

Ethnobotany and Phytopharmacology of Avena *sativa*: A Qualitative Review

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Keywords: Ethnopharmacology, Phytochemicals, Avenanthramides, Oat, Toxicity profile. Abstract: Among all cereals, oat is considered to be one of the goods consumed in functional grain, nutraceutical, and pharmaceutical components. The review article aims to explore plant profile, phytochemical constituents present in different parts, and potential therapeutic agent which prevents people from different diseases with their respective mechanism of action it also includes toxicity studies, dosage form, marketed formulation, and industrial application. The information on Avena sativa is collected from the different databases available in Science Direct, PubMed, Scopus, and Google Scholar to search for research papers for literature and data. Reviewed information suggests that the A. Sativa is a good source of a range of phytochemicals including lignans, saponin, anthocyanidins, and avenanthramides, which might be directly and/or indirectly linked with beneficial nutraceutical and/or pharmacological effect(s). The review states, that A. sativa is a promising candidate as a functional and/or non-functional food because of various phytoconstituents. The clinical report has described that the utilization of oats can provide several health benefits. However, systematic rational investigations for such indications and safety profiles are yet to be explored.

Introduction

Traditional medicines, particularly herbal medicines, are gradually increasing, it provides healthcare benefits around the world, particularly in rural and city areas (1). According to the world health organization (WHO), traditional or alternative medicines are employed based on beliefs or popular culture to prevent, diagnose, improve, or treat the prevention, diagnosis, improvement, or treatment of health, whether physical or mental problems. The WHO also suggests using traditional medicines, including herbal medicines in its 2014-2023 strategy, to keep the population well by providing a gain of effective and several acceptable alternatives to medicine to provide healthcare choices along with people's cultural practices (2). One of India's oldest systems of traditional medicine is Ayurveda. In Ayurveda, single or multiple herbs (polyherbal) are used to cure various ailments (3). Moreover, over the past decades, there has been a surge in demand for the different extractives obtained from various plants for nutritional and therapeutic purposes (4).

Avena sativa L., (Family: Poaceae), known as 'Oat' is a major cereal grain. The word Avena is derived from the Sanskrit word 'avi' meaning 'sheep' or 'avast' meaning 'foodstuff' (5). It is considered a weed of wheat and barley. It is the third leading crop in the United States and is also found in Russia, Sweden, Finland, Alaska, and Europe (6). However, in India, Avena is majorly grown in Haryana and Punjab and it was considered a weed of wheat and barley. Functionally, oats are used in varieties of ways like meal grains, crushed into oatmeal, meal, or flour, it is healthier to be taken as breakfast cereal. Edible oil obtained from grains is appropriate for the manufacturing of breakfast cereals (7). The bran of oats is used in the treatment of gout, liver and skin disease, and diuretics (8). The straw of oats is used as a building board, paper making, and material for the mattress (9). It is a good source of lipids, minerals, protein, lipids, avenanthramides, indole alkaloids, βglucan, flavonoids, and triterpenoid saponins. β-glucan, an important phytocomponent, is rich in non-starch polysaccharides that help in the reduction of blood

cholesterol (10) and possess protective responses against nervous necrosis virus (NNV) infection that is underway to harness its potential application to boost vaccination (11). Further gums from oats have proven pharmaceutical applications as an alternative to gelatin due to their thickening and stabilizing properties (12). Moreover, a wide spectrum of pharmacological activities has also been shown by oats including, demulcent, antitumor, antispasmodic, stimulant, diuretic, neurotonic, and tonic. Examine sequence of genome profile confirms the presence of unbalanced translocation of chromosomes from 1C to 1A. Such types of rearrangements appear in oats where it causes recombinant suppression, segregation, and pseudo-linkage (13). Therefore, efforts have been made to compile a piece of review work, emphasizing the traditional indication(s), phytochemical characterization, and reported pharmacological profile of oats, to develop state-of-arts in understanding its potential as one of the leading phytopharmaceuticals and/or nutraceutical components for the betterment of human well-being.

