Natural Excipients-An Alternative to Synthetic Excipients: A Comprehensive Review
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ABSTRACT
Though the utilization of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials, but the added advantages offered by these natural excipients are their being non-toxic, less expensive and freely available. The performance of the excipients to some extent determines the quality of the medicines. The traditional concept of the excipients as any constituent other than the active substance has undergone a substantial evolution from an inert and cheap vehicle to an essential constituent of the formulation. Earlier used natural excipients are carrageenan, thaumatin, lard, shilajit, aerosil, myrobolan, storax. Excipients are any component other than the active substances deliberately added to formulation of a dosage form for it proper formulation. Novel drug delivery systems are developed to address the challenges of drug development such as bioavailability, permeability, and poor solubility. Global excipients markets are expected to grow rapidly with the emerging trends in the pharmaceutical industry. The pharmaceutical industry is marketing refinement in the physical structure of active pharmaceutical ingredients (APIs). The present review would facilitate to comprehend various natural excipients and their role in pharmaceutical products.

1. Introduction
An excipients (derived from words excipere to take out, receive) may be defined as any substances mixed with the active pharmaceutical ingredient to give it consistency or used as a vehicle for its administration. It is impossible for any active pharmaceutical ingredient to have properties that allow incorporation in a therapeutic product that meets all the mentioned requirements. Therefore, every therapeutic product is a combination of drug and excipients.

The traditional concept of the excipients as any component other than the active substance has undergone a substantial evolution from an inert and cheap vehicle to an essential constituent of the formulation. The pharmaceutical industry is marketing refinement in the physical structure of active pharmaceutical ingredients (APIs). This article gives an overview of natural excipients which are used in conventional dosage forms as well as novel drug delivery systems[1-3].

Natural Excipients
Natural excipients and derivatives occur ubiquitously throughout the plant and animal kingdoms. Examples of polymers or derivatives that have been used or investigated as vaccine adjuvants are:-

- Individual saponins derived from the South American tree Quillaja saponaria.
- Keyhole limpet hemocyanin (KLH), a nonheme copper containing protein found in anthropods.
- MPL, a monophosphoryl derivative of the Lipid A molecule found in gram-negative bacteria.
- Leishmania elongation initiation factor (LeIF), a protein produced by the parasite leishmania.
- Ricin, a potent immunotoxin obtained from the seeds of castorbean plants[2].

Classification of Excipients
Excipients are commonly classified according to their application and function in the drug products:

- Binders, Diluents
- Lubricants, Gildants, Disintegrants
- Polishing agents, Film formers and coatings agents
- Plasticizers, Colorings
- Suspending agents Preservatives, antioxidants
- Flavorings, Sweeteners, Taste improving agents
- Printing inks, Dispersing agents[4]

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Gums and Mucilage

Gums are considered to be pathological products formed following injury to the plant or owing to unfavorable conditions, such as drought, by a breakdown of cell walls (extra cellular formation; gummosis). Mucilage’s are generally normal products of metabolism, formed within the cell (intracellular formation) and/or are produced without injury to the plant. Gums readily dissolve in water, whereas, mucilage form slimy masses. Muclilage’s are physiological products.

Tamarind Gum

Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, *Tamarindus indica*, a member of the 21 evergreen families. Tamarind Gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds. Microspheres formed were in the size range of 230 - 460 µm. In another study, Diclofenac sodium matrix tablets containing TSP was investigated. The tablets prepared by wet granulation technique were evaluated for its drug release characteristics [5].

Guar gum

Guar gum comes from the endosperm of the seed of the legume plant *Cyamopsis tetragonolobus*. Refined guar splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing. Strong acids cause hydrolysis and loss of viscosity, and alkalies in strong concentration also tend to reduce viscosity. It is insoluble in most hydrocarbon solvents [6].

