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Phytochemical and Biological Activity of Rice Bran: A Review

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Abstract: ***Rice is the most commonly consumed food by human beings all over the world. The various countries easily cultivate it. Rice is an annual plant. It grows in an area with a rich supply of water. The height of rice bran depends on the depth of water. Approximately 13,500 years ago, Oryza sativa was the first rice plant cultivated in the Yangtze River basin. Rice bran is a milling product of rice. Various studies have shown that rice bran contains a range of phytochemical constituents. This constituent consists of vitamin E, thiamine, Niacin, and minerals, Tocotrienol, oryzanol, tocopherol, gallic acid, vanillic acid, etc and nutritional components like carbohydrates, protein, fat and dietary fiber, vitamins, and minerals, etc. rice valuable bran for health and contain antioxidant property due to presence of tocopherol, tocotrinol and gama-oryzanols. Traditionally, rice bran has been used as a treatment for various diseases, including diabetes, cancer, liver disease, and heart disease. It is also used as a skincare product. Due to the presence of tocopherol, Tocotrienol, and gama-oryzanols rice bran is used for the treatment of various diseases or disorders like cancer, hypertension, lowering serum cholesterol, skin-related problems, insulin sensitivity, etc. during various studies shown by multiple scientists that rice bran has a rich source of a nutritional constituent, medicinal value as well as neutraceutical value. Various food industries use rice bran as a nutraceutical ingredient. Rice bran is a rich source of gamma-oryzanol. Hence, it is used to improve disease conditions. Several studies have demonstrated the biological effects of rice bran in improving hypertension, diabetes, and hypercholesterolemia, while also lowering cholesterol levels and reducing the risk of various diseases, including cancer and skin problems.***

Keyword: ***Rice bran, Oryza Sativa, Vitamins, Minerals, Gama-Oryzanols, Tocotrienol.***

I. INTRODUCTION

Rice is the most important crop and food in the world because 20% of dietary energy is obtained from rice [1]. Rice is a plant that grows in both water and on land, making it an amphibious plant. Rice belongs to the family Poaceae. It is a monocotyledon plant. Rice is the most commonly consumed cereal grain by the human population (50%) (Liu1). In Africa and Asia, it is the third highest agricultural plant after maise and sugarcane [1]. Rice produces the maximum energy required by the body for various uses of human beings. The traditional method for cultivating rice plants involves first developing them in a nursery.

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After one month, the nursery was shown on the irrigated land. High irrigation planting reduces the growth of weeds and pest plants. Various methods are required for pest and weed control, including fertilising the soil during the growth period. Rice cultivation is prevalent in regions with high rainfall, most commonly in Asia and Africa. Rice plant height is 1-2m (3-6 ft.). The height of the plant depends on the soil variety and soil fertility. It bears long leaves, i.e. 50-100 cm (20-40 inches long), 2-2.5 cm (3/4-1 inch) broad. Rice flower is tiny and pollinated by the wind. Flowers are produced in branched, arching, and pendulous inflorescences 30-45 cm long. Seed lengths are 5-12mm and 2-3mm thick. Production of rice all over the country is about 25% of all cereal production. Rice bran is a brownish portion of rice. It is collected during the dehusking and milling of paddy rice. 20% of rice seeds constitute the hull. Rice contains white rice kernels. Rice kernel is made up of starch and covered with bran, inside a rigid siliceous hull. After removing the rice husk, the bran layer comes into contact with air. When bran comes in contact with air, it produces off-flavour in the presence of endogenous lipase. Further milling of bran produces white rice [2]. The percentage and composition of rice bran depend on rice variety, degree of milling, type of milling, etc. Rice bran has a sweet taste, a light colour, a nutty flavour, and is slightly oily [2]. It contains fibre, 10% oil, 20% moisture, 13 % protein, 16% ash, and 18%. It is also a rich source of vitamin E, thiamine, Niacin, and minerals [2]. Rice bran is a rich source of nutritional compounds like tocotrienol, oryzanol, and tocopherol. The protein in rice bran contains lysine, which is why it is used in food recipes. Rice bran consists of 9% of the total rice weight and 65% of the nutrients of the whole rice grain. Rice bran oil is extracted from rice bran. This is produced and consumed by Asian countries. Medicinally, it is considered a healthy oil due to its antioxidant properties, anti-inflammatory activity, and other medicinal benefits. Hence, it is used for its antidiabetic, antihypertensive, anti-obesity, and anti-carcinogenic properties. The main active ingredient responsible for medicinal value is gamma-oryzanol, ferulic acid esters of cholesterol. In 2020, 756 million metric tons of rice were produced. India and China account for 52% of the world's total production. The other major rice-producing countries are Bangladesh, Indonesia, and Vietnam. They produce 72% of the total rice. A comprehensive study reveals that 8-26% of the total rice produced by developing countries is lost each year due to poor harvesting techniques, inadequate knowledge, and other factors.3].

Fig. 1: Bran of Rice

II. BOTANICAL CLASSIFICATION

Taxonomy

Kingdom:- Plantae
Subkingdom:-Tracheobionta
Superdivision :- Seed plant(spermatophyta)
Division: Flowering plant (magnoliophyta)
Class: - Liliopsida Monocotyledons
Subclass :- Commelinidae
Order :- Cyperales
Family :- Poaceae
Genus :- Oryza L.
Species :- Oryza sativa L.

III. BOTANICAL DESCRIPTION

Rice is an annual plant belonging to the family Poaceae. There are various varieties available, but only two species, i.e., Oryza sativa and Oryza glaberrima, are commercially available. Oryza sativa is found worldwide; it is most commonly cultivated by humans, while Oryza glaberrima is more commonly found in West Africa. Rice is a self-pollinated, semi-aquatic plant. It consists of arenchymatic tissue. Arenchymatic tissue helps in the movement of oxygen downward, from the areal part (leaf) to root. The height of the plant depends on the depth of water, which ranges from 1m to 5m (in deep water).

Root: Rice consists of fibrous roots. Initially, Rice produces seminal roots. Seminal roots are temporary. The primary root is an adventitious root that is made from the column node.

Shoot:-Rice shoots are known as Colum. It is hollow. It consists of nodes and internodes. Leaf and buds develop from nodes. Buds develop into shoots and tillers/plants. Tillering is the vegetative phase of the plant. During the reproductive phase, some tillers die due to a shortage of nutrients.

