

Psyllium Husk, A Potent Natural Biomaterial Against Colorectal Carcinogenesis

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ABSTRACT

Psyllium husk, a well-known natural polysaccharide derived from *Plantago* sp. is frequently used in the biomedical and pharmaceutical sectors. The mucilage present in this husk has immense health benefits including prevention of carcinogenesis, reducing high blood glucose levels, cholesterol, obesity, inflammatory bowel syndrome, haemorrhoids, etc. Among all these, the laxative nature of this husk along with its bioavailability, thermal stability, and chemical modifications for generating bioactive derivatives make it more influential against colon cancer. The review article will give us a clear picture on the efficacy of Psyllium husk against colorectal carcinogenesis, its physico-chemical nature, mechanism of action and the precautions that should be taken during intake.

Keywords: Psyllium Husk, Colon Cancer, Biomaterial, Bioavailable, Toxicity.

INTRODUCTION

Colorectal cancer (CRC) is ranked as the third most common cancer in the world with high death rates (700000 deaths per year) [1]. Based on gender, Report shows CRC is the second most common cancer in female (9.2%) and the third most in male (10%) [2]. Nowadays, it is the third most leading cause of cancer-related death [3]. At diagnosis, metastases are present in about 20% of CRC patients, and metastatic CRC (mCRC) is typically an incurable condition [4,5]. There have been reports of a decline in the incidence of colorectal cancer (CRC) in high-incidence countries recently. This decline may be attributed to changes in the population's lifestyle choices, more colonoscopy screening, and improved treatment options [6].

There is ample proof that nutrition plays a significant part in the development of colon cancer [5]. According to certain experimental and

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analytical research, consuming dietary fibre, vegetables, whole-grain cereals, and calcium may protect against colorectal cancer and adenomas. Specifically, certain epidemiological research states consuming large amounts of calcium and fibre in the diet lowers the risk of colon cancer [4,5,7]. Among all others, psyllium husk (PH) is a highly fermentable water-soluble fibre that has a positive role in reducing colorectal carcinoma.

PH is derived from the *Plantago* sp. plant seeds called 'horse flower' from where it procures the popular name 'isabgol' [8-11]. The laxative nature of the husk is responsible for its mucilaginous properties. The white-coloured, fibrous, hydrophilic mucilage is processed by milling of *Plantago* seeds [12]. *Plantago psyllium* and *Plantago arenaria* are the main husk-producing plant.

An important herb that has been utilized for ages in South Asia's medical system is *Plantago* psyllium. It is used extensively worldwide for therapeutic purposes. Psyllium is an ayurvedic herb that grows in Afghanistan, India, and Iran. It is also indigenous to Pakistan, Europe, and the regions bordering the Mediterranean, including Northern Africa. Because this plant requires little water, it may be cultivated in a variety of dry environments worldwide [13]. The primary producers and the world's top exporters of PH are the western Indian states of Madhya Pradesh, Gujrat, Rajasthan, and Haryana [14].

Chemically the husk is made up of branched polymer arabinoxylan consisting of arabinose and xylose (xylose 74.6%, arabinose 22.6%,) having limited digestibility in humans. Intestinal microbiota can absorb these oligosaccharides as their nutrient source and help enhance intestinal prebiotic potentiality [15,16].

The high fibre content (\sim 76 %) of PH makes it more populous to people [12]. Maintaining a healthy digestive tract, encouraging regular bowel movements, and avoiding constipation fibre is very important.

The mucilage present in the PH helps in easy movement of colonic content and subsequently is involved in preventing constipation, which is one reason for colonic unease [17-19].

Through two independent randomized placebo-controlled intervention trials, researchers sought to ascertain the impact of PH supplementation on the intestinal microbiota of patients suffering from chronic idiopathic constipation as well as healthy individuals. The samples used in this investigation are from two related, published clinical trials [20], which examined the impact of PH on intestinal water content and colonic volume in adult patients who were either healthy or chronically constipated.

This is consistent with earlier research on the supplementation of PH [21] and the consensus that the microbial makeup of healthy individuals is resistant to alterations in the environment [22]. The degree of microbial change may reflect the fact that the constipated patients had a greater environmental change than the healthy subjects, as indicated by the change in colonic T1, an MRI (Magnetic resonance imaging) time constant reflecting the fluidity of the colonic chyme [22].

