Review On: Role Of Herbal Excipients In Pharmaceutical Formulations

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ABSTRACT:
The use of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials.With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to use most of them in their formulationPharmaceutical formulation development involves various components in addition to the active pharmaceutical ingredients. However advantages offered by these natural excipients are their being non-toxic, less expensive and freely available. The performance of the excipients partly determines the quality of the medicines. 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.This article gives an overview of natural excipients which are used in controlled drug delivery systems. Therefore, we conclude that the natural excipient proposed can be used as binder, diluent and disintegrant in oral disintegrating tablets and immediate release dosage forms. Mainly the natural excipient used is biocompatible, cost effective and provides as nutrition supplements.

KEYWORDS:

Herbal excipients, Polysaccharides, Natural excipient, Pharmaceutical application Pharmaceutical excipient.

INTRODUCTION:

Excipients are defined as 'the substance used as a medium for giving a medicament'. Excipient in past mainly used to form bulk of formulations as it contain potent drugs which could not be taken alone and to assure uniformity of drug in dosage form. In recent years, plant derived polymers have evoked tremendous interest due to their diverse pharmaceutical applications such as diluent, binder, disintegrants in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppository , they are also used in cosmetics, textiles, paints and paper-making. Due to advancement in drug delivery system, there is need of novel excipients to fulfill the multi-functional role like affecting release pattern, improvement of bioavailability and stability, enhancement of patient acceptability. For these purpose researchers have been investigated both natural and synthetic excipients.

As the establishment of toxicity and approval from regulatory authorities poses a problem with synthetic excipients, of late more interest is being shown by researchers in herbal excipients. The drawback posed by heavy metal contamination often associated with herbal excipients is superseded by their lack of toxicity, easy availability, and economic considerations in pharmaceutical industry as compared to their synthetic counterparts. Present day consumers look for natural ingredients in food, drugs, and cosmetics as they believe that anything natural will be more safe and devoid of side effects.

CLASSIFICATION OF EXCIPIENTS:

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

- Binders, Diluents
- Lubricants, Glidants, Disintegrants
- Poolishing Film formers and coatingsagents
- Plasticizers, Colorings
- Suspending agents Preservatives,antioxidants
- Flavorings, Sweeteners, Taste improvingagents
- Printing inks, Dispersing agents

TYPES OF HERBAL EXCIPIENTS:

Gums:

Gums are translucent and amorphous substances produced by the plants. Usually pathological products, gums are produced when the plant is growing under unfavorable conditions or when injured. Gums are plant hydrocolloids and may be anionic or non ionic polysaccharides. On hydrolysis gums yield sugar and salts of uronic acid.

Guar gum:

Guar gum derived from the seeds of cyamopsis tetragonolobus (Family Leguminosae) is a naturally occurring galactomannan polysaccharide. It is made up of a linear chain of β-D-mannopyranose joined by β-(1–4) linkage with α-D-galactopyranosyl units attached by 1, 6- links in the ratio of 1:22