A leaf develops from a node. Leave consists of the following parts:

***Leaf Sheath*:** The leaf sheath develops from the column node. It encloses the column and is part of the leaves.

Leaf blade- it originates from the node and extends to the upper part of the leaf. The leaf sheath helps in joining the leaf blade and the node.

Auricle: It is a hairy outgrowth. It is found on the base of the leaf blade.

***Ligules*:** It is situated above the auricles. It is a thin and paper-like structure. Flag leaf- it is the last leaf present just below the panicle. It is shorter than other leaves and is erect at a certain angle.

Panicle: Panicle originates from the flag leaf. The flower of the rice plant is attached to the terminal shoot. It is known as a panicle. At maturity, the flower dropped from the terminal shoot. The panicle consists of spikelets.

Spikelets: Flower units of rice plants are known as spikelets. It consists of a flower, a lemman, and a palea.

***Lemma*:** It is a complex and branched structure with filiform outgrowths known as awns.

***Palea*:** It is thinner than the lemma.

***Flower*:** it consists of a bilobed anther, six stamens, one pistil, a pair of stigmas, and a single ovary.

***Grain*:** ripe ovary converted into a rice grain. Lemma and palea remain attached to the rice grain. During milling, lemma and palea are removed with the hull. Rice seeds consist of an embryo and endosperm. The embryo consists of a radicle and a plumule. On sowing, plumules develop into the shoot and radicles grow into the root.

Cultivation: Oryza sativa, the first rice plant, was domestically cultivated in the Yangtze River basin approximately 13,500 years ago. A wide variety of rice is now grown in different geographical locations. Rice is the most important crop as well as food all over the word [4].

Fig. 2: Plant of Rice

IV. GEOGRAPHICAL SOURCE

The most common rice-producing countries are Asia, Africa, and America. Rice is the second most consumed grain in the world, particularly in Asian countries such as China, India, Bangladesh, Indonesia, and Vietnam. It is a primary food for 40% of the world's population [5]. It is found in India in states such as Tamil Nadu, Karnataka, West Bengal, Andhra Pradesh, and Assam. It is a typical food in West Bengal, Bihar, and Uttar Pradesh, among others.

Rice is an annual plant. The height of the plant is up to 1-2 meters. The height of the plant depends on the type of fertiliser and soil. The leaves are 50-99cm long and 2-3 cm wide. The flower is small and pollinated by the wind. The grain length is 5.1-11.9mm and 2-3 mm thick. The temperature required for rice cultivation is 200 °C- 400 °C [6].

V. CHEMICAL CONSTITUENTS AND BIOACTIVE COMPOUNDS

Rice bran is a rich source of fibre, fat, protein, saturated and polyunsaturated fatty acids, and phenolic compounds [7]. Rice bran consists of nutritional and bioactive compounds. Nutritional compounds comprise carbohydrates, proteins, fats, etc, while bioactive compounds consist of gamma-oryzanol, phenolic compounds, and antioxidants. Due to its nutritional value, rice bran is used in the production of bread, ice cream, cornflakes, and other food products. Rice bran protein is of high quality, hence it is used in pharmaceutical preparations and the food industry.

Rice bran contains anthocyanin. It is a potent antioxidant. There are several anthocyanin monomers, dimmers, and polymers present in rice bran e. g. Apigenin, cyanidin glucoside, luteolin, hesperetin, etc. Major anthocyanins to be found in rice bran are peonidin-3-O-glucose, cyanidin 3-O-glucoside, followed by Flavan [8]. Flavonoids are found in rice bran in a free or bound form in black rice bran. The most commonly extracted phenolic compounds of rice bran are p-coumaric acid and ferulic acid. Brown and red rice bran extracts contain myricetin, while Apigenin and quercetin are obtained from black rice bran. Zhou et al found that brown rice consists of a large amount of ferulic acid and a smaller amount of gallic acid, vanillic acid, etc [9].

Table-1: Rice Bran Extracts Contain Several Chemical Constituents. The Details Are Given Below:

S. No.	Chemical Constituents	Figure No.
	Fiber	
1	Cellulose	1
2	Hemicellulose	2
3	1,6-Anhydro-beta-D-glucopyranose	3
4	Pectin	4
5	beta glucan	5
	Fatty Acid	
6	Linoleic acid	6
7	Linolenic acid	7
8	palmitic-acid	8
9	Myristic acid	9
10	Stearic acid	10
	Oryzonol	
11	gamma-Oryzanol	11
12	β-sitosterol	12
13	Cycloartenyl ferulate	13
14	24-methylenecycloartanyl ferulate	14
15	Campesterol ferulate	15
16	Vitamin E	16
17	Tocotrienol	17
18	Tocopherols	18
19	Ferulate	19
	Protein	
20	Gluten (prolamins) protein	20
21	Albumin	21
22	Human Gamma Globulin	22

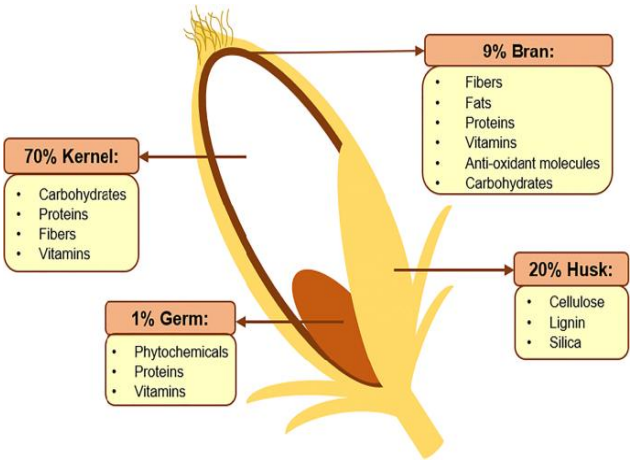


Fig. 3 Part of Rice Bran Through Which Different Chemical Obtained.

Dietary fiber

Rice bran contains 6–14% fiber. The central part of dietary fiber is cellulose and hemicelluloses. Cellulose is the most abundant polymer on Earth. Cellulose contains carbon, hydrogen (44 to 45% and 6 to 7 %), and a large amount of oxygen. Cellulose is polysachiride whose formula is $(C_6H_{10}O_5)_n$. It is a linear chain of beta 1-4 linkage of D-glucose unit (D-anhydrobeta-glucopyranose, AUG). This unit is linked together by a beta (1-4) glycosidic linkage formed between carbons no 1 and carbon no 4 of adjacent of glucose molecules [10].

