RESEARCH PAPER

Gamma Oryzanol: A Boon for Human Health

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ABSTRACT

Gamma oryzanol obtained from rice bran is a unique chemical constituent of natural origin having a plethora of applications in cosmeceuticals, nutraceuticals and pharmaceuticals. It is considered to be the most potent antioxidant. γ-Oryzanol has health properties due to the antioxidant and anti-inflammatory activities of its structure. Gamma oryzanol is a ferulic acid isolated from Oryza Sativa L.; it consists of components like trans-ferulic acid, phytosterols, cycloartenol, β-sitosterol, 24-methylenecycloartenol and campesterol, each of these components have their own specific health benefits. It was first shown to be effective in the treatment of menopausal symptoms, including hot flashes. Since then, research has been done continuously for its anti-diabetic activity, anti-inflammatory activity, anticancerous activity and activity against obesity. This article will aim at introducing various therapeutic properties of GOZ. Since it is a waste product obtained from rice bran during the process of milling, its extraction techniques are also being mentioned in this review using different solvents. There are many ways to extract gamma oryzanol from rice bran depending upon the feasibility. Apart from being a waste product, it has a variety of health benefits. There are a variety of pharmaceutical applications of gamma oryzanol. In the current review we will enlist the chemical components and applications in the therapeutic field while focusing mainly on therapeutic activity against cancers with special reference to colon cancers. Recently, a large number of studies are being conducted to study the usefulness of gamma oryzanol and special attention is being given to its activity against cancer. The review also focuses on the number of patents that have been recently done on GOZ.

Key Words: Gamma oryzanol, supercritical fluid extraction, microwave assisted extraction, colorectal cancer.

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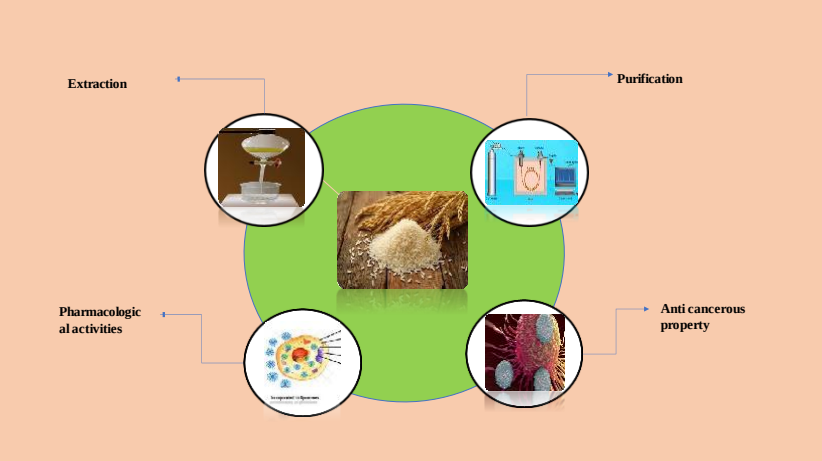
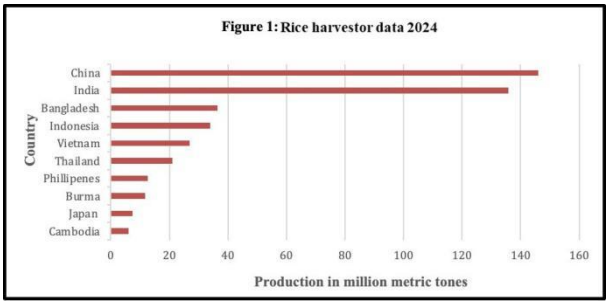
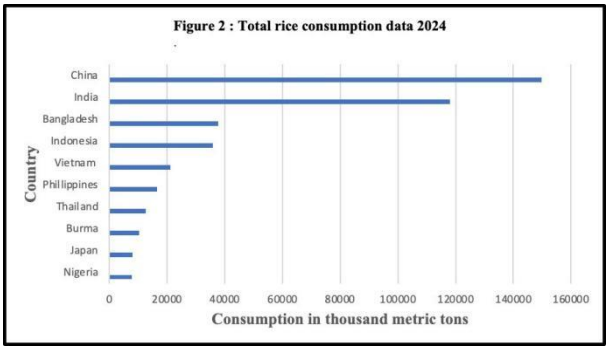


1. INTRODUCTION

Rice is considered as staple food crop in many countries across the globe. The consumption of rice has shown to be increased over the last few years [1]. Based on rice production data (2016), estimated by the Food and Agriculture Organization of the United Nations,

approximately 740 million tons of rice is harvested worldwide and 90% (approximately 670 million tons) is produced and consumed in Asia. **(Figure 1).** As per the latest report China is known to consume the maximum amount of rice worldwide **(Figure 2).** India is the second highest harvester of rice across the world after China. Among various phytochemicals in rice (Oryza sativa L.), GOZ is the one present in the highest amount, particularly in rice bran.





