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Review Article

A Rigorous Analysis of the Pharmacological Properties, Extraction, Stabilization Method, and Nutritional Content of Wheat Germ Oil

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Abstract

Wheat Germ Oil (WGO) is a potent herbal product. The major derivative of WGO extraction is defatted (the fat was removed during extraction) germ meal that is rich in albumin, globulin, and a rational profile of amino acids. It has many minerals like magnesium, potassium, calcium, manganese, and zinc, has a high nutritional value, and is used as a nutraceutical. The most abundant phytoconstituent in wheat germ oil is linoleic acid. It has a wide range of pharmacological actions, like potential antioxidant properties, reproductive activity, anti-inflammatory, neurodegenerative, and anti-cancer properties because vitamin E and antioxidants act as protective agents against toxicity. The stability of oil was the major issue for its acceptability in the market, but now different microencapsulation techniques should be widely used to increase the shelf life of oil and improve its use in cosmetics, dietary supplements, and pharmaceuticals. For the stability of the oil, different microencapsulation techniques should be widely used to increase the shelf life.

Keywords: Wheat germ oil; Pharmacological property; Pharmacological action; Bioactive compound; extraction method; Nutraceuticals; Phytoconstituent

Abbreviations

WGO: Wheat Germ Oil; PUFA: Poly Unsaturated Fatty Acid; DIAAS: Digestable Indispensable Amino Acid Score; DM: Decimeter; FO: Fish Oil; STZ: Streptozocin; FSH: Follicular Stimulating Hormone; LH: Luteinizing Hormone; AMH: Anti Mullerian Hormone; E2: Estradiol; GSH-Glutathione; MDA: Malondialdehyde; CAT: Catalase; GST: Glutathione S-Transferase; SOD: Superdioxide Dismutase; GSSG: Oxidized Glutathione; ROS-Reactive Oxygen Species; PGB: Pregabalin; TNF: Tumor Necrosis Factor; MCF: Michigan Cancer Foundation; G6PD: Glucose 6 Phosphate Dehydrogenase; PCNA: Proliferating Cell Nuclear Antigen; UV-B: Ultraviolet; Nrf2: Nuclear Factor Erythroid2-releated Factor 2; BCL-2: B-cell Lymphoma2; ALT: Alanine Transaminase; ALP: Alkaline phosphate; VLDL: Very Low-density Lipoprotein, HDL: High Density Lipoprotein; CVD: Central Vascular Disease; IBS: Inflammatory Bowel System; CNS: Central Nervous System

Practical Application

Wheat germ oil is believed to be an efficacious health nutrient widely used in nutraceuticals as well as therapeutic agents to treat and control abnormal diseases by showing pharmacological properties through good bioactive compounds and phytoconstituents. Because of their antioxidant properties, PUFA and octasonol have demonstrated a variety of biological activities. This assessment aims to examine the use of WGO in various disorders, different extraction approaches, and its chemical constituent. It will be helpful in the field of medication to have different effective constituents for numerous ailments.

Introduction

The demand for vegetable oils is increasing year after year due to increased awareness of herbals and oils because of their economic availability, and they also cure many diseases because they are used in various fields such as nutraceuticals, feedstock for industrial polymers, and many other industrial products. Thus, the demand for vegetable oils is rising even more rapidly every year [1]. Wheat, one of the primogenital foods with 652 million metric tonnes of worldwide production, is a major food intake and an essential commodity for third-world populations around the globe [2]. Wheat grain constituents are divided into bran (13% to 17%), endosperm (80% to 85%), and germ (2% to 3%) [3]. The primary source of energy during germination is the embryo of wheat grain. During the milling process, the germ portion separates grain from grain [4]. Wheat germ is enriched in macronutrients like lipids, and protein-peptide carbohydrates, as well as other constituents that show major health benefits. There are carotenoids, tocopherols, saponins, flavonoids, phytosterols, thiamin, niacin, phenolics, -aminobutyric acid (GABA), thiamin, riboflavin, and quinones, as well as anti-nutritional factors such as raffinose and phytic acid [5]. Good contents of essential amino acids like lysine, threonine, and methionine [6]. WGO has potent protective activity because of its antioxidant properties, as it has a high number of fat-soluble carotenoids, particularly lutein, beta-

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carotene, and zeaxanthin, which have high antioxidant properties [7]. Despite its advantages and importance, WGO is susceptible to oxidation because of the high amount of linoleic acid, and color intensity is affected. It is also unstable during storage conditions and has unfavorable baking properties, so during milling, the germ is removed from the endosperm and is mainly used for oil production and fodder [6,7]. WGO has different extraction processes like commercial hexane extraction, pressurized solvent extraction, supercritical CO_2 extraction, cold pressing, ethyl acetate extraction, and aqueous enzyme extraction. The content of bioactive compounds depends on different extraction processes. WGO, due to its potent bioactive compound and chemical constituent, is used in many life-threatening diseases like cancer, diabetes, hypertension, parasitic disease, atherosclerosis, ulcers, inflammation, wound healing, acute radiation injury, reproductive activity, vitamin E and D deficiency, muscular dystrophy, microbial infection, neurodegenerative disease like Alzheimer's and Parkinson's, hepatosteatosis and dyslipidemia, hepatotoxicity, and a protective role in hepatorenal toxicity, nephrotoxicity [8]. The description's information was compiled by merging numerous research papers and review articles from multiple sources, including Elsevier, Hindawi, Research Gate, the NCBI [National Centre for Biotechnology Information], and from 1981 to 2021.