Methods

A comprehensive literature search was conducted using the keywords like Oat and/or Avena sativa with Phytochemicals 'Pharmacological', 'Anticancer', 'Antioxidant', 'Review', Phytopharmacological, and/or 'Phytochemistry' were entered in the search engines, including Pub Med, Scopus, and Web of Science up until May 2022. Further, the hypothesized objective data was compiled.

Plant Profile

Oat, or *A. sativa* L., is an annual grass that grows to a height of 1.5 meters. It has tufted culms, is solitary, and can be either upright or bent at the bottom. It has blunt, membrane ligules, non-articulate, green, and non-articulate leaves. The inflorescence may be a

diffuse raceme with 2-3 florets, bisexual, or distal one; it may also be reduced, in which case the male is sterile; the glumes are subequal and patterned, measuring 7-11 mm; the longer glumes, measuring 17-30 mm; the lemmas, measuring 7-9 mm; and the lowest lemma, measuring 12-25 mm. Lemmas are uncommon in farmed oats with rachilla, which do not separate at maturity. The labor-intensive lemma and palea closely seal the grain. Seed size is found to vary according to the variety (14). Common name: Oat, Jai, Groats, Haber, Hafer, Avena, Straw, Oatmeal; Taxonomic information: Kingdom - Plantae, Super division - Spermatophyta, Division -Magnoliophyta, Class - Liliopsida, Order - Cyperales, Family - Poaecae, Genus - Avena, Species - sativa (7); Parts used: bark, fibers, fruits, leaves, roots, and seeds.

Phytochemicals

Oats contain various phytochemicals, including organic acids, flavonoids, polyphenolics (15, 16), alkaloids (17), tannins, anthocyanins, carbohydrates, sterols (18, 19), lignans, tocols (20), carotenoids, and triterpenoid saponins (21) (see Table 1) (22-24). Key flavonoids include kaempferol, quercetin, amentoflavone, naringenin, luteolin derivatives, tricin, and hetrodera (15, 16). Major avenanthramides are ferulic, coumaric, and caffeic acids (16). Oats also contain β -glucan and carbohydrates like neokestose, bifurcate, and kestose (18). Oat leaves have sterols such as sterol glycoside, stigmasterol, sitosterol, and campesterol (19). Tocols (tocotrienols and tocopherols), particularly α tocotrienol, act as antioxidants (20). Triterpenoid saponins include avenacin (in roots) and avenacoside A and B (in leaves) (21). Lignans in A. sativa include pinoresinol, larciresinol, and medirescinol. Oats are the only grain with high selenium, supporting immunity and preventing cancer and aging (1). Among its phytochemicals, β -glucan and avenanthramides play key pharmacological roles.

Table 1. List of the phytoconstituents reported from A. sativa.

Phytoconstituents	Class	References
Catechin, Kaempferol, Syringic acid, Quercetin, Caffeic and Rosmarinic acid, Ferulic acid, Myricetin Avenanthramides Amentoflavone, Naringenin	Phenolics and flavonoids	(23, 24)
Gramine, Avenanthramides	Alkaloids	
β-glucan	Carbohydrates	
Campesterol, β -Sitosterol, Sitosteryl glucose, Campesteryl ferulate, Sitosteryl, ferulate	Sterols	
Campestanol, Sitostanyl glucose, Campestanol ferulate, β -Sitostanol, Sitostanyl ferulate	Stannols	
δ-tocopherol, α and β , -tocopherol, γ -tocopherol	Tocols	
Lutein, α and β -carotene	Carotenoids	
Pinoresinol, MatairesinolCyanidin-3-galactoside, Mediresinol, Larciresinol, Secoisolariciresinol,	Lignans	
Cyanidin-3-galactoside and glucoside	Anthocyanins	
Avenacins, Avenacoside A & B	Triterpenoids saponins	