In the 2024/25crop year, about 530.239 million metric tons of rice were consumed all over the world out of which China and India were the two largest consumers, with China consuming approximately 145.475 million metric tons and India consuming around 121 million metric tons[2]. Numerous processing steps are involved to obtain rice from the paddy plants. The composition of ingredients in rice kernels depends upon rice variety, area where it is cultivated and extent to which it is milled. Generally, it is composed of starch, husk, and rice bran (RB).After milling the rice obtained is used for consumption by humans while broken rice, rice husk, and rice bran are considered as by-products which is commonly used as feed for animals as well as used for industrial applications. Among these by-products, rice bran has shown considerable importance due to the presence of significant phytoconstituents which have nutritional and medicinal importance. Rice bran is highly nutritious due to presence of high contents of protein (14–16%), dietary fibre (8–12%), phytic acid (8.7%), and oil (16–23%).The therapeutic importance is due to the o rice bran oil present in the rice bran which comprises of chemical constituents such as Gamma-oryzanol (GOZ), vitamin E (tocopherols and tocotrienols), and phytosterols[3]. Some of the research studies based on rice bran oil has highlighted t the presence of GOZ and its therapeutic activity which include anti-oxidant(Mahsan Alizadeh et al 2025), anti-inflammatory properties, controls the aggregation of platelets (Yi-Shan Liu et al,2025), lowers the plasma cholesterol level (Alvin Berger et al 2004),[4].In 1954, Kaneko and Tsuchiya isolated GOZ in its crystalline form from unsaponified part of rice bran. . In the initially stages of GOZ isolation, it was considered as a single chemical moiety but later studies confirmed that it is a mixture of ferulate esters and campesteryl ferulate. Since then, researches are being done to explore the composition of GOZ and finally its structure was obtained based on their composition which is mentioned in Figure 3.

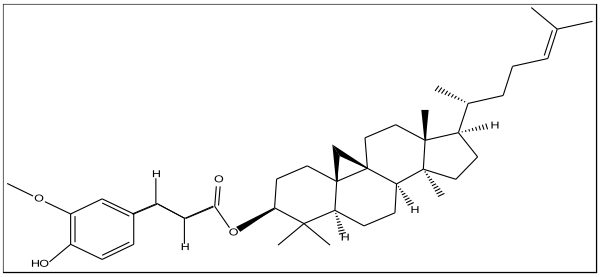


Figure3: Structure of GOZ

2. EXTRACTION OF GOZ

Rice bran makes up approximately 8–10% of paddy rice by weight and represents a significant portion of global production of this high-value byproduct. Rice bran is made up of the outer layers of the rice kernel which are the pericarp, tegmen, aleurone, and sub-aleurone. Crude rice bran oil contains moderate amounts of gums and waxes, free fatty acids (2–4%), a rich unsaponifiable fraction (4–5%), and neutral lipids (88–90%). The major bioactive components found in the unsaponifiable fraction of rice bran oil are GOZ and tocols. Other minor components reported are carotenoids, squalene, lecithin, tricin, and long-chain alcohols that too present in traceable amount [5]. When the rice is subjected to milling process, certain type of lipids present in it undergo hydrolysis and convert them to free fatty acids which are characteristized by a foul smell and bitter taste which make it inappropriate for consumption. [6].

Various methods are used for the extraction of GOZ which includes liquid - liquid phase extraction, solid

phase extraction, supercritical fluid extraction, maceration method and direct solvent extraction. All the above mentioned methods involve repeated extraction process where rice bran oil is subjected to expose with suitable solvent. Under optimal extraction conditions, the most commonly used solvents are hexane, isopropanol, acetone, isopropanol, acetate and alcohols . In one of the research done by Bo Ra Yi & Mi-Ja Kim in 2019 showed that extraction γ-oryzanol from rice bran using edible oils which increased the oxidative stability. Even though hexane extracts more GOZ [7,8,9].

2.1 Liquid – Liquid extraction:

This method is more of a separating method which is used to extract GOZ from rice bran oil by dissolving it in two immiscible solvents. The process is done by using separating funnel. Two solvents are chosen as per feasibility and shaken together along with rice bran oil. The aqueous layer is then removed which generally contains GOZ and further purification is done. One of the research have used this method to extract GOZ.