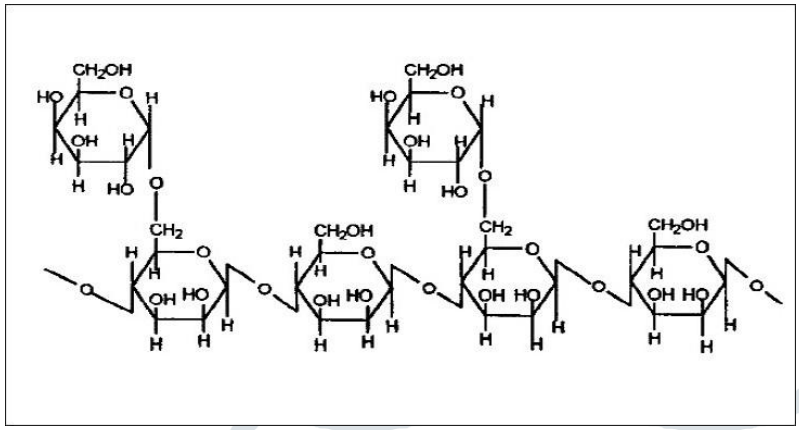

Fig 1: Structure of Guar gum

Guar gum is used in colon-delivery systems due to its drug release retarding property and susceptibility to microbial degradation in the large intestine. Core tablets containing 5-aminosalisylic acid (5–ASA) were prepared by wet granulation with starch paste and were compression coated with coating formulations containing different quantities of guar gum The study confirmed that selective delivery of 5–ASA to the colon can be achieved using guar gum as a carrier in the form of a compression coating over the drug core21. Further, guar gum-based matrix tablets of rofecoxib were prepared for their intended use in the chemoprevention of colorectal cancer. In vivo studies showed delayed Tmax, prolonged absorption time and decreased Cmax indicating that rofecoxib was not released significantly in stomach and small intestine, but was delivered to colon resulting in a slow absorption of the drug and making it available for local action in human colon.

In an attempt to design oral controlled drug delivery systems for highly water-soluble drugs using guar gum as a carrier in the form of three-layer matrix tablets, trimetazidine dihydrochloride was chosen as a model drug because of its high water solubility. Both matrix tablets as well as three layer matrix tablets were prepared and evaluated. The three-layer guar gum matrix tablet provided the required release rate on par with the theoretical release rate for guar gum formulations meant for twice daily administration.

The results indicated that guar gum, in the form of three-layer matrix tablets, is a potential carrier in thedesign of oral controlled drug delivery systems for highly water-soluble drugs such as trimetazidine dihydrochloride23. The same study was carried out by using metoprolol tartrate a model drug with high solubility. The results indicated that guar gum, in the form of three-layer matrix tablets, is a potential carrier in the design of oral controlled drug delivery systems for highly water-soluble drugs such as metoprolol tartrate. Another water soluble drug, diltiazem HCl has given controlled release comparable with marketed sustained release diltiazem HCl tablets (D-SR tablets), which are prepared in the form of matrix tablets with guar gum using the wet granulation technique.

Bhara gum:

This yellow coloured natural gum obtained from plant Bahera; when extracted from bark of Terminalia bellerica belonging to family combretaceae. The main components which are giving film forming property to the gums are tannins. Bhara gum has wide application as it is hydrophilic and biocompatibility, in various cosmetics it is used as emulgent 31. Microencapsules of famotidine using bhara gum when examined by in vitro drug release profile shown slow release of drug over 10hrs thus could be used for sustained drug delivery system.

Gum acacia:

Gum acacia or gum arabic is the dried gummy exudate obtained from the stem and branches of Acacia senegal (Linne) Willdenow and other related species of acacia (Family Leguminosae). The gum has been recognized as an acidic polysaccharide containing D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid. Acacia is mainly used in oral and topical pharmaceutical formulations as a suspending and emulsifying agent, often in combination with tragacanth. It is also used in the preparation of pastilles and lozenges and as a tablet binder. Sustained release of ferrous sulfate was achieved for 7 h by preparing gum arabic pellets. Release was further sustained for more than 12 h by coating the pellets with polyvinyl acetate and ethylene vinyl acetate, respectively. An increase in the

amount of gum arabic in the pellets decreased the rate of release due to the gelling property of gum arabic. The gel layer acts as a barrier and retards the rate of diffusion of FeSO4 through the pellet.

Gum arabic was used as an osmotic, suspending and expanding agent in the preparation of a monolithic osmotic tablet system (MOTS) with two orifices on both side surfaces. Water-insoluble naproxen was selected as the model drug. The optimal MOTS was found to be able to deliver naproxen at a rate of approximately zero order up to 12 h in pH 6.8. Cumulative release at 12 h is 81%, and is independent of environment media and stirring rate. Therefore, these MOTS can be used in the oral drug-controlled delivery field, especially for water-insoluble drugs.