Dietary fiber is a polysaccharide. Humans cannot absorb it, and intestinal enzymes are unable to break it down. Dietary fibre is a crucial component of a healthy diet. It has several health benefits, including improved body weight, reduced serum lipids, and lower cholesterol levels. Dietary fibre is obtained from rice bran through a milling process. Dietary fibre comes in two types: soluble and insoluble. Dietary fibre obtained from rice bran is primarily insoluble, and trace amounts of soluble fibre, i.e. Pectin and beta-glucan, are present. Soluble dietary fibre is superior to insoluble fiber [11].

Fatty acid

Rice bran oil contains 40.5% oleic acid, 35.8% linoleic and linolenic acid and 23.2% palmitic, myristic, and stearic acid. Fatty acids are two types i.e. essential (body not synthesized, taken from diet) and nonessential fatty acid (synthesis in the body). Essential fatty acids are used in the cosmetic industry because they regenerate skin and prevent ageing [12]. Unsaturated fatty acid undergoes oxidation or thermal decomposition during cooking. Rice bran oil contains some amount of unsaponifiable substance and gamma oryzanol. Rice Bran oil consists of quercetin, ferulic acid, some fraction of sterol, gamma-oryzanol, and squalene. These are unsaponifiable substances. The high-temperature stability of rice bran oil is due to the presence of these substances. Rice bran oil has low viscosity; hence, during frying, less oil uptake occurs. The smoke point of rice bran oil is high; therefore, it is a good cooking oil.

Several researchers have investigated the stability of rice bran oil, as well as its stability when mixed with other oils, including groundnut oil, sunflower oil, and mustard oil. They found that oil and its mixture show better stability than the other oils [13].

Gama Oryzonol

Rice Bran oil contains 1-2% gamma-oryzanol, which serves as a natural antioxidant. Initially, it is considered that gama oryzanol is a single compound present in rice bran oil. However, after several studies (1999), it was found that polysteryl ferulate ester is present in gamma-oryzanol. This ferulate ester contains beta-sitosteryl ferulate as a main bioactive compound, and also consists of campesterol ferulate, cycloartenyl ferulate, and methylenecycloartanyl ferulate [14].

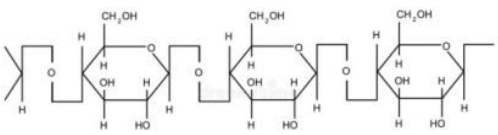
γ-Oryzanol helps reduce cholesterol and lipoproteins, inhibits platelet aggregation, and increases high-density lipoprotein. Several studies show that γ-oryzanol has potent antioxidants. Other compounds, such as vitamin E, tocotrienols, and tocopherols, are fat-soluble. These compounds cannot be synthesised in the body and are taken from the diet or food sources. These compounds have antibacterial and antioxidant properties. 182-313mg/kg of tocopherol and tocotrienols are present in bran oil, while rice bran oil contains 585 mg/l of total tocotrienol. In 2015, Pengkumsri et al. observed that gamma-oryzanol obtained from regular rice is less than that from red and brown rice. Tocopherols and tocotrienols are natural antioxidants. Tocotrienols have more antioxidant properties than tocopherols. However, the composition and amount of γ-oryzanol depend upon the variety of rice plants and extraction methods [15].

Protein

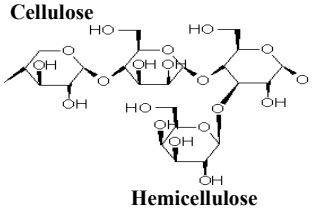
Generally, a whole rice grain contains 5.8-7.7% protein. White rice has a soft texture and a gorgeous appearance; hence, it is eaten by most humans. The velvety texture of rice contains 76.7% carbohydrate and 7.4% protein. Specific research indicates that it is the source of approximately 13-15% hypoallergenic and high-quality protein, with a protein efficiency ratio (PER) of 1.5-2, compared to casein (2.5). Starch is the most abundant constituent in milled rice and the second most abundant in protein. The protein content ranges from 10% to 16%, depending on the cultivar. According to protein solubility by Osborne fractionation, proteins are divided into four types, i.e. 32.6% glutelin, 31% albumin, 25% globulin, and 11.5% prolamine (11.6%) [16].

Gluteline consists of a significant component of rice protein. It contains 23-40.3 % of the total protein of rice bran [16]. Glutelin has limited solubility in water due to the presence of disulfide bonds and hydrophobic interactions [17]. Glutelin is soluble in 1- 3 pH and above pH 10. Its molecular weight ranges from 64 to 500 kDa. Its molecular weight is higher than that of other rice proteins. Rice glutelin consists of two types of subunit, i.e. acidic and basic subunits. The molecular weight of the acidic subunit is 30-39 kDa, and the basic subunit is 19-25 kDa. Both subunits come from 57kDa polypeptide precursors. In 1997, Hamada observed that the molecular weight of glutelin protein was 46-149 KDa, while in 2009(Chanput) and 2012(scientist Xia) observed the molecular weight of glutelin was 11- 61 KDa.

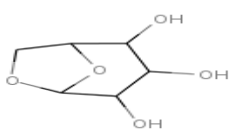
Water-soluble protein is albumin. Albumin is contaminated by globulin protein during extraction with water because minerals present in the rice grain dissolve in the water solvent and contaminate it. About 6.3 -10 % albumin is present in rice grains [16]. The molecular weight of albumin is approximately 100 kDa or less when analysed by size exclusion HPLC. In 2009, Cao et al. found that albumin has a major polypeptide with a molecular weight of 18-20 kDa. In the same year (2009), Chanput et al. found the two prominent bands of albumin using SDS-PAGE. Globulin is a sulfur-rich protein. It is soluble in salt. It contains 12.5 to 25% of the total storage protein in rice bran [16]. In 2012, Xia et al found that the molecular weight of globulin is 26 kDa in broken rice, and also the molecular weight of Thai rice variety globuline is about 15.4 and 50 kDa [16]. Prolamine is soluble in alcohol. Prolamine is extracted at the end of the extraction of protein i.e. albumin and globuline. Prolamines contain 3.3-11.5 % of total protein in rice bran [16]. Prolamine is extracted by ethanol (70%) or propanol (50 %). In 2009, Chanput et al. observed various prolamine fractions, i.e., 10, 15, and 25 kDa. In the same year (2009), Cao et al. proved that prolamine consists of three subunits of polypeptide, with molecular weights of 10 and 16 kDa.