Numerous uses of PH in food and pharmaceutical industries make it a natural powerful ingredient along its successful application in lowering blood glucose level, weight management, cardiovascular disorders etc., [6]. PH is prized for its use in therapeutics, medicines, and nutraceuticals. It is primarily used as a laxative, which has many health advantages and is beneficial for treating several illnesses, including ulcerative colitis, diabetes, bowel syndrome, high cholesterol, obesity, and atherosclerosis [23]. PH has been shown to have effects on diarrhoea, constipation, excessive cholesterol, and obesity in children and adolescents. The pictogram in Figure 1 demonstrates how PH may be used to treat several human diseases. Given the pharmacological importance of PH polysaccharides in reducing the absorption of glucose and the existence of hydrogel-based drug delivery strategies, PH can enhance novel drug delivery systems provided it is suited for synthesizing hydrogels [24].

Additionally, some population-based research indicates that consuming more fibre may reduce the risk of colon cancer [24]. PH, a powerful source of fibre that inhibits the development of colorectal cancer, is discussed in detail in this article, along with the safe dosage and safety measures.

We gather information from the most recent literature review of published studies in order to study the national and worldwide state of PH research, and our article's commentary is based on this information. Standard references are used to support all comments and closing statements.



Figure 1. Pictogram shows the therapeutic applications of PH against various diseases.

Physical and Chemical features of PH:

Plantago ovata Forsskaol's dried, ripe seeds are the source of the 'isapghula' husk or PH. Commercial psyllium seed production involves using the seeds to make mucilage. The outer covering of the seeds is mechanically ground to release the mucilage from the seed coat. It absorbs water and turns into a gummy gel. The literature has reported on the gel type and composition of the polysaccharide isolated from P. ovata seeds [25].

Physical features:

Psyllium's surface morphology was examined by Sen et al., using scanning electron microscopy (SEM), and it was discovered that psyllium had a uniform, smooth structure. [26].

Fourier transfer infrared spectra (FTIR) of the husk were recorded by Kaith and Kumar [27], where alcohol's –OH stretching band, C-C stretching band of alkanes, C-O-C stretching bands of ether, and bands for polymer chain bending were observed. The thermogravimetric analysis of the PH was done to reveal the thermal characteristics caused by graft copolymerization with acrylic acid and acrylamide under various reaction conditions by Kumar et al. [28].

Chemical features:

Moisture, crude fat, crude fibre, crude protein, total ash, and nitrogen-free extract (NFE) measurements were used to assess the chemical composition of the husk. The PH is a bioactive substance that contains both primary and secondary metabolites, including amino acids, flavonoids, polyphenols, alkaloids, phenolic acid derivatives, terpenoids, and iridoid glycosides. [29-31].

Psyllium seeds are typically composed of proteins, fixed oil, and 10% w/w mucin in the testa's epidermis. Aldobionic acid and pentosan make up the mucilage [31]. Polysaccharides are chemically an arabinosyl rhamnosylxylan.

According to a research report, the average values for moisture, ash, crude protein, crude fat, crude fibre, and NFE in husk were 6.43 ± 0.05 , 3.85 ± 0.04 , 2.08 ± 0.06 , 0.09 ± 0.01 , 3.83 ± 0.02 , and $83.72\pm0.08\%$, in that order [32]. The results are comparable to those of Marlett and Fischer (2003), who found that the protein, ash, and total carbohydrates in husk were, 35.0, 33.5, and 902.4 mg/g respectively [33]. The findings of Guo et al. (2008), reported that the moisture, ash, protein, fat, and nitrogen-free extract (NFE) values in PH were 6.83 ± 0.04 , 4.07 ± 0.02 , 0.94 ± 0.00 , 0.04 ± 0.11 , and $84.98\pm4.26\%$, respectively [34].

PH against colon cancer:

Over the last few years, researchers have accumulated substantial evidence supporting the use of PH as a treatment for colon cancer [35,36]. A clinical study with 75,214 participants for eight years disclosed that non-fibre laxatives increased the risk of colon cancer rather than the application of laxatives with high fibre [37]. The same authors later revealed that the intake of high fibre in the diet is inversely proportional to the risk of colon cancer [38].

