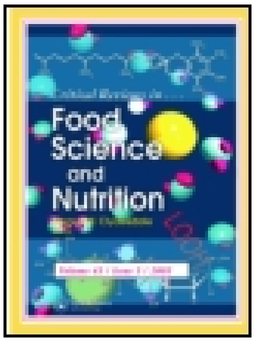

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RICE BRAN NUTRACEUTICS: A COMPREHENSIVE REVIEW

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Abstract

Agro-industry yields ample quantity of several byproducts with considerable importance. These byproducts are mostly under-utilized, often used as animal feed or rejected as waste, hence their true potential is not harnessed. The use of such superfluous resources is not only of economic significance but also a form of commercial recycling. Rice bran is an important byproduct of rice milling industry with a global potential of 29.3 million tons annually. It is gaining great attention of the researchers due to its nutrient rich composition, easy availability, low cost, high antioxidant potential and promising effects against several metabolic ailments. Bioactive components of rice bran, mainly γ-oryzanol, have been reported to possess antioxidant, anti-inflammatory, hypocholesterolemic, anti-diabetic and anti-cancer activities. Rice bran oil contain appreciable quantities of bioactive components and has attained the status of “Heart oil” due to its cardiac friendly chemical profile. Nutraceutics have successfully been extracted from rice bran using several extraction techniques such as solvent extraction, supercritical fluid extraction,

microwave assisted and ultrasonic assisted extraction. Current paper is an attempt to highlight bioactive moieties of rice bran along with their extraction technologies and health benefits.

Keywords

Rice bran, γ-oryzanol, bioactive components, hypercholesterolemia, diabetes

Introduction

Rice (*Oryzae sativa*, Family: Oryzeae) is a major cereal crop around the globe. About half of the world's population consume rice as dietary staple. It is second most grown food crop globally after wheat. Rice is grown in approximately 114 countries which produce more than 650 million tons rice annually (Sharif et al., 2014). In terms of per capita energy, human are gaining 23% energy globally from rice (IRRI, 2012).

Rice processing industry is well developed and produce a number of products along with a large quantity of byproducts. These byproducts include rice bran (5-8% of the rough rice) and polishing (2-3%). These byproducts are frequently used as animal feed in developing countries (Sharif et al., 2014). Rice bran is the outer layer of rice kernel which is mainly comprised of pericarp, aleurone, sub aleurone layer and germ. Appreciable quantities of antioxidants like γ oryzanol, tocopherols and tocotrienols has been reported in rice bran (Gong and Yao, 2001; Moldenhauer et al., 2003).

Rice bran has been known as a potential source of edible oil. Rice bran oil (RBO) is not popular worldwide but its demand is increasing due to its health benefits. It comprises 15-20% oil, depending upon variety, degree of milling and other agro-climatic factors (Lima et al., 2002). During last few decades, efforts are being made to explore the nonconventional sources for oil extraction and value addition. In this context, agro-industrial by-products are gaining special attention of food processing industry. Rice bran oil has good fatty acid profile which is in part responsible for its nutraceutical value along with other phytochemicals (γ oryzanol, tocopherols and tocotrienols). It is largely used in Japan, Taiwan, China, Thailand and Korea as a "Premium Edible Oil" (Ghosh, 2007). In Japan and some western countries, it is more commonly

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recognized as a “Heart Oil” and attained the status of “Health Food” (CAC, 2003). Rice bran and its oil can be consumed for value addition of cereals based food products to achieve multiple benefits.

Nutritional profile of rice bran

Rice bran is rich in lipids, protein, dietary fiber and other food components (Table 1). It contains significant quantity of mineral elements including phosphorus, potassium, magnesium, calcium, manganese and other trace elements (Gurpreet and Sogi, 2007).

Rice bran oil (RBO) contains significant quantities of linolenic acid (2.2%), linoleic acid (34.4%), oleic acid (38.4%) and other unsaturated fatty acids. However, saturated fatty acids such stearic acid (2.9%) and palmitic acid (21.5%) are also present. In spite of having similar fatty acid profile, RBO offers several benefits over the other oils owing to the presence of tocopherols, γ-oryzanol and tocotrienols which give oxidative stability along with health benefits (Kim and Godber, 2001; Wilson et al., 2000). It also contain 4.2% unsponifiable substances, mainly phytosterols. Studies on the bioefficacy of rice bran oil showed a direct relationship between its consumption and lower serum total cholesterol and low density lipoproteins (LDL) levels (Wilson et al., 2000; 2007; Most et al., 2005). Defatted rice bran contain 8.37% moisture, 14.27% protein, 1.8% crude fiber, 14.59% ash, 58.41% carbohydrates and 12.44% reducing sugars (Sirikul et al., 2009).

Proteins isolated from rice bran are nutritionally superior and hypoallergenic in nature ((Kennedy and Burlingame, 2003; Tsuji et al., 2001). Amino acid profile of rice bran proteins is better as these are rich in essential amino acids like lysine which is a limiting amino acid in cereal grains.

