Development and Evaluation of Plant-Derived Polymers as Novel Pharmaceutical Excipients

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Abstract

The ever-growing demand for plant-derived, safe, Biodegradable and ecologically sound ingredients for pharmaceuticals has promoted research in this field for finding natural polymers for substituting synthetic compounds in pharmaceutical formulation. There are several natural polysaccharides with beneficial Physicochemical characteristics (e.g.,Biocompatibility, Safety, Biodegradability, Lower Cost) from variety of botanical sources suitable to employ as alternative pharmaceutical excipients. The purpose of this study was development and evaluation of some plant-based polymeric pharmaceutical excipients for formulation purpose and their utility and efficacy. Polysaccharides were isolated and purified from some plant source and evaluated PhysiochemicallypH, viscosity, swelling Index, Moisture content, Ash content, solubility in water, Flow parameters, etc were studied. Studies of compatibilty with Model Drugs were performed to investigate. The prepared and characterised plant derived polymers were found suitable for use as excipients possessing good organoleptic properties, excellent water absorptive ability, swelling and favourable flow properties. They can act as binder, disintegrants and controlled released agents. Plant-derived polymers gave good performance equivalent to conventional commercial agents and showed more ecological benefits. The stability of the polymers shows the absence of major physiochemical alterations on storage.These results indicate that plant-derived polymeric materials are a promising alternative multifunctional excipient in pharmaceutical formulation, and offer a greener route for developing pharmaceutical excipients which, to some extent, can be of value in terms of development of green pharmaceutical technologies and expanding use of naturally-derived substances in pharmaceutical application.

Keywords: Plant-derived polymers, pharmaceutical excipients, natural polymers, biocompatibility, biodegradable materials, drug delivery systems, sustainable pharmaceuticals.

Introduction

Plant Based Pharmacuetical Excipients – A Review Pharmaceutics Pharmacologically inactive compounds that are included in dosage forms to aid drug delivery, enhance stability, improve processing and increase the therapeutic benefit are called pharmaceutical excipients. In the last several decades synthetic and semi-synthetic excipients have widely been used for formulation of pharmaceuticals due to the reproducible process and well controlled physiochemical property. With the increasing concerns over drug toxicity, environmental friendliness and biocompatibility and regulatory agencies' stringent norms the exploration of natural resources-based excipients has accelerated. Plant derived polymers represent potential alternatives, due to their wide availability, biodegradability, non-toxicity and low cost(Rowe et al., 2009).

Natural polymers obtained from plants are predominantly polysaccharides and hydrocolloids that possess excellent swelling, binding, film-forming, thickening, emulsifying, and controlled-release properties. Commonly investigated plant-based polymers include guar gum, xanthan gum, pectin, starch, gum acacia,

locust bean gum, tamarind seed polysaccharide, psyllium husk mucilage, and aloe vera mucilage. These biopolymers exhibit favorable physicochemical characteristics and have found applications in tablets, capsules, suspensions, emulsions, gels, and sustained-release formulations (Shirwaikar et al., 2008). Their natural origin and renewable nature make them attractive alternatives to synthetic polymers such as hydroxypropyl methylcellulose and polyvinylpyrrolidone.The natural polymers extracted from plants mainly comprises polysaccharides & hydrocolloids, which have a wide range of valuable properties i.e., swelling, binding, film forming, thickening, emulsifying & controlled release characteristics. The most commonly explored plant derived polymers are Guar Gum, Xanthan gum, Pectin, Starch, Gum Acacia, Locust bean gum, tamarind seed polysaccharide, psyllium husk mucilage & Aloe vera mucilage, which show good physio-chemical properties and can be utilized in Tablets, capsules, suspensions, emulsion, gels & sustained release forms (Shirwaikar et al. 2008). As they are derived from natural & renewable sources and thus can be used as substitute for synthetic polymer.

Growing concerns on green chemistry and eco-friendly manufacturing of drugs have spur to the studies on application of naturally originated materials in pharmacy. The important features of these biopolymers derived from plants are biodegradability, biocompatibility, low antigenicity, availability, cost effectiveness etc. It is well known that plant-derived polymers are regarded as GRAS (generally regarded as safe) substances that have a long history of usage in food and drug industries. Various gums and mucilages from plant sources can perform diverse functions such as bind-ers, disintegrants, suspending,matrix-formulating and controlling-release materials which lead to sustained drug-release and improve the rate of acceptance by the patients as opined by Kamel et al. (2008).