Chemical Constituents

Essential oils show different activities because of their different chemical constituents. WGO is an admirable source of vitamin E and PUFA. The major component that WGO shows is a wide variety of sterols. 4-methyl sterols, triterpenoid alcohols, -sitosterol, and campesterol are all plant sterols [9]. Linoleic acid is the most abundant WGO fatty acid, accounting for 42% to 59% of total triglyceride content, followed by oleic acid (18:1) and palmitic acid (16:0). [10] A long-chain aliphatic alcohol, octacosanol [HO-CH2-(CH2)26CH3], with 67% content, shows much pharmacological activity [11]. WGO has a peroxide value of 20 me/kg [12]. Phosphorus (389.5), potassium (1567.6), and zinc are all present, as are good sources of essential amino acids with a high protein content (35.81 g per 100 g of protein) [13]. Wheat germ contains little glutamine and proline, but plenty of lysine, glycine, arginine, alanine, and threonine. The protein content is 36.5 percent, and the essential amino acids range from 33.3 g/kg DM (arginine) to 3.01 g/kg DM (tryptophan). Lysine content is 22.8 g/kg, and leucine content is 22.8 g/kg DM. The DIAAS value of wheat germ is 93% isoleucine and 82 % (leucine [14,15]). WGO carbohydrate content included 14.9 lipids, 4.8% fructose, 57.6% raffinose, 16.8% total sugars, 37.6% sucrose, and a small amount of glucose. WGO has a 10% to 15% content of lipids, 26% to 35% of proteins, 1.5% to 4.5% of fiber, and contains 4% minerals: phytosterols (24-50 mg/kg), policosanols (10 mg/kg), carotenoids (4 mg/kg-38 mg/kg), riboflavin (6 mg/kg-10 mg/kg), and thiamin (15 mg/kg-23 mg/kg). Contains 11% oil hydrolytic lipase enzyme. Wheat germ has various beneficial effects due to benzoquinones; the contents of 2-methoxy benzoquinone and 2,6-dimethoxy benzoquinone in oil vary from 10% to 15%, depending upon the variety, extraction method, and purity. Different extraction methods show different percentages of oil content and purity values [16]. The chemical structure of different bioactive is shown in Table 1.

Different chemical constituent of wheat germ oil which contain different phytoconstituent which areVitamin E, Asparticacid, arginine, policosonal, glutamic acid, valine, glycine, phenlalinine, leucine and isoleucine, β-carotene, Raffinose, Glucose, Fructose, Oleic acid, Linoelic acid, Thiamine, Riboflavin. Palmitic acid Octacosanol, primarily obtained from sugarcane, is the main active component of WGO and is mainly used to improve exercise performance by acting as an ergogenic supplement and delaying fatigue by increasing the immobilization of free fatty acids within muscle from the fat cell [17]. When dosed at 20 mg/kg, inhibiting thromboxane A2 reduced platelet aggregation to the same extent as 100 mg/kg aspirin [18]. Vitamin E is abundant in WGO oil and increases the vitamin E content in the whole body. A deficiency of vitamin E changes the intensity of lipid peroxidation [19], and improves the antioxidant defense mechanism. Polyunsaturated fatty acids, also present in high abundance in WGO, decrease arachidonic acid-derived eicosanoids, which have major anti-inflammatory action [20], as inflammation damages blood vessels, leading to heart disease. Omega-3 PUFA prevents cardiovascular disease by decreasing triglycerides [21]. Different constituent which has pharmacological properties reported are mentioned in above table which shows these constituents reused to treat different diseases.

Extraction Methods

There is various extraction methods used for extracting WGO, like commercial hexane, pressurized solvent extraction, supercritical CO_2 extraction, cold press, and ethyl acetate extraction shown in Figure 1. Every extraction method has its advantages and disadvantages. The traditional n-hexane extraction process was used, but because n-hexane is inflammable and causes pollution, the new method of supercritical CO_2 extraction is widely used as it is nontoxic, nonflammable, nonhazardous, less expensive, and can be easily separated from the extracts [22-24].

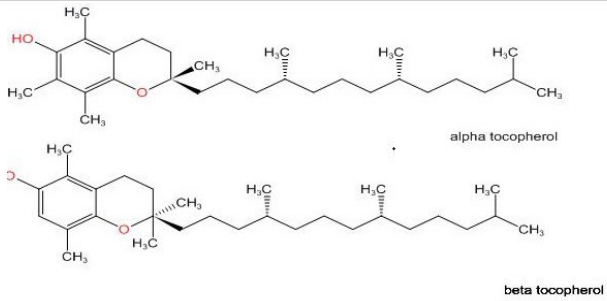
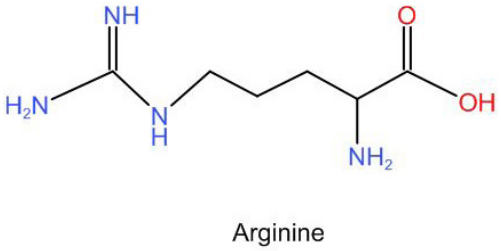
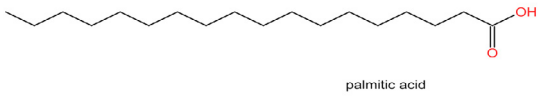
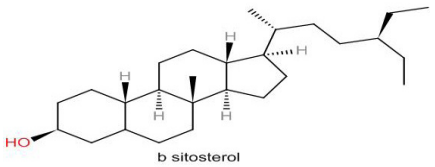
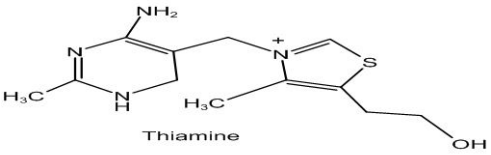
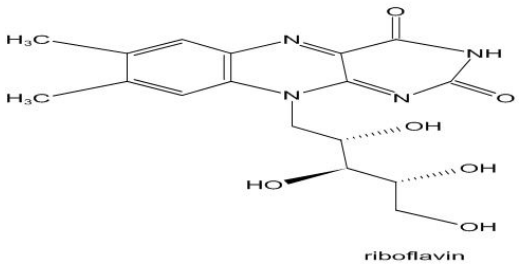
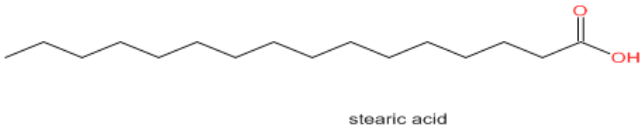
Extraction by commercial hexane

