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REVIEW ARTICLE

Exploring *Ispaghula* Husk in Drug Delivery: A Comprehensive Review

K. B. Rakshitha[1], G. B. Kiran Kumar[1], Butchi Raju Akondi[2], D. Umamaheswari[3], Prakash Goudanavar[1], N. Venuka Devi[4] and T. Mallamma[1]*

[1]Department of Pharmaceutics, Sri Adichunchanagiri College of Pharmacy, Adichunchanagiri University, B.G. Nagar - 571448, Karnataka, India; mallammareddy89@gmail.com

[2]Clinical Pharmacy and Pharmacology Department, Ibn Sina National College for Medical Studies, Jeddah, Saudi Arabia

[3]Department of Pharmaceutics, College of Pharmacy, Madurai Medical College, Madurai -625020, Tamil Nadu, India

[4]Nitte College of Pharmaceutical Sciences, Bangalore – 560064, Karnataka, India

Abstract

This comprehensive review provides an in-depth exploration of *Ispaghula* husk as a natural polymer in the pharmaceutical landscape. Beginning with an overview of natural polymers, emphasising their eco-friendly attributes, the article classifies and elucidates the significance of these polymers in pharmaceutical applications. Focused on the *Ispaghula* husk, the review delves into its properties, pharmaceutical applications and stability considerations. A key emphasis is placed on the importance of polymer modification in advancing formulation development, covering diverse methodologies applied to *Ispaghula* husk. The article elucidates various drug delivery systems formulated using this natural polymer, showcasing its adaptability in controlled-release formulations and mucoadhesive drug delivery. Recent patents on *Ispaghula* husk provide a contemporary perspective. The review concludes with forward-looking recommendations, positioning itself as a valuable resource for researchers and pharmaceutical professionals navigating the potential of *Ispaghula* husk as a natural polymer in pharmaceutical contexts.

Major Findings: This review highlights *Ispaghula* husk as an eco-friendly and biocompatible natural polymer with significant pharmaceutical applications. It possesses excellent swelling, gel-forming, and bioadhesive properties, making it suitable for controlled-release and mucoadhesive drug delivery systems. Various chemical and physical modifications enhance its solubility, stability, and drug-carrying capacity. Recent patents demonstrate its growing importance in novel pharmaceutical formulations. Future research should focus on advanced modifications and expanding its role in innovative drug delivery platforms.

Keywords: Controlled-release, *Ispaghula* Husk, Natural Polymer, Polymer Modification

Abbreviations: APIs: Active pharmaceutical ingredients; DNA: Deoxyribonucleic acid; FTIR: Fourier transforms infrared; **g**: Gram; IBS: Irritable bowel syndrome; IPN: Interpenetrating polymer network; Kcal: Kilocalorie; LDL: Low-density lipoprotein; NMR: Nuclear magnetic resonance; RNA: Ribonucleic acid; SCFA: Short-chain fatty acids; UV: Ultraviolet; XRD: X-Ray diffraction.

1. Introduction

The use of natural polymers in pharmaceutical drug development has gained significant importance due to several advantages they offer. Due to their unique properties, natural polymers which come from biological sources like plants, animals, or microorganisms are beneficial at numerous stages of the drug development process[1]. Exceptionally biocompatible, or well-absorbed by the human body, is an inherent characteristic of natural polymers. Being able to minimise the side effects and improve patient safety is vital for medication delivery methods and formulations[2]. Natural polymers frequently exhibit a lower immunogenicity than generated polymers. This is important in preventing undesired immune reactions when utilising polymers as implanted device

*Author for correspondence

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components or as pharmaceutical delivery systems[3]. Natural polymers are flexible in their composition, facilitating the development of a variety of drug delivery systems, comprising films, hydrogels, microparticles and nanoparticles. This adaptability is necessary for improving drug release patterns and personalising pharmaceutical formulations to satisfy specific therapeutic needs. As many natural polymers can break down into more basic, non-toxic components, they are biodegradable. This attribute helps mitigate the adverse consequences that pharmaceutical product disposal has on the environment[4]. Drugs that are not readily soluble in water might become soluble to a greater extent when they are in natural polymers like proteins and certain polysaccharides. This is especially crucial to improving the bioavailability of certain drugs, which enhances the therapeutic value of those medications as treatments[5]. Natural polymers can be engineered to respond to specific physiological conditions, enabling targeted drug delivery[6]. pH-responsive, temperature-sensitive, or enzyme-triggered release systems can be designed using natural polymers to enhance drug targeting and reduce off-target effects[7]. In pharmaceutical formulations, the use of natural polymers may assist in reducing toxicity. Natural polymers typically have a lesser risk of adverse effects, but synthetic polymers can introduce undesirable by-products or impurities. When compared to certain synthetic alternatives, natural polymers can be more affordable[8]. This is particularly relevant for pharmaceutical companies aiming to develop affordable medications, especially in the context of global healthcare access.

2. Classification of Natural Polymers

Natural polymers, integral to the biological fabric of living organisms, can be classified into distinct categories based on their composition and functions. Proteins, complex macromolecules constructed from amino acid monomers, exhibit remarkable diversity in form and function, ranging from enzymes and antibodies to structural components like collagen. Nucleic acids, such as Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA), carry genetic information and are fundamental to cellular processes. Polysaccharides, composed of monosaccharide units, play key roles in energy storage (e.g., starch, glycogen) and structural support (e.g., cellulose in plant cell walls, chitin in arthropod exoskeletons). Cellulose, a linear glucose polymer, contributes to plant cell wall rigidity, while chitin provides strength to arthropod exoskeletons and fungal cell walls. Other notable natural polymers include collagen, offering structural support in connective tissues, elastin providing elasticity to tissues and glycoproteins involved in cell recognition and signalling. This intricate classification underscores the significance of natural polymers in the architecture and functionality of living systems, each type uniquely contributing to the complexity and resilience of biological structures[9].