The major category of plant based natural polymers used in formulation of medicines is Polysaccharide. Starch and its derivatives as well as cellulosic compounds has been used in pharmaceutical formulation for many years as an integral part such as diluents, binders and disintegrants. Currently research interests are focusing more on the application of various plant derived mucilage and gums having good hydrating properties and gel-forming nature. For example, various studies indicate that natural plant mucilages have a higher tendency towards swelling property and can control the release rate of drugs in matrix dosage form due to interaction between the drug and matrix, which has been investigated and established by Malviya et al. (2011). Due to microbial degredation in large intestine of our body, pectin and Guar Gum can be utilised as a useful vehicle for colonic drug delivery and sustained drug release.

In addition to this, the biocompatibility profile of polymers of botanical origin is better than synthetic excipients. Sometimes due to their chemical reactivity some synthetic compounds can cause reactions, intolerance or interactions with drugs. On the other hand, biodegradable natural polymers show good tolerance with the drug substance and the biological environment. The gums and mucilages extracted from plant species do not have toxicity or allergy problems and have been used as drug carriers in oral, topical or timed-release pharmaceutical dosage forms (Kulkarni et al., 2002). Their renewability can favor more sustainable pharmaceutical productions without any petroleum dependence.

Some studies have evaluated extraction, purification and characterization of plant polymers for assessment of pharmaceutical applications of those polymers based on variables such as swelling index, moisture, viscosity, pH, flow behavior, and interactions with drugs which determine the efficiency of such polymers as excipients. Physical properties related to their functional characteristics such as swelling power, binding characteristics and disintegrating abilities have been dependent on the structure and the chemistry of these polymers (Jani et al., 2009). Development in extraction and chemical modification technologies have resulted in numerous innovative approaches towards new drug delivery designs and nanotechnology.

Although significant advancements have been achieved, there is still a lack of sufficient controls over various factors such as batch-to-batch variations, microbial contaminants and standardize production of these polymers. Environmental origin of the plant material, geographic location, extraction processes all

have a impact on the properties and the functional performance of the polymers, thus there is need for systematic studies oncharacterization and control of these polymers.

Here, an attempt was made to prepare and characterize pharmaceutical excipients using various types of natural biopolymers obtained from plants to serve as novel alternatives to commercially available materials used in various drug formulations such as binders, disintegrants and controlled-release devices. The research aims at establishing effective methods for isolation and purification, physicochemical characterization, and functional evaluation, ultimately aiming to formulate green and eco-friendly and multi-tasking drug carriers.

Pharmaceutical Excipients and Their Importance

A pharmaceutical excipient, otherwise called a non-active constituent, is an inactive material present in the dosage system (i.e., tablet, capsule or injection). Excipients are a part of dosage systems that help make the dosage system stable, workable or more suitable for administration of the drug, or that facilitate the uptake or delivery of the drug (Rowe et al. 2009). Though a non-active element in pharmaceutical compositions, the excipient's composition and performance are considered in deciding the quality of an inactive component in a given prescription product; it provides better quality and can prevent deterioration and improve the biological absorption and drug supply system.

Plant-Derived Polymers as Natural Excipients

Plant based polymers consist mostly of polysaccharides and hydrocolloids, which are usually derived from the different part of a plant like seed, fruit, leaf, root and bark for instance gum acacia, guar gum, pectin, tamarind seed polysaccharide, starch, psyllium mucilage and locust bean gum. Theses biopolymer are best suited for pharmaceutical applications due to their inherent film-forming property, ability to form viscous gels, swell ability, and water-holding capability. As per Kamel et al. (2008), natural gums and mucilages exhibit multifarious property as they can replace effectively the synthetic excipients, since these are bio-degradable and bio-compatible.

Advantages of Natural Polymers over Synthetic Excipients

There are many advantages in comparing natural polymers with their synthetic counterparts which includes biodegradation,biocompatibility,low cost and it are also abundant in nature (i.e., the use of readily available renewable resources). Whereas conventional synthetic polymers utilize non-renewable petrochemical sources as a precursor and cause harm to the environment, plant-based polymers cause less environmental damage and are environment friendly; thereby supporting the environmentally friendly pharmaceutical preparations (Santhi et al., 2011; Patel, et al., 2014; Jain et al., 2014). Natural gums and mucilages are relatively non-toxic and well accepted by patients as stated by Kulkarni et al. (2002) because of their low immunogenicity and good safety profile for application by topical, oral and modified release methods (Patel et al., 2013; Veni, et al., 2014; Gadiyaret al., 2014). Formation of hydrogels and matrices from these polymers provides modification of drug release pattern and can provide enhanced therapeutics.