In a test tube 10g of Rice bran and 50 ml distilled water was taken, followed by addition of 2 g ascorbic acid. The mixture was then vortexed and incubated at different temperatures, time durations, Varying volumes and ratios of solvents which were regarded as factors. Then vortexed for 30 s followed by centrifugation at 1320 × *g* for 15 min. The organic layer was separated using separating funnel. The residue was re-extracted with (10 mL) hexane: isopropanol and the entire process was repeated. The combined organic layers were evaporated in a rotary evaporator at 70°C [10].

2.2 Solid phase extraction:

This technique utilizes a solid phase called as stationary phase and a liquid phase called as mobile/solvent phase. The component to be separated is adsorbed on the solid phase and then eluted with desired solvent. This method is widely used in pharmaceuticals, food testing, environment analysis and natural product isolation. In the literature we found that Lv, L.; Zhang, L.; Gao, M.; Ma in 2023 isolated GOZ from different agriproducts using silica as solid phase. Firstly, to remove the impurities silica gel adsorbent was washed with n-Hexane, then the agriproduct extract is loaded at a controlled flow rate. The loaded sorbents were washed with 2 mL of acetone/n-hexane (4:96, v/v) to remove the most of triglycerides and other unwanted components. At last all the analytes were eluted with 4 mL of ethyl acetate and dried under nitrogen stream at 25 ◦C. The residue was reconstituted with 100 µL of methanol for further analysis [11].

2.3 Maceration method:

Maceration is highly economic extractive method that requires very less quantity of solvent which is called as menstrum. This method has certain advantages over other extractive methods like economical and drug not exposed to higher temperatures and shorter extraction time. Hence, it is known to be favorable technique for extraction with higher extraction efficiency. While doing literature survey we got research done by Duangkamol Ruen-Ngam *et al* in 2014 where gamma oryzanol was extracted by maceration method. Firstly, Rice bran is mixed with solvents like hexane, ethyl acetate, acetone, isopropanol and ethanol in varying ratios with constant agitation at room temperature for 1 hour. After the process is completed, the solvent is removed with the help of rotary evaporator and the amount of oil extracted is measured [12].

2.4 Supercritical fluid extraction:

SFE is a method used for extracting bioactive components from the parent compound. It was first used by Emteborg et al. and Cela-Torrijos et al SFE for mercury speciation. This technique utilizes supercritical CO2 as an extracting media. The temperature of CO_2 is maintained at approximately 31° C, under pressure, so that it behaves like a fluid and dissolves the CO_2-soluble constituents with it. During the literature survey many research came to our focus which uses SFE extraction of gamma oryzanol using supercritical CO2, in one of the novel work supercritical fluid extractions (SFE) apparatus was used, composed of a CO2 storage tank (T), the gas is pressurized and heated up to the supercritical condition, and allowed to enter into the extractor filled with the rice matrix. Later, the fluid enters into the gravimetric separator where pressure and temperature are lowered down so that CO_2 can again turn to its gaseous form. The gaseous CO2 goes for the next slot while the extracted phase falls to the bottom of the separator, from where it can be recovered. The extraction was performed with a constant solvent flow of 20 kg/h for 3 h, filling the extractor with 1 kg of rice bran and metal rings to promote the solid and solvent contact [13].

2.5 Direct solvent extraction:

This is most simple method with least hustle. The drug component needs to be dissolved in appropriate solvent and vortexed for 30 minutes after that the drug solvent mixture is centrifuged to separate the supernatant from

the extract. The process is repeated thrice to ensure complete extraction from the parent compound. Then the extract is washed and filtered. During the data collection we came to one research where different components of rice bran are extracted using direct solvent extraction method. M.-H. Chen & C.J. Bergman (2003) isolated tocopherols, tocotrienols and GOZ.50 mg of rice bran sample was extracted using solvents like hexane, isopropanol and methanol. Sample vortexed with the solvents at room temperature and then centrifuged to remove the supernatant repeated the procedure of removing supernatant three times. The solvent remaining in the final extract was washed and filtered [14].