3. Polymer Modification

Polymer modification is important in natural polymers for several reasons. It can enhance their properties, extend their applications, and improve their performance in various industries. Modification allows the adjustment of physical, chemical and mechanical properties of natural polymers to meet specific application requirements. This tailoring can include changes in strength, flexibility, solubility and thermal stability[10]. Natural polymers are often modified to enhance their biocompatibility, making them more suitable for medical and biological applications. Biomimetic modifications aim to mimic natural structures and functions, allowing for better integration with biological systems[11]. Natural polymers can be made easier to handle during the manufacturing process by altering them to increase their processability. This might entail adjustments to melt flow, viscosity, or other rheological characteristics. To make natural polymers more stable and resistant to environmental elements including humidity, temperature and microbial deterioration, they can be modified. This is particularly significant for applications that require consistency over the long run[12]. It is possible to modify natural polymers to add functional groups and give them certain properties. For instance, adding chemical groups can facilitate the attachment of bioactive molecules for use in medicine or improve adhesion and cross-linking. Drug delivery systems are frequently developed through the modification of natural polymers[13]. Through structural modifications of the polymer, researchers can regulate drug release rates, optimise drug encapsulation, and improve targeting to certain cells or tissues. Natural polymers can be altered to make them less immunogenic and so more suited to human health. When employing polymers in implants or drug delivery systems, it is essential to prevent adverse

responses in medical applications[14]. Natural polymers have many potential applications when they are modified. These polymers' characteristics may be changed to make them useful in a wide range of new and inventive industries, such as packaging, textiles, food technology and cosmetics. Natural polymers can also be modified in ways that improve their environmental or economic viability. For example, changing the structure of the polymer might increase its biodegradability or lessen its reliance on finite natural resources[15].

Polymer modification of natural polymers involves a range of techniques aimed at tailoring their inherent properties for specific applications. One common approach is chemical modification, where natural polymers such as proteins or polysaccharides undergo grafting or cross-linking reactions. Grafting introduces functional groups or side chains onto the polymer backbone, altering properties like solubility or reactivity[16]. Cross-linking, on the other hand, forms covalent bonds between polymer chains, enhancing structural integrity and resistance to degradation[17]. Enzymatic modification utilises biological catalysts to induce controlled changes in the polymer structure, offering a sustainable and specific way to tailor properties[18]. Physical modifications, like blending or the incorporation of fillers, allow for adjustments in mechanical strength, flexibility, or other characteristics. Surface modifications, such as plasma treatments, can enhance the biocompatibility or adhesion properties of natural polymers[19]. These tailored modifications are crucial for expanding the utility of natural polymers in diverse industries, including medicine, food and materials science.

Polymer modification enhances mechanical strength, toughness and durability crucial for applications like biomedical implants or structural materials. In medicine, it improves biocompatibility, reducing adverse reactions in implants or medical devices. Thermal changes or cross-linking boost stability for high-temperature environments. Modifications control degradation rates, crucial for applications requiring specific lifespans. Chemical alterations influence the solubility and swelling, adapting polymers for processing or interactions in drug delivery. Improved resistance to moisture, Ultra Violet (UV) and microbial degradation extends polymer lifespan. Functional groups enable targeted drug delivery or enhanced adhesion. Modified polymers find use in food and cosmetics, offering improved stability. Processability is enhanced for various manufacturing techniques. Environmentally friendly modifications contribute to polymer sustainability, aligning with eco-friendly material demand[20].

4. Psyllium Husk

Psyllium is a plant which is indigenous to tropical climates and is technically known as *Plantago* (family *Plantaginaceae*). The term "*psyllium*" is frequently applied to more than 200 *Plantago* species. In the common Indian language, it is also referred to as *Ispaghula* and *Ispaghula*. The name *Ispaghula* comes from the Persian word "*band ghoul*", which means "horse flower" and describes the form of psyllium seeds. Psyllium was an indigenous plant of Persia. This plant is a short-stemmed annual herb which usually grows between 10 and 18 inches. It goes by several names in different regional languages, including *Ispaghula*, *Aspaghol*, *Ashwagolam*, *Bazarqutuna*, *Aspagol* and blond psyllium. This plant is grown extensively across the world. Psyllium is often grown for its mucilage, a white, fibrous material with hydrophilic features[21].

The seeds of the *Plantago ovata* plant as shown in Figure 1 are a source of psyllium husk. Dried, fully developed seeds from the *Plantago ovata* plant are known as psyllium seeds. These are obtained by thoroughly washing seeds to remove any contaminants such as iron particles, trash, stones, agri-farm fibres and dust. The appearance of psyllium seeds is light brown and has a faint odour. Linoleic acid, a key fatty acid, comprises nearly 40% of these seeds. In addition, it might have



Figure 1. *Plantago ovata* plant[22].

