest for abundant sources, low cost and security. Addition of antioxidant peptides to foods is considered to be a reasonable way to prevent food corruption and promote good health [31]. It was stated that peptides are characterized by their strong potency, specificity, and favorable safety profile, making them a highly attractive group of compounds for emerging and effective therapeutic options that may fill the gap between small molecules and protein drugs [32]. It was found that functional millet bran peptides had antioxidant and life-prolonging effects, which are important for the development and utilization of millet bran proteins as resources of active ingredients [33]. An investigation found that millet bran peptides could have anti-inflammatory activities [34]. Three novel antioxidant peptides were identified in foxtail millet bran glutelin-2 hydrolysates. These peptides had excellent antioxidant activities [35]. In another study a novel tetrapeptide identified in foxtail millet bran globulin hydrolysate. These findings revealed the possible use of peptides in the food or pharmaceutical sectors [36]. Fermented foxtail millet bran is a rich source of bioactive peptides, which have notably higher antioxidant activity [37]. Peptides obtained from the bran of foxtail millet could be incorporated into food products as antihypertensive agents. In silico studies indicated that foxtail millet bran glutelin-2 peptide fractions are potential natural Angiotensin-Converting Enzyme inhibitors [38].

3. Therapeutic properties of millet bran

3.1. Antioxidant activities

Antioxidants are substances that can interact with free radicals safely, stop the reaction, and transform them into a non-harmful compound by providing an electron. This process lowers oxidative stress, thereby safeguarding cells from damage caused by oxidation [39]. Formulation of new antioxidant substances has turned into a critical health issue due to the extensive harm to the cellular macromolecules that reactive oxygen species can inflict [40]. Additionally, the findings revealed that the bran-rich fraction demonstrated significant antioxidant potential determined by reducing power assay due to elevated tannin, phytic acid, and flavonoid content [11]. It was stated that bran, a byproduct of the milling process, contains antioxidant properties because it is rich in phenolic acids like p-coumaric acid and vanillic acids, which are particularly concentrated in the bran part of cereal kernels [41]. The antioxidant power of five bran extracts showed significant amounts of total phenolics, flavonoids, and the ability to neutralize DPPH radicals. Similarly, it was reported bran had the greatest antioxidant power when compared to decorticated grain and whole millet grain [16]. Millet bran polysaccharide -1 an extract from millet bran possessed strong antioxidant and hypoglycemic activities [42]. The results indicated that the soluble dietary fibre from millet bran had good antioxidant activity [43].

3.1.1. Antioxidant activity of Finger millet bran

It was observed that Xylo-oligosaccharides (XO) from finger millet bran exhibited higher antioxidant activity which is more than the antioxidant activity exhibited by rice, maize, and wheat bran XO mixtures in DPPH and FRAP assay [44]. Similarly, dose-dependent addition of finger millet seed coat polyphenols inhibited free-radical formation in peanut oil, thereby preventing oxidative rancidity and deterioration in oils during regular and accelerated storage of 7.8 weeks, respectively [45].

3.1.2. Antioxidant activity of Foxtail millet bran

It was found that the methanol, ethanol and water extracts of whole flour and bran-rich fractions of foxtail millet bran were found to contain terpenoids and tannins whereas flavonoids, alkaloids, phenolics, and reducing sugars were found only in methanol and aqueous. Bran-rich fractions had the highest antioxidant activity compared to the whole flour [46]. It was demonstrated that the ethanol: water extracts of defatted foxtail millet bran had good phenol content. Total phenolic content was highest in ethanol: water extract. Thus, demonstrated good antioxidant potential reducing power, and scavenging abilities on DPPH, ABTS and superoxide radicals [47]. It was reported that the different varieties of foxtail millet extracts exhibited antioxidant activity [48]. Similarly, it was indicated that bran rich fraction of foxtail millet, showed radical scavenging activity [46].

3.1.3. Antioxidant activity of other millet brans

The kodo bran and defatted Kodo bran, which are by-products of polishing and oil extraction exhibited antioxidant activities [49].

It was reported that phenolic compounds influence the antioxidant properties of proso millet grains with different colors [50].The sorghum bran shows higher oxygen radical absorption capacity values compared to fruits, suggesting it has a high antioxidant potential [51]. Procyanidin-rich extract of sorghum bran exhibited antitumor and antimetastasis potential. It reduced the induced oxidative stress by improving the activities of antioxidant enzymes, superoxide dismutase and glutathione peroxidase [52].