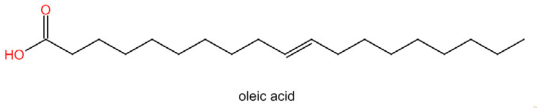
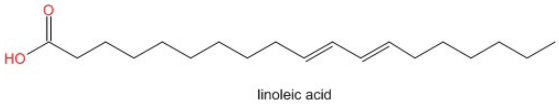
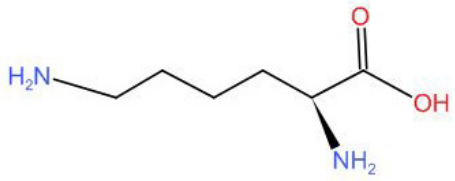
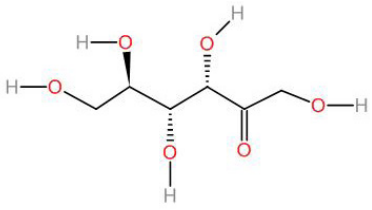
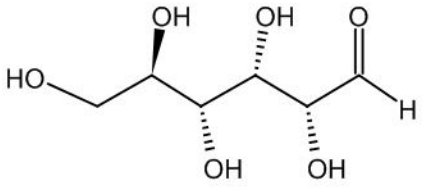
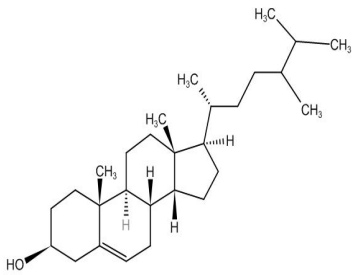
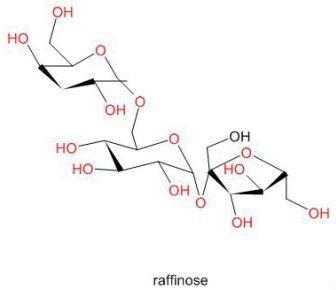
It is widely accepted that for oil extraction from seeds containing 6% to 8% oil content, which are difficult to press, the common solvent hexane was used. This extraction process was conducted with about 400 g of wheat germ [25]. The extraction is done at a different ratio at room temperature; at 250 rpm, the solid-solvent combination was stirred mechanically for 120 min, then the miscella was filtered and the solvent evaporated. The oil extracted is weighed, and the recovery of oil is estimated. The study also shows that the oil that was recovered by this process did not show any effect when the extraction mixture was heated throughout the extraction process and during the storage period, which led to the development of peroxides and free acids [26].

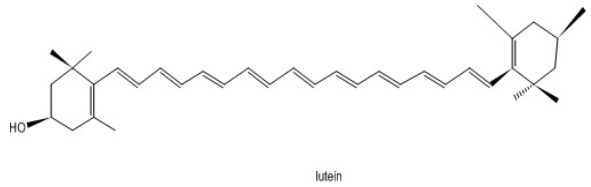
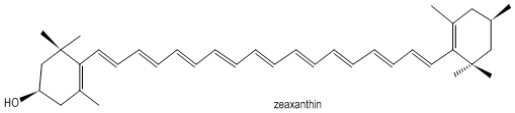
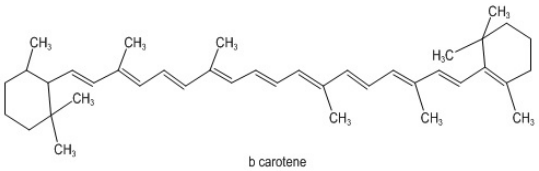
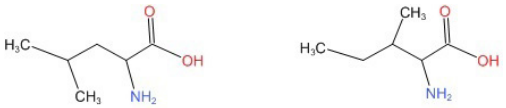
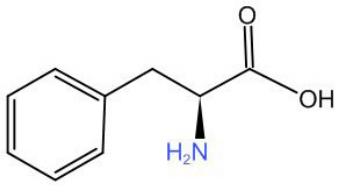
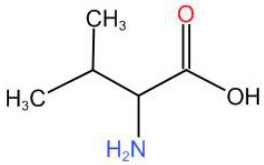
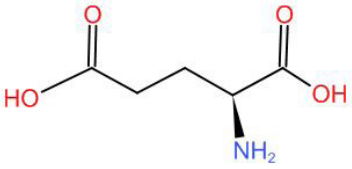
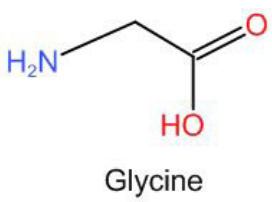
Supercritical CO_2 extraction

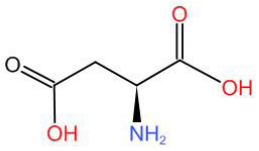
Because it is non-corrosive, non-inflammable, and has a high purity (about 99%), supercritical CO_2 is widely used in pharmaceuticals. It also has the property of having a low critical temperature without degrading the solvent [27]. Extraction can be performed in a laboratory setting with a 400 cm^3 to 450 cm^3 extraction vessel and two centrifuge containers of 300 cm^3 and 200 cm^3 linked in a uniform sequence. This process is carried out at 40°C and 250°C pressure in the extraction vessel [28]. In 1985, an extraction procedure was conducted at 73 atm pressure and 31.1°C critical temperature, which made it easy to grip CO_2 as a solvent, and removing CO_2 from any solute with supercritical CO_2 showed more tocopherol extraction than another extraction method [29]. It was determined in 2000 that temperatures of 40°C and pressures of 150 psi provided the best conditions for oil extraction. Eliminated the solvent distillation phase [30]. In 2002, it was stated that when extraction was done by supercritical CO_2, the content of a-tocopherol was significantly higher than the extraction method of solvent chloroform/methanol [31] and the fatty acid content remained unchanged from that of n-hexane

Table 1: Structure of different chemical constituents of Wheat germ oil.