18.8% protein, 19% fibre and 10% to 20% triglycerides. It might include both soluble and insoluble fibre. Mucilage polysaccharide fibre, found in seeds, is naturally soluble. Psyllium seed grades are determined by the quality and purity of the seeds[23]. The outer layer of the seed, which is composed of mucilage, is called the psyllium husk. This is the primary component of the plant that is utilised to make psyllium products and contains nutritional value. Proteins, polysaccharides, glycosides, vitamin B1 and choline are included in this. It has a high fibre content, mostly made up of hemicellulose. Although hemicellulose is an indigestible complex polysaccharide, it is partially digested in the colon and provides nourishment to the intestinal flora. Hemicellulose may be found in cereals, vegetables, and fruits. Psyllium husk is produced by processing seeds to remove their outer covering. Its fibre composition is around 70% soluble and 30% insoluble. Husk is a white, fibrous material that is utilised in several sectors, including cosmetics, pharmaceutical and food products as shown in Figure 2.



Figure 2. *Ispaghula* seed and husk[25].

Depending on the user's requirements, different grades of psyllium husk based on purity and mesh size are available. The basic material utilised to create psyllium mucilage is psyllium husk. After being precipitated with alcohol in an aqueous solution, it is dried and cleaned with acetone. Moreover, psyllium husk powder is made from the husk by utilising grinders with different particle mesh sizes[24].

4.1 Characterisation of *Ispaghula* Husk

Ispaghula husk, also known as psyllium husk, is a natural dietary fibre derived from the seeds of the *Plantago ovata* plant. It has been used for centuries in traditional medicine and culinary practices for its health-promoting properties. *Ispaghula* husk is renowned for its unique physical properties, which play a crucial role in its effectiveness and versatility in various applications[26]. Its chemical composition is primarily characterised by a rich content of soluble fibre, along with various other constituents such as proteins and minor compounds[27]. The bioavailability of *Ispaghula* husk, primarily composed of soluble fibre, is limited as it undergoes fermentation in the colon rather than absorption in the small intestine. Its gel-forming properties aid in stool softening and regular bowel movements, but it doesn't directly contribute to nutrient absorption. *Ispaghula* husk consumption may promote satiety and regulate appetite, impacting weight management. Individual variability in gut health and microbiota composition can influence its effectiveness[28]. In Table 1 we mention the overall characteristics of the *Ispaghula* husk.

Table 1. Concise overview of the physical characteristics, biocompatibility and chemical composition of *Ispaghula* husk[26-28]

Component	Concentration/Content	Function/Characteristics
Appearance	Fine, fibrous material	Light brown or white flakes/powder
Texture	Fibrous	Absorbs water; forms a gel-like substance when hydrated
Swelling capacity	High	Absorbs water and expands
Water retention	High	Retains water, forming a gel-like consistency
Biocompatibility	Generally considered safe	Suitable for biomedical and pharmaceutical applications
Polysaccharides	High	Provides fibrous structure; water-absorbing properties
Proteins	Variable	Source of amino acids; potential biological activity
Glycosides	Variable	Secondary metabolites with potential therapeutic effects
Vitamins	Variable	Contributes to nutritional value (e.g., Vitamin B1)
Minerals	Variable	Provides additional nutritional content

4.2 Nutritional Value of *Ispaghula* Husk

The importance of the nutritional value of *Ispaghula* husk lies in its rich content of soluble fibre, predominantly composed of mucilage polysaccharides. This fibre exhibits various physiological effects, including increased faecal bulk, enhanced bowel motility, and improved stool consistency, thereby promoting gastrointestinal health and alleviating constipation. Moreover, the soluble fibre in *Ispaghula* husk contributes to metabolic benefits such as lowered cholesterol levels, regulated blood glucose levels, and heightened satiety, which collectively supports cardiovascular health and weight management. These scientifically substantiated properties underscore the significant role of *Ispaghula* husk in enhancing overall nutritional intake and promoting holistic well-being. Table 2 showcases the dietary fibre content in the *Ispaghula*[29].

4.3 Distinguishing Features of Psyllium Husk and Psyllium Seeds

Psyllium husk and psyllium seeds, derived from the *Plantago ovata* plant, represent two distinct forms of the same botanical source with notable differences in composition and application. Psyllium husk, the outer covering of the seed, contains a higher concentration of soluble fibre compared to the seed itself. This soluble fibre, primarily composed of mucilage polysaccharides, contributes to its effectiveness in promoting bowel regularity, relieving constipation and supporting digestive health. Physically, psyllium husk presents as a fine, pale brown to off-white powder with a slightly gritty texture, facilitating its dispersion and absorption of water in the digestive tract. In contrast, psyllium seed encompasses the entire seed, including the husk and inner kernel, and is typically larger with a darker colour due to the presence of the outer seed coat. While both forms can absorb water and form a gel-like substance, psyllium husk's finer texture allows for easier incorporation into various applications, such as dietary supplements, pharmaceuticals, and food products. Psyllium seeds, often ground into powder, serve a similar purpose but may offer slightly different textural characteristics due to the inclusion of the inner kernel. Ultimately, the choice between psyllium husk and seed depends on specific dietary needs, functional properties desired in formulations, and intended applications in various products. Table 3 demonstrates the physical characteristic features of Psyllium husk and seed[30].

Table 2. The dietary fibre content in *Ispaghula*[24]

Nutrient	Percentage (%)
Protein	0.94
Albumin	35.8
Globulin	23.9
Prolamin	11.7
Total Carbohydrates	84.98

5. Pharmaceutical Applications

It has been claimed that psyllium helps with constipation, diarrhoea, Irritable Bowel Syndrome (IBS), ulcerative colitis, diabetes, colon cancer and high cholesterol[32].

5.1 Constipation

Psyllium husk relieves constipation through its soluble fibre, which forms a gel in the digestive tract. This gel increases stool bulk, stimulates intestinal contractions, and softens stool, ensuring smooth and regular bowel movements. Its water-retention properties further enhance stool hydration, making it an effective remedy for digestive health[33].