<mark>β-glucan</mark>

Oat mainly contains linear, viscous polysaccharide $(1\rightarrow 3)$, $(1\rightarrow 4)$ β -D-glucan and is often called β -glucan, non-digestible polysaccharide. It is made up of a unit of monosaccharides D-glucose, extracted from oat kernels (25). Oat kernel contains about 85% insoluble dietary fibers (26). It is present in the endosperm layer which is adjacent to the aleurone layer. It mainly contains >90% off $(1\rightarrow 3)$ which prevents close packing of molecules makings the molecule partly soluble and β -(1→4) provides close packing of crystalline structure (27). These are the several species of oats having various amounts of total β -glucan like A. strigosa, A. byzantine, A. fatua, A. damascene, A. hirtula, A. wiestii, A. sterilis, A. atlantica, A. canariensis, A. clauda, A. agadiriana, A. insularis, A. magna, A. fatua, A. ludoviciana, and A. occidentalis. Its extraction is done depending on the solubility in hot water and alkaline solutions, and dissolved protein gets separated by isoelectric precipitation. Its precipitation is done by ethanol, propranolol, and ammonium sulphate (18).

β-Glucan Lowers Cholesterol Level

The cholesterol-lowering effect of β glucan is because of the ability to entrap whole micelles which contain bile acid in intestinal contents it shows this activity because of more viscosity of beta-glucan which excludes the interaction with luminal membrane transporter on intestinal epithelium which leads to decrease absorption of cholesterol and bile acids, further increases faecal output (28). Due to more elimination of cholesterol, it leads to a decrease in endogenous cholesterol which causes increased activation of 7α -hydroxylase and HMG-CoA reductase to make up for the loss of these two components from the liver. Further, it stimulates the upregulation of LDLreceptors synthesis which further decreases the LDL concentration in the blood. This all activity is primarily due to increased viscosity on diffusion rates and thickness of the layer on-site of absorption (29). Additionally, human has a shortage of intestinal enzymes to separate glucose molecule from β -glucan so they entered the large intestine in undigested form. It further decreases enterohepatic recirculation of bile acid and cholesterol (30).

β-glucan in the Management of Diabetes

Studies show that when more concentrated oat extract is taken in boiled, cooked, or baked form, it lowers the response of insulin and glucose. Several scientists studied the mixture of oats containing β -glucan with different viscosity and it shows linearity between viscosity and glucose and insulin relationship, so they concluded that the reduction in insulin and glucose response is due to viscosity (31). β -glucan present in oats has high significance in the management of type-2 diabetes by lowering peak glucose levels concurrently with insulin response (32). Long-term intake of oat β - glucan in breakfast for 4 weeks in men shows a significant decrease in cholesterol level and lower postprandial glucose peaks but shows no effect on insulin, fasting plasma glucose, and HbA1c (33). Comparing oat bran flour and oat bran crisp shows that AUC for plasma glucose for postprandial was higher for oat bran crisp, it signifies that oat bran flour lowered more rapidly postprandial than oat bran crisp.

Anticancer Potential of β-Glucan

 β -glucan exhibits the ability to inhibit the growth of tumors in a variety of experimental models (34). Its efficacy due to (1, 3)- β -glucan depends on the type of tumor, the route, time of administration, genetic background, and tumor load (35). The antitumor and anticancer effect of the β -glucan present in oats is because of the modulation of lymphocyte, neutrophil, and natural killer (NK) cells activity and innate immune system (36). Apart from oats β -glucan several other components contain (1, 3)- β -glucan like mushroom and fungi also shows antitumor properties. Recent research shows that combining orally administered β -glucan with antitumor monoclonal antibodies activates the mechanism that shows a broad range of efficacy against cancer (37). Orally delivered β -glucan actively proliferate and activate monocyte in the peripheral blood of patients with advanced breast cancer (38).

Antimicrobial and Immunostimulant Properties of $\beta\mathchar`-$ Glucan

Administration of natural β -glucan either orally, IV, or IM results in the elimination of bacteria by increasing clearance of bacteria, bacteria activity, modulation of cytokine production, and increases the number of monocytes and neutrophils resulting in antibiotic potential (39). Fungi-derived β -glucan also has immunostimulants on the immune system leading to resistance against bacterial, fungal, viral, and parasitic pathogens. Few scientists have reported that oat β glucan taken orally alone or in combination with sucrose shows high efficacy against HSV-1 respiratory infection and macrophage antiviral resistance following stressful exercise (40). IP administration of β -glucan enhances immune activity and protects Aeromonas hydrophila bacterial pathogen in zebrafish (41). It provides resistance against microbial infection via cellular and antigen-specific humoral immunity, it is upregulated by both parenteral and oral administration of oat β -glucan.