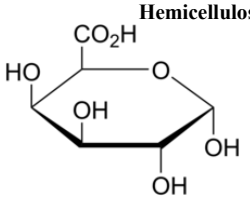
Cellulose



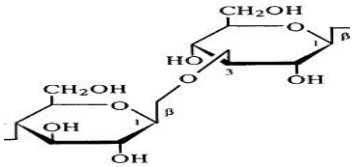
Hemicellulose



1,6-Anhydro-beta-D-glucopyranose



Pectin beta-glucan



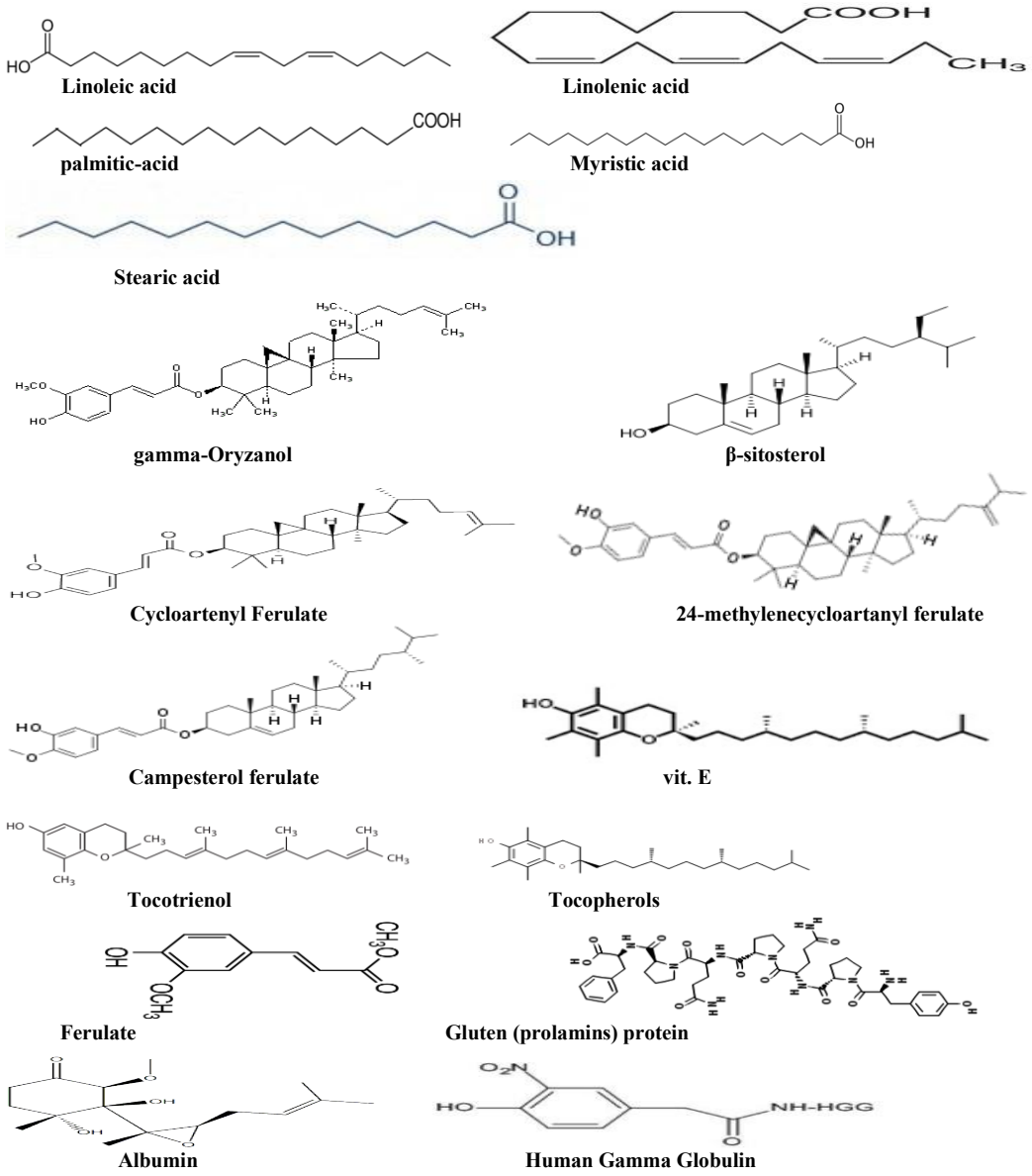


Fig. 4: Chemical Structure of Phytoconstituents of Rice Bran

VI. TRADITIONAL USE

Traditionally, rice is considered to have medicinal value in Chhattisgarh, India. Insects that attack rice are used as traditional healers for common and complicated diseases. Laicha rice variety is used to treat Laicha disease. Hence, it is known as Laicha. Laicha is a type of skin infection. Anciently, rice plants and rice bran were used as animal feed. Rice bran oil is now extracted from rice bran. It has high medicinal value. Rice straw is used to make bags, mats, and other products. These bags help in the packaging of nuts, beans, potatoes, etc [18]. Some Indian rice varieties, such as Black Kavuni rice, possess antimicrobial properties, as seen in Kaivara Samba, which helps lower blood glucose levels. Kuruvi kar rice is a variety grown in drought-prone areas and consumed by the local population for its health benefits. The Poongar Rice variety, consumed by women after puberty, is associated with the reproductive system. Kuliyal variety rice is used in special dishes. Mappillai Samba has hypocholesterolemic properties and anticancer properties, and it also improves men's fertility. Rice is stored in the form of paddy instead of milled rice because husk prevents the degradation of the rice grain and protects against insects.

VII. FOOD AND NUTRITIONAL COMPONENTS

The amount and quality of rice grain depend on the genetic factor, type of fertiliser, milling process, storage condition, and environmental effect [19]. Rice bran consists of dietary fibre, carbohydrates, protein, vitamins, fatty acids and minerals. There are two types of nutrients present in rice bran: micronutrients and macronutrients.

A. Macronutrients

Macronutrients are established by autoclaving and parboiling at 4 to 8% milling. The milling degree also affects the chemical and nutritional quality of the bran. Rosniyana et al. in 2005 [20] observed that milling rice at a 4% milling degree yields more nutritional compounds compared to milling at other degrees. The macronutrients of rice bran are carbohydrates, fat, and protein. The composition of

carbohydrates, fats, and proteins is 26%, 20%, and 17%, respectively.

These amounts of macronutrients are obtained if rice is milled at a 4% milling degree.