5.2 Diarrhoea

Psyllium husk helps manage diarrhoea through its soluble fibre, which forms a gel in the intestines. This gel absorbs excess water, firms stools and reduces stool frequency. Its prebiotic effects support gut health by promoting beneficial bacteria, while long-term use helps restore intestinal balance and regulate bowel function[34].

5.3 Ulcerative Colitis (Crohn's Disease)

Psyllium husk may help manage Crohn's disease, a type of Inflammatory Bowel Disease (IBD), through its soluble fibre and anti-inflammatory properties. The fibre produces Short-Chain Fatty Acids (SCFAs) like butyrate, which reduce inflammation in the intestinal lining. Psyllium husk also absorbs water, increases stool bulk and regulates bowel movements, addressing symptoms like diarrhoea and urgency. Additionally, its gel-like substance forms a protective barrier,

Table 3. Characteristics features of psyllium husk and psyllium seed[31]

Characteristic	Psyllium Husk	Psyllium Seed
Composition	The outer seed coat of *Plantago ovata* seed.	Entire seed of *Plantago ovata* plant.
Fiber Content	Rich in soluble fibre and mucilage.	Contains soluble fibre, but the exact composition may vary.
Consistency	Forms a gel-like substance when mixed with water.	May have a slightly different texture compared to psyllium husk.
Pharmaceu tical uses	Commonly used in laxatives, fibre supplements and gastrointestinal health products.	Used as a bulk-forming laxative or as a source of dietary fibre.
Formulation	Often processed into powder or capsules.	May be used whole or processed into various forms.
Dosage	Dosage may vary depending on product formulation.	Dosage may vary depending on product formulation.
Specific applications	Relieves constipation, promotes bowel regularity and supports digestive health.	Relieves constipation, provides dietary fibre and supports digestive health.
Variability	Generally consistent in composition and properties.	The composition may vary based on the inclusion of inner seed components.

supporting intestinal healing. While promising studies show symptom improvement and enhanced quality of life, more research is needed. Patients should consult healthcare providers before using psyllium husk as part of their treatment[35].

5.4 Irritable Bowel Syndrome

Psyllium husk helps manage IBS by regulating stool consistency through its bulking properties without causing excess gas or discomfort. Its gel-like substance forms a protective barrier in the intestines, reducing inflammation and irritation linked to symptoms like abdominal pain and bloating. Clinical studies show it can improve overall IBS symptoms, including discomfort, bloating, and irregular bowel movements. However, individual responses vary, so consultation with a healthcare provider is advised before use[36].

5.5 Diabetes

Psyllium husk supplements help manage blood sugar by slowing glucose absorption and preventing spikes after meals. They also promote satiety, aiding in weight management for diabetes. Pharmaceutical companies may include psyllium in functional foods like meal replacement shakes or snack bars, designed to provide controlled glucose release and support glycemic control[37].

5.6 Cholesterol Lowering

Psyllium husk forms a gel-like substance in the digestive tract that traps cholesterol and bile acids, promoting their excretion and preventing absorption into the bloodstream. The soluble fibre in psyllium binds to cholesterol-rich bile acids, reducing cholesterol reabsorption and lowering the Lower Density Lipoprotein (LDL) ("bad") cholesterol levels without affecting HDL ("good") cholesterol. Clinical studies show that psyllium husk effectively lowers LDL cholesterol, especially in individuals with hypercholesterolemia[29].

5.7 Cancer Prevention

Psyllium husk may help mitigate the risk of cancers associated with hyperglycaemia and insulin resistance, such as pancreatic and colorectal cancers. Its anti-inflammatory properties can reduce chronic inflammation, which plays a role in cancer development. Additionally, psyllium husk's antioxidant activity helps protect cells from oxidative damage caused by free radicals, a factor in cancer initiation and progression. By promoting detoxification and aiding the elimination of toxins and carcinogens, psyllium husk further supports cancer prevention. While more research is needed to fully understand its mechanisms, psyllium husk shows promise in cancer risk reduction[38].

6. Stability Issues or Drawbacks

When compared to their conventional equivalents, biopolymers derived from natural sources are currently associated with several disadvantages, including poor production rates, inferior mechanical and thermal

strengths, processability, compatibility, excessive water absorption and feasibility issues[39]. *Ispaghula* husk, with its water-absorbing tendency, can increase volume and viscosity, posing stability concerns in formulations sensitive to water absorption. The hygroscopic nature of natural polymers like *Ispaghula* husk may lead to microbial contamination, affecting the stability of pharmaceutical or food products. Variability in quality due to factors like source and processing methods can pose challenges in maintaining consistent product performance. In some formulations, the rheological properties of the *Ispaghula* husk may change over time, impacting flow behaviour and stability. Although *Ispaghula* husk can form gels when hydrated, beneficial for controlled drug delivery, it may be problematic in formulations where gelation is undesired[40]. It's possible that some formulation elements or active medicinal substances won't work well with *Ispaghula* husk. Compatibility issues could occur and impact the end product's performance and stability. The husk of *Ispaghula* could be susceptible to changes in humidity and temperature. The stability and quality of the polymer may be impacted by modifications to these circumstances during storage or transit. The flavour and texture of *Ispaghula* husk in dietary supplements or pharmaceutical formulations may not be to everyone's taste, which might cause difficulties with patient compliance. *Ispaghula* husk particles may tend to clump or agglomerate in dry powder formulations, making it difficult to process and ensure uniform distribution in the finished product[41].