Another study by Jacobs and White mentioned that only fibre among other market-available laxatives can play a positive role against colonic carcinoma [39]. According to research by Sierra et al., PH exhibits anti-carcinogenic features, particularly in cases of colon and breast cancer. PH is employed to shorten transit times and enhance stool volume moreover, it decreases the intestinal wall's disclosure to lethal substances, some of which are present in feces. While the underlying methods by which PH can prevent cancer are currently unknown and incredibly obvious, a substantial amount of study has been conducted to disclose the potential outcomes [40]. PH's established mechanism of action against colorectal carcinogenesis has been depicted diagrammatically in Figure 2.

Mechanism of action of PH against carcinogenesis:

It is well understood that PH inhibits carcinogenesis by reducing the Tumour necrosis factor, TNF- α , and NO responsible for intestinal inflammation. [41,42]. The husk performs its role by increasing faecal volume after absorbing water. Finally, it reduces the carcinogens if present inside the colon by diluting it and turning it into a mucogel-like structure after binding with it [43].

The PH also can turn down the glucuronide-conjugate carcinoma cells by impeding bacterial glucuronidase activity. The non-starch polysaccharide like cellulose, hemicellulose, lignin, etc., present in this husk forms short-chain fatty acids viz. propionate, butyrate, and acetate in the intestine after aerobic fermentation [44]. This butyric acid has a role in preventing neoplasticity, hindering cell proliferation in the distal colon and transforming colon epithelial cells into cancerous cells. The P. ovata seeds are very rich in fermentable fibres and can produce higher concentrations of butyric acid through fermentation [45].

As the husk comprises only the seed epidermis, the butyric acid-forming fibres content is lower than that of the whole seed. In this way, it may also be helpful in the treatment of ulcerative colitis. In a clinical trial, individuals with colorectal carcinogenesis who received a daily dose of 20 grams of psyllium seeds for three months showed a roughly 42 % increase in the synthesis of butyric acid. The study's findings revealed a lower percentage of resected patients receiving pre-treatment within two months [46,47]. For the colon bacterial colony, PH furnishes nutrition supplements and helps to fabricate short-chain fatty acids. These fatty acids indirectly reduce carcinogenesis minimizing faecal mutagenicity [48]. Elevated cholesterol can potentially lead to colon cancer. PH lowers high cholesterol by encouraging the synthesis of cytochrome 7A, also called 7 alphahydroxylase, or CYP7A, the rate-limiting enzyme responsible for bile acid synthesis [49]. The husk generally slows down the LDL cholesterol by reviving the synthesis of bile acids which in turn let down cholesterol absorption and intensify the fractional turnover of cholic and deoxycholic acid [50]. The general mechanism of action of PH against CRC has been mentioned in Figure 2.



Figure 2. Diagrammatic representation showing the mechanism of action of PH against CRC. The arrows indicate step by step action to perform the involvement of PH towards its action.

Probable dose:

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It has been proposed that dietary fibre lowers the risk of colorectal cancer by shortening the transit time of feces through the colon. Table 1 depicts the survey data collected after clinical studies from various time periods, analyzed by several European medical associations, suggested that dietary fibre consumption lowers colon cancer, which is dose-dependent. Dose at 13-24 g/d for female and 14-28 g/d for male exhibited best result according to this data.

Table 1. Survey data collected from different time periods of people intake dietary fibre at different doses againstcolorectal carcinogenesis. Positive results depict good for +, better for ++ and the best for +++

Time frame	Applied person	Total no of people	CRC detected	Dose/Day	Effect	References
1986-2000	Male	47766	597	21g/d	++	51,52
1986-1993	Male	58279	646	27g/d	+++	52
1980-1987	Male	30363	492	28g/d	++++	53
1985-1999	Male	26987	321	19 g/d	+	54
1986-1993	Female	62573	501	24g/d	+++	55
1986-2000	Female	68502	648	17g/d	+	56
1987-2003	Female	61459	714	20g/d	++	57
1993-2002	Female	38384	201	17g/d	+	58

Studying from background knowledge, the suggested daily dosage of PH, based on various research, is between 10 and 30 g, split into smaller amounts [59]. To lessen all-around irritable bowel syndrome (IBS) symptoms, the Polish Society of Gastroenterology advises consuming 10-25 g of soluble fibre daily [60]. For all indications except constipation, PH therapy should be initiated gradually. The first week's dose should be 3.4 g/day, and it should then be raised by one daily dose per week until the therapeutic objective (about 10.2 g/day) is attained [61,62]. Supplementing a diet lacking in variety with bigger doses of PH supplements can also be a healthy way to add essential fibre to an otherwise unbalanced diet. A 2003 WHO expert opinion states that adults should consume more than 30–40 g of fibre per day [63]. This advice is based on preventative health initiatives meant to avert illnesses linked to metabolic diets and gastrointestinal issues. The European experts state that for children older than one year, the standard of adequate intake of dietary fibre is 10-21 g/day, or 2 g/MJ (8.4 g/1000 kcal) of fibre, depending on the child's age [47]. The recommended daily intake of fibre for adults (≤ 65 years old) is 25 g, and for the elderly (> 65 years old), it is 20 g. This is after dietary and medical guidelines are considered to modify the consumption in the oldest age group [64].