Locust bean gum

Locust Bean Gum (LBG) (also known as Carob Gum) is obtained from the refined endosperm of seeds from the carob tree *Ceretonia siliqua* L. It is an evergreen tree of the legume family. Carob bean gum is obtained by removing and processing the endosperm from seeds of the carob tree.

Honey locust gum

It is known botanically as *Gleditsia triacanthos*, and belongs to the order Leguminosea (suborder Mimoseae). The gum is obtained from the seeds.

Khaya gum

Khaya gum is a polysaccharide obtained from the incised trunk of the tree *Khaya grandifoliola* (family Meliaceae). The fact that the gum is naturally available, inexpensive and non-toxic has also fostered the interest in developing the gum for pharmaceutical use. Further work has also shown its potential as a directly compressible matrix system in the formulation of 61 controlled release tablets [7,8].

*Aloe Mucilage*

Aloe mucilage is obtained from the leaves of *Aloe barbadensis Miller*. The aloe parenchyma tissue or pulp has been shown to contain proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and small organic compounds in addition to the different carbohydrates. Many investigators have identified partially acetylated mannan (or acemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide [9].

*Hakea Gum*

Hakea gum a dried exudate from the plant Hakea gibbsa family Proteaceae. Gums that are acidic arabinogalactans (type A). Molar proportions (%) of sugar constituents Glucuronic acid, Galactose, Arabinose, Mannose, Xylose is 12:43:32:5:8.

*Konjac glucomannan*

Konjac glucomannan, which is extracted from the tubers of Amorphophallus konjac is a very promising polysaccharide for incorporation into drug delivery systems. Highly hydrophilic galactomannan is obtained from the seeds of Mimosa scabrella (a brazilian leguminous tree called bracatinga) of the Mimosaceae family. Its seeds provided 20–30% of galactomannan (G) with a mannose: galactose ratio of 1.1:1.

*Mimosa pudica*

Mimosa pudica, commonly known as sensitive plant belongs to family Mimosaceae. Mucilage of *M.pudica* is obtained from seeds, which is composed of d-xylose and d-glucuronic acid. Mimosa seed mucilage hydrates and swells rapidly on coming in contact with water. Earlier the seed mucilage was 75 evaluated for binding and disintegrating agent [10].

*Fenugreek*

Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage. Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage-containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids [9].
Pharmaceutical Applications of Gums

In the presence of counter ions, this polymer is capable of forming gels that are particularly strong when formed with divalent ions. Important parameters, like the gel strength, were studied to find a reliable indicator of the gel ocular bioavailability. A recent study reports the preparation of microspheres obtained by the emulsion cross-linking method of gellan and poly (vinyl alcohol) in the presence of different amounts of glutaraldehyde as a cross-linking agent and of an antihypertensive drug. The new microspheres were spherical, with smooth surfaces and with a narrow unimodal size distribution. By increasing the cross-link density, microspheres with smaller size were obtained due to the formation of a more rigid network[11].

Mucilage in Plant Parts

Mucilages found in rhizomes, roots and seed endosperms may act primarily as energy reserves whereas foliar mucilages appear not to serve as storage carbohydrates. Generally, it has been assumed that foliar mucilages are merely secondary plant metabolites, but there are reports, the ionic balance of plant cells and as carbohydrate reserves. It has been suggested that the ability of mucilage to hydrate may offer a mechanism for plants to resist drought.

Intra Cell Mucilage: Source Part

Orchids sp. -Corn Musa paradisiacal -Pulp Aloe -Succulent plant

• Cell-Membrane Mucilage: Secondary Wall

Parenchyma Cells of Wood and Bark

• Cherry-gum, yielded by some of the Amygdalaceae.

Various Cells of the Bark

Acacia senegal, yielding Gum arabic; primary wall as an intercellular substance: making up the pith, medullary ray, parenchyma and other Thallus of Chondrus crispus, Stackhouse and of the origin of mucilage[12].