7. Importance of Polymer Modification of Natural Polymers for Formulation Development

Natural polymers, such as cellulose derivatives and starch, become more soluble in water or organic solvents when they undergo chemical changes like etherification or esterification. They are now suitable for a wider range of formulations, including oral dosage forms, thanks to this enhancement. By incorporating certain functional groups or altering the chemical structure, customized polymers allow for the modification of drug release patterns and allow for controlled or sustained release. This is essential for creating formulations that have precisely the right release kinetics to provide the best possible therapeutic outcomes. It's usual to struggle with a drug's low bioavailability; however, modified natural polymers come in handy by increasing the drug's solubility and rate of dissolution, which guarantees sufficient absorption into the circulation[42]. Under some circumstances, natural polymers can degrade or show instability. These polymers may be modified to increase their stability and increase their resistance to environmental elements including humidity, temperature, and enzymatic destruction[43]. Controlled swelling and gelation behaviour may be achieved by modifying natural polymers, particularly in hydrogel compositions. This is helpful in situations where the swelling pace influences medication release or tissue contact, such as regulated drug administration and wound healing. Certain natural polymers may lead to allergies or immunological reactions, but chemical changes might lessen these effects and reduce the possibility that patients would have undesirable side effects. This offers formulators more alternatives and is essential for creating safe and friendly pharmaceutical formulations[44]. It is feasible to develop a variety of dosage forms, like tablets, capsules, gels and films, by adjusting factors including viscosity, adhesion, and mechanical qualities. Chemical changes improve the compatibility of natural polymers with Active Pharmaceutical Ingredients (APIs), preventing problems such as drug-polymer incompatibility and assuring consistent drug distribution. Through polymer changes, rheological parameters such as viscosity and flow behaviour may be tailored, which is important for formulation manufacture and administration via various routes (oral, topical, or injectable)[38].

8. Polymer Modification of *Ispaghula* Husk

8.1 Micronisation

Ball milling enhances psyllium husk arabinoxylan by reducing particle size and altering its structure, improving accessibility, extractability, and solubility. This modification boosts its compatibility with *Ispaghula* husk and may serve as a reinforcing agent with improved mechanical properties. It has potential applications in controlled release, gel formation and strengthening in food, pharmaceutical and biodegradable polymers. Further research using techniques like Fourier

Transforms Infrared (FTIR), X- Ray Diffraction (XRD) and Nuclear Magnetic Resonance (NMR) is needed to fully understand its effects[45].

8.2 Chemical Functionalisation

8.2.1 Carboxymethylation

Carboxymethylation of arabinoxylan, isolated from *Ispaghula* seed husk, involves reacting with chloroacetic acid. This process enhances reactivity, water solubility, and allows controlled modification of the substance's properties. The Schematic representation of the synthesis of carboxymethyl arabinoxylan was shown in Figure 3. The chemical functionalisation improves compatibility, leading to better stability, increased mechanical strength and more adaptable features[46].

8.2.2 Ethylation

Ethylation adds ethyl groups to arabinoxylan, altering its xylose backbone and arabinose side chains. This modification, achieved by reacting with ethyl halides, enhances the polymer's compatibility, reactivity and solubility[47].The Conversion flow has been shown in Figure 4.

8.2.3 Thiolisation

Thiol groups are added to arabinoxylan and psyllium husk mucilage to create thiolated mucilage. These thiol groups enhance adhesion to mucosal tissues, extending contact duration. This modification improves the mucoadhesive properties of *Ispaghula* husk, enabling sustained therapeutic effects and controlled drug delivery[48].

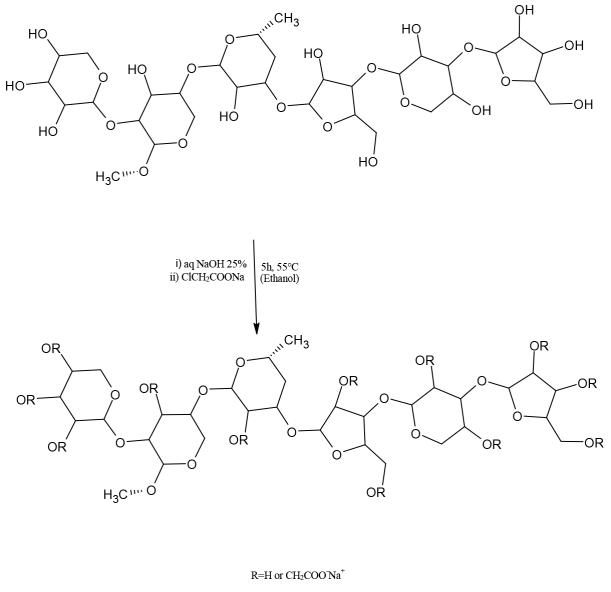


Figure 3. Schematic representation of the synthesis of carboxymethyl arabinoxylan[46].