Rice bran proteins are highly digestible and can be utilized as an effective food ingredient (Wang et al., 1999). Dietary fiber is an important food component which is rich in cereal by-products including rice bran. With increasing awareness about its health perspectives, more fiber enriched food commodities are being prepared and marketed. Functional foods with added dietary fiber are in great demand nowadays. Rice bran is a good choice in this context with high dietary fiber contents varying from 20-51%. Rice bran fiber has laxative effect which improve fecal production and stool rates. Soluble fibers works like a sponge and absorbs water in the intestine, produce bulk and slows down digestion and absorption. Researchers have observed 29% less danger of coronary heart disease for each extra intake of 10g of fiber daily (Abdul-Hamid and Luan, 2000).

Though, overall composition and nutritive profile of rice bran is good however, existence of anti-nutritional compounds such as trypsin inhibitors, phytates, pepsin inhibitors, hemaglutinins, antithiamine are the main hindrance in its food applications. Lipases are also present in considerable quantity and become free during milling process, act upon triglycerides thereby increasing the free fatty acid contents and deteriorate oil quality (Lima et al., 2002).

2. Oryzanol; bioactive component of rice bran

Recently, research on phytochemistry of rice bran has demonstrated that it contain hundreds of different bioactive components. Most important of these are tocopherols, tocotrienols and oryzanols. These components have high antioxidant potential than other minor components of rice bran and alongside their health benefits as bioactive components they are also being utilized to increase storage stability of different foods. It has been observed that cholesterol lowering ability of rice bran oil is better than it is predictable from its fatty acid profile. This suggests that along with fatty acids, other constituents (mainly γ-oryzanols) present in the oil are also responsible for the hypocholesterolemic effect of rice bran oil (Moldenhauer et al., 2003).

Among agro-industrial byproducts, rice bran is an exclusively good source of bioactive components that finds applications in pharmacy, cosmetics and nutrition (Danielski et al., 2005). The unsaponifiable constituents of rice bran oil mainly comprises of γ-oryzanol, tocotrienols and tocopherols. Whereas, other compounds which are found in less concentration are carotenoids, lecithin and long chain alcohols such as 1-octacosanol, squalene & flavone tricin (Patel and Naik, 2004). The concentration of γ-oryzanol and tocols ranges from 0.9-2.9% and 0.10-0.14% respectively and are mainly dependent on environmental and genetic factors (Lloyd et al., 2000). β-sitosterol, γ-oryzanol and tocotrienol have been reported to possess hypolipidemic effect. Rice bran oryzanol have demonstrated significant antioxidant potential which protect the cells from damaging effects of VLDL (Xu et al., 2001).

The chemical constituents of γ-oryzanol includes transferulic acid esters, triterpenic alcohols and sterols (phytosterols). Previously, γ-oryzanol was considered as single component but later work on it chemistry has revealed that it is a combination of at least 10 components. The dominating constituents are β-sitosterol, cycloartenol, campesterol and 24-methylenecycloartenol (Lloyd et al., 2000). In addition to these components, caffeic acids, cis-ferulic acid esters as well as minute quantity of trans-ferulic acid esters with stigmasterol, D7-campesterol, D7-stigmasterol, sitostenol campestenol and D7-sitostenol are also found in γ-oryzanol (Akihisa et al., 2000; Fang et al., 2003). Oryzanol is named as it was first isolated from rice bran oil. The γ-oryzanol has an effect similar to that of vitamin E in growth promotion, facilitating blood circulation and hormonal secretions. The most available natural source of γ-oryzanol is rice bran. It comprises about 9.8 g/kg oryzanol (Fang et al., 2003). The γ-oryzanol is 13-20 times more in concentration than that of total tocotrienols and tocopherols in rice bran (Bergman and Xu, 2003). It has been reported that unsaponifiable fraction of RBO is about 20% oryzanol with high melting point (137.5-138.5°C) resulting in high thermal stability.

3. Antioxidant potential of rice bran extracts

Antioxidants are the entities that protects the tissues from degenerative processes and diseases caused by the free radicals in the body. Rice bran contains considerable amount of various phytochemicals with antioxidant potential in addition to other health benefits. Amongst these, γ-oryzanol and vitamin E (four tocopherols and four tocotrienols) fractions has gained special attention of researchers owing their antioxidant potential (Akihisa et al., 2000). Many clinical trials have reported that γ-oryzanol is an effective anti-diabetic, anti-cancer, anti-inflammatory and hypolipidemic agent (Xu et al., 2001). In view of these health benefits, rice bran oil and isolated antioxidant components have a potential use as food additives to prolong storage stability along with providing protection against many metabolic ailments (Nanua et al., 2000; Kim and Godber, 2001).