Vitamin E [alpha and beta tocopherol]	
Arginine	
Polcosonal	
Palmitic Acid	
B Sitosterol	
Thiamine	
Riboflavin	
Stearic acid	

Oleic Acid	 oleic acid
Linoleic Acid	 linoleic acid
Lysine	 lysine
Fructose	 fructose
Glucose	 glucose
Campesterol	 campesterol
Raffinose	 raffinose

Leutin	 lutein
Zeaxanthin	 zeaxanthin
B-Carotene	 b carotene
Leucine and Isoleucine	 leucine and isoleucine
Phenylalanine	 phenylalanine
Valine	 Valine
Glutamic Acid	
Glycine	 Glycine

Aspartic Acid	 aspartic acid

[32]. A 2006 study discovered that extracted petroleum ether oil had the highest value of fatty acids and tocopherol [33,34].

Aqueous enzymatic oil extraction

The hydro-enzymatic oil extraction method is an extraction process that is both environment-friendly and authentic. The extraction process decreases the energy and price requirements while stimulating health responsibility and improving the nutritional content of oil [35].The basic steps are grinding (wet or dry), mixing the comminated material with an aqueous solution, incubation with enzymes, separation of the liquid and solid phases by centrifugation or filtration, and recovery of oil from the liquid phase [36]. Emulsified oil, free oil, and oil are three forms that are produced by this method in the skin [37]. Extraction was performed in 2011AEE using a multienzyme preparation at 48, 49, and 6 hours. The content of free fatty acids was high when compared to organic solvent extraction, oxidative stability was higher, and the tocopherol content and peroxide value were lower. The yield and quality of oil are increasing [38].In 2014, the yield of oil increased when the content of moisture in oil was reduced in the oven for 4 min and pretreated at 180°C [35], by the enzyme (*Bacillus licheniformis*. At pH 8, the highest free oil yield (64%) was obtained [39].

Cold press (hydraulic press)

The cold press technique to obtain WGO is a very simple and easy-to-perform process in which, without heating and under a hydraulic press, the wheat germ flakes are pressurized [40]. WGO was attained by the cold press extraction process in the medicinal and chemistry industries in a hermetically closed container below the nitrogen atmosphere [41]. A study was conducted, and it showed that extraction by the cold press was approved at a power of 1.1-4 kW. A comparison of cold pressing and supercritical CO_2 found that the fatty acid content was nearly identical and the tocopherol content was higher (1.27 mg/g) than that 0.79 mg/g [28]. In 2021, it was determined that the cold-pressed oil extraction process contained the highest levels of linolenic acid, octacosanol, oleic acid, and sitosterol, all of which have potent ani-cyclooxygenase activity [42].

Ethyl acetate extraction

The wheat germ was assorted with Ottawa sand and positioned in about 11 mL of cells. The cells were then tapped off with Ottawa sand, and further extraction was done with the solvent ethyl acetate. The following parameters were used for accelerated solvent extraction: 1000 psi, temperature 100°C, preheated time of 0 minutes, heated time of 5 minutes, static time of 10 minutes, static cycle 3, flush volume 100% (11 ml cell), and purge time of about 1 minute [43].

Accelerated pressurized solvent extraction

Accelerated pressurized Solvent Extraction (ASE) was developed in 2002 to investigate the extraction of WGO at high pressure and high temperature (200°C and 1500 psi fixed), which increased the rate of extraction even though increased pressure avoided boiling at those temperatures and reduced solvent consumption compared to other extraction techniques.

Wheat Germ Oil as a Nutraceuticals

Nutraceuticals, widely used in today's population, are a combination of nutritive and pharmaceutical products that provide health benefits in the daily diet or in the prevention or treatment of diseases. Nutraceuticals, which have no side effects, are gaining popularity due to their potential health benefits in vitamin deficiency treatment and as health supplements [44,45]. It is used in various formulations as a nutraceutical and cosmetic anti-aging cream and as a face serum because its vitamins and high-quality fatty acids repair the skin and restore an even tone because of vitamin E's antioxidant properties and PUFA WGO's properties as a PUFA [46]. Soaps and shampoos with a high content of linolenic acid nourish and condition hair by combining other essential oils with cationic surfactants, showing innovative products for both scalp and shaft hair damage repair [47,48].Supplement tablets are an essential oil also used in perfumes. Exercise endurance was high and systolic because octasonal is a dietary supplement. Blood pressure is low [49]. Performance swimming in rats was also increased [50], as a supplement, it also increases the volume of semen, spermatozoa concentration, and motility of spermatozoa in bulls (Table 2).

Pharmacological Properties

Wheat germ oil shows different pharmacological actions because of the constituents present in this plant shown in Figure 2.

Reproductive activity

In 2016, a study was done to see the protective result of a combination of FO and WGO, which was given orally for 3 weeks with 100 mg WGO and 1000 mg FO in hyperglycemia-induced female albino rats with ovarian dysfunction. Hyperglycemia was introduced by an I.P. of 65 mg/kg (STZ). Antioxidant activity was assessed by reducing and measuring Glutathione (GSH) levels and Malondialdehyde (MDA), the GSH: oxidized glutathione (GSSG) ratio, and Superoxide Dismutase (SOD) and Catalase (CAT) activities. The combined supplement increased the levels of FSH, LH, E2, and AMH and the count of follicles. Additionally, MDA was decreased, which indicates that FO-WGO supplementation maintained ovarian function in STZ-induced diabetic rats and enhanced the defense mechanisms of antioxidants in rat ovaries, as shown in Figure 3 [51]. Another study in 2019 was conducted and showed that, because of SRT, there was a testicular injury in albino rats. It was reported that SRT-induced damage to reproductive organs was due to oxidative stress and ROS generation. The disruption between the generation and removal of ROS causes injury to the cell with a decreased level of GSH and lipid peroxidation. WGO, because of its abundant constituents of ALA, sterol tocopherols (vitamin E), and policosanols, has a very beneficial role in the treatment and protection of diseases with oxidatively damaging effects *via* cell defense from free radicals. As a result, the current study aimed to evaluate the potential defensive

Table 2: Constituent of wheat germ oil used in different disorder.