Karaya gum:

Karaya gum is obtained from Sterculia urens (Family sterculiaceae) is a partially acetylated polymer of galactose, rhamnose, and glucuronic acid. Swellable hydrophilic natural gums like xanthan gum and karaya gum were used as release-controlling agents in producing directly compressed matrices. Caffeine and diclofenac sodium, which are having different solubilities in aqueous medium were selected as model drugs. Gum erosion, hydration and drug release studies were carried out using a dissolution apparatus (basket method) at two agitation speeds. In case of xanthan gum neither agitation speed nor drug solubility had any significant effect on water uptake, but matrices with the lower proportion of gum produced a lesser degree of hydration. In contrast, karaya gum displayed a much lower hydration capacity and a higher rate of erosion, both markedly affected by agitation speed. Hence it was concluded that drug release from xanthan and karaya gum matrices depended on agitation speed, solubility and proportion of drug. Both xanthan and karaya gums produced near zero order drug release with the erosion mechanism playing a dominant role, especially in karaya gum matrices. That mucoadhesive tablets prepared by karaya gum for buccal delivery, had superior adhesive properties as compared to guar gum and was able to provide zero-order drug release, but concentrations greater than 50% w/w may be required to provide suitable sustained release.

Xanthan Gum:

Xanthan gum is a high molecular weight extra cellular polysaccharide produced by the fermentation of the gram-negative bacterium Xanthomonas campestris. The primary structure of this naturally produced cellulose derivative contains a cellulosic backbone (β-D-glucose residues) and a trisaccharide side chain of β-D-mannose-β- D- glucuronicacid- α- D-mannose attached with alternate glucose residues of the main chain. The terminal D-mannose residue may carry a pyruvate function, the distribution of which is dependent on the bacterial strain and the fermentation conditions. The non-terminal D-mannose unit in the side chain contains an acetyl function. The anionic character of this polymer is due to the presence of both glucuronicacid and pyruvic acid groups in the side chain 11.

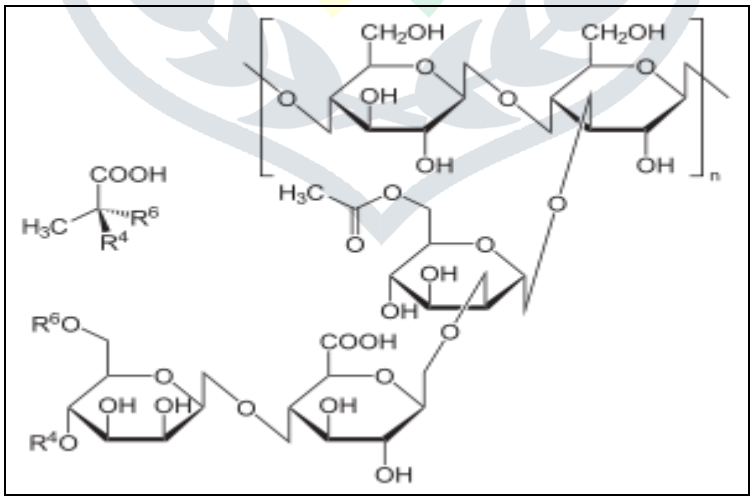

Fig2: STRUCTURE OF XANTHAN GUM

In one of the trials, xanthan gum showed a higher ability to retard the drug release than synthetic hydroxypropylmethylcellulose . Compaction and compression properties of xanthan gum pellets were evaluated and drug release from tablets made of pellets was characterized. Two types of pellets were prepared by extrusion-spheronisation. Formulations included xanthan gum, at 16% (w/w) and diclofenac sodium or ibuprofen, at 10% (w/w) among other excipients. Physical properties of pellets and tablets were analysed. Pellets showed close compressibility degrees (49.9% for pellets comprising diclofenac sodium and 48.5% for pellets comprising ibuprofen). The release of the model drug from both type of tablets revealed different behaviours. Tablets made of pellets comprising

ibuprofen released the model drug in a bimodal fashion and the release behaviour was characterised as Case II transport mechanism (release exponent of 0.93). On the other hand, the release behaviour of diclofenac sodium from tablets made of pellets was anomalous (release exponent of 0.70). For the latter case, drug diffusion and erosion were competing mechanisms of drug release .