Clinical studies have depicted the health promoting properties of oryzanol like reduction of total plasma cholesterol, increase in HDL levels, reduction in LDL, improvement of blood lipid profile and inhibition of platelet aggregation (Cicero and Gaddi, 2001). It also exhibits significant *in vitro* antioxidant potential as it lowers down the cholesterol oxidation accelerated

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by 2,2-azobis(2-methylpropionamidine), pyrogallol autoxidation and lipid peroxidation induced in porcine retinal homogenate by ferric ion (Juliano et al., 2005).

Rice bran extracts obtained by using different solvents showed significant antioxidant activities. Enzymatic extracts of rice bran have also exhibited good antioxidant potential. A number of mechanisms has been reported in this regard (Xu et al., 2001). It has been inferred that the antioxidant properties of γ-oryzanol is mainly due to its chemical structure that contains ferulic acid which exhibit radical-scavenging activity (Srinivasan et al., 2007). Similarly, tocols also exhibit strong antioxidant activity. This activity is attributed to their potential to donate phenolic hydrogens to different redicals. Numerous research studies have concluded that tocotrienols are better antioxidant moieties than tocopherols. Additionally, tocotrienols also showed greater ability to address free radical mediated metabolic dysfunctions. However, the concentration of γ-oryzanol is about 13 times greater than tocols in the enzymatic extract of rice bran (Qureshi et al., 2002).

Chotimarkorn et al., (2008) investigated the antioxidant prospective of rice bran extracts using various reputed *in vitro* systems, such as total reducing power, ferrous ion-chelating activity, inhibition of lipid peroxidation and 2, 20-diphenyl-1-picrylhdrazyl free radical-scavenging (DPPH). They also determined the flavonoid and total phenolic contents, tocopherol, tocotrienol and γ-oryzanol isomer contents of these extract by high performance liquid chromatography (HPLC) and colorimetric assay. The methanolic extracts of rice bran showed best results with reducing power (EC_{50} 0.10-0.53 mg/ml), DPPH free radical-scavenging (EC_{50} 0.38-0.74 mg/mL), inhibition of lipid peroxidation (EC_{50} 0.14-0.57 mg/mL) and ferrous ion-chelating activity (EC_{50} 0.11-- 0.55 mg/ml). The concentration of total phenolic, γ-oryzanol, flavonoid, tocotrienol and tocopherol were reported as 2.2-3.2, 0.56-1.08, 0.03-0.10, 0.22-0.46 and 0.35-0.77 and mg/g rice bran, respectively.

In a subsequent study, Tabaraki and Nateghi (2011) applied ultrasonic technology for the extraction of polyphenols and antioxidants from rice bran. They reported that total phenolic content (TPC) of ultrasonic assisted extracts of rice bran ranged from 2.37 to 6.35 mg gallic acid equivalent/g on dry weight basis. Antioxidant potential of rice bran extracts was determined by scavenging activity of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical and the ferric reducing antioxidant power (FRAP) assay. DPPH and FRAP values were 31.74 and 57.23 µmol Fe^{2+}/g respectively on dry weight basis.

4. Extraction of active ingredients from rice bran

4.1. Conventional solvent extraction

As γ-oryzanol is readily soluble in conventional organic solvents, hexane has classically been employed in its extraction. However, the components of γ-oryzanol have an alcoholic group in the ferulate part, which makes the molecule highly polar. Some polar solvents like ethyl acetate and isopropanol and nonpolar solvents like heptane and hexane may also solubilize these components. The extraction rate of γ-oryzanol can be significantly effected by the polarity of solvent.

Different solvents have been utilized in earlier literature for the extraction of γ-oryzanol and other bioactive components from rice bran. Imsanguan et al., (2008) extracted bioactive components of rice bran by using different solvents as well as modified methods. Extraction was carried out using 100 mL hexane at varying temperature (32 °C to 60 °C) and a rotating speed of

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200 rpm, for 24 hours. Moreover, rice bran extract was also obtained using vacuum soxhlet apparatus with 300 mL of hexane at variable pressures (500-550 mmHg) and temperatures (65-70 °C) for 24 h. The extracts were also obtained by using ethanol as solvent and rest of the conditions remained the same. Ethanol exhibited better extraction yield as compared to hexane with an extraction yield of 9414.02 mg/kg on dry basis.

Afterwards, Heinemann et al., (2008) reported a rapid extraction technique for γ-oryzanol and tocols. In this experiment, 3 mL hexane having 0.02% BHT was used for extraction at 60 °C for 20 min. Centrifugation of the mixture was done at 3000 g for 10 min and the supernatant was collected. The separated residues were twice subjected to hexane extraction followed by the evaporation of hexane. The resultant extracts showed high extraction rate of γ-oryzanol and tocols. Azrina et al. (2008) determined the total lipid and oryzanol content in rice bran. Four different isomers of γ-oryzanol were successfully obtained using conventional solvent extraction followed by quantification. These four fractions were campestryl ferulate, 24-methylene cycloartanyl ferulate, cycloartenyl ferulate and mixtures of cycloartanyl ferulate and β--sitosteryl ferulate. The oryzanol content of different rice brans varied from 23.7 to 43.0 mg/g. The oryzanol content may depend on different factors such as plant processing methods, solvent to bran ratio, rice varieties, nature of extracting solvent as well as temperature of extracting solvent.