Pharmaceutical Application of Muclilages

Mucilages are most commonly used as adjuvant in pharmaceutical preparations, with wide range of applications such as thickening, binding, disintegrating, suspending, emulsifying, stabilizing and gelling agents. Mucilages may be used as sustained and controlled release formulations[13].

Polyssacharides

Pectin

Pectins are non-starch, linear polysaccharides extracted from the plant cell walls. The blended alginate and pectin polymer matrix increased the folic acid encapsulation efficiency and reduced leakage from the capsules as compared to those made with alginate alone, they showed higher folic acid retention after freeze drying and storage[14].

Alginates

Alginates are natural polysaccharide polymers isolated from the brown sea weed (Phaeophyceae). Alginic acid can be converted into its salts, of which sodium alginate is the major form currently used. Various applications in drug de-livery are in matrix type alginate gel beads, in liposomes, in modulating gastrointestinal transit time, for local applications and to deliver the bio molecules in tissue engineering applications.

Uses of alginates

Alginates have proven to be effective for the symptoms of malignant wounds. • Bleeding in malignant wounds is caused by the absence of platelets and the abundance of friable capillaries. Because bleeding occurs easily, it is essential that dressings do not adhere or cause trauma. Alginates are ideal for bleeding wounds as they have haemostatic properties[15].

Starch

Starch that is a natural polysaccharide polymeric material widely exists in fruit, root, pedicle, and leaf of plants.

Starch is classified into

I. Raw starch

II. Physical-modified starch or chemical-modified starch.

Modified starch was tested for general applicability of a new pregelatinized starch product in directly compressible controlled-release matrix systems.

Amphoteric Starch

Amphoteric starches have been used as wet-end and size-press papermaking additives by aid in retention, drainage and strength properties. They can also be used as ceiling tile additives drilling fluid additives, viscosity modifiers and agents in ore recovery operations[16].

Chitosan

Chitosan is a natural positively charged (cationic) biopolymer derived from the hydrolysis of the polysaccharide chitin. Chitin is an amino polysaccharide (combination of sugar and protein) abundantly available natural biopolymer found in the exoskeletons of crustacean like shrimp, crab, lobster and other shellfish.
Properties of Chitosan

Chitosan is a linear randomly distributed, hetero polysaccharide consisting of S (1→4) linked 2-acetamido-2-deoxy-S-D-glucopyranose and 2-amino-2-deoxy-S-D-glycopyranose units.

Physicochemical Properties

Chitosan is highly basic polysaccharides due to presence of primary amino group in its structure. The main factors which may affect the CS properties are its molecular weight and degree of deacetylation (DD). These factors enable the researcher to formulate different grades of CS which differ primarily in molecular weight and degree of deacetylation.

Biological Properties

Due to its bioadhesive property, it can adhere to hard and soft tissues and has been used in dentistry, orthopedics and ophthalmology and in surgical procedures. It also has a fungistatic or bacteriostatic, anticancerogen and anticholestermic action[17,18].

Application of Polysaccharides

Natural polysaccharides are extensively used for the development of solid dosage forms. These polymers of monosaccharide’s (sugars) are inexpensive and available in a variety of structures with a variety of properties. They are highly stable, safe, non-toxic, and hydrophilic and gel forming in nature. Pectin’s, starch and amylase are a few polysaccharides commonly used in controlled release dosage forms[19].

Conclusion

Nowadays the hassle is on patient compliance and to achieve this objective there is an eruption in the developing NDDS. As the herbal excipients are promising biodegradable materials, these can be chemically compatible with the excipients in drug delivery systems. Besides this, herbal excipients are non-toxic, freely available, and less expensive compared to their synthetic counterparts. They have a major task to play in pharmaceutical industry. Therefore, in the years to come, there is going to be constant interest in the natural excipients to have better materials for drug delivery systems.

References

[7]. Pawar H., D’mello P., Isolation of seed gum from Cassia tora and preliminary studies of its applications as a binder for tablets, Indian Drugs, 2004; 41:465-468.


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