8.3. Cross Linking

Crosslinking modifies arabinoxylan-rich *Ispaghula* husk by forming covalent bonds, enhancing strength, stability, and mucoadhesion. This improves drug release control, making it suitable for sustained therapeutic effects and mucoadhesive microspheres. It also alters rheological properties, increasing viscosity and mechanical strength, and supports controlled swelling for targeted drug delivery. Thiolation reaction of PSY with thioglycolic acid was shown in Figure 5. Crosslinking tailors *Ispaghula* husk for diverse

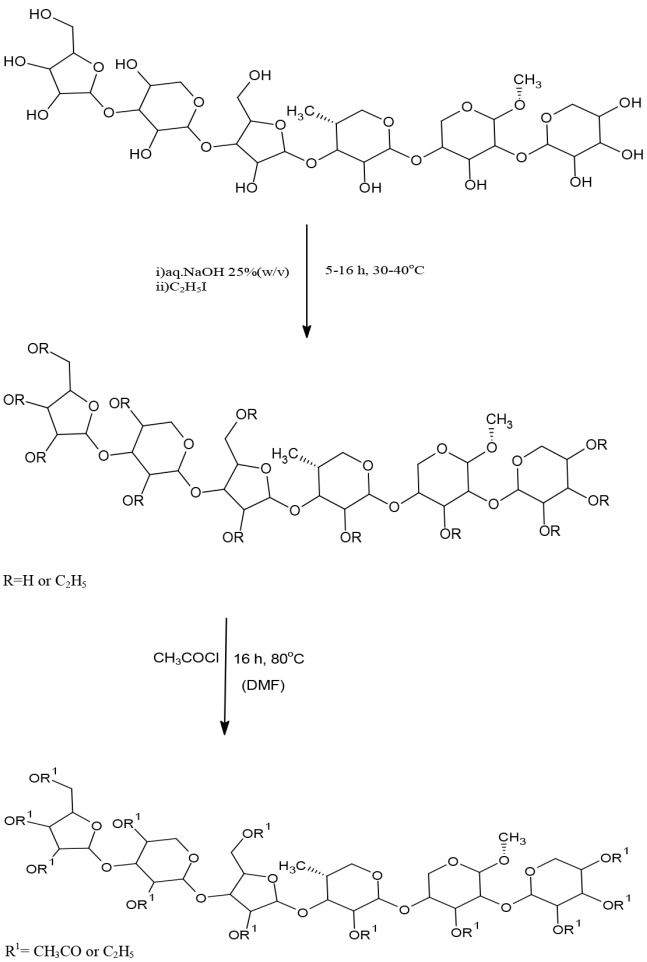


Figure 4. Conversion of arabinoxylan with ethyl iodide and sodium hydroxide under heterogeneous reaction conditions and subsequent peracetylation[47].

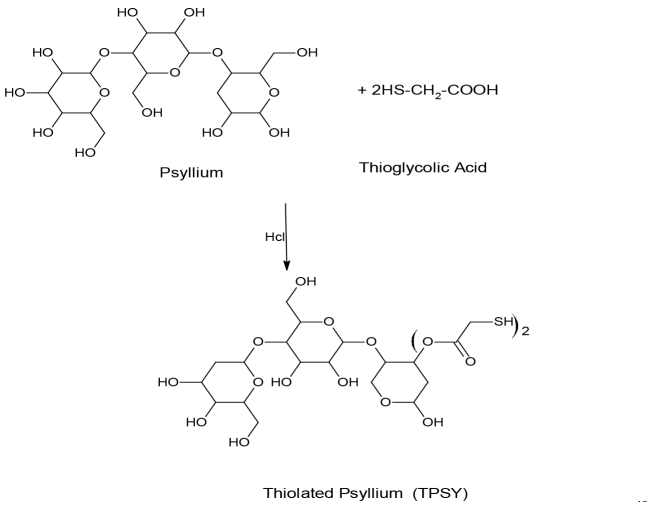


Figure 5. Thiolation reaction of PSY with thioglycolic acid[48].

applications in pharmaceuticals and biomedical engineering[28].

8.4 Blending with Other Polymers

Blending *Ispaghula* husk with other polymers customises the material properties for specific needs in industries like pharmaceuticals, food and biomedicine. This enhances compatibility with various formulations, preserving its beneficial properties. The synergistic effects of blending can also create novel material properties and applications that combine the unique attributes of both components[29].

8.4.1 3D Printing Technology

In 3D printing, blends of gelatin and psyllium husk (*Ispaghula*) are studied for their mechanical and rheological properties. Rheological tests assess the viscosity and flow behaviour at different temperatures and shear rates to ensure a homogeneous mix. Mechanical characteristics, including tensile strength, compression and elasticity, are evaluated. Extrusion tests assess print uniformity and extrudability, while printing quality, layer adhesion and resolution are analysed through standardised samples. The study aims to establish correlations between mechanical and rheological properties to optimise the psyllium husk-to-gelatin ratio for improved 3D printing materials[26].

8.4.2 Wound Dressing Application

Antibiotic-loaded psyllium husk hemicellulose and gelatin-based polymeric films offer an innovative approach to wound care. These films provide a controlled, prolonged release of antibiotics directly at the wound site, enhancing therapeutic efficacy. The combination of psyllium husk hemicellulose and gelatin ensures biocompatibility while imparting mechanical strength to the films. This study highlights the potential of using polymeric films for targeted antibiotic delivery, marking a significant advancement in wound care technology[49].

8.4.3 Tissue Regeneration

Electrospun psyllium husk-based nanofibers show promise in tissue engineering by supporting tissue regeneration. The study focuses on the development of nanofibrous scaffolds through electrospinning, which provide an ideal environment for cell adhesion and proliferation due to their biomimetic structure, resembling the extracellular matrix. Psyllium husk is an attractive raw material because of its biocompatibility and natural properties. Characterisation of the nanofibers reveals essential qualities like mechanical strength and porosity, making them suitable for various biomedical applications in tissue engineering[50].