4.2. Supercritical Fluid Extraction

Recovery of biological components from plant materials like rice bran using solvents is the conventional method of extraction. This practice mostly uses flammable and often highly toxic solvents like isopropanol, hexane and petroleum ether. The use of such solvents is not environment friendly as there are problems associated with their disposal. Another concern is the presence of toxic residues of solvent in final product. These problems triggered scientists and technologists to find out nonhazardous and environment friendly alternative extraction techniques.

A prominent technique for the purpose is supercritical fluid extraction (SFE). This is a promising technique to address an increasing demand for green, natural and organic fractions from food and other biological materials. The use of SFE technique is environmentally safe and advantageous as compared to conventional methods like enzyme and solvent extraction for the separation and purification of bioactive moieties (Herrero et al., 2010). SFE makes use of supercritical fluid as solvent. Every supercritical fluid is distinguished by a specific critical point which depends upon critical pressure and critical temperature of that gas/liquid. Irrespective to the pressure applied, a gas cannot be converted to liquid above its critical temperature but may attain a state close to liquid. Above its critical pressure and temperature, a substance is said to be a supercritical fluid. Viscosity, thermal conductivity, density, heat capacity and diffusivity are the important properties of a supercritical fluid. Low viscosity provide frictionless flow and penetration into the material while high densities provide a greater dissolving power. The ability of supercritical fluids to penetrate and extract desirable moieties from food materials are significantly affected by the pressure and temperature above the critical points (Lang and Wai, 2001).

The most extensively used supercritical solvent in food industry is supercritical carbon dioxide (Rozzi and Singh, 2002). In addition to the non-flammable and non-toxic nature of carbon dioxide, supercritical CO_2 also provide advantage of flexibility in its extraction power by varying operating conditions like temperature, pressure and flow rate. This flexibility offers fractionation and selective extraction abilities to the process. CO_2 is converted to its supercritical state above 7.38 MPa and 31.1 °C which makes it best solvent for the recovery of heat-sensitive substances from food matrices. Moreover, it also offers better extraction of fat soluble components with a high recovery rates (Dunford et al., 2003). Previously, many studies have been conducted to use supercritical fluid extraction technique to recover natural antioxidant components from agro-industrial waste products using carbon dioxide as supercritical solvent (Braga et al., 2008).

Soares el al. (2016) compared the extracted rice bran oil through SFE and liquefied petroleum gas (LPG). Effect of temperature (40-80 ^{o}C) and pressure (150-250 bar) on extraction yield was evaluated for SFE. Results showed maximum oil yield (12.68%) through supercritical fluid extraction. Moreover, highest antioxidant activity was exhibited by SFE extract (71.67%). Chen et al. (2008) conducted a study for the extraction of oryzanol from rice bran by employing supercritical fluid extraction (SFE) technique. They investigated the effect of process parameters (temperature and pressure) on extraction efficiency of rice bran oil from rice bran samples using CO_2 as supercritical fluid trailed by the separation and concentration of γ-oryzanol by using column partition purification. SFE at 313K temperature and 350 bar pressure recovered 17.5% oil with 84.9% extraction efficiency, consuming 1.2 Kg of CO_2 over 4 hr. Temperatures ranging from 313-333 K and pressures ranging from 250-350 bar were reported to be best for the extraction of rice bran oil and γ-oryzanol based on response surface methodology. It was observed that the effect of pressure on γ-oryzanol concentration was more pronounced than the effect of temperature.

Likewise, Imsanguan et al. (2008) investigated the effect of different operating mode (continuous and batch + continuous), solvent, pressure and temperature on γ-oryzanol and α-tocopherol

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extraction from rice bran and also compared the extraction efficiency of different extraction techniques including solvent extraction, supercritical carbon dioxide extraction and soxhlet extraction. Solvent extraction of rice bran was carried out using ethanol and hexane at 55-60 MPa and 32 ^{o}C. Results showed that ethanol at 60 ^{o}C was good for the extraction of γ-oryzanol while α-tocopherol could not extracted by any of the solvents. Finally, supercritical fluid extraction was performed using CO_2 as solvent at different ranges of pressures and temperatures (38 and 48 MPa at 45-65 ^{o}C), and at a flow rate of 0.45 mL/min. The results indicated that continuous mode at 65 ^{o}C, 48MPa was best for the extraction of γ-oryzanol while for the extraction of α-tocopherol, batch plus continuous mode at 55 ^{o}C, 48MPa provided most suitable conditions for extraction. Thus, supercritical fluid extraction was regarded as best technique for the extraction of both γ-oryzanol and α-tocopherol with higher extraction rate and yields.