Sources and Classification of Plant-Based Polymers

The use of plant-derived polymers based on the source of polymers & chemical composition has classified them. Seed gums viz. Guar gum and Locust bean gum comprise substantial quantities of Galactomannans and Pectin extracted from the fruits is an important galacturonic-based polymer. Starch extracted from Maize, potato, cassava are composed of amylose and amylopectin, respectively, which impart binding and disintegration property. The Mucilage isolated from Plant source e.g. Psyllium, aloe vera has also constituted by the polysaccharides complicated in structure. These polymers also exhibit high water-holding ability. According to Malviya et al. (2011), these natural polymers exhibit various types of rheological and physicochemical properties which ultimately influences its use in pharmaceutically designed formulations. Based on their structural uniqueness, it is possible to create multifunctional excipients to be suitable to any type of formulations.

Pharmaceutical Applications of Plant-Derived Polymers

Plant-derived polymers offer a wide variety of functions that have contributed to their successful utilization in a diverse range of pharmaceutical applications including tablets binders, disintegrant, matrix, suspending agents, viscosity control agents, emulsifying and film coating materials. Both pectin and guar gum are currently well-evaluated natural polysaccharides for use in sustained and colonic drug delivery systems because they readily form gel upon wetting with aqueous fluid and are susceptible to enzymatic cleavage within the GI lumen. Shirwaikar et al. (2008) studied the properties of natural mucilage as tablet binders and have successfully reported that they can be utilized to replace synthetic excipients. The capacity of these substances to modify and increase drug delivery and provide stability to the formulations, has attracted attention.

Extraction and Characterization of Plant Polymers

The suitability and viability of plant extractives used as polymers in the formulation of pharmaceutical products can be characterized after carrying out efficient extraction, purification and analysis techniques of these plant based polymers. Usually, plant material is extracted in an aqueous medium, and thereafter, the filtrate is filtered, and after precipitating, drying and grinding, these properties are evaluated to see how fit it can be used as an excipient in pharmaceutical formulation based on physiochemical properties like; pH, viscosity, swelling index, moisture content, ash content and flowability. Characterization studies of these plant derived polymers are required to achieve reproducibility and quality assurance for the reproducible and satisfactory formulation, (Jani, 2009 et al.)Furthermore, the evaluation of the functions is required which include compatibility and stability studies.

Challenges and Future Prospects

Plant-based polymers are hampered by the problem of batch-to-batch variability in terms of physicochemical characteristics, microbial contamination, geographical and environmental effects. Standardization and quality control for them should be important criteria before for its pharmaceutical regulation and large-scale application. Improved knowledge of purification, modification andnanotechnology of natural polymers gives potential ways to imbue them with new functionalities. Growing concern in the area of green chemistry and green pharmaceuticals should make way for more study and promotion of plant-derived excipients.

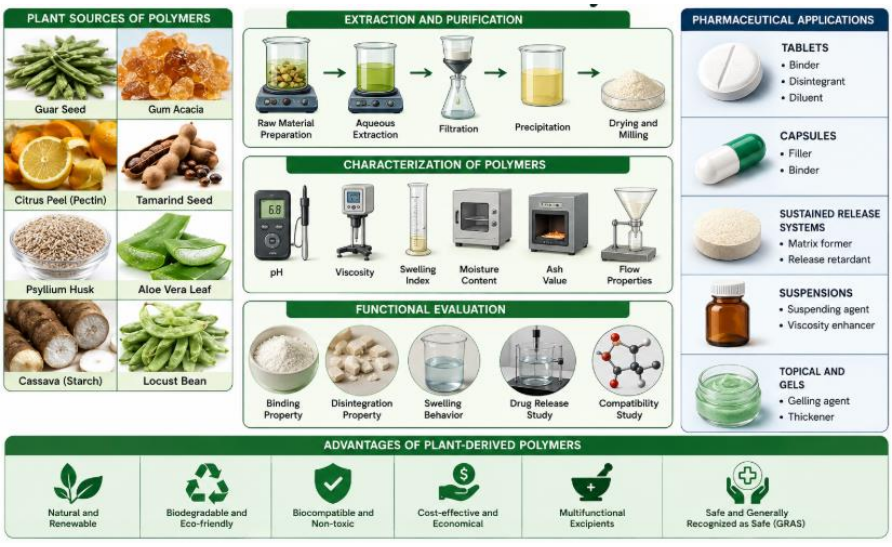


Figure 1. Schematic Representation of the Development and Pharmaceutical Applications of Plant-Derived Polymers as

The figure explains the important plant origin of polymer such as guar seed, gum acacia, citrus peel (pectin), tamarind seed, psyllium husk, aloe vera, cassava starch, and locust bean gum. Figure demonstrates the general schematic representation of the extraction and purification of plant origin polymers (raw material processing, aqueous extraction, filtration, precipitation, drying, milling). It contains different characterization parameter of extracted polymers (pH, viscosity, swelling index, moisture content, ash value and flow property). Also represent the functional valuation of plant origin polymer and its uses in pharmaceuticals. Plant origin polymer is use as binder, disintegrant, matrix forming, suspending and gelling agent for various pharmaceutical dosage form, i.e. Table, capsules, sustained release formulation, suspension and topcial formulation. Advantage of these plant origin polymer are, biodegradability, biocompatibility, non-expensive, and eco-friendly.