Constituent Of Wheat Germ oil	Use
Tocopherol (Alpha and Beta B-Sterol+ Vitamin E Reduce ageing, Reduce plasma and liver cholesterol	Antiprotective, Stable
Fatty Acid (Linoleic Acid)	Reduces Oxidative Stress and Mild Hypercholesteremia
Octasonal	Reduces Obesity, Antifatigue, Cryoprotective, and Cardiac disease Cholesterol lowering, platelet aggregation, antiprotective
Vitamin E	Prevent hair loss and Improve blood circulation
Other Nutrients (A, B) Iron, zinc, K	Used in nutraceuticals
Omega 3 and Omega-6 [PUFA]	Lower inflammation, cholesterol, and support the nervous system
-Sterol+ Vitamin E	Reduce aging, Reduce plasma and liver cholesterol

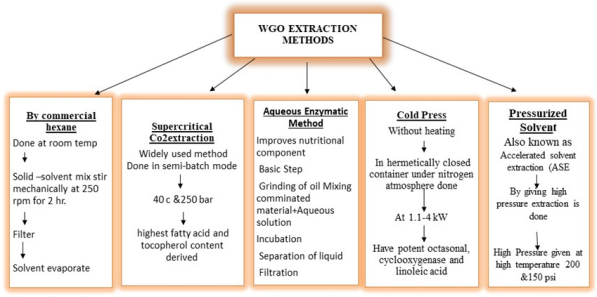


Figure 1: Different Extraction method of wheat germ oil commercial hexane, aqueous enzymatic, cold press, pressurized solvent, cold press.

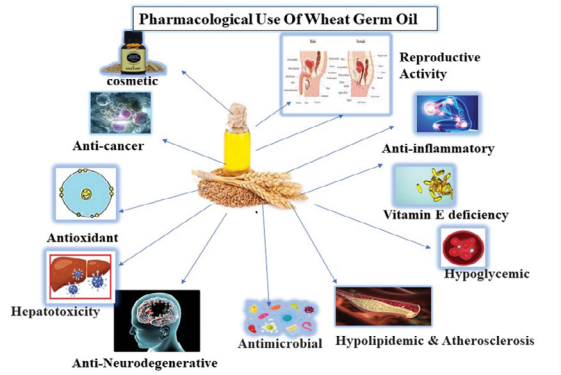


Figure 2: Different pharmacological properties of wheat germ oil use to treat different disorder like Parkinson, alzhmeir, hypertension, immunodefecicency, liverdamage, inflammation, potent antioxidant, cholesterol, diabetes.

role of WGO against sertraline-induced reproductive system damage in rats due to its antioxidant activity [31]. Glutathione content and catalase activity were decreased in the testicular tissue of sertraline-administered rats. The serum testosterone level was elevated. WGO improved antioxidant defenses by reducing lipid peroxidation in testicular tissue. Orgasmic, impotent, and decreased libido are the most common SSRI side effects, all of which are reproductive dysfunctions [52]. A study was conducted to examine the harmful effect of the epileptic drug pregabalin on the body weight of the animal and reproductive function, and the ameliorative effect of WGO was evaluated by giving the WGO at 1.5 mL/kg by gastric gavage. PGB affected male rats' reproduction by inhibiting spermatogenesis and reducing testosterone levels. In females, reproductive toxicity was triggered when pituitary steroids were lowered, gonadal hormones were raised, and the atretic ovarian follicle count was increased. It has a protective role because of its antioxidant properties, and it also increases weight loss and can be used in the long term [53]. In 2021, a study was conducted to study the protective effect of WGO on diabetes mellitus-induced erectile and sexual dysfunction at 3 mg/ml and 6 mg/ml by oral gavage for 35 days. A daily beneficial effect appeared at higher doses, with an observed increase in the parameter of oxidative stress. These observations suggest that antioxidant property has no effect on the improvement of vascular or erectile function, and more experiments and research are needed to be conducted to know the mechanism [54].

Neurodegenerative disease

Uncontrolled (DM) shows damage in neurons that was caused by increasing the level of intracellular glucose. Natural products like WGO and FO as supportive therapy can decrease neuronal problems. According to the findings, the main mechanisms of FO and WGO co-supplementation in STZ-diabetic rats were anti-inflammatory and antioxidant. They could correct the cholinergic function by decreasing Ache activity, restoring ACh levels in brain synapses, and rebuilding the cognitive deficiency. Thus, this combination, when combined with other medications, is an effective therapy, as shown in Figure 3 [55]. Due to its antioxidant and anticholinesterase activities, WGO (180 mg/kg) increased the level of GSH, decreased activity of cholinesterase, and increased the content of TNF- in the brains of scopolamine-induced amnesic rats [56].

Anticancer activity

In 2015, a study was conducted to see the potential biological effect of Black Cumin Seed Oil (BCSO) and Wheat Germ Oil (WGO) on different cell lines by microscopic observation of the protective effect against ROS in NIH-3T3 cell, phenolic content, and antioxidant activity of each oil was detected. Apoptotic and necrotic rates were investigated with help of flow cytometry [57]. Another study published in 2019 examined the effect of WGO on human breast cancer cells MCF-7, which demonstrated anticancer and ant proliferative activity attributed to its constituent high tocopherol, by reducing cell viability and inducing cell death in cancer cells. In conclusion, this study showed that WGO in MCF-7 has an anticancer effect [58]. In 2019, anticancer activities of bioactive peptides from wheat germ protein hydrolysates were studied, and hydrolysates of wheat germ protein prepared with Alcalase, pepsin, or proteinase K had significant antioxidant activities and the potential to reduce A549 cell viability in a concentration-dependent manner. Peptides with the highest activities were cytotoxic [59]. Chemometric studies of WGO germ plants can be determined for studying anticancer properties, as this study in man plants was done in 2020 and showed significant results [60]. A recent study in 2022 was conducted and evaluated the possible protective role of Vitamin E, (WGO), (WGP) against environmental induced carcinogen 7,12-dimethylbenzanthracene (DMBA) breast cancer in Sprague Dawley albino rats [61]. Reduced PCNA expression was used to observe movements in tumour cell proliferation (mammary carcinoma) and ant proliferative properties. Vitamin E was given to DMBA rats along with WGO and WGP