In another investigation, Xu and Godber (2000) investigated the effect of process parameters on the extraction efficiency of γ-oryzanol and lipids from rice bran with SFE and organic solvents. Among the solvents, the highest yield (1.68 mg per gram of rice bran) of γ-oryzanol was obtained with a mixture of 50% isopropanol and 50% hexane (v/v) at 60°C for 45-60 min extraction time. SFE yielded four time more γ-oryzanol (5.39 mg/g of rice bran) than the peak yield of solvent extraction under a pressure of 680 atm (68901 kPa), temperature of 50°C and time of 25 min.

Later, Jesus et al. (2010) conducted studies to compare supercritical fluid extraction with soxhlet technique for the extraction efficiency of γ-oryzanol from rice bran. The effect of different process variables on supercritical fluid extraction was evaluated by comparing γ-oryzanol recovery rate, γ-oryzanol content, global yield and fatty acid composition of the recovered fraction. Overall extraction curve was also studied by mathematical modeling. Highest γ-oryzanol recovery rate (31.3%, w/w), maximum global yield (39±1%, w/w), relatively high γ-oryzanol content (3.2%, w/w) and presence of considerable amount of poly and mono-unsaturated fatty acids was noted at 30 MPa pressure and 303 K temperature.

4.3. Microwave assisted extraction

Microwave assisted extraction makes use of electromagnetic radiations in the range of 0.3 to 300 GHz. These waves penetrate the material and produce heat upon interaction with polar molecules like water present in the material. Resultantly, microwaves can heat the whole material and offer fast delivery of energy to the total mass of solid plant matrix and liquid solvent. Cell disruption is promoted by internal heating process thereby increasing the yield of bioactive components (Kaufmann *el al*., 2001b).

Zigoneanu et al. (2008) studied the antioxidant compounds in rice bran oil extracted through microwave assisted extraction and reported good antioxidant potential of resultant RBO as shown by DPPH assay (59.85 µmol Trolox Equivalent per gram). They observed no significant differences in oil yield and total vitamin E content of rice bran oil extracted through conventional methods and microwave assisted extraction. Terigar et al. (2011) compared microwave assisted extraction of rice bran oil with conventional extraction methods. They delineated that microwave extraction give better oil extraction and thus can be employed commercially for better recovery of good quality oil.

Pretreatment with microwaves prior to extraction with conventional and novel techniques improves the extractability of desired nutraceutics. Wataniyakul et al. (2012) observed improved recovery of phenolic compounds by pretreating the defatted rice bran with microwaves before subcritical water extraction. Less extraction time was required for pretreated rice bran. Microwave pretreatment resulted in 55% more total phenolic extraction as compared to untreated one. The antioxidant activity was also greater for pretreated samples. Likewise, Duvernay et al. (2005) conducted a trial to extract antioxidants from rice bran using microwave assisted extraction. The results concluded that microwave assisted extraction is one of the superior extraction modes for the extraction of tocopherols and tocotrienols from rice bran.

4.4. Ultrasonic assisted extraction

The extraction of biologically active moieties from plant material using ultrasounds (20--100 KHZ) has been emerged as another promising technique (Chemat et al., 2008). This technique involves passing sound waves (>20 kHz) from a solvent containing the raw material. The sound waves travel from extraction medium (solvent) and produce alternate compression and expansion cycles. A negative pressure is produced during expansion due to bubble formation. Bubbles form, grow in size and eventually collapse. This results in high speed jets of liquid solvent which has a strong impact when comes in contact with solid material (Luque-Garcia and Luque de Castro, 2004). Major advantages associated with this extraction mode are high extraction yield, shorter time, high reproducibility, less solvent utilization, low temperature and reduced energy input (Chemat et al., 2008). The mechanical properties of ultrasound waves bring about greater solvent penetration in the cellular materials thereby improving mass transfer. These waves also disrupt biological membranes and cell walls to facilitate the release of cellular contents therefor increasing extraction yields (Wang and Curtis, 2006).

While investigating the effect of ultrasound treatment on the yield of rice bran oil, Khoei and Chekin (2016) reported that yield of rice bran oil affected significantly with ultrasound pre-treatment. Their results showed that the yield of RBO with ultrasound assisted aqueous extraction was close to the yield of oil with soxhlet extraction using hexane as solvent. Furthermore, RBO extracted through ultrasonic treatment had lower coloring pigments and free fatty acids as compared to soxhlet extracted oil. Earlier, Tabaraki and Nateghi (2011) studied the extraction of polyphenols and antioxidants from rice bran using ultrasound assisted extraction and ethanol as the solvent. Their results showed that ultrasonic extraction is a promising technique for the extraction of bioactive components from rice bran with high antioxidant potential and better yield. Moreover, they concluded that the extraction of polyphenols from rice bran using ultrasonication is a green and environment friendly process to obtain antioxidant-rich fractions.