3.2. Anti-cancer property

Cancer ranks among the leading causes of mortality, imposing a substantial health burden globally due to its significant cost of management for individuals affected by it [53]. Certain bioactive substances assist in stimulating various biological responses that may contribute to combating cancer cells. Additionally, some of these stimuli regulate the action of proteins and enzymes, which have a specific role in the biology of cancer [54].

3.2.1. Anti-cancer property of foxtail millet bran

BPIS from foxtail millet bran contains ferulic acid and p-coumaric acid, which provides new perspectives into developing nutraceuticals and drugs for breast cancer patients [55]. BPIS from foxtail millet bran has a significant inhibitory effect on α-glucosidase activity which proves that it is an important functional component of the anti-diabetic potential of bran [56]. A peroxidase enzyme from foxtail millet bran was found to inhibit cell migration in human colon cancer cells through antagonizing epithelial-mesenchymal transition via STAT3 signaling pathways [57]. It was reported that the millet bran-derived BPIS is a potential anti-inflammatory therapeutic agent for attenuating LPS-mediated inflammation in colorectal cancer [58].Thus, the foxtail millet bran-derived peroxidase has a therapeutic potential in the management of colon cancer [59]. It was indicated that the foxtail millet bran peroxidase exhibits anti-colon cancer activity and has the potential as an outstanding chemotherapeutic agent against colon cancer [60].

3.2.2. Anti-cancer property of other millet brans

It was demonstrated that finger millet bran supplementation to high-fat diet-fed mice for 12 weeks can prevent body weight gain, improve lipid profile and anti-inflammatory status, reduce oxidative stress, modulate the expression of several obesity-related genes, boost the proliferation of beneficial gut bacteria (Lactobacillus, Bifidobacteria, and Roseburia) and inhibit Enterobacter in caecal contents [61]. Bran of certain sorghum lines especially black sorghum possess 3- deoxyanthocyanidins. This compound showed strong antiproliferative activities when tested against various human cancer cell lines and its potential was comparable to that of quercetin, one of the most potent antioxidant molecules [62]. The red sorghum bran has been reported to contain an antiproliferative anthocyanin pigment [63].

3.3. Anti-diabetic potential

Diabetes mellitus is characterized by elevated blood sugar levels that result from issues with insulin production or the body's inability to use insulin properly. Some people may have both of these factors contributing to their condition [64]. Bioactive compounds are the basic essential element of current medicines, because of their accessibility, minimal adverse reactions, and affordability [65].

Millet bran accounts for 18% of the millet's fiber content making it a very important source of dietary fibers, and some researchers have shown that millet bran dietary fiber modified by combined ultrasonic-microwave treatment inhibits alpha-glucosidase activity more effectively [66]. Millet bran is also rich in phytochemicals that have antioxidative properties, which may contribute to its antidiabetic effect [67]. It was reported that millet bran polyphenols exhibit high biological activities, including antioxidant, antitumor, immunomodulatory, antifungal, and hypoglycemic effects [68]. Several studies indicate that the millet bran-derived products can be used in the development of functional ingredients and foods for the prevention and management of diabetes. A study proved that millet extracts from finger Italian millet and barnyard millet showed strong antioxidant activities. The soluble phenolics of these millets, mainly flavonoids, showed a strong ability to inhibit the actions of α-glucosidase and α-amylase enzymes, suggesting they could reduce postprandial hyperglycemia by retarding carbohydrate digestion. Additionally, the flavonoid-rich parts of these millets demonstrated strong abilities to prevent glycation, showing their potential to reduce the harmful effects of advanced glycation end products [69].

3.3.1. Anti-diabetic potential of finger millet bran

It was showed that a diet containing finger millet bran reduces the buildup of body weight, glucose intolerance, and oxidative stress in highfat diet-fed mice, and its effect was more pronounced than that of a diet containing whole grain [61]. An animal study evidenced the hypoglycaemic, hypocholesterolemic, nephroprotective and anti-cataractogenic properties of finger millet seed coat matter, suggesting its utility as a functional ingredient in diets for diabetics to derive beneficial effects in the regulation of glucose homeostasis and prevention of dyslipidemia, thus helping manage diabetes and its complications. The health-beneficial properties of the millet seed coat matter can be attributed to its dietary fibre, phytate and phenolic constituents [70,71]. In another research, the phenolic compounds from the millet seed coat were extracted with acidified methanol showed strong inhibition towards [alpha]-glucosidase and pancreatic amylase. The study indicated the therapeutic potentiality of millet phenolics in the management of postprandial hyperglycemia [12]. It was concluded that, tannins showed best inhibitory activity followed by phenolic acids, water soluble polysaccharides and xylooligosaccharides derived from finger millet bran towards the inhibition of a-amylase and α-glucosidase activity when used separately. The phenolic compounds extracted from the finger millet seed coat were showed strong inhibition towards α-glucosidase and pancreatic amylase [44].