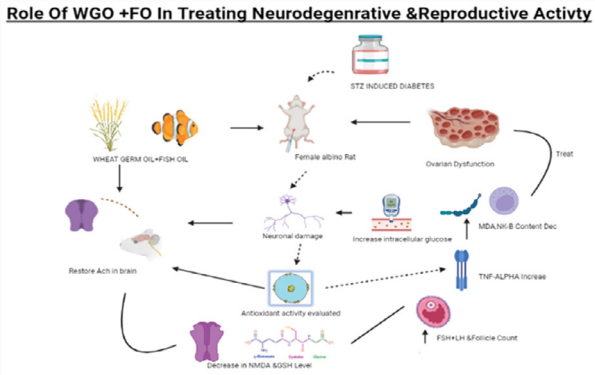


Figure 3: Mechanism of action of FO and WGO in treating neurodegenerative disease and improving reproductivity activity in diabetes induced female albino rat by evaluating antioxidant activity the ach level in rat was restored, decrease in NMDA level increase the FSH, LH count ad treat ovarian dysfunction b dec MDA, NK-B content.

and demonstrated good anti-protective activity as reduced PCNA expression was used to observe movement in tumour cell proliferation (mammary carcinoma) and anti-proliferative properties. The main role is played by cell proliferation and observing the constituents used in the inhibition of breast cancer [62]. By suppressing cell proliferation, WGO encourages the apoptosis of cancer cells. Furthermore, WGO, Vit E, and WGP contain an antioxidant enzyme that inhibits the effect by scavenging free radicals, lowering oxidative damage, and inhibiting the development of [63]. Oleic acid and linoleoyl chloride can be given with WGO, as they both can generate apoptosis by inhibiting the proliferation of cancer cell lines. Thus, when combined with WGP and Vit E, WGO is beneficial, acting as a protective agent against oxidative stress and lipid peroxidation, and lowering the risk of breast cancer [64-66]. As this study was conducted in the man plant in 2020 and yielded significant results [60], Chemometric studies of the WGO germ plant can be determined for investigating anticancer properties.

Improved vitamin D deficiency

In 2022 a study was conducted which showed that UV-B exposed WGO 23.7 µg showed improved vitamin d in animals by increasing the circulation of ergocalciferol after 3 weeks and 6 weeks of administration but did not have much effect on the total serum level of ergocalciferol [67].

Antioxidant protection in tissue

Wheat germ oil is the richest in vitamin E (tocopherol). This linolenic-rich PUFA from an experimental plant, wheat germ, has abundant vitamin E (tocopherol) [68]. WGO inhibited rapeseed oil oxidation due to unsaponifiable matter isolated from WGO [69]. Another study found that WGO administration changed the strength of lipid peroxidation in animal tissues [70].

Gastroprotective effect

In 2022, a study was conducted that showed a good gastroprotective effect against gastric ulcers that were induced by ethanol. They prevented ulceration of gastric damage induced by ethanol by reducing the index of the gastric ulcer, nitric oxide, and malondialdehyde levels in the stomach, showing the same effect as omeprazole. WGO increased the expression of Nrf2, Bcl2, HO-1, and antioxidants. WGO had anti-inflammatory effects by inhibiting TNF-, IL-1, and 10. In inference, WGO reduced the toxicity of the stomach, which was shown by chemical ethanol, by affecting variable genes that are involved in inflammation, oxidative stress, and apoptotic pathways [42].

Anti -inflammatory

A study conducted in 2021 showed WGO contains abundant amounts of vitamin E, omega-3 fatty acids, and sterols that show anti-inflammatory properties. Cold-pressed oil extraction contained the highest levels of -sitosterol, -linolenic acid, octacosanol, and trypsin inhibitors, all of which are powerful bioactive compounds for inflammatory disease [42]. In 2017, the study showed the anti-inflammatory properties of WGO on RAW 264.7 The croton-oil-induced edema in the ears of the mouse was reduced by WGO cells by modulating the JNK/ERK MAPK and NF-κB signaling pathways. Inhibiting cyclooxygenase-2 (NF-B) inhibited nitric oxide secretion, which inhibited the production of LPS-induced NO, and pro-inflammatory cytokines (IL-6, TNF, and IL-1) reduced the expression of phosphorylated ERK [71].

Nephrotoxic effect

In 2021, a WGO nanoemulsion formulation will use lecithin-layered WGO Nanoemulsion (WGOL-NE) or Triton X-layered WGO Nanoemulsion (WGOT-NE) to reduce the nephrotoxic effect of cisplatin. The major side effect shown by Cisplatin is nephrotoxicity, which causes apoptosis, oxidative stress, and inflammation. WGO contains Fatty Acids (FA) like linoleic acid, -linolenic acid, and oleic acid; policosanol and Octacosanol have anti-inflammatory antioxidant properties that reduce inflammation, oxidative stress, and cell death by decreasing caspase-3 levels as well as urea and creatinine levels [72]. A 2018 study with WGO and vitamin E found that when rats were given gentamycin, they had significantly lower BCL-2/BAX ratios, MDA, increased catalase activity, and total antioxidant capacity. Wheat origin showed improvements in the function of the kidneys of rats as measured by urea, serum creatinine, potassium, and sodium levels [73].

Hepatosteatosis and dyslipidemia

WGO supplementation improved hematocrit and haemoglobin concentrations and normalized the altered lipid profiles by normalising fatty acid synthase and hydroxymethylglutaryl CoA reductase mRNA expression. Research on WGO protected rats against sucrose-induced dyslipidemia and hepatosteatosis by monitoring Chol estrogenic in addition to lipogenic gene expressions, indicating that WGO is a favourable mediator against sucrose-induced dyslipidemia and hepatosteatosis [74].