5. Health claims of rice bran and its bioactive components

Changing dietary patterns, urge for refined foods and poor socioeconomic conditions have led mankind to a dilemma of malnutrition and diet related disorders. Of the various diseases being faced, cardiovascular diseases (CVDs), cancer, arthritis, diabetes and hypercholesterolemia are notable cause of illness and mortality in both developing and developed world. Novel nutritional approaches have successfully been employed as therapeutic interventions against various ailments. Scientific evidences have supported dietary intervention as an effective tool for health promotion (Shahidi, 2000). In this context, rice bran and its bioactive components have been reported to be effective against aforementioned ailments.

5.1. Hypolipidemic aspects

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Cardiovascular diseases are widespread cause of morbidity and mortality around the globe. The risk factors for CVDs are elevated level of plasma cholesterol, decreased level of high density lipoprotein (HDL) and increased low-density lipoprotein (LDL). Therefore, lowering of blood cholesterol level is crucial for the prevention and treatment of CVDs (Roberts et al. 2007). The transportation of plasma cholesterol of all higher animals is carried out by lipoproteins that need a number of molecules with different sizes, HDL, LDL, IDL and VLDL. Increased concentration of lipoproteins (hyperlipoptoteinaemia) is genetic ailment related with the elevated level of plasma total cholesterol and LDL, suggesting a greater risk of cardiac disorders. Diet is the foremost way to treat hyperlipoproteinaemia. In this context, rice bran oil and its constituents have demonstrated the capability to restore the normal blood lipids profile in animal and human studies, decreasing total triglyceride, LDL and plasma cholesterol whereas, elevating the HDL cholesterol level. Important therapeutic effects of rice bran oil and γ-oryzanol includes antioxidant action, inhibition of gastric acid secretion, modulation of pituitary excretions and inhibiting the aggregation of platelets (Cicero and Gaddi, 2001).

Risk of CVDs is high with the onset of oxidative stress (Marini, 2003). Oxidized-LDL is formed by the oxidation of the LDL in subendothelial space of arteries and is extremely atherogenic. Cell have several defense systems such as antioxidant enzymes and small antioxidant molecules to protect them against reactive species (Hori et al., 2008). To address hyperlipoproteinaemia and atherosclerosis, the first and most effective choice is to modulate diet. The growth of atherosclerotic lesions is considerably suppressed if the diet contain a mixture of cholesterol lowering phytochemicals and antioxidants. In the last two decades, rice bran has gained special attention by the researchers for its anti-atherogenic, cholesterol lowering and free radical scavenging potential (Ha et al., 2006; Jariwalla, 2001; Parrado et al., 2003).

Experiments have revealed that γ-oryzanol is the main component in rice bran with anti-atherogenic potential. This naturally occurring γ-oryzanol along with vitamin E have pronounced free radical scavenging activity which is helpful to shield the cells from oxidative stress (Kennedy and Burlingame, 2003). In this context, Tsuji et al., (2003) conducted rat modeling to study serum cholesterol levels of rats and the effect of hypocholesterolaemic diet containing rice bran oil with varying levels of γ-oryzanol on serum cholesterol. The control group was given with lard as dietary lipid source. They observed that total serum cholesterol level in rat fed on rice bran oil reduced significantly as compared to the control group.

Many studies has been conducted to evaluate the comparative effect of rice bran oil, γ-oryzanol and its components on plasma lipid profile. Wilson et al. (2007), for example evaluated cholesterol lowering potential of trasnferulic acid, γ-oryzanol and rice bran oil in an experiment. The control group (I) was fed on high cholesterol diet (HCD), group II was given HCD with 10% rice bran oil, group III was given 0.5% transferulic acid plus HCD while the diet of group IV comprised of HCD with 0.5% γ-oryzanol. Serum biochemistry after 10 weeks exhibited that LDL+VLDL and total plasma cholesterol levels were considerably lower in test groups fed on diet with γ-oryzanol (77% and 70% respectively), diet with rice bran oil (70% and 64%) and diet containing trans-ferulic acid (24% and 22%) as compared to control group. The groups fed on diet containing γ-oryzanol and rice bran oil showed significant reducing trends for lipid hydroperoxides and plasma triglycerides levels. The study revealed that γ-oryzanol possess better potential to decrease LDL and VLDL levels and to maintain normal blood lipid profile by raising HDL cholesterol than transferulic acid.

Earlier, Ausman et al. (2000) analyzed various unsaturated vegetable oils (rice bran, canola and corn) for their effect on serum lipoprotein levels. A diet containing rice bran oil reduced LDL cholesterol (30%) and serum total cholesterol (25%) levels. The cholesterol lowering abilities of the rice bran oil diet was greater than those anticipated from the constituent fatty acids of rice bran oil. Later, Accinni et al., (2006) evaluated the effect of γ-oryzanol, tocols, niacin and omega-3 polyunsaturated fatty acids on oxidative stability, lipid profile and inflammatory response in volunteers with abnormal blood lipid levels. In a four month trial, all groups with different dietary supplements exhibited a shift from abnormal to normal blood profile and the best results were seen in the group containing γ-oryzanol in diet.