B. Micronutrients

Rice bran contains a high degree of vitamins and minerals. Hence, its consumption leads to a high intake of minerals and vitamins. The amount of minerals and vitamins depends on the milling process and stabilisation process [21]. Rice bran contains niacin, pyridoxine, thiamine, and riboflavin. The niacin content in rice bran is high. Minerals present in rice bran are potassium and phosphorus. Other trace amounts of minerals include calcium, sodium, iron, and magnesium. The amounts vary from autoclaved to parboiled rice bran. The amount of these minerals is higher in autoclaved rice bran than in parboiled rice bran. Iron is higher in parboiled rice bran than in autoclaved rice bran. The outer covering of rice is known as rice bran. It is brown. Rice bran consists of a seed coat, pericarp, and aleuronic layer. Rice bran is composed of various nutrients like carbohydrates, protein, fat and dietary fibre. The nutritional composition of rice bran depends on the milling system and the variety of rice [22]. The nutritional components of rice bran are listed in the table.

Table. 2: Composition of Nutrients in 100 Grams of Rice Bran

Sn	Nutrient	Amount	Sn	Nutrient	Amount
1	Energy	316 (Kcal)	13	Manganese	780 mg
2	Saturated Fat	4.15 g	14	Calcium	57 mg
3	Fat	20.8 g	15	Mangnesium	780 mg
4	Unsaturated fatty acid	15 g	16	Thiamine	2.7 mg
5	Protein	13.5 g	17	Pantothenic acid	7.4 mg
6	Carbohydrate	50 g	18	Folate	63 mg
7	Dieatory fiber	21 g	19	Riboflavin	0.28 mg
8	Iron	18.5 mg	20	Vitamin B6	4 mg
9	Potassium	1485 mg	21	Niacin	34 mg
10	Phosphorus	1677 mg	22	Choline	32 mg
11	Selenium	14.2 mg	23	Vit K	2 mg
12	Zinc	6 mg	24	Vit E	5 mg

VIII. BIOLOGICAL ACTIVITY

A. Antioxidant

Natural antioxidants are present in rice bran and rice bran oil. These antioxidants have significant health benefits. This study is supported by several previous studies that show rice bran has disease-preventing properties, including cancer prevention. It is an essential source of antioxidants and phytochemicals [23]. Antioxidant activity was observed in rice bran in another study by the DPPH radical method. Rice bran is a rich source of antioxidant compounds like tocopherol, tocotrienols, gamma-oryzanol, polyphenols, etc. They prevent oxidative degradation of body tissue DNA. Some components of rice bran show a synergistic effect, potentiating antioxidant activity, such as tocotrienols and tocopherols. In 2011, Norhaizan et al. observed the antioxidant activity of phytic acid in rice bran extract. They observed antioxidant activity using the thiobarbituric acid (TBA) method, ferric reducing antioxidant power (FRAP) assay, Thiocyanate capacity (FTC) test, and beta-carotene bleaching method. They also discovered the antioxidant mechanism of phytic acid in reducing the production of oxygen-free radicals. Antioxidants work at both the molecular and cellular levels. They deactivate the metabolic byproducts, which are free radicals. Rice bran contains gama-oryzanol, phytosterols. They have antioxidant properties. Ferulic acid is a component of gamma-oryzanol. It is a potent antioxidant and stable at very high temperatures [24]. Vitamin E also has antioxidant properties. Several studies show that gama-oryzanol more potent antioxidant than vitamin E for cellular oxidation. The pharmaceutical industry utilises the various properties of rice bran for the development of nutraceuticals and other food ingredients. The antioxidant activity of rice bran is produced due to the presence of flavonoid and phenolic compounds such as hydroxycinnamic acid, haempferol and hydroxybenzoic acid. Total flavonoid and phenolic content of rice bran is approx 2.9 to 3.5 mg retinol equivalent/g and 3 to 4 mg/ gallic acid, respectively [25]. Rice bran is a good source of fibre. The amount of fibre present in rice bran is 3-5 mg/g. tocopherols present in alpha and gama form, with concentrations varying from 63-95 µg/g and 5-5.2 µg/g, respectively[25]. Antioxidant effect significantly shows on the liver and serum levels of rats [26]. Hypercholesterolemia is produced by the formation of active oxygen free radicals and reduces serum antioxidant activity. A nutrition supplement containing an aqueous enzymatic extract of rice bran at 750 mg/kg body weight (BW) was administered for 42 days. They restore the antioxidant capacity in rats fed a high-fat diet. Rice fed a high-fat diet and rice bran supplementation increase liver catalase and reduce carbonyl protein content in the liver compared to rats fed only a fatty diet [26]. A clinical study in hyperlipidemic adults shows that consuming 30 ml of rice bran oil containing more than 4000 ppm gamma-oryzanols for 28 days significantly increases plasma oxygen-free radical scavenging capacity. Hence, the antioxidant activity of rice bran is also shown by the presence of bioactive peptides [27]. Boonla et al proved that rice bran supplements containing rice bran protein hydrolysate 60-99 mg/kg given for 42 days reduce plasma malondialdehyde (MDA) and protein carbonyl [27].

B. Anticancer

Rice bran contains various biologically active compounds that have beneficial effects for the treatment and prevention of many cancerous diseases. Phytonutrients present in rice bran help prevent certain types of cancer, including lung, liver, Breast, colon, and other cancers. Rice bran consists of Inositol. It exhibits a chemoprotective effect with low cytotoxicity. These compounds prevent and inhibit the development of cancer in various organs, such as the mammary glands, lungs, and colon [28]. Several scientists, including Nishino et al. in 1998 and Shamsuddin & Ullah in 1989, have proven the effects of rice bran on liver carcinogenesis in mice and colon carcinogenesis in rats, respectively. Nurul-Husna et al. (2010) and Shafie et al. (2013) demonstrated the

chemoprotective properties using in vivo and in vitro models [29]. Shafie et al. (2013) observed anticancerous properties of phytic acid in rats by administering phytic acid to their drinking water [29].

Norazalina et al in 2010 and Shafie et al in 2013 observed reduced formation of crypt foci and tumor growth by administration of 0.2% phytic acid in the diet [29].