Hepatorenal toxicity

In 2017, potassium bromate hepatorenal toxicity was reduced by orally administering WGO at various levels of dose for 4 weeks of treatment, showing a decrease in serum amounts of (Cr), blood urea nitrogen, and enzymes present in the liver such as (ALP, ALT, ALT). WGO, because of its natural antioxidant properties, excellent source of vitamin E with tocopherol, reduces the damage to the liver, and provides greater antioxidant protection when wheat germ and WGO are given in the diet [68].

Muscular hypertrophy

In 2008, a study investigated that WGO has a potent role in increasing the muscle strength in gamma radiation skeletal damage in rats when administered orally for 14 days through oral gavage, resulting in oxidative stress by increasing quantities of (TBARS) with

decreasing levels attributed to glutathione (GSH), SOD, and G6PD. Moreover, total levels of iron, copper, and calcium improved in muscles and maintained skeletal muscle integrity by having vitamin E, linoleic acid, and octacosanol, which are beneficial in neutralizing free oxygen radicals [75].

Acute radiation damage

In 2011, the combined effect of Ginseng and WGO demonstrated a prophylactic role against radiation injury when WGO was administered orally at 80 mg/kg B.W. by reducing oxidative damage, it reduced high-level serum signs of liver impairment as Alanine Transaminase (ALAT), Aspartate Aminotransferase (ASAT), ammonia, and butyrylcholinesterase were associated with a decrease in serum total protein and thiobarbiturate. When the comparison is done with irradiated rats, the combined treatment significantly showed no toxicity, rapid improvement, and less severe damage in all the measured parameters. A study was conducted to study the effectiveness of WGO, on radiation-induced oxidative damage in rats' liver and skeletal muscle. Exposure to radiation causes oxidative stress and damages muscle and liver tissues. The outcomes showed that oxidative stress was induced in skeletal muscle and liver when whole-body exposure to gamma radiation was induced by an increase in the quantity of (TBARS) xanthine oxidase linked. Exposed rats showed declines in creatine phosphokinase, glutamate dehydrogenase, and lactate dehydrogenase activities, whereas lactate dehydrogenase quantity was amplified. In skeletal muscle and liver, the content of total calcium, copper, and iron was increased in the irritated rat when compared with the control. Rats treated with WGO orally at different dosages for 4 weeks showed good improvement and less severe damage in all the parameters that were measured. It was determined that WGO preserves liver and skeletal muscle integrity by reducing the severity of oxidative stress caused by radiation and neutralising free radicals *via* vitamin E, linolenic acid, and Octacosanol [76].

Hypoglycemic activity

When combined with Aloe vera and *Coriandrum sativum*, the polyherbal composition of WGO demonstrated blood-glucose-lowering activity. This was studied in diabetic rats, in which alloxan was induced after administration at dosages of 2.0 ml/kg and 1.0 ml/kg orally. Serum plasma glucose was estimated by the POD/GOD (glucose peroxidase and glucose oxidase) method. The polyherbal preparation produced a significant drop in the serum glucose level of diabetic rats in the 30-day study when compared with control and glibenclamide [77,78]. WGO (1.5 ml/kgBW/day orally) has an ameliorative effect on sucrose-induced hepatosteatosis and hyperglycemia. It also induced low glucose levels by increasing the expression of mRNA pyruvate kinase and reducing the expression of mRNA pyruvate carboxylase, and it reestablished the analysis of hepatic tissue [74]. Wheat germ in the diet is also helpful in lowering blood sugar levels in diabetic patients [79].

Alleviating abnormalities in infants

A study found that aspirin, a major nonsteroidal anti-inflammatory drug, administered during pregnancy increased the risk of organogenesis abnormalities, so WGO was orally administered at a dose of 250 mg/kg to see if it had a protective role by reducing free radicals like malondialdehyde and alkaline phosphate. The total protein content returned to normal, fetal mortality was reduced, and its antioxidant properties were beneficial [80].

Wound dressing

In 2021, a WGO hydrogel created by combining textile and polymer layers and cross-linking poly (ethylene glycol) Sodium Alginate (SA) with diglyceryl ether (PEGDGE) demonstrated wound healing and increased NIH/3T3 cell proliferation by 1% [81].

Hepatotoxicity

Cyclosporine, a major immunosuppressive drug, causes hepatotoxicity by increasing the levels of liver serum enzymes (ALT and AST), increasing NF-B expression, and increasing lipid peroxidation. When WGO was given orally through gavage for 21 days, liver toxicity was reduced, and by inhibiting ROS and iNOS (Akool 2015), liver toxicity was reduced.

Hypolipidemia and atherosclerosis

WGO contains nearly 273 mg/100 gm (62% PUFA) tocopherols and carotenoids, indicating that it has the potential ability to lower cholesterol in rabbits, as dietary saturated fat raises cholesterol and polyunsaturated fatty acids lower cholesterol [82] and inactivate acyl transferase and antioxidant properties (vitamin E) demonstrated potent hypercholesterolemia potential [83,84] showed a decrease in the level of LDL, total cholesterol, VLDL, and HDL content, increased HDL content, and a reduction in malondialdehyde production in plasma [85]. The presence of too many fatty acids in the composition lowers triglyceride and fibrinogen levels in the liver [86]. So it was concluded that the presence of vitamin E and the reduction of monoaldehyde are the reasons for the lowering effect of triglycerides [87,88]. It also increases enzyme activity like CAT, GST, and SOD [89]. Policosanol, a major bioactive compound with the ability to alter serum concentration and hepatic mobility, was shown to be a better drug than the statin-marketed product in 1999, as policosanol has the same pathway as statin but inhibits 3-hydroxy-3-menthyl glutarate one step earlier than statin [90,91]. Another study found that when WGO was administered orally for 60 days, serum total cholesterol was reduced by more than 90%, and triglycerides were reduced by 44%. VLDL-C was 53% and LDL-C was >95% when hyperlipidemia was induced orally in rabbits [92]. In 2021, it was evaluated and concluded that WGO controlled hyperlipidemia by protecting the body against oxidative stress and reducing expansion in addition to risk related to diseases like CVD, along with protecting the tissues of the aorta because of its antioxidant and anti-inflammatory effects, which showed a more potent effect than a statin [93], shown in Figure 4.