A considerable cholesterol lowering effect of enzymatically recovered rice bran extracts has also been reported by Revilla et al. (2009). Two different diets were given to experimental rats to induce hypercholesterolemia. The addition of 0.33% enzymatic extract of rice bran in diets of both experimental groups affected total cholesterol and HDL significantly. An increase in HDL and decrease in cholesterol levels was observed. The cholesterol lowering potential of enzymatic extract of rice bran is primarily due to its constituent phytochemicals, which are mainly sterols in nature. This effect is due to the transformation of side chain structures between cholesterol and phytosterols. Due to their proven potential in lowering cholesterol, plant sterol have successfully been exploited in different food products as additive to aid in decreasing blood LDL cholesterol levels (Scoggan et al., 2008).

The enzymatic extract of rice bran is rich in γ-oryzanol which is mainly responsible for its therapeutic effects. Numerous mechanism have been delineated for hypocholesterolemic effect of γ-oryzanol including hindrance in intestinal absorbance of cholesterol, increase in bile flow and higher fecal excretion of cholesterol (Cicero and Gaddi, 2001). All these effects are mainly attributed to the phytosterols which are part of γ-oryzanol complex. Another target point of γ-oryzanol in lowering LDL-cholesterol is decreased formation of apoprotien B. Apoprotien B is the major constituent of low density lipoprotein and decreased levels of it limits formation of LDL and ultimately results in lower serum LDL levels (Sasaki et al., 1990). Moreover, increase in the HDL-cholesterol level is also positively correlated with decreased plasma total cholesterol. The recovery of extra lipoproteins and cholesterol from the peripheral cells by the help of HDL also alleviate the risk factors for the onset of atherosclerosis. Enzymatic extracts of Rice bran have been reported to increases HDL-cholesterol levels and may play an important role in prevention of cardiovascular disorders by decreasing the risk of atherosclerosis. There are number of clinical trials that provide a clear evidence that the HDL-cholesterol levels of hypercholesterolemic human subjects can be significantly improved by consuming RBO rich diet (Berger et al., 2005).

Wilson et al. (2007) proposed that rice bran γ-oryzanol show better results in reducing LDL, VLDL cholesterol levels and increasing HDL cholesterol compared to that of ferulic acid alone, which may be, to a great extent, due to a rise in excretion of cholesterol and its metabolites in feaces. Nevertheless, a better antioxidant potential may be exhibited by ferulic acid due to its ability to uphold vitamin E levels of serum in comparison to oryzanol and RBO. So, both ferulic acid and γ-oryzanol may exert comparable anti-atherogenic potential, but through different mechanisms. Also, it has been concluded that triterpene alcohols also have cholesterol lowering activity which are part of oryzanol.

5.2. Anti-diabetic potential

Considering the major impact of increasing worldwide occurrence of diabetes due to the absence of effective and affordable interventions, a large number of medicines are available. Nevertheless, there are numerous side effect associated with these anti-diabetic synthetic medicines such as diarrhea, liver problems and lactic acidosis. Therefore, currently the major focus of researchers and scientists is to search for more affordable remedies of natural origin that retain the therapeutic efficacy and are devoid of side effects (Inzucchi, 2002).

Besides insulin injection, dietary interventions aimed at reducing consumption of processed and refined carbohydrate and improving intake of dietary fibers have been established to reduce postprandial glycosuria. These practices have also been proven good to ameliorate glucose level by increasing the sensitivity of cells to insulin as well as reducing the rate of absorption. Nevertheless, these measures are still unable to regulate the variation in blood sugar levels to a required extent. Nutraceuticals have been extensively studied in order to explore their possible role in this regard. Rice bran and its components have showed promising potential to mitigate hyperglycemia and associated abnormalities (Kahn *el at.*, 2001).

Furthermore, previous studies investigating the effects of oryzanol supplementation, as a constituent of experimental diets on the levels of serum glucose in diabetic rats reported a lower concentration of fasting glucose. Subsequent studies indicated that adiponectin secretion might be regulated by the use of hydroxycinnamic acid derivatives such as oryzanol, which regulate the process by inhibiting the activation of NF-kB. Since there is a direct relationship between insulin sensitivity and adiponectin, it was proposed that oryzanol may play an effective role against type 2 diabetes (Ohara et al., 2009). Son *et al* (2011) illustrated that oryzanol could regulate secretion of insulin as well as glucose, normalize liver enzymes activities and thus can lower down the risks of hyperglycemia induced with high fat diet. Later, Somsuvra et al. (2012) investigated hypoglycemic potential of oryzanol. Streptozotocin induced diabetic rats having elevated serum glucose levels (340-400 mg/dL) experienced a decline in serum glucose within 2-4 hr at a dose of 50 and 100 mg/kg oryzanol. A single dose of 100 mg/kg of body weight resulted in 13.09% decline in serum glucose as compared to the 12.38% decrease by administrating 50 mg/kg oryzanol.