Pros and Cons of the use of PH against colon cancer

The level of processing and purity of these goods determines the safety of psyllium as a functional component in supplements [65]. The Food and Drug Administration, USA declared in a statement that it was safe and lawful to use PH in food items and dietary supplements in amounts required to have the intended therapeutic benefit (i.e., 10.2 g/day) when *P. ovata* husk was used with a high level of purity, at least 95%. Furthermore, it should not be overlooked that during the production of supplements and food items, there may be protein contamination with other allergies (such as sesame or mustard). Therefore, after ingesting psyllium-containing supplements or food items, doctors, pharmacists, and consumers should be informed of the possibility of allergic responses, including anaphylaxis. Regarding PH's allergenicity, the FDA has said that PH purity is a crucial safety factor in this regard as well. As a result, the FDA established a minimum 95% purity standard (with a protein level of no more than 3%), as stated in [66]. Regarding the safety of psyllium ingestion, the U.S. Food and Drug Administration has also recognized as significant the potential for oesophageal or intestinal blockage. Insufficient fluid consumption when using psyllium supplements may prevent the product's ingested dose from passing through the body properly. Additionally, swelling in the upper gastrointestinal system may obstruct the oesophagus or throat, potentially leading to choking. As such, patients must be made aware of the potential adverse consequences of using the PH when dehydrated.

Researchers are considering the safety of long-term PH supplementation by considering its potential impact on the nutritional status of high-quality patients and the bioavailability of nutrients from the gastrointestinal system. It was formerly believed that taking PH supplements might decrease the absorption of fat-soluble vitamins [65]. Additionally, it has been proposed that psyllium's mucilaginous-gel-like structure may help bind minerals including calcium, potassium, magnesium, zinc, and iron. Nonetheless, P. ovata husk supplementation is safe, well tolerated, and does not negatively impact the gastrointestinal bioavailability of vitamins and minerals, according to the findings of clinical investigations that have been published in the literature. The effects of an 8-week intake of 10.5 g/ day PH on laboratory parameters, such as magnesium, calcium, iron, ferritin, haemoglobin, vitamins A and E, and prothrombin time (as an indirect indicator for assessing vitamin K levels), were investigated by Solà et al. in 28 men (age: 61.4 ±8.6 years) with ischemic heart disease [67]. The mentioned woman's sole prior interaction with psyllium occurred while she was a nurse and was giving patients a laxative that contained psyllium. Specific IgE levels and the outcome of point skin tests indicated that the patient was allergic to psyllium [65].

A 60-year-old lady experienced an anaphylactic response after eating breakfast cereals containing psyllium, according to a case report published by Lantner et al. [67]. It is important to consider the potential for inhalation or gastrointestinal allergic responses following consumption or contact with psyllium-containing goods when discussing the safety concerns associated with *P. ovata* husk. Additionally, cases of occupational asthma linked to psyllium exposure through skin contact or dust inhalation have been reported. A literature survey indicates that employees in the medical field, the pharmaceutical industry, and particularly those working directly on psyllium preparations may be more susceptible to allergic responses because of regular inhalation exposure to the allergen [68].

CONCLUDING REMARKS

The review article concludes the possible health advantages of PH and its prospective application in the management and prevention of CRC. Since herbal PH preparations are inexpensive, generally safe, and show encouraging therapeutic results rapidly, it may be suggested that they should be taken consideration as a natural dietary supplement for use in the nutrition of patients with colon cancer-related gastroenterological issues. The medicinal qualities of PH discussed in this article could assist medical professionals in providing patients with ulcerative colitis, irritable bowel syndrome, and people at risk for colorectal cancer with useful advice. Furthermore, it will educate the general public on the consumption of PH, its dosages, and its application in preventing colon problems, particularly colorectal cancer.

DECLARATION OF INTEREST

The author has no conflict to declare.

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