3.3.2. Anti-diabetic potential of other millet brans

An investigation showed that BPIS from foxtail millet bran could significantly inhibit α-glucosidase activity and the type of inhibition is non-competitive inhibition [72]. It was found that water-soluble foxtail millet bran polysaccharide possessed strong antioxidant and hypoglycemic activities [73]. The strong scavenging ability to hydroxyl radical, DPPH, superoxide radical and ABTS radical, and strong Fe^{2+} chelating activity, and the high inhibition rates of α-glucosidase and α-amylase in vitro indicate that millet bran polysaccharide possessed strong antioxidant and hypoglycemic activities.

It was revealed that Japanese barnyard millet bran had preventive effects on postprandial hyperglycemia in normal rats and ameliorative effects in STZ-induced diabetic rats. Bran of the millets is rich source of dietary fibre, which is termed as complex unavailable polysaccharides [67]. It was determined that the blood glucose level of non-obese patients with non-insulin-dependent diabetes mellitus, who consumed sorghum bran papadi, showed considerable reduction [74]. Barnyard millet bran-based diet reduced diabetic polyuria, water intake, and HbA1c levels in diabetic rats [67]. Pearl millet bran is also a potential source of dietary fiber as it contains a significant amount of soluble dietary fiber and could be employed for several health benefits. Arabinoxylan extracted from pearl millet bran demonstrated anti-glycation effects [75]. Research findings of suggested that feruloylated xylooligosaccharides from pearl millet bran can be utilized as a constituent of functional foods with antiglycation and antioxidant properties [76]. Cakes made with the addition of whole proso millet flour and fermented dietary fiber from defatted proso millet bran had polyphenols and enhanced antioxidant properties, in addition to decreasing glycemic index values. Consequently, it showed less adverse sensory impact and possessed the potential to decrease postprandial blood glucose levels resulting purely from cake consumption [77].

3.4. Cardiovascular health

The leading cause of global public health challenges is cardiovascular diseases, which are responsible for a significant burden of mortality and disability [78]. Latest developments in the health benefits of bioactive compounds offer novel therapeutic approaches, which have significantly contributed to the decrease of cardiovascular disease globally [79]. Millet brans have been validated to impart antilipaemic, antiatherogenic, antihypertensive and hypoglycaemic properties. They have been verified to combat oxidative stress, attenuate insulin resistance, avert obesity risk by inducing satiety, and alleviate cardiovascular complications [80]. It was indicated that active polyphenols extracted from millet bran have great potential in preventing the development of atherosclerosis. It was also reported that active polyphenols were extracted from millet shells, and their main components including 3-hydroxybenzylhydrazine, luteolin-3′,7-diglucoside, *N*-acetyltyramine, *p*-coumaric acid, vanillin, sinapic acid, ferulic acid and isophorone exhibited the anti-atherosclerotic potential *in vitro.* Thus, millet bran phenolic acids prevent atherosclerosis by remodeling the gut microbiota [81]. Furthermore, a research study investigated the physicochemical and functional properties of foxtail millet bran dietary fiber and found good adsorption capacities to lipophilic substances such as lard, peanut oil and cholesterol. Its bile salts adsorption capacity indirectly reflected its cholesterol-lowering effect [82].

3.5. Anti-inflammatory activity

Inflammation is a physiological response of the immune system, serving to protect the body against various inflammatory triggers, such as toxic compounds, infections, and tissue injury [83]. Inflammation is a defense mechanism that enables the body to protect itself against infection, burns, toxic chemical allergens, or any other harmful stimuli [84]. Inflammation can be acute or chronic and untreated acute inflammation can lead to the development of several chronic inflammatory diseases, including diabetes, heart disease, cancer, stroke, and obesity, which are among the world's leading causes of mortality [85].