TABLE 1: Extraction techniques used in various researches

S. No.	Source compound	Extraction technique	Solvent utilised	Phytoconstituent's identified	Pharmacological activities	References
1.	Vegetable oil	liquid to liquid extraction & dispersive solid phase extraction	Hexane, Acetonitrile, Methanol & Isopropanol	Gamma oryzanol	Nutritional property	[15] 2024
2.	Rice bran	Maceration	Hexane	Gamma oryzanol	Anti - oxidant activity	[16] 2016
3.	Rice bran	Supercritical fluid extraction	Liquid CO_2	Gamma oryzanol & fatty acids	Antioxidant and antiproliferative effect	[17] 2025
4.	Black rice bran	Maceration	Ethanol	Cycloartenyl ferulate methylene cycloartenyl ferulate, campesterol ferulate, and Sitosteryl ferulate	Tyrosinase inhibition activity	[18] 2020
5.	Red rice bran	Direct solvent extraction	Ethanol, dichloromethane & hexane	γ-oryzanol, γ-tocotrienol & proanthocyanidin	Anti-cancerous activity	[19] 2014
6.	Rice bran oil	Supercritical fluid extraction	Liquid CO_2 & liquified dimethyl ether	γ-oryzanol	Cholesterol lowering activity	[20] 2025
7.	Rice bran oil	Direct solvent extraction	Hcl & NaOH	γ-oryzanol	Anti-oxidant activity	[21] 2016
8.	Rice bran	Supercritical fluid extr	Liquid CO_2	γ-oryzanol	Anti-oxidant activity	[22]2010

		action				
9.	Rice bran oil	Soxhlet extraction	Hexane	γ-oryzanol	Anti-hyperlipidemic activity	[23] 2012
10.	Rice bran	Microwaved Assisted Extraction	N-hexane & $NaNO_3$	γ-oryzanol	Gastro protective Activity	[24] 2018
11.	Rice	Liquid - liquid extraction	Acetonitrile & methanol	γ-oryzanol	Anti-cancerous activity	[25] 2020
12.	Rice bran	Microwaved Assisted Extraction	Hexane	γ-oryzanol	Tyrosinase inhibition activity	[26] 2020
13.	Rice bran	Supercritical fluid extraction	Liquid CO_2	γ-oryzanol	Anti-oxidant property	[27] 1999

3. Purification of gamma oryzanol

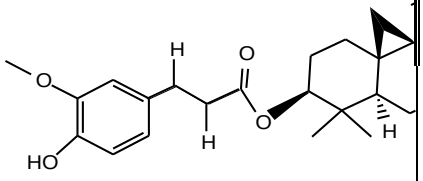
After extraction it is necessary to purify the extract to get the desired compound of choice in purest form. In general, while extracting GOZ from the feedstock along with GOZ, there are many other components like triglycerides, lipids, ferulates, tocopherol, tocotrienol etc which also gets extracted. Hence it is ultimate requirement to purify the extract for which variety of solvents and methods are used. Maryono and others in 2021, purified the GOZ extract using vacuum column liquid chromatography, the glass column was packed with silica grade 60. For solvent hexane and ethyl acetate were used in the ratio 9:1 which was later evaporated.

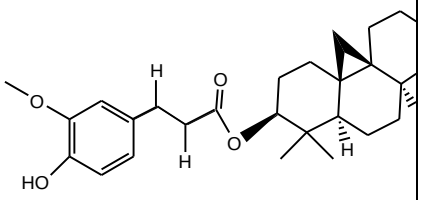
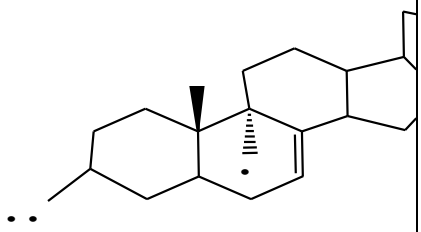
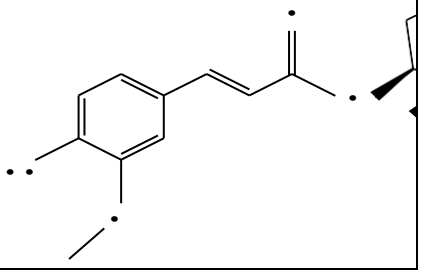
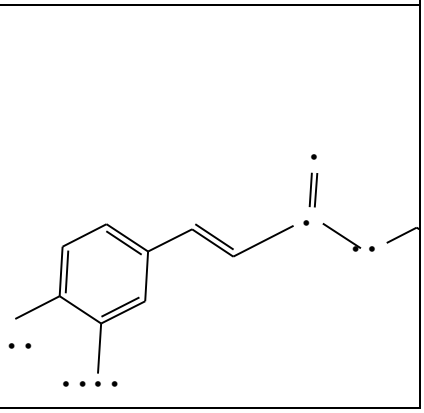
Anchana Anjinta and other in 2023, used column chromatography for separating GOZ from mixture of components. Further they studied the effect of purification parameters like size of silica gel particle, elution mode, ratio of solvent. They concluded that column containing 10 g of silica with 25-40 μm particle size gave the highest yield (84%) of GOZ with highest amount of purity around (95%).