These studies demonstrate that phytic acid inhibits various pathways of carcinogenesis, which are responsible for cancer formation. Phytosterols can inhibit chemically induced cancer in animal cells—the formation of coprostanol, sterol and bile acid by colonic microorganisms is accountable for the inhibition of colon cancer. Several studies also show that the intake of phytosterols reduces faecal cholesterol by inhibiting the proliferation of epithelial cells. Bingham et al proved that dietary fiber intake is inversely proportional to the occurrence of colorectal cancer. The less protective effect is shown on the rectum, and the highest protective effect is shown on the left side of the colon [30]. Not all cancer is hereditary. Only 5% to 10% of cancers are hereditary. The most common causes of cancer are a modern diet and lifestyle habits. By improving dietary habits, the incidence of cancer is reduced by up to 30% in humans. Phytic acid is extracted from rice bran. It exhibits anticancerous activity against hepatocellular carcinoma cells (HepG2) and induces their apoptotic activity, as observed by the expression of apoptosis regulatory genes, such as p53 and Bcl-2. Tocotrienol is present in Rice bran oil. δ δ-Tocotrienol is effective against colorectal cancer. In an in vivo study, oral administration of tocotrienols 10 mg/day in mice significantly inhibits tumor growth in nude mice. The cancerous cell produces free oxygen radicals, which are responsible for the progression of cancer. Cycloarttenyl ferulate is a component of ɣ-oryzanol. It is an antioxidant, hence it reduces the proliferation of colorectal adenocarcinoma [31].

C. Anti-Hypercholesterolaemic

Tocotrienol reduces cholesterol levels by inhibiting 3-hydroxy 3-methyle-gluteryl coenzyme A (HMG-CoA) reductase enzyme. In endogenous cholesterol synthesis, it is a rate-limiting enzyme. A study shows that the combination of tocotrienols and the American Heart Association Step 1 diet reduces serum cholesterol and LDL-cholesterol in individuals with hypercholesterolemia. RBO reduces total cholesterol and LDL cholesterol, as demonstrated in the human model. In 2005, Most et al [32] observed that rice bran oil given with a controlled oil blend has a significant effect on serum cholesterol concentration, due to the presence of unsaponifiable compounds. Various types of literature indicate that RBO lowers cholesterol levels in various laboratory animals, including rats, humans, and hamsters. Multiple studies show that rice bran oil decreases cholesterol levels in hypercholesterolemic patients. Who takes rice bran oil instead of cooking oil, and elderly and middle-aged people take rice bran oil and a low-fat diet [33]. Rice bran oil has significantly reduced Low-density Lipoprotein (LDL) cholesterol levels. This property of rice bran oil is due to the presence of Phytosterol, Tocotrienol and oryzanol. In the 1950s, phytosterols were reported as cholesterol-lowering agents. Several studies have shown that beta-sitosterol can reduce LDL and circulating cholesterol levels. These results show that rice bran contains lipid-lowering agents. Which reduces lipid concentration by affecting lipid metabolism [34]. Feeding 4 weeks of rice bran oil containing low and high gamma-oryzanol reduces 6% of total plasma cholesterol, 10.2% of low-density lipoprotein cholesterol. Various studies on human models conducted for an 84-day intervention with 20g/day rice bran show a decrease in total cholesterol, LDL, and LDL to HDL ratio [34]. When gamma-oryzanol was given with PUFA n-3 and Vitamin E was given to dyslipidemic patients, they maintained a standard lipid profile after 4 months of intervention as compared to a placebo given with PUFA n-3 and Vitamin E. A study on obese Japanese individuals with high LDL cholesterol, who were given rice bran extract 50 mg/day for 84 days, showed a significant reduction in total cholesterol and LDL levels. In 1998, Jariwala [35] It was said that phytic acid present in rice bran reduces cholesterol and triacylglycerol in blood, resulting in a significant reduction in heart disease. In hyperlipidemia, total cholesterol and triglyceride levels become high in the blood. It is associated with cardiovascular disease. A diet high in phytic acid and cholesterol, given to rats, shows reduced serum cholesterol and triglyceride levels, and regulates markers of hypercholesterolemia, including the zinc and copper ratio. This lipid-lowering compound (phytic acid) has no toxic effect in rats. In 1998, Katayama showed the combined effect of inositol and phytic acid. They show that the combination of phytic acid and inositol significantly reduces hepatic lipid and triacylglycerol via inhibition of lipogenesis enzyme rather than enzyme inhibiting intestinal enzyme. Phytic acid is also responsible for inhibiting aggregation of platelets to increase inflammatory response, and calcification ofaorta and lipid peroxidation in the kidney [36].

D. Anti-Diabetic

Type 2 diabetes is caused by the pancreas producing less insulin, leading to hyperglycemia that results in reduced glucose entry into cells, which in turn leads to decreased glucose utilisation in the body. As a result, glucose levels become high [36]. In various human studies, the consumption of rice bran by insulin-dependent diabetic patients has been shown to reduce blood glucose levels. Which is the active component of diabetes? This study demonstrated that 25% of patients experienced a significant reduction in hyperglycemia, accompanied by a decrease in daily insulin injections and hypoglycemic medications [37]. In vivo studies on mice and rats demonstrate the antidiabetic effect of rice bran. Fermented rice bran regulates adiponectin expression and induces insulin resistance by neutralizing free radicals. Gama-oryzanols stimulate insulin secretion by the pancreas. Various in vitro studies proved that rice bran extract increases the uptake of glucose in 3T3-L1 adipocytes and reduces α-glycosidase and α-amylase activity. Hence, it reduces glucose absorption and glycemic response [38]. Rice bran extract activates glucose reabsorption in cells by activating messenger ribonucleic acid (mRNA) by expressing glucose transporters (GLUT1 and GLUT4) and reducing insulin signalling pathway proteins. These insulin signalling pathways include the insulin receptor gene (INSR) and the insulin receptor substrate (IRS)1[38]. The glucokinase enzyme is a

regulator of blood glucose that activates the utilisation of glucose in the liver by promoting the phosphorylation of glucose to glucose-6-phosphate.

Other studies show that a diet containing low fibre and 40g/day of rice bran fibre for 7 days has a significant effect in lowering glucose levels in diabetic patients compared to a low-fibre diet alone. After 12 weeks of a diet containing 20g/day stabilised RB, there was a significant reduction in glucose level in fasting conditions, glycated haemoglobin, and postprandial glucose [39]. Rice bran supplements increase insulin resistance by increasing the level of adiponectin. Adiponectin is related to insulin sensitivity.

E. Anti-Allergic

The allergic reaction is triggered by exposure to environmental substances, such as proteins, pollen, and spores, within the body. Substances that produce allergies are known as allergens. β- The bleach rice bran inhibits hexosaminidase and histamine. In vitro study: Allergic reaction mediated by mast cells and basophilic leukaemia cells was inhibited by black rice bran. Rice bran activates the natural killer cells, monocytes, and T cells. In vitro studies have shown that it also activates monocyte-derived dendritic cells. Hence, it is used as a dendritic cell-based vaccine against various infections and potentiates dendritic cell maturation [40].