Avenanthramides

Oats containing an important phenolic amide i.e., avenanthramides (AVA), possess a greater number of health benefits because of their anti-inflammatory, antioxidant, and antiproliferative properties. It is an ester of 5-hydroxy anthranilic acid and a kind of hydroxycinnamic acid-like p- coumaric (AVA-A), ferulic acid (AVA-B), or caffeic acid (AVA-C) as shown in **Figure 1** (42). The bran and outer layer of the kernel of oats contain all the AVAs differing from each other in terms of functional groups (43, 44). The studies regarding stability showed that AVA-B is sensitive to neutral and alkaline conditions and increases with an increase in temperature, whereas AVA-A and AVA-C are more stable in this condition (45). The solvent used for the extraction of avenanthramides is ethanol, acetonitrile, methanol, and formic acid and their combinations. Determination of the number of AVAs is done by high-performance liquid chromatography (HPLC) with high-resolution tandem mass spectrometry-mass spectrometry (HRMS/MS), and ionexchange chromatography.



Figure 1. Structure of avenanthramides (AVA) i.e., pcoumaric (AVA-A), ferulic acid (AVA-B), and caffeic acid (AVA-C).

Health Benefits of Avenanthramides

• It shows strong antioxidant effects which have been proven in *in vitro* and *in vivo* studies. It shows potent antioxidant effects by acting as a free radical scavenger for reactive oxygen and nitrogen species or by chelating it (46).

- Oat bran is believed to lower LDL cholesterol and avenanthramides also helps in preventing free radical from low-density lipoprotein cholesterol (9).
- Consumption of oats and oat-related products reduces the risk of cardiovascular disease (47).
- Due to the presence of active constituents, avenanthramides reduce the risk of colon cancer (48).
- A study performed on laboratory animals shows that intake of 100 mg/kg oats in the diet reported increasing superoxide dismutase (SOD) activity in the liver, kidneys, and skeletal muscles and glutathione peroxidase activity in the heart and skeletal muscles (49).
- Oats AVAs contribute to the reduction of the risk of atherosclerosis and inhibit the proliferation of vascular smooth muscles (50).
- Synthetic AVAs (CH3 -AVA-C) inhibit activation of the NF-k-B transcription factor, which plays a key role in infection and inflammation (51).
- AVAs show similarities with tranilast (an antiallergic drug) used to treat asthma and autoimmune disease (52).
- Lowers blood pressure by dilating blood vessels due to increased production of nitric oxide (53).

Pharmacological Studies

Recent scientific studies have highlighted the detailed medicinal importance of different parts of *A. sativa* against a variety of human ailments, which are mentioned in **Table 2**.

Table 2. Highlights of pharmacological activity of selected parts of A. sativa with their possible mechanism of
action(s).

Plant parts	Activity	MOA	References
Oat product and oat soluble fiber	Hypocholesterolaemia activity and cardiovascular ailments i.e., antihypertensive, atherosclerosis	Lowering bile acid reabsorption increases bile acid excretion. Reduction of blood pressure prevents thrombosis.	(55)
Whole grain food	Antineoplastic behavior modulates the immune system	When macrophages are activated by β -glucan, they aid in the release of cytotoxic chemicals by T lymphocytes or lytic enzymes. These substances eliminate the tumor.	(22)
Oat bran (β- glucan)	Antidiabetic activity	enhancing the body's absorption of glucose for use in energy breakdown and converting glucose into glycogen.	(56)
Oat (phenolic compound)	Antioxidant potential	Antioxidant scavenges free radicals and prevents chain reactions.	(4)
Oat (β-glucan)	Weight management	Dietary fiber in oats absorbs water, causes swelling, and boosts volume. The individual's happiness is impacted by the higher volume due to stomach distension.	(55)
Oat (gluten-free)	Celiac and gastrointestinal disease	Enhance bowel movements and encourage the growth of good bacteria in the colon. It enhances a person's health in terms of celiac disease.	(57)