Zhimin Xu and J. Samuel Godber in 1999 , used a glass column of dimensions 2.5 cm × 25 cm packed with 20 g of silica. The rice bran oil was mixed with the solvents (hexane/ethyl acetate) 9:1) and flushed through the column. Then 50 mL of solvent (hexane & ethyl acetate in the ratio7:3 was allowed to flow through the column, and the eluant was collected. At The column was then washed with 50 mL of hexane/ethyl acetate.

Various chemical constituents of gamma oryzanol quantified using HPLC are enlisted in **Table 2.**

TABLE 2: CHEMICICAL CONSTITUENTS PRESENT IN GOZ AND THEIR STRUCTURES

S. No.	Constituent	Structure
1.	Stigmasteryl ferulate	

2.	Campesteryl ferulate	
3.	Δ7 Stigmasteryl ferulate	
5.	Cycloartenyl ferulate	
6.	Sitosteryl ferulate	

3.1 GAMMA ORYZANOL AS ANTI CANCER AGENT

Recent studies have showed that conventional therapies for cancer treatment like chemotherapies and radiation therapies have more of adverse reactions rather than therapeutic efficacy along with that the drug delivery systems have plenty of limitations like toxicity, lack of bioavailability & specificity etc. On the other hand, various compounds of natural origin have shown to be highly effective in treating cancer with reduced side effects and least limitations. Gamma oryzanol which is of natural origin economic and foremost important obtained from rice bran which is discarded part of rice. Many researches have proved its effective property against different cancers, few of which are described in Table 4.

TABLE 4: POTENTIAL OF GAMMA ORYZANOL AS ANTI CANCEROUS AGENT BASED ON RECENT RESEARCH

S.NO.	CANCER TYPE	Evaluation studies (in vitro/ in vivo/ ex vivo)	Findings	References
1.	Prostate Cancer	In vitro	γ-oryzanol decreases cell viability and culture biomass by apoptosis and/or necrosis death in androgen unresponsive (PC3 and DU145) and responsive (LNCaP) cell lines, and signals through pERK1/2 in LNCaP and DU145 cells [28].	Jan 25

2.	Skin Cancer	In vitro	In Vitro Anticancer Activity of Gamma Oryzanol in Skin Cancer [29].	July 22
3.	Skin Cancer	In vivo	GO-NEs could effectively prevent UVB-induced skin cancer [30].	October 2021
4.	Colon Cancer	In vitro	The cytotoxic activity of rbNPs to murine colon adenocarcinoma colon26 cells was significantly greater than DOXIL® or other pdNPs. The rbNPs induced cell cycle arrest and apoptosis, and reduced the expression of proliferative proteins, including β-catenin and cyclin D1[34].	March 2024
5.	Prostate Cancer	In vitro	All concentrations of gamma-oryzanol, 0.1-2.0mg/ml, significantly inhibited cell growth in a dose- and time-dependent fashion in both prostate cancer cell lines, DU145 and PC3[35].	September 2013
6.	Tumor	In vitro	The improved anticancer efficacy of the nanoparticles could be attributed to the enhanced solubility and bioavailability of γ-oryzanol and the selective targeting of cancer cells by the albumin nanoparticles [36].	June 2023
7.	Tumor	In vivo	ELISA of tumor cells confirmed reduced expression	June 2012

			of COX-2 and 5-LOX up to 30%. Reduced COX-2 and 5-LOX expression downregulated VEGF and inhibited neo angiogenesis inside the tumours. Induction of NK activity, activation of macrophages, and inhibition of angiogenesis seem to contribute to the inhibitory mechanism of tumor regression by γ-oryzanol [37].	
8.	Cervical and stomach cancer	In vitro	Exhibited strong inhibition on leukaemia, cervical, and stomach cancer cells [38].	Sep 2012
9.	Colorectal Cancer	In vitro	Inhibition of CRC cell growth [39].	Nov 2013
10.	Breast Cancer	In vitro	Moderate cytotoxicity effect against MCF-7 cells [40].	Jan 2005
11.	Colorectal Cancer	In vitro	Markedly inhibited the growth of LS174T cells [41].	April 2011
12.	Colorectal Cancer	In vitro	Inhibited the proliferation of HT-29 cell line [42].	June 2015

3.2 COLON CANCER

Colon cancer is a type of cancer that develops in the tissues of the colon, which is a key part of the body's digestive system.

The digestive system is responsible for breaking down food to absorb nutrients—such as vitamins, minerals, carbohydrates, fats, proteins, and water—and for eliminating waste from the body. It consists of several organs, including the oesophagus, stomach, small intestine, and large intestine.