Pectins:

Pectins are non-starch, linear polysaccharides extracted from the plant cell walls. They are predominantly linear polymers of mainly (1–4)-linked D-galacturonic acid residues interrupted by 1,2- linked L-rhamnose residues with a few hundred to about one thousand building blocks per molecule, corresponding to an average molecular weight of about 50 000 to about 1 80 0002. Being soluble in water, pectin is not able to shield its drug load effectively during its passage through the stomach and small intestine. It was found that a coat of considerable thickness was required to protect the drug core in simulated in vivo conditions2. Hence the focus was shifted to the development of less soluble derivatives of pectin which get degraded by the colonic microflora. Calcium salts of pectin reduced their solubility by forming an egg-box configuration. To overcome the drawback of high solubility of pectin, mixed films of pectin with ethyl cellulose were investigated as a coating material for colon-specific drug delivery. These films combined the colon specific degradation properties of pectin with the protective properties of the water insoluble polymer ethyl cellulose.

Polymeric hydrogels are widely used as controlled-release matrix tablets. Sungthongjeen investigated the high-methoxy pectin for its potential value in controlled-release matrix formulations. The effects of compression force, ratio of drug to pectin, and type of pectin on drug release from matrix tablets were also investigated. The results of the in vitro release studies showed that the drug release from compressed matrix tablets prepared from pectin can be modified by changing the amount and the type of pectin in the matrix tablets. A very low solubility pectin-derivative (pectinic acid, degree of methoxylation 4%) was found to be well suited as an excipient for pelletisation by extrusion/spheronisation. The capacity as an extrusion aid was found to be high; even formulations containing only 20% pectinic acid resulted in nearly spherical pellets. All pectinic acid pellets were mechanically stable, had an aspect ratio of approximately 1.15–1.20 and released 30–60% of a low solubility model drug within 15 min both in simulated gastric fluid (0.1M HCl) and intestinal fluid (phosphate buffer pH 6.8).

Micro particulate polymeric delivery systems have been suggested as a possible approach to improve the low bioavailability characteristics shown by standard ophthalmic vehicles (collyria). In this context pectin microspheres of piroxicam were prepared by the spray drying technique. In vivo tests in rabbits with dispersions of piroxicam-loaded microspheres also indicated a significant improvement of piroxicam bioavailability in the aqueous humour (2.5–fold) when compared with commercial piroxicam eyedrops.

Musabayane investigated the suitability of amidated pectin as a matrix patch for transdermal chloroquine delivery in an effort to mask the bitter taste when orally administered. The results suggest that the pectin-chloroquine patch matrix preparation has potential applications for the transdermal delivery of chloroquine and perhaps in the management of malaria. Calcium pectinate nanoparticles to deliver insulin were prepared as a potential colonic delivery system by ionotropic gelation. In relation to the food industry, folic acid incorporated microcapsules were prepared using alginate and combinations of alginate and pectin polymers so as to improve stability of folic acid. Folic acid stability was evaluated with reference to encapsulation efficiency, gelling and hardening of capsules, capsular retention during drying and storage. 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. In relation to cosmetics, using citronellal as a model compound, pectin gel formulations were evaluated for controlled fragrance release by kinetic and static methods. These formulations showed a prolonged duration of fragrance release and limitation of fragrance adsorption to the receptor skin layers. The increase in pectin concentrations suppressed the fragrance release by a diffusion mechanism, thereby proving that pectin/calcium microparticles are promising materials for controlled fragrance release.

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. A linear polymer consisting of D-mannuronic acid and L-guluronic acid residues arranged in blocks in the polymer chain, these homogeneous blocks (composed of either acid residue alone) are separated by blocks made of random or alternating units of mannuronic and guluronic acids. Alginates offer various applications in drug delivery, such as 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.

In a comparative study, alginate formulation appeared to be better than the polylactide-co-glycolide (PLG) formulation in improving the bioavailability of two clinically important antifungal drugs-clotrimazole and econazole. The nanoparticles were prepared by the emulsion-solvent-evaporation technique in case of PLG and by the cation-induced controlled gelification in case of alginate.