Green oat extracts, immature oat seeds	Mental performance	Nitric oxide generation in the smooth muscles of the human aorta is reduced as a result of avenanthramides. inhibits nuclear factor- $\kappa\beta$ activity while inhibiting inflammatory cytokines and causing vasodilation in cerebral artery walls.	(58)
Oat root (Avenacins)	Bactericidal activity	Focus on clearing the bacteria by getting rid of them. Production of cytokines ultimately leads to an increase in monocyte and neutrophil production, which in turn boosts the effectiveness of antibiotics. Moreover, it boosts humoral and cellular immunity.	(59)
Oat flour	Wound healing	Induce the cellular responses involved in wound healing	(60)
Green top of oats	Cure insomnia, anxiety, opium, obsession, burn, eczema, erythema, pruritis.	Nerve stimulant	(55)

Celiac Disease

It is a disease related to the small intestine which leads to hypersensitivity to gluten-containing products, its usual treatment is a lifetime intake of gluten-free food. Apart from other fiber food, clinical studies suggested that the part of oats seed flour is also widely used to prevent celiac disease, and its methods of extraction are by sequential digestion of it purified pepsin and trypsin and the constituents present in it, which helps in the prevention are avenin, it improves bowel movement and bacterial proliferation in the gut and helps to improve the celiac health of an individual (62, 63). Intake of oats in the diet helps in the eradication of celiac disease as it has a high fiber content of foods and cereal character (63). Uncontaminated oats containing wheat, and barley also show activity against celiac disease.

Cerebral Cavernous Malformation Disease

It is a major cerebrovascular disease affecting up to 0.5% of the human population, implying inflammation and oxidative stress as the main pathogenic events. Clinical trials suggested that it gets prevented by the intake of extracts of oatmeal which contains major phytoconstituents like avenanthramides, and phenolic amides which contain anthranilic acid and hydroxycinnamic acid, apart from it, eating high-fiber food helps in the prevention of disease. Oats were found to be effective in reducing reactive oxygen species (ROS) levels in experimental rats (65, 66).

Human Skin Fibroblast

Dermal fibroblast is a cell that is present within the dermal layer of skin are responsible for the cause of connective tissue and allowing the skin to recover from the injury of the skin, injury in this cell leads to inflammatory and oxidative stress. Sometimes hydrogen peroxide free radicals are involved in the human skin fibroblast causing cell damage and apoptosis, so preincubation of human skin fibroblast with oat reverses the effect and also reverses the hydrogen peroxide inducing a decrease of SOD and inhibition of malondialdehyde (66). This oxidative stress is prevented by oat groats (crushed grain of oats), which is performed by *in vitro* assay to see its activities due to the presence of vitamin E (tocols), phytic acid, phenolic acids, and its main constituents AVA-C (67).

Atopic Dermatitis

Atopic dermatitis is a common chronic inflammatory skin disease, highly pruritic, leads to dysfunction of the epidermal barrier, and is witnessed by the increased loss of transepidermal water from lesions. It is one of the common skin disorders seen in children and infants. It affects the quality of life of patients (68). The simple decoction was done on dry seeds to relieve the symptoms of eczema as seeds have a soothing effect that decreases itching and nourishes the skin (69). It is found that fiber, 'Rhealba' an oat plantlet extract contains flavonoids and saponins, avenacoside A and B, which prevent it from microinflammation and its skin barrier. Protein-free oat plantlet extract is protected by three international patents viz., WO2010/054879A2, WO2010/054878, and FR2938439 (70, 71).