The colon, also known as the large bowel, forms the main portion of the large intestine and is approximately 5 feet long. At the end of the colon are the rectum and anal canal, which together are about 6 to 8 inches long. The anal canal ends at the anus, the opening through which waste exits the body.

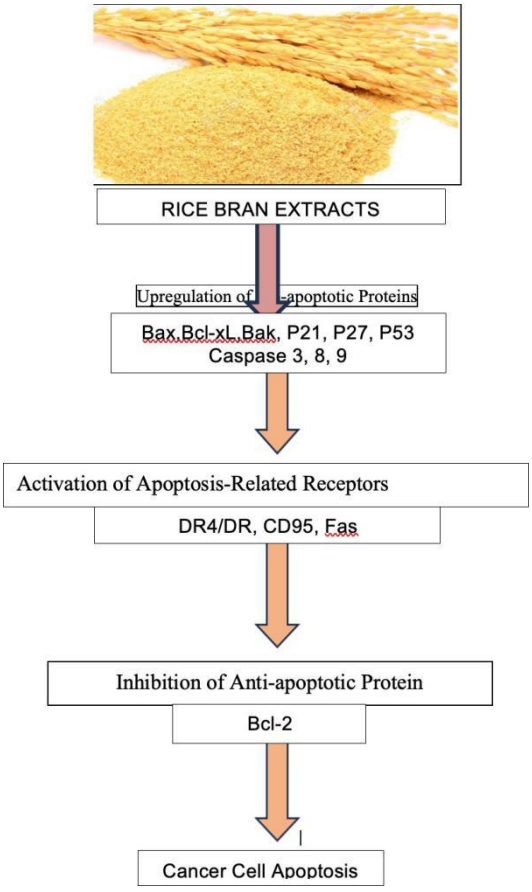
Colon cancer takes years to develop generally it takes around 10 to 15 years for a polyp to convert into a malignant tumor. For this reason, regular screening, detecting, and removing polyps at the early stage is utmost important by the help of which colon cancers can be prevented to a great extent. Current diagnosis can detect only 40% of Colon cancer cases in the early stages, and such type of cancers might recur following surgery and post-surgery treatment

3.3 MECHANISM OF ACTION OF GAMMA ORYZANOL FOR CANCER

Rice bran extracts and fermented rice bran (FRB) promote cancer cell apoptosis which is blocked in case

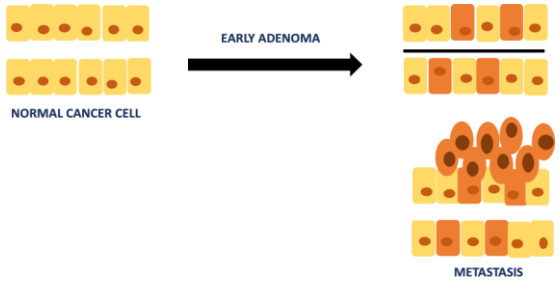
of cancer. Compounds derived from rice bran such as phytic acid, cycloartenyl ferulate, gamma/delta-tocotrienol, and Bio bran as well as fermented rice bran administration have been shown to dramatically induce apoptosis in cancer cells. They achieve this by:

- Upregulating pro-apoptotic proteins such as Bax, Bcl-xL, Bak, P21, P27, P53, and caspases 3/8/9.
- Activating apoptosis-related receptors like DR4/5, CD95, and Fas.
- Inhibiting the expression of anti-apoptotic proteins, particularly Bcl



3.4 EFFECT OF GAMMA ORYZANOL ON COLON CANCER

Colorectal cancer (CRC) or colon cancer is a type of cancer which comprises of colon and/or rectum cancer, represents a significant health problem as the world's third most commonly diagnosed and second most fatal cancer globally [43]. Around 9.4% of cancer-related deaths were due to colon cancer in 2020. However, in view of the significant increase in the number of identified cases in the older population, it is assumed that the incidence of CRC around the globe will more than double by 2035.CRC is a disorder that effects colon or rectum and is caused by the colon's aberrant proliferation of glandular epithelial cells. There are three major types of CRC: Sporadic, hereditary, and colitis-associated. Both environmental and genetic factors determine the risk of developing CRC. In addition, the risk of developing CRC in patients with long-standing ulcerative colitis and Crohn's disease increases with age [44].



Germline abnormalities in genes such as *adenomatous polyposis coli* (APC), DNA mismatch repair genes, *K-Ras*, and *p53* can lead to uncontrolled cell proliferation and contribute to the development and progression of colorectal cancer (CRC), often corresponding to distinct stages in the adenoma–carcinoma sequence [45,46,47]. The mutated genes produce the mutated protein that cannot give the normal cellular response alongside damaged DNA continues to proliferate and accumulates further genetic mutations leading to a malignant phenotype. These cellular changes are not evident at the early stage of Colon cancers. Therefore, early detection of Colon cancer is complex, and this limitation causes a high death rate. Apart from the difficulties in early detection problem, there are also other plenty of issues in diagnosis such as heterogeneous clinical presentations, overlapping symptoms with benign conditions, and limitations in current diagnostic tools.