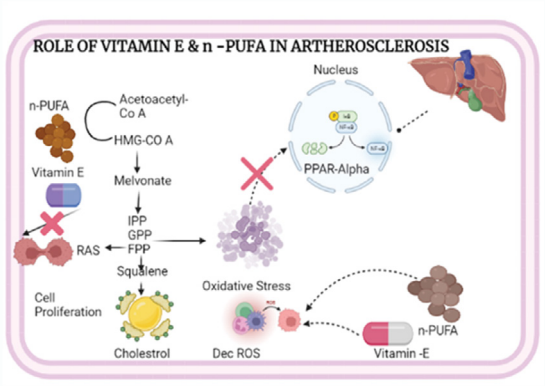


Figure 4: Role of vitamin E and n-PUFA in atherosclerosis they inhibit oxidative stress because of antioxidant activity dec Reactive oxygen species and inhibit cell proliferation.

Antimicrobial

An antioxidant from oil was extracted and showed very good antimicrobial activity [94] as wheat germ extract is very repressive to S. aureus. Cereus as it contains 2,6-dimethoxy-1,4-benzoquinone (DMBQ) [95].

Antiparasitic activity

In 2022, it was determined that WGO has potent antiparasitic activity against cryptosporidiosis and can control tumorigenesis in chronically infected immunocompromised hosts. In 2022, immunocompromised mice were infected with *Cryptosporidium parvum*, and WGO demonstrated a potent action because *Cryptosporidium parvum* occurs in those whose immune systems are not functioning properly, antioxidant carotene can treat immunodeficiency, and the antimicrobial action of WGO treated this pathogen; more research is needed to determine the exact mechanism of action [96].

Stability Techniques

Wheat germ oil is prone to oxidation, which degrades food's flavor, aroma, color, and nutritional value [97]. Encapsulation is a potential technique for protecting delicate food ingredients from environmental challenges, covering up off-tastes, and delivering active minerals. Microencapsulation can prevent the oxidation of wheat germ oil [98]. The effects of various homogenization techniques on the physical-chemical characteristics and storage stability of wheat germ oil in capsules. Silent crushing, microfluidization, and ultrasonication were applied as homogenization techniques. Compared to Ultrasonication methods, silent crushing and microfluidization methods produced more stable emulsions. On the effectiveness of capsule encapsulation, the effects of maltodextrin in conjunction with sodium caseinate, gum arabic, chitosan, or whey protein concentrate, as well as Whey protein concentrate and chitosan combination at various ratios, were investigated. For the most effective encapsulation of wheat germ oil, sodium caseinate was shown to be a superior coating material to chitosan, whey protein concentrate, and gum arabi [99].

Extrusion, microwave heating, infrared radiation therapy, steaming, dehydration, atmospheric cold plasma, as well as chemical preservation, such as the addition of antioxidants or alkalis, have all been used to reduce the wheat germ's enzymatic activity. Dry heating and steaming are now the heat treatment techniques used most frequently to avoid oxidation. However, steaming caused the most -tocopherol to be destroyed, which is related to the samples' lowest measured levels of radical scavenging activity [100].

Infrared radiation increased the stability of wheat germ oil from 15 to 90 days. The optimal processing conditions to stabilize wheat germ without significantly reducing the tocopherol content included an infrared radiation intensity of 4800 W/m^2, a 3-minute treatment, at 0.2 m between the emitter and sample [101]. Nanoemulsion has high storage stability, fast digestion, resistance to degradation, regulated release, and strong drug-enhancing potential [102]. Production of wheat germ oil WGO nanoemulsions had, respectively, delayed by 36.1%, 20.5%, 32.2%, 37.7%, and 68.4% the increase in the cooked fish fillets' TBARS, FFA, PV, CD, and CT values. Cooked fish fillets treated with WGO nanoemulsions showed more persistent changes in sensory quality, b* value, and lipid nutritional quality indicators. Because WGO-loaded nanoemulsions gave the cooked fish fillets' surface a wider contact area, the oil quality of the fish fillets treated with WGO nanoemulsions was successfully preserved [103]. To extend the shelf life of the oil, more stabilizing methods need to be assessed and research is required.

Future Prospective

This review presented the most recent data on WGO pharmacological properties, chemical constituents, extraction, as WGO has excellent nutritional demand and is used in the cosmetic industry, as a health supplement but many more areas are still needed to be researched and reviewed properly. Comprehensive research is required in many diseases like parasitic infection, infertility, neurodegenerative, hemorrhoids, constipation, IBS, and CNS-related problem like anxiety. Improvement needed in stabilizing process as its shelf life is less research should be done to expand the shelf life of oil so it can compete with other edible oils in the market with microencapsulation technique.

Conclusion

The current review reveals all scientific research conducted on WGO and its bioactive compound which gives a brief review of plants pharmacological mechanism of action the plant also gives many marketed products especially in nutraceuticals and cosmetic and if stability of oil is improved it can compete with marketed formulation. WGO when used as nutraceutical observe with man potent pharmacological properties like cancer, diabetes, hypertension, parasitic disease, atherosclerosis, ulcer, inflammation, wound healing, acute radiation injury, reproductive activity, vitamin E and D deficiency, muscular dystrophy, microbial infection, neurodegenerative disease like Alzheimer, Parkinson, Hepatosteatosis and dyslipidemia, Hepatoxicity and protective role in hepatorenal toxicity, nephrotoxicity. WGO when given with traditional medicine decrease the side effect and enhance pharmacological properties are also reported. Comprehensive research is required in many diseases like parasitic infection, infertility, neurodegenerative, hemorrhoids, constipation, IBS, and CNS related problem like anxiety.

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