Antioxidant and Anti-Inflammatory Activity

Antioxidants are those compounds that help in the prevention of oxidation of free radicals as oxidation leads to damage to cells. Free radicals like ROS and reactive nitrogen species are formed in our bodies due to various types of endogenous systems or pathological conditions. The antioxidant activity of oats is by the presence of the phenolic compound (71). The outer portion of oats grain contains several antioxidants like tocols, phenols, and phytic acids. The phenolic compound also exhibits other activities like anti-inflammatory and anti-allergic (72). An oat variety called CDC dancer inhibits tumor necrosis factor- α and it also induces nuclear kappa- β activation which results in antioxidant and anti-inflammatory activity with the help of flavonoids, guercetin, and resveratrol present in whole oat groats extracted with the help of the

advanced form of HPLC and HRMS (73, 74).

Cancer and Inflammatory Bowel Disease

Cancer is a major cause of leading of death throughout the world, it is the uncontrolled growth of malignant cells and it is the second leading after cardiovascular disease, which can be prevented by a high-fiber diet like Barley, Oranges, or Oats (75). Clinical studies suggested that increased intake of dietary fiber and fiber-related chemicals leads to a reduction of estrogen levels in the blood (76). It has been hypothesized that a diet that has high fiber content is shown to cause the risk of breast cancer in pre-and post-menopausal women by reduction of circulating estrogen and also for those who went for hormone replacement theory (77). β -glucan not only eradicates or destroy cancer but also modulate the neutrophils, lymphocyte, and NK cells. When it combines with other antibodies, neutrophils are triggered to look for and bind tumor cells to kill them. It also increases the proliferation of monocytes in a person who is suffering from breast cancer (36). Oat fiber help to eradicate such kind of inflammatory disease in part of the entire digestive tract because of the presence of its active constituent, avenanthramides, eradicating cancer as well as IBD (78, 79).

Type 2 Diabetes

Non-insulin-dependent diabetes mellitus (NIDDM) is a metabolic disorder affecting the largest population in the world and is very common in India. It affects in a way that the body either does not produce sufficient insulin or resists insulin. Natural sources of food like broccoli, apples, barley, and oats are proven to be effective in diabetes. Oats have been proven to be effective in lowering the glycemic response. β -glucan provides viscosity which shows linearity between glucose and insulin response, converts glucose to glycogen, or increases its uptake (80). Because of the large molecular weight of β -glucan, it improves viscosity, demonstrating β-glucan's beneficial impact on lowering blood glucose levels. A diet rich in oat is very helpful in this disease which is confirmed by randomized clinical trials. People taking white bread and those taking a diet rich in β -glucan show large differences in blood glucose levels as those who take a diet rich in β -glucan show a significant decrease in blood glucose levels (81). Phytoconstituent, avenanthramides, and β -glucan are found to be effective in treating diabetes (57, 82).

Anti-Allergic Inflammatory Effects

Allergic disease is very common affecting 20% of the world's population. Its occurrence is continuously increasing and it is linked to the presence of environmental allergens (82). Mast cells play an important role in allergic disease via the secretion of inflammatory mediators (83). Histamine also plays a

key role in allergic response which leads to hypothermia and increases vascular permeability (84). While there is no correlation between the intake of fruits, vegetables, and dairy products and asthma, the combination of whole grains (oats) and fish has been suggested to be effective in treating asthma. The children taking together, fish and whole grains had shown the incidence of reduction in wheezing sound in asthma. Its anti-allergic inflammatory effects are shown by germinated oats having phytoconstituent AVA-C, which is confirmed by an *in vitro* study using RBL-2H3 mouse bone marrow-derived from mast cells and rat peritoneal mast cells (85).

Cognition and Mental Fitness

Oats have been proven by researchers to be effective in improving overall mental fitness and cognitive improvement under stress condition as it affects all activity of brain enzymes in vitro. Preclinical and clinical studies show that oats interact with neurotransmitters present in the brain implicated in cognition, motivation, and memory (86). The extract of green oats helps in the enhancement of human health, it also provides its effectiveness in those who have a high risk of mild cognitive disorder. Immature oats seed also helps to cure tension and anxiety whether acute or chronic (25). Seeds of immature oats extracted from ethanolic extracts contain an active category of phytoconstituents like polyphenols and flavonoids, avenacin showing improvement in mental illness and performing multitasking tasks (88, 89).