Numerous studies have been performed to study the role of gamma oryzanol in colon cancer. These researches were done to explore the novel effect of rice extract which is gamma oryzanol rich fraction. And effect of its other ingredients, on bacterial lipopolysaccharide - induced colon cancer metastasis via adhesive and invasive ability as well as gelatinase secretion and activity.

In one of the research projects done in 2012, it was found that Colonic SOD activity and COX-2 expression were improved in group fed with 0.8 % gamma oryzanol rich

diet. Male F344 rats were fed control diet (C group), diets containing 0.8% γ-oryzanol (O group) or 0.8% UM (U group). 1,2-Dimethylhydrazine (DMH) and dextran sodium sulphate (DSS) were used to induce colon carcinogenesis. After 16 weeks, colons were examined for preneoplastic lesions including aberrant crypt foci (ACF) and mucin-depleted foci (MDF). Catalase and superoxide dismutase (SOD) activities in livers and colons, as well as total antioxidant capacity (TAC) in plasma were measured. Colonic expression of cyclooxygenase-2 (COX-2), a pro-inflammatory protein, was also assessed.

4. OTHER THERAPEUTIC POTENTIALS OF GAMMA ORYZANOL

Apart from anti-cancer activity, gamma oryzanol is having plethora of other therapeutic potentials. In recent years, numerous researchers have conducted both *in vitro* and *in vivo* studies to investigate the bioactivities of γ-oryzanol. Many of these studies have demonstrated its potential therapeutic effects in various medical conditions.

4.1 ANTIOXIDANT PROPERTY

The antioxidant properties of γ-oryzanol helps to the regulate the major antioxidant enzymes in the body. Among these enzymes, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase play critical roles in reducing oxidative stress by neutralizing reactive oxygen and nitrogen species. Superoxide dismutase initiates this defence by catalysing the dismutation of superoxide anions into oxygen and hydrogen peroxide (H_2O_2). The resulting H_2O_2 is subsequently converted into water by Catalase and G. The SOD-mimetic activity of γ-oryzanol has been evaluated through its capacity to inhibit pyrogallol autoxidation, a reaction driven by superoxide radicals. Experimental findings show that γ-oryzanol significantly reduces pyrogallol autoxidation, suggesting it exhibits functional properties similar to those of SOD. [48].

4.2 ANTI-OBESITY PROPERTY

The potential health benefits associated with the consumption of rice bran was evident in a study conducted in individuals with metabolic syndrome. Brown rice consumption resulted in decreased body weight, total cholesterol, and LDL-cholesterol level when compared to individuals consuming white rice. However, dietary fibres from rice have a minimal effect on total cholesterol, triglycerides, and free fatty acids blood levels Thus, these effects may be promoted by Oryzanol and Fatty acids, as they showed a significant decrease in the body weight of rodents that were fed diets rich in fat and sugar (Keshun Liu et al., 2016). [49].

4.3 ANTI-INFLAMMATORY ACTIVITY

The anti-inflammatory property of GOZ is due to non-polar structure of cycloartenyl ferulate which is capable of sequestering the immunoglobulin E and inhibit the allergic reaction mediated by mast cell degranulation [50]. The ferulic acid moiety in oryzanol esters contributes to these actions via radical scavenging and anti-inflammatory signalling (Cicero et al. 2020). The presence of inflammation increases the production Reactive oxygen species inside the cell, with the help of mechanism like NADPH oxidase or the mitochondrial electron transport chain [26].Among the transcription factors, nuclear factor-kappa B is involved in the regulation of proinflammatory genes, which represents a key step in the production of proinflammatory cytokines such as tumour necrosis factor-α (TNF-α), IL-1β, IL-6, and IL-8 . The role of Oryzanol in regulating these cytokines had been verified in an experimental model of colitis done previously. Significant reductions in the mRNA expression of TNF-α, IL-1β, IL-6, and cyclooxigenase-2 were observed in mice treated with Oryzanol (Kim SP et al., 2013) [50].