8.5 Surface Modification

The surface characteristics of *Ispaghula* husk particles can be changed by using surface modification techniques like coating or grafting. This might facilitate the production of pharmaceutical formulations by improving their flowability or compatibility with specific excipients. To improve the chemical and physical characteristics of the polymer backbone, acrylic acid moieties are introduced during the grafting process onto *Plantago* psyllium mucilage[51].

8.6 Hydroxypropylation

The effects of hydroxypropylation on the functional characteristics of psyllium, provide important information on how to alter this organic polymer. This work outlines the experimental techniques used in the hydroxypropylation of psyllium and how this chemical modification affects its functional properties, such as viscosity, solubility and thermal behaviour. These alterations are crucial for potential commercial applications, advancing the field of biomaterials and expanding the uses of this versatile natural polymer[52].

8.7 Encapsulation

Ispaghula husk can be encapsulated to improve stability, control release and protect against external factors. This work introduces a novel method of microencapsulating annatto extract using psyllium husk mucilage polysaccharides[53].

8.8 Microwave Assisted Modification

Microwave-assisted binary grafting of psyllium enhances its properties for medical use, particularly in anticancer formulations. This technique modifies the psyllium structure, potentially improving its effectiveness in drug delivery and advancing cancer treatment strategies[54].

9. *Ispaghula* Husk-Based Formulations for Enhanced Drug Delivery

Ispaghula husk, recognised for its unique properties, is increasingly being explored as a versatile ingredient in pharmaceutical formulations aimed at enhanced drug delivery. This natural fibre, derived from *Plantago ovata* seeds, offers distinct advantages for drug delivery systems due to its high water absorption capacity, swelling ability and biocompatibility. Researchers are focusing on harnessing these characteristics to develop controlled release systems, where *Ispaghula* husk's ability to form a gel-like matrix upon hydration allows for prolonged drug release, enhancing therapeutic efficacy and patient compliance. Moreover, its mucoadhesive properties make it suitable for mucoadhesive drug delivery systems, enabling improved drug absorption and bioavailability by extending contact time with mucosal surfaces. *Ispaghula* husk-based formulations can also be tailored for gastrointestinal targeting, facilitating drug delivery to specific regions such as the colon, which is beneficial for treating conditions like inflammatory bowel disease. Furthermore, *Ispaghula* husk enhances the solubility and stability of poorly water-soluble drugs, offering potential solutions for enhancing their bioavailability. Its compatibility with various formulation techniques allows for the development of diverse drug delivery systems, including tablets, capsules and multi-particulate formulations. With its biodegradability, safety and natural origin, *Ispaghula* husk emerges as a promising excipient for pharmaceutical formulations (Table 4), offering opportunities for advancing drug delivery strategies and improving therapeutic outcomes. Continued research in this area holds the potential to further optimise the efficacy, safety and patient acceptability of pharmaceutical products utilising *Ispaghula* husk[12].

9.1 Case Studies Showcasing Psyllium in Drug Delivery

Psyllium has demonstrated its utility across various drug delivery systems. In controlled-release formulations, its high viscosity and gel-forming properties have been used effectively to prolong drug release, aiding in chronic disease management. Its application in colon-targeted drug delivery systems has proven beneficial for treating conditions like ulcerative colitis, where it remains intact until reaching the colon. Additionally, combinations of psyllium with sodium alginate have shown promise in improving bioavailability and enabling controlled drug release, particularly in microsphere formulations for antibiotics. Innovative approaches, such as psyllium-based hydrogels for transdermal delivery, further underscore its potential to enhance drug permeability and patient compliance.

10. Literature Survey on *Ispaghula* Husk

European patent (EP 4 275 515 A1) is described to introduce a dietary food product for weight loss with low nutritional value. This patent focuses on providing a low-calorie food product supplemented with psyllium, glucomannan, and grounded pumpkin seeds. The incorporation of *ispaghula* husk ensures increased dietary fiber content, promoting weight reduction effectiveness without compromising taste and texture. This innovative product addresses the need for effective weight management solutions while offering convenient serving sizes and minimal organoleptic impact[59].

Patent (WO 2023/131835 A) introduces a ground-breaking granular psyllium formulation designed to promote digestive health by incorporating a novel delayed gelation property. With a gelation retardant ranging from 10 to 60%, this innovative formulation offers enhanced liquid dispensability, ensuring a viscosity below 1000 cP for convenient administration. Psyllium husk is treated with the gelation retardant along with optional excipients and then subjected to

Table 4. *Ispaghula* husk-based drug delivery system

Application	Components	Concentration	Technique Used	Physico-Chemical Properties	Entrapped Active Compound(s)
IPN Microspheres for Medication Delivery	*Ispaghula* husk, polymers	Varies	Emulsion Cross-linking	Improved material qualities, regulated medication delivery	Diclofenac sodium[55]
pH-Sensitive Smart Hydrogels	Psyllium husk	100 gm.	Alkali Extraction	pH-responsive, stimuli-responsive, superabsorbent	Anhydrous Theophylline[56]
Biocomposite Films for Packaging	Psyllium seed husk, husk flour	Varies	Hot Water Extraction	Mechanical strength, barrier properties, biodegradability	*Plantago* psyllium seeds[27]
Oral Dispersible Pills	*Ispaghula* husk	Varies	Sublimation Process	Taste-masking, improved tablet qualities, dispersibility	Domperidone[57]
Mucoadhesive Drug Delivery Systems	*Ispaghula* husk	Varies	Microwave-assisted	Mucoadhesive properties, extended contact with mucosal surfaces	Ciprofloxacin[58]

a specified granulation process to produce granules ranging in size from 50 to 1000 microns. Notably, the inclusion of *Ispaghula* husk further amplifies the benefits to the gastrointestinal system, enhancing digestive health. This formulation's regulated particle sizes, delayed gelation mechanism, and synergistic effects with *Ispaghula* husk present a flexible and efficient treatment option for various digestive issues[60].