Laxative Effects

Constipation is a gastrointestinal disorder that leads to difficulty in the evacuation of faeces (89). Foods that help relieve constipation and keep you regular are kiwi, apples, pears, and fibrous food like oats, and cucumber. Apart from this oats bran is involved in the physiology of gastrointestinal disorders which helps in regulation by delaying gastric emptying, increasing faecal bulk, and intestinal transit speeds (90). The extract shows a laxative effect by causing changes in colonic movement. It is important in preventing bowel obstruction thereby enhancing the movement of the intestine. Its long-term intake is found to be useful in inflammatory bowel disorder. Oat bran increases stool weight and decreases constipation. The aqueous root extract of oat bran contains insoluble fiber arabinoxylans and to a lesser extent cellulose and β glucans which show effectiveness against loperamideinduced constipated rats (91).

Sciatic Nerve Disorder

It is a disorder that occurs due to the narrowing of the which spine, compresses the part of the nerve. In a reported work, the increased formation of perineurium and epineurium in the oat extract-treated groups (100, 200, 400 mg/kg), when compared with that of the

Anti-Hypoxia

Hypoxia is a pathological condition in which there is tissue cell metabolism leads to a change in morphological structure due to a lack of oxygen. It not only damages physiological function but also affects metabolism (94). In hypoxic condition energy which is produced by aerobic respiration are not sufficient enough to meet the tissue needs due to which there is excessive formation of lactic acid, lowering of pH value causing intracellular acidosis under anaerobic condition (95). Clinical studies suggested that oat oligopeptide eradicates the anti-hypoxic effect which is analyzed by whole blood cell analysis using a blood analyzer. It shows this effect due to the presence of flavonoids, aventhramides, tocotrienols (96).

Protease Inhibitory Action

In a study, a comparison was made between the structural the functional entity of protease inhibitors from four plants namely *A. sativa*, *T. durum*, *S. hispanica*, and *C. quinoa*. In the study, the influence of these plants on hepatocarcinoma models was determined. However, it was reported that the plants had different levels of protease inhibitory action. The plant with more protease inhibitory action showed more propensity to be active as a chemo-preventive agent (97). Protease including enzymes like trypsin, thrombin, urokinase, elastase, and cathepsin B gets inhibited by preparing a methanolic extract of a mature grain of oats due to the presence of flavonoids and polyphenols (98).

Antihelminth Activity

It is an activity that is used to treat or kill the worm and oust it from the body (99). Green leaves of oats contain avenacoside B and 26-desglucoavenacoside B (saponins) treating infections of animals with parasitic worms (59). The biological activity of saponin is due to its amphiphilic nature, it is purified and extracted from green leaves of oats which reduces the pathogenicity from *Heligmosomoides bakeri* larvae in a mouse model and avenacoside leads to morphological changes in larvae, enhances IL-4 production and block glycoprotein pump activity (59). It shows harmful effects on pathogens by irreversibly binding to cell membranes and increasing their permeability (100).

Chronic Kidney Disease

Oat intake is effective in kidney function. Several in

vitro and *in vivo* studies reported that oats have scavenging activity (101), and the people who intake flour are shown to have favorable effects on inflammation and oxidative stress, and the lipid profile of a patient who suffers from chronic kidney disease (102). Oat bran containing insoluble fiber such as arabinoxylans which assess the extent of cellulose and beta-glucan which is found to be effective in chronic kidney disease shows this effect in randomization performed using SPSS 20 software (103).

Hepatic Liver Damage

Oat bran found which is in the endosperm layer of oats contains several chemical constituents i.e., AVA – A and B, vanillin, and sinapic acid, and its ethanolic and water extracts are used to treat hepatic liver damage (73, 104). The ethanolic extract of oats shows an inhibitory effect on oleic acid-induced hepatic steatosis *in vitro* test (105). The ethanolic fraction of oats protects against alcohol-induced acute liver damage in a mouse model by boosting endogenous antioxidants and preserving liver function, mitochondrial respiratory enzyme activities, and inhibiting activation of the NF- β signaling pathway (106).