4. Advanced drug delivery system formulation and polymer functions:

4.1 Injectable Depots and Hydrogels:

Hydrogels made of natural polysaccharides (such as alginate, chitosan, and gelatine) expand when exposed to water, enabling the controlled release of medications. The ionic gelation process, physical entanglement, chemical crosslinking with epoxide derivatives or diamines, and crosslinking with CaCl2 are the methods used to create alginate hydrogels. Injectable drug carriers based on gelatine and hyaluronic acid have been created and effectively used for cancer treatment delivery in the past ten years. Drug diffusion and release characteristics, swelling ratio, gelation duration, and mechanical qualities are important considerations.

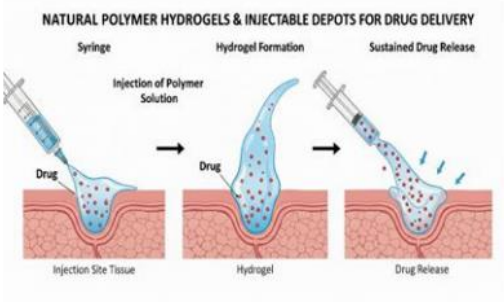


Figure 1: A medication delivery device utilising natural hydrogels and injectable depots.

Formulation:

Thermosensitive in situ gelation: Injectable depots can be made by subjecting polymers like Pluronic or chitosan/β-glycerophosphate to a sol-gel transition at room temperature.

Ionotropic gelation: Made by crosslinking gellan or alginate solutions with Ca2+ ions, depot gels can have their medication release controlled.

GelMA, or covalent/enzymatic crosslinking, is a technique for making mechanically stable hydrogels injectable from modified natural polymers.

Nanoparticles / Nanocarriers:

To provide targeted distribution and protection, natural polymers such as chitosan, albumin, and gelatine can encapsulate nucleic acids, tiny compounds, and peptides. Methods such as nanoprecipitation, emulsion polymerisation, and solvent evaporation are employed to create nanoparticles. Anticancer medications and nucleic acids can now be delivered by nanoparticles made of chitosan. Particle size, encapsulation efficacy, zeta potential, and in vitro release patterns are important assessment criteria.

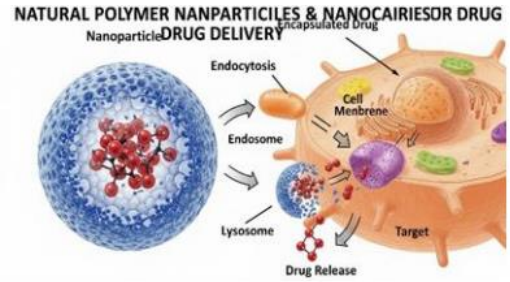


Figure 2: Nanoparticles / Nanocarriers drug delivery.

Formulation:

Nanoparticles of chitosan and tripolyphosphate interact electrostatically in aqueous solution to form an ionic gel (Chitosan-TPP). The emulsion-solvent evaporation procedure involves dissolving the polymer and medicine in an organic solvent, creating an emulsion in water, and then removing the solvent to solidify the combination. Through the process of nanoprecipitation, nanoparticles with a limited size distribution are created when a solution of polymer and drug diffuses quickly into the water phase in a solvent that is miscible with the drug.

Conclusion

In the present study, plant derived polymers proved a promising avenue as multifunctional pharmaceutical excipients with added sustainability and functionality in sustainable approach. The phytochemical profiles of the plant-derived polymers showed satisfactory physical-chemical characteristics such as optimum swelling, viscosity, moisture content, flow properties etc which are critical factors for solid dosage forms. Functional characterization indicates that polymers prepared could successfully serve as binders, disintegrants, suspending agents, suspending agent, thickening agent, sustained-release matrix in drug dosage forms. As a counterpoise to present-day synthetic excipients, the natural origin of plant-derived materials contributes advantages like biocompatible nature, easily biodegradable, very few or none side effects, widely available and low cost of preparation. Eco friendly “green” nature is also another valuable point. Although a matter of concern remains with regard to low-to-lot variation and Standardization; nevertheless, adequate efforts may be made for establishing satisfactory extraction procedures, purification and standardizition. So, it can be said that plant derived polymers show a promising option against current synthetic drugs and present opportunities for application in innovative formulations and other applications of future products.

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