The Canadian patent (CA 3155818) introduces a novel pharmaceutical formulation combining curcumin with a psyllium husk matrix and, enhanced with an enteric coating. Utilising a 25% ethanol solvent, curcumin's medicinal potential is optimised through regulated and delayed release. This innovative approach integrates unique coatings, solvents and fibres to create a sophisticated delayed-release drug delivery system, promising targeted and controlled release in pharmaceutical research and development[61].

11. Challenges in Using Psyllium and Other Natural Polymers in Drug Delivery

Natural polymers like psyllium hold immense potential, but their application in drug delivery is not without challenges. Scalability remains a significant issue, as variability in raw material quality due to natural sourcing complicates standardisation and consistency. Stability concerns also arise, with formulations being sensitive to environmental factors such as temperature, humidity, and microbial contamination, affecting their shelf life. Regulatory hurdles add another layer of complexity, as natural polymers often require extensive testing to meet stringent quality and safety standards. Additionally, processing challenges such as poor solubility and difficulty in advanced techniques like encapsulation can limit their utility. Impurities during extraction and potential biocompatibility issues necessitate advanced purification methods to ensure safety. Moreover, the economic and environmental constraints of sourcing and processing natural polymers sustainably can impact their widespread adoption. Addressing these challenges is essential for realising the full potential of natural polymers in pharmaceuticals.

12. Future Recommendation

Ispaghula husk, derived from the seeds of the *Plantago ovata* plant, holds immense potential for various biomedical and industrial applications. Comprehensive characterisation of its chemical and physical properties is essential for understanding its structure and behaviour. Advanced analytical techniques such as spectroscopy, chromatography, microscopy and rheology can provide valuable insights into these properties, aiding in the development of innovative applications.

One promising avenue is the exploration of *Ispaghula* husk in biomedical applications. Its use in drug delivery systems, wound healing, tissue engineering and regenerative medicine shows great promise. Evaluating its biocompatibility and interactions with biological systems is crucial for ensuring safety and efficacy. Modifying *Ispaghula* husk to enhance its performance in drug delivery systems through chemical modifications, encapsulation techniques or the development of composite materials can further improve its utility in medical applications.

Moreover, there is growing interest in utilising *Ispaghula* husk or its derivatives in sustainable and biodegradable packaging materials. With increasing demand for environmentally friendly alternatives, investigating its feasibility in this area aligns with current market trends. In the food industry, *Ispaghula* husk's potential as a functional ingredient is being explored. Its role in improving texture, stability and nutritional content in food formulations, particularly as a dietary fibre, presents opportunities for developing healthier food products.

Additionally, research is underway to develop nanostructured materials based on *Ispaghula* husk. Synthesising nanoparticles or nanocomposites for applications in sensors, catalysis or novel materials with unique properties holds promise for technological advancement. Optimizing extraction and modification processes is crucial for industrial scalability, ensuring efficiency and cost-effectiveness in large-scale production. Clinical studies are needed to further explore the health benefits of *Ispaghula* husk, especially in gastrointestinal health, cholesterol management and diabetes. Investigating its potential role in preventive medicine and overall well-being is also important. Furthermore, exploring synergistic effects by combining *Ispaghula* husk with other natural polymers can enhance specific properties or functionalities for various applications. Lastly, considering regulatory aspects is essential, particularly for its use in pharmaceuticals, food products, or other regulated industries, compliance with safety and quality standards is paramount to ensure consumer safety and product efficacy.

13. Conclusion

In conclusion, this paper has explored the diverse facets of *Ispaghula* husk, a natural polymer with significant potential in various applications. We have delved into its origin, properties and traditional uses, shedding light on its unique characteristics as a soluble fibre. The importance of *Ispaghula* husk in pharmaceutical drug development has been underscored, considering its role in formulations for gastrointestinal health, drug delivery and beyond. While *Ispaghula* husk holds promise, it is crucial to acknowledge the stability issues and drawbacks associated with its use. The hygroscopic nature, potential for microbial contamination, and challenges related to rheological changes present considerations for formulation development. Additionally, the variable quality and limited compatibility with certain active ingredients emphasise the need for careful consideration and optimisation in diverse applications. Looking ahead, future research on *Ispaghula* husk should focus on addressing these stability issues through advanced characterisation techniques, innovative formulations, and process optimisation. Exploring its potential in biomedical applications, sustainable packaging materials and nanostructured materials could open new avenues for this natural polymer. In navigating the complexities of the *Ispaghula* husk, it is imperative to strike a balance between harnessing its beneficial properties and overcoming its limitations. Continuous research, collaboration across disciplines and a commitment to addressing regulatory considerations will contribute to unlocking the full potential of *Ispaghula* husk in pharmaceutical and other industries. As we move forward, the evolving landscape of natural polymers invites researchers to explore novel avenues and innovations, ensuring that *Ispaghula* husk continues to play a significant role in shaping the future of materials science and healthcare.

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15. Authors Contributions

Rakshitha KB: Writing-original draft, formal analysis. Prakash S Goudanavar and D Umamaheswari and Venuka Devi N: Resources, writing-review and editing, formal analysis, Kiran Kumar GB and Mallamma T: Conceptualization, validation, supervision, writing-review and editing, formal analysis. Butchi Raju Akondi: Project administration.

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