Herpes Simplex Virus (HSV) Infection

Herpes simplex virus is most commonly encountered by humans. HSV-1 and HSV-2 are two types of HSV infections. The former usually causes orolabial disease and the latter is associated with genital and new-born infection (107). β -glucan derived from the cell walls of fungi, algae, and oats has been indicated to enhance the activities of both specific and non-specific immune responses (108). The oat beta-glucan preparation which is made from oat bran concentrate is found to be effective in the herpes simplex virus (109).

Nervous Necrosis Virus (NNV) Infection

Beta-glucan has shown an effect in treating nervous necrosis virus by activating the antiviral immune response, primarily many macrophages were involved in activating the antiviral response to NNV and showed proinflammatory cytokines (110). In vitro studies showed that increasing the viability of macrophages against NNV infection is linked with the activation of inflammatory cytokines gene expression (111). An *in vivo* study showed that NNV-infected fish given β -glucan showed high survival rate than those fish kept under control NNV infected fish. Further, studies are revealing that studies are underway to develop a potential agent for prime and boost vaccination strategies (11).

Traditional Uses

Oats are a powerful antitumor, antispasmodic, cyanogenetic, diuretic, stimulant, and tonic. They are used to treat sleeplessness, neurological weariness, and nerve weakening. Oat tea is beneficial for treating water retention and rheumatic disorders. (12). A green top of oats helps in withdrawal from tobacco and opium addiction. It is used to treat insomnia, anxiety, and various skin diseases. including burn eczema. Seeds are used in tumors as folk remedies and straws in rheumatism (112). The herb of oats is used as a combination therapy with tea for internal use, and in homeopathy, it is used in the form of mother tincture and dilution. This tea is taken frequently throughout the day and also just before going to bed. Tincture of the fresh herb of *A. sativa* is taken 3 to 40 drops per day for effect on the central nervous system. If we take it as a homeopathic dosage it is recommended to be taken as a tablet or 5 to 10 globules, 1 ml of injection solution twice weekly (113).

Toxicological Studies

The toxicity study revealed that oats containing active constituent avenanthramides are not found to cause any cytotoxicity effect on aortic endothelial cells of humans when taken up to 40 μ g/ml. Further, the colloidal extract of oats had not found any ocular and cutaneous toxicity in irritation tests (50). Avena colloidal extract is used in a variety of cosmetic formulations, including shampoo, cream, ointment, soap, emulsions, and gels. Colloidal fractions are also used to prepare bath water and to treat dry skin, both of which are frequently used for a longer time. However, no data on carcinogenicity, mutagenicity, and reproductive toxicity as well as sub-chronic and chronic oral use is available (114).

Industrial Application

Oats are considered to be more beneficial products among people. Industrial and commercial products are emerging vastly as it is most commonly used in porridge. A variety of marketed oat products are available in the market, those marketed products are Muscle Milk Oats, Oatrim, Oat well, Oat flakes, Oat milk, Granola, and ice cream. Oats flakes are commonly used in breakfast alone or combination (115). The popularity of oats consumption is mainly in the form of bread food products. Oats cake is UK based product (116). It is a substitute for bovine milk. Oat milk contributes to the nutritional and practical qualities of cereal as a probiotic food. Oat milk is nowadays due to increasing consumer demand (117).

Conclusion

Oat is examined to be a boon for human beings due to several pharmacological effects shown by its related products. Apart from food it also shows non-functional food activity. It has high nutraceutical values and the presence of several phytochemical constituents. Daily intake of oats helps us to get rid of several complications related to our health. With the presence of varieties of phytoconstituents, FDA has approved its usage in coronary heart diseases. It is also an important source of various formulations due to the absence of acute, subacute, and chronic toxicity. A rational investigation of the mechanism of action and its other toxicity-related profile, solubility, phase balance, and bioavailability still needs to be done. Its clinical studies on a larger scale have to be done. As nowadays people are so much conscious about their health so to enhance this now the demand for oats has been increasing. Due to scientists' intense interest in oats and their qualities, there are numerous products on the market now and many more will emerge in the future.

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