F. Anti-Inflammatory

Methanolic extract of rice bran contains feruloyl ester of triterpene alcohols. Feruloyl ester of triterpene alcohols shows an anti-inflammatory effect against 12-O-tetradecaolylphorbol-13-acetate-induced inflammation in mice [41]. Feruloyl ester of oligosaccharide suppresses inflammatory mediators, demonstrating its effectiveness as an anti-inflammatory agent. Hydrolysed rice bran contains immunomodulatory properties, and therefore, it is used to prevent the common cold syndrome in elderly individuals. RBO contains cycloartenyl ferulate, which reduces nitric oxide production induced by lipopolysaccharide and expression of mRNA of NO synthetase and COX-2, as well as upregulates superoxide dismutase activity. This evidence demonstrated its effectiveness in treating inflammatory diseases. Previous studies proved the inhibitory effect of rice bran on pro-inflammatory enzymes like COX-1, 5-LOX, and COX-2 [42]. In vivo, the study also demonstrated that the prebiotic form of rice bran mediates immune cell differentiation, inhibits the growth of Clostridium, and increases the content of short-chain fatty acids in colitis. Hou et al in a 2013 study on the effect of anthocyanin-rich extract of black rice bran for 49 days at a concentration of 200,400, and 800 mg/kg in tetrachloride-treated mice [43]. The results of this study show that the anthocyanin-rich extract of rice bran increases plasma antioxidants (SOD and glutathione peroxidase), normalises liver enzymes, and lowers the amount of thiobarbituric acid-reactive substances (expressed as MDA, TBARS) and 8-hydroxy-2-deoxyguanosine (8-OHdG). 8-OHdG is a biochemical substance that is responsible for the oxidative stress, similar to guanine in DNA. During the repair process, Guanine is transformed into 8-oxo-guanine and subsequently removed from the body as 8-oxo-7,8-dihydro-2'-deoxyguanosine (8-OHdG). Release of 8-OHdG increases in certain diseases like atherosclerosis and diabetic mellitus [43]. MDA is released during lipid peroxidation as a secondary byproduct. It is widely used as a biomarker of oxidative stress. The level of MDA becomes high during various inflammations related to diseases like cancer, cardiovascular disease, liver disease, diabetes mellitus, Alzheimer's disease and Parkinson's disease. RBP exhibits an anti-inflammatory effect by reducing pro-inflammatory cytokines, such as TNF-α and IL-6, and increasing anti-inflammatory cytokines, including IL-10, in macrophage cells. RBP is obtained by hydrolysing rice bran protein through flavourzyme or alcalase. These hydrolyzed proteins contain ACE inhibiter and antioxidant properties [44]. The fraction of RBP lower than 3kDa has potent antioxidant activity, a high amount of phenolic compounds and potent ACE inhibitor activity [44]. A study was performed on 105 obese and overweight adults. They administered rice bran at 70 mg/day, rice husk at 25 g/day, and a placebo along with an energy-restricted diet. After 84 days of administration, they observed that high-sensitivity C-reactive protein (hs-CRP) was reduced in serum. Reduction of hs-CRP level is greater in the Rice bran-treated group than in the placebo-treated group. The placebo-treated group does not show a significant change in hs-CRP concentration. Weight management. Obesity is an essential factor for many diseases like type 2 diabetes, cardiovascular diseases, cancer and hypertension [45]. It is not only common in adults but also in children. There is a specific region through which obesity is produced, like economic imbalance, changing dietary patterns and globalisation [45]. Giacco et al. found that grain intake lowers body weight by reducing the glycemic index, lowering energy density, modulating gut bacteria, and increasing short-chain fatty acids (SCFAs). However, the recent study fails to explain the mechanisms by which consuming grain promotes weight loss. Justo et al [46] studied the enzymatic extract of rice bran (1% and 5% supplemented diet) on biochemical, metabolic and adipose tissue change in diet-induced obesity mice. Mice fed a high-fat diet with 1% and 55% rice bran extract did not show any changes in body weight compared to mice fed only a high-fat diet.

G. Gastrointestinal Effect

Consumption of fibre improved gut health. Excess amount of fiber in the diet produces blotting and gastrointestinal disturbance due to the fermentation of fiber in the colon by gut bacteria [47]. In colorectal cancer patients, a diet containing 30 g of rice bran for 4 weeks helps maintain a significant amount of dietary fibre (DF) without causing gastrointestinal discomfort or altering stool consistency. Other studies show that arabinoxylans obtained from rice bran, when given to inflammatory bowel syndrome (IBS) patients for weeks, will improve diarrhoea, reflux, and constipation [48]. Fermentation of rice bran stimulates mucosal balance and shifts gut microbacteria in the intestinal tract. Hence, consumption of rice bran improves gut health [48].

H. Prebiotic Properties of RB

Some studies have shown that dietary fibre has prebiotic properties. [49]. Kurdi and Hansawadi in 2015 demonstrated that rice bran treated hydrothermally at 0.22 MPa and 135 °C for 0.5 to 3 hours produced oligosaccharides. This oligosaccharide is

suitable for the growth of Bifidobacterium and lactobacillus and increases the population of F.prausnitzii, without affecting the production of SCFAs. Zhang et al [49].

Performed in vitro study in gastrointestinal digestion and colonic fermentation of dietary fiber fraction of rice bran and phenolic removed rice bran dietary fiber. The study proved that rice bran dietary fiber increases the population of lactobacillus after 24 and 48 hours. At the same time, phenolic-rich rice bran dietary fibre improved bifidobacteria, A. muciniphila. Finally, this study shows that the fibre fraction of rice bran, as well as the phenolic compounds in rice bran dietary fibre, help to confer prebiotic properties to rice bran. A diet containing 4% enzyme-treated RB for 6 days prevents colitis by decreasing clostridium and Eubacterium and increasing the production of SCFAs; hence, the final result is reduced inflammation in colitis [50]. 1-5 g/day intake of rice bran for 6 months in Nicaraguan infants of 6-12 months of age reduced the diarrhea. This intake of rice bran changes the gut bacteria such as Lachnospiraceae, Bifidobacterium, Veillonella, Bacteroides, and Lactobacillus [51].