4.4 ANTI DIABETIC PROPERTY

These effects may be explained by the results reported by Son et al., who discovered in his experiment that mice fed a HFD supplemented with either 0.5% gamma oryzanol or 0.5% Ferulic acid exhibited significantly lower blood glucose levels, and (glucose-6-phosphatase) and phosphoenolpyruvate carboxykinase activities, as well as higher glycogen and insulin concentrations, and glucokinase activity. Research suggests that oryzanol prevents Endoplasmic Reticulum stress-induce apoptosis (programmed cell death), and it consequently enhances β-cell insulin production (Yoshino S, Awa R, Miyake Y, et al. 2010) [51].

4.5 IMMUNITY BOOSTING AGENT

Soon Young Shin, et al. 2017 investigated the capability of GOZ to increase immunity response of body. They showed that GOZ extract increased the expression of CD14 and Toll-like receptor 4 and enhanced the phagocytic activity of RAW264.7 macrophages[52].Further we found that S. Sierra MSc , et al. in 2005 conducted an experiment where mice were fed with the diet rich in GOZ for one month and after that they were observed by extracting samples from spleen,

macrophages and lymphocytes. Results showed that T_H1–type cytokines such as IL–2 and B–lymphocyte proliferation was modulated which are responsible to fight against intracellular pathogens. As per the data collected from literature survey, we can say that GOZ can be used as an effective immunomodulator [52].

4.6 CHOLESTROL LOWERING PROPERTY

Increased cholesterol level comes along with complications like Dyslipidemia, Cardiovascular diseases, myocardium infarction, ischemic stroke, and peripheral organ ischemia. Kutcharin Phunikhom, *et al* in 2021 conducted a clinical study on 54 patients with problem of high cholesterol level. This clinical trial was conducted at out-patient Department, Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand. The findings confirmed that consuming GOZ rich diet reduces absorption of both cholesterol and LDL [54]. N Rong , *et al* in 1997 did a experiment on hamsters where he made hamsters hypercholesterolemic by feeding them with high cholesterol diet and GOZ treatment resulted in a significant reduction in plasma total cholesterol [55].

5. PATENTS

Ikeda mohandou kk filed a **patent (JPS5616409A)** in which a pharmaceutical preparation was formed for skin infections. As we all know for preparing a gamma oryzanol formulation we need solvents like acetone, isopropyl alcohol, ethanol which makes it difficult to prepare formulations meant for external use because it causes precipitation of drug. Also give rise to skin irritation with skin stimulation. Hence GOZ is dissolved in different composition consisting of one or two or more solvents selected from the groups like liquid higher alcohol, liquid higher fatty acid, liquid higher fatty acid ester, and liquid higher hydrocarbon, and a solid fatty acid ester.

Another **patent (US 20160243185A1)** was filed by Natarajan et al. to prepare various composition using constituents derived from rice bran and checked their efficacy against LDL , HDL and blood glucose levels.

Tsuno Food Industrial Co Ltd filed a **patent (JP5868330B2)** where they used a two-step alkali-acid treatment that extracts out γ-oryzanol from raw oils into the edible oil fraction, enabling high-yield, flexible, low-cost production of γ-oryzanol-rich edible or cosmetic oils, without external additive use and with regulatory advantages in certain jurisdiction.

5. CONCLUSION

As discussed in this article and supported by a growing number of scientific evidence, γ-oryzanol (GOZ) exhibits a wide spectrum of pharmacological properties that hold significant promise for addressing a variety of human ailments. Its already established roles in nutraceuticals, functional foods, and cosmeceuticals underscore its versatility; while emerging clinical interest has led healthcare professionals to recommend it as a dietary supplement. Although many of γ-oryzanol's therapeutic activities—such as its antioxidant, anti-inflammatory, lipid-lowering, and anti-diabetic effects—have been well characterized, several unique biological properties remain under investigation. Notably, advancements in formulation design (e.g., nano emulsions, liposomal carriers, and biopolymer matrices) are being developed to enhance its bioavailability, stability, and targeted delivery.

Most Importantly, γ-oryzanol is a naturally derived phytochemical, which is witnessed by low toxicity and minimal adverse effects, especially when compared to synthetic pharmaceutical agents. Its biocompatibility and eco-friendliness make it a unique compound for long-term therapeutic use and for incorporation into sustainable pharmaceutical platforms. In oncology research, GOZ is being explored as a potential alternative to conventional chemotherapeutic agents, which are often costly and associated with severe side effects. Its ability to promote site-specific drug delivery, while maintaining affordability and safety, may offer a valuable breakthrough in cancer therapeutics.

From promising in vitro findings and preclinical models to emerging real-world applications, it is evident that γ-oryzanol has a long and promising journey ahead in both medical and pharmaceutical sciences. Continued research, formulation innovation, and clinical validation will be critical to fully harness the therapeutic potential of this unique, naturally derived compound.

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