Rice bran as a whole can be utilized as dietary supplement to control both types of diabetes mellitus in humans and other primates**.** Qureshi et al. (2002) conducted studies to investigate the effect of stabilized rice bran on insulin dependent diabetes (Type I) and non- insulin dependent diabetes (Type II) in human subjects. Subjects with both type of diabetes mellitus were fed on stabilized rice bran and its selective components for 60 days to check the effect on blood profile including serum lipid, hemoglobin and carbohydrate. Subjects with type I diabetes were fed on water extract of rice bran, AHA (American Heart Association) Step 1 diet plus stabilized rice bran and fiber concentrates of rice bran. Fasting serum glucose levels showed a considerable reduction by using stabilized rice bran (9%), water extract (29%) and fiber concentrates of rice bran (19%). Similarly, Subjects with type II diabetes mellitus were fed on fiber concentrates and water extract of rice bran plus AHA Step 1 diet. A reduction in fasting glucose levels and glycosylated hemoglobin (33 and 22% respectively) was observed. Water extract of rice bran increased serum insulin levels by 4% in both type of diabetes. This increase in serum insulin levels coupled with a reduction in glycosylated hemoglobin suggests that intake of rice bran water extract can check the serum glucose levels in diabetics. Kozuka et al. (2012) suggested that brown rice, rich in γ-oryzanol, improves glucose metabolism in mice fed on high fat diet. Serum glucose levels of mice were significantly lower (132±3 mg/dL) in the brown rice group against the control high fat-fed group (156±4 mg/dL).

5.3. Anti-cancer potential

Cancer is one of the leading cause of morbidity and mortality around the globe. Only 5-10% of all the cancers are due to genetic factors, rest of the 90-95% are directly or indirectly linked with lifestyle and dietary habits (Anand et al., 2008). If properly practiced, dietary interventions can help to cure about 30% of human cancers (Willett, 2002). Anticancer drug therapies are associated with a number of risk factors. So, there is a “scientific and economic greed” for the identification and use of natural chemopreventive components from different sources having no safety issues as with synthetic drugs in practice for the same purpose.

Active components from rice bran has effectively been utilized against certain oncogenic events in a number of studies. Revilla et al. (2013) investigated the anticancer potential of enzymatic extract of rice bran (EEBR) against viability and propagation of leukemic cell line and normal lymphocytes. They observed a significant decrease in cell proliferation in dose dependent manner by using 5-10 mg/mL EERB. This study explained the possible mechanism of active components from rice bran to attenuate cell proliferation acclaiming the free radical scavenging activity for this effect. Tumor cells generate reactive oxygen species (ROS) which help them to diffuse through normal tissues by damaging their integrity. So there is a strong link between

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antioxidant potential and cell proliferation. γ-oryzanol possess high antioxidant activity so it would be helpful to deal with ROS and in turn limit cell proliferation. Kong et al., (2009) reported the growth inhibitory effect of rice bran polyphenols, mainly oryzanol and its derivatives. They observed that cycloartenyl ferulate (CF), a major component of γ-oryzanol, exhibited promising growth inhibition on human colorectal adenocarcinoma SW480. It was further noted that the health benefits of whole grains and bran portion, like rice bran, is not just due to their fiber content but also due to other bioactive components. These bioactive moieties act as chemopreventive agent on target cells to suppress their growth directly or indirectly.

The antitumor activity of bran from different rice verities differ considerably as the chemical profile differ across the rice verities. Forster et al. (2013) analyzed seven varieties of rice bran for their growth inhibition potential against human colorectal cancer cells and reported 0 to 99% inhibition depending upon rice bran variety. They found a positive correlation of γ--tocotrienol and total phenolics with the reduction of colorectal cancer cells. Nam et al. (2005) investigated tumor suppression activities of bran from different pigmented and non-pigmented rice varieties. They reported that 70% ethanolic extract of bran from pigmented rice inhibited phorbolester-induced tumor promotion better as compared to bran from non-pigmented variety.

Conclusion

Rice bran is a rich source of basic nutrients as well as several components with considerable bioactivity and associated health benefits. Dietary fiber, essential fatty acids, γ-oryzanol, tocopherols and tocotrienols are some important nutrients from rice bran with proven health benefits on. However, the true potential of rice bran has not been utilized. There is a dire need to use rice bran and its components in different diet based approaches to mitigate lifestyle related disorders. Research studies on functional foods and nutraceutics must include rice bran as a major source of bioactive components for the developments of designer foods.

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Table 1. Basic composition of rice bran

Components	Quantity (%)
Carbohydrates	34-62
Lipids	15-20
Protein	11-15
Crude fiber	7-11
Ash	7-10

(Cicero and Gaddi, 2001)

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