It has been reported that natural remedies with very little side effects, proven efficacy, and safety are required for as substitutes for chemical therapies [86]. Phenolic compounds from millet have been reported to show anti-inflammatory properties under vivo and in vitro experimental models. BPIS from foxtail millet bran displayed anti-inflammatory effects in LPS-induced HT- 29 cells and in nude mice [87]. It was found that millet bran extracts had potent suppressive activities against the production of nitric oxide and inflammatory cytokines such as IL-6 and TNF-α in the activated macrophages [88]. It was concluded that the presence of strong anti-inflammatory and anti-fibrotic phenolic compounds in the finger millet bran methanol extract, which attenuates lung inflammation and fibrosis probably via inhibition of PLA2 and 5-LOX enzymes activity [89].

3.6. Prebiotic activity

Finger millet seed coat represents an abundant and alternative source for the extraction of xylan and its use for prebiotic xylooligosaccharides (XOS) production. Compared to commercial XOS and dextrose, the finger millet seed coat XOS was an efficient substrate for accelerating the growth rate and cell mass of L. plantarum [90]. Several prebiotic compounds such as arabinoxylans, inulin, and XOS are isolated in the bran and seed coat of different millets[19]. It was investigated the prebiotic potency of the multi-millet functional beverage and reported that millets stimulated the growth of the gut microflora which appears to be a result of prebiotic activity [91].

3.7. Gut health

Polyphenols from foxtail millet bran and shell could remodel the gut microbiota to prevent tumor and atherosclerosis in mice, respectively [92]. A study revealed that active polyphenols were extracted from millet shells regulate the integrity of the gut barrier and the structure of the gut microbiota, ultimately inhibiting the development of atherosclerotic plaques [81]. It was suggested that BPIS might be used as a new inhibitor of glycolysis for enhancing intestineshealth benefits [93].

3.8. Body weight Management

Obesity poses a serious threat to worldwide public health [94]. Recent research on the natural bioactive compounds found in foods has associated them with effects on cell functions in obesity, including a reduction in the inflammatory response [95]. Phytochemicals may influence anti-obesity outcomes through various mechanisms, including the inhibition of digestive enzymes such as pancreatic lipase and amylase, the regulation of appetite, and the reduction of white adipose tissue formation or the enhancement of white adipose tissue browning [96]. It was stated that finger millet bran supplementation could be an effective strategy for preventing high-fat diet-induced changes and developing finger millet bran-enriched functional foods. Therefore, finger millet bran can be used as a nutraceutical ingredient for the development of functionally enriched food products for the management of obesity and associated metabolic complications [61]. A study evidenced that kodo millet supplementation alleviates high-fat diet-induced changes and hence can be incorporated as a functional ingredient for the management of obesity [97].

3.9. Other therapeutic properties

It was found that a combination of modified finger millet bran, modified kodo millet bran, and modified rice bran could be used as a nutraceutical or functional food ingredient for preventing high-fat diet-induced gut derangements and associated metabolic complications [98]. It was showed that the polysaccharides from proso millet bran had good antibacterial ability [99]. Oil extracted from foxtail millet bran is capable of attenuating ethanol-induced hepatic injury [100]. It was indicated that millet and millet polyphenols could exert neural protective effects under high-fat diet-induced oxidative stress by upregulating the expression of antioxidant enzymes and downregulating the expression of AD-related genes [101]. It was showed that millet bran protein hydrolysate possesses an anti-non-alcoholic fatty liver disease effect *in vitro* and *in vivo*, characterized by the alleviation of hepatic steatosis and the reduction of lipid accumulation in mice model [102].

4. Conclusion

Millet bran is becoming more significant because of its bioactive constituents and health benefits. Millet bran shows a greater degree of biological function compared to millet grains, especially when it comes to antioxidant content, which can aid in promoting health and preventing diseases. When properly treated, bran can serve as an important ingredient that can serve as active component in the prevention or management of various diseases such as obesity, diabetes, cardiovascular diseases, and so on. With more thorough research on millet bran, it is projected that its potential applications in the food and medical industries will expand. Additionally, this potential applicability helps to reduce agricultural waste. The current review explored the applicability of millet bran in various disease conditions. It can be therefore concluded that there are several possibilities of extending the range of applications for millet bran in pharmaceutical and food processing fields. In this review, many relevant scientific studies were gathered and reviewed to provide information on the bioactive compounds and therapeutical properties of millet bran.

Future scope of the study

Further research in the future should be oriented towards the isolation of each compound from millet bran and explored for their therapeutic properties.

Conflict of interest

The authors declare that there is no conflict of interest regarding this Review article.

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