I. Kidney and Liver Function

The kidneys maintain the body's water and electrolyte balance. Various diseases, such as cardiovascular disease and diabetes mellitus, affect kidney function by producing inflammatory mediators. In diabetic nephropathy, albumin and creatinine levels increase in urine, which makes complications in the kidney. Diabetic mice fed rice bran containing food 100 to 500 mg/kg/day for 8 weeks show a reduction in the creatinine and albumin levels in urine. Certain studies proved that gamma-oryzanol or its combination with gamma-oryzanol and rice bran oil improved liver and kidney function in rats. Which was treated with a high-fat and cisplatin diet [52]. Cisplatin helps to reduce kidney complications in rats treated with sucrose/high-fat feed. These rats treated with gamma-oryzanol 50mg/kg with/ without rice bran oil 300 mg significantly improved health [52]. During this study, it is believed that the gama-oryzanol inhibits inflammatory mediators like PG2 which is responsible for kidney disease [52]. High-fat diet produces nonalcoholic fatty liver disease (NAFLD) and increases the secretion of liver enzymes. NAFLD is produced by the accumulation of fatty acid and triglyceride in the liver. This leads to oxidative stress, mitochondrial dysfunction, and the stimulation of inflammatory mediators. Dietary supplements of Gama - oryzanol alone or in combination with rice bran oil improved liver function by reducing alanine and aspartate transaminase levels in rats previously treated with high-fat, high, and cisplatin [46]. Intake of food containing 0.5% gama-oryzanol for 49 days improved Glucokinase activity in the liver, which reduced glucose -6-phosphate (G-6-P) and phosphoenol pyruvate carboxylase kinase (PEPCK) enzyme in mice [53].

J. Effect on Metabolic Disorder

Abnormal metabolism produces various metabolic diseases like hyperglycemia, hypercholesterolemia, hypertriglyceridemia, insulin resistance, cardiovascular disease, etc. Rice bran products reduce metabolic risk. Enzymatic extract of rice bran-containing diet prevents the change of adipose and macrophage in obese mice [54]. Lowering triglyceride and cholesterol levels is known as antihyperlipidemia. Antihyperlipidemic effect of α-tocopherol proved in F344 rats fed a western diet. Anthocyanins and proanthocyanidins are present in the pigment of the rice bran layer, Which activate the uptake of glucose by 3T3-L1 adipocytes. 3T3-L1 cells are a key factor in glucose homeostasis. Fatty acid ester and gama-oryzanol with phytosterol are abundant in rice bran. Gama-oryzanol, a fatty acid ester, prevents metabolic syndrome induced by a high-fat and high-fructose diet. Treatment with gama-oryzanol significantly reduces the liver index and hepatic triglyceride concentration. Reduction of serum C-reactive protein and IL-6 and increased concentration of serum adiponectin proved that gama-oryzanol and fatty acid esters were used as a dietary supplement to reduce the risk of high-fat and high-fructose (HFFD) diet. Adenosine is responsible for the reduction of SHRSP syndrome. Single-dose and long-term use of adenosine improved hyperinsulinemia and hyperlipidemia. Several studies show that the administration of adenosine for three weeks reduces the synthesis of glucose-6-phosphatase enzyme by inhibiting mRNA regulation. The glucose-6-phosphatase enzyme is a rate-limiting enzyme of hepatic gluconeogenesis. Adenosine is also involved in β-oxidation, fatty acid synthesis and AMP-activated protein kinase by regulating hepatic mRNA expression [55].

K. Health Improvement

Rice bran and its active compound have immunomodulatory effects. Rice bran consists of gamma-oryzanol, phytosterol and other antioxidant compounds that stimulate the immune system. A rice bran-rich diet enhances gut health by improving the growth and colonisation of Lactobacillus rhamnosus and protects against rotavirus diarrhoea in pigs by altering gut permeability. A long-term RB-containing diet improved brain mitochondrial function and altered Alzheimer's disease. It also controls menopausal symptoms like bone loss in older women who have osteoporosis and hot flashes. Rice bran is a plant-derived active compound and an alternative source of various vitamins [56]. Bodybuilders and athletes use rice bran as an ergogenic supplement. Driselase enzyme-treated rice bran is used to prevent high blood pressure, hyperglycemia, and hyperlipidemia. Driselase is an esterase-free plant cell wall degrading enzyme consisting of cellulase, laminarinase and xylanase. Rice bran derivatives containing beta-sitosterol induce apoptosis in cancerous cells. Many coloured rice varieties are rich in β-carotene. B-carotene is converted into vitamin A, which is essential for eye disease [57].

L. Anti-Ageing Property

Gama oryzanol protects against light-induced lipid peroxidation by UV rays. It is used as a sunscreen agent. Gama-oryzanol consists of ferulic acid and its ester. Ferulic acid and its ester stimulate hair growth and skin ageing [58]. Rice bran also consists of tocotrienols. It is also an antioxidant agent. Tocotrienol easily penetrates the skin, is rapidly absorbed and acts as the first line of defence by accumulating in the stratum corneum. Free radicals are produced within the skin when the skin is exposed to toxic rays. They stabilized free radicals produced in the skin by exposure to poisonous rays. They protect the skin from exposure to UV rays-induced skin damage and also aid in skin repair [58].

IX. CONCLUSION

According to various research studies, rice bran has significant biological and nutritional value. The rice plant is a common herbal plant traditionally used for the treatment of multiple diseases and has diverse pharmacological value. Various chemical constituents present in plants have more pharmacological activity. Hence, further research and evaluation are necessary to identify the chemicals present and their applications, which will ultimately benefit human welfare.

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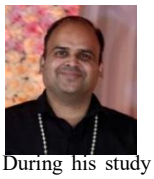

Dr. Neeraj Sharma provides support and guides the author to write the article Phytochemical and Biological Activity of Rice Bran: A Review. He has a good moral character and friendly behaviour, hence students are easily attracted to communicating their problems. Dr. Neeraj Sharma received his initial education in his hometown. During his study period, he was a brilliant student. After completing his pharmacy degree, he joined Bhagwant University, Sikar Road, Ajmer (Rajasthan), India. Dr. Neeraj Sharma is a highly diligent individual. During his teaching period, he published in various national and international journals. They also published several journals indexed in Scopus. Based on their intelligence and hard-working nature, after some time, he became H.O.D. in the Department of Pharmacy of Bhagwant University, Sikar Road, Ajmer (Rajasthan), India. During his teaching period, he guided several Ph.D. scholars. Currently, he is one of the best faculty members at Bhagwant University.