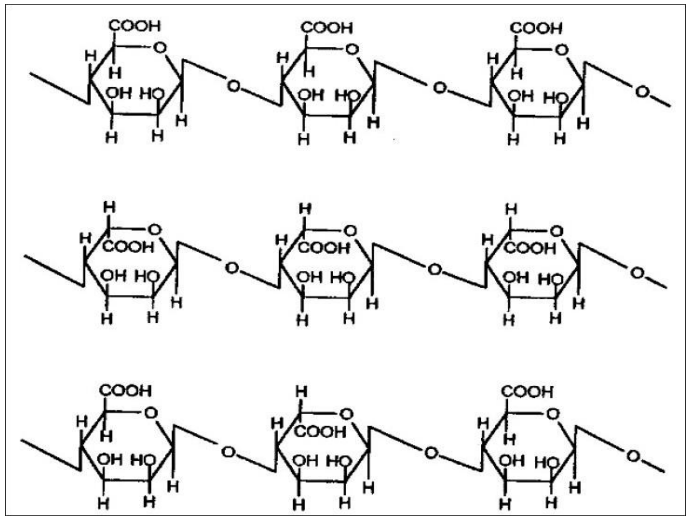

Fig3: Structure of Alginates

MAJOR ROLE OF HERBAL EXCIPIENT IN NOVEL DRUG DELIVERY SYSTEM:

Excipients of natural origin are of particular interest to us for reasons of reliability, sustainability and avoiding reliance upon materials derived from fossil fuels. Plant products are therefore attractive alternatives to synthetic products because of biocompatibility, low toxicity, environmental "friendliness", and low price compared to synthetic products.

PHARMACEUTICAL APPLICATIONS OF POLLYSACHARIDES/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 amonts 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.

- 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.

FORMULATIONS PREPARED WITH NATURAL EXICIPIENTS:

TAMARIND GUM

Tamarind xyloglucan is obtained from endosperm of the seed of the tamarind tree, Tamarindus indica, a member of evergreen family. Tamarind gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds. The seeds are processed in to gum by seed selection, seed coat removal, separation, hammer milling, grinding and sieving. Tamarind gum is polysaccharide composed of glucosyl : xylosyl : galactosyl in the ratio of 3:2:1 xyloglucan is a major structural polysaccharide in the primary cell walls of higher plants5. Tamarind seed polysaccharide (TSP) which is obtained from the seed kernel of Tamarindus indica, Tamarindus indica belonging to family leguminacy , Xyloglucans (XGs), also called amyloids, are widespread in nature in plants.

Tamarind gum is non Newtonian and yield higher viscosities than most starches at equivalent concentration. This has led to its application as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries.

Tamarind seeds consist of:-

Polysaccharide (35 - 55%),Proteins (18-20%)Tamarind bean – raw,Lipids (6-10%),Fiber (7 - 18%),Fat (3 - 7.10%),Inorganic salts,Freesugars,Moisture (4 – 10%),Ash (1 - 3%).

The white kernel obtained of tamarind seeds are utilized for producing Tamarind Kernel Powder. Tamarind kernel is rich in Protein, Carbohydrates, Fibers and Oils.Tamarind Kernel Powder is the combination of Galactoxyloglucan polysaccharide (55-65%).

The white kernel obtained of tamarind seeds are utilized for producing tamarind kernel powder. Tamarind kernel is rich in protein, carbohydrates, fibers and oils. In a study the tamarind seed polysaccharide (TSP) was isolated from tamarind kernel powder and this polysaccharide was utilized in the formulation of matrix tablet containing Diclofenac sodium by wet granulation technique and evaluated for its drug release characteristics.

OCIMUM SANCTUM LINN

Ocimum sanctum Linn (known as Tulsi in Hindi), a small herb seen throughout India.Ocimum sanctum (Family Labiatae) is a many branched, erect, stout and aromatic herb about 75 cms high. This small herb is found throughout India and is cultivated, worshiped in temples and houses of Hindus. The leaves, seeds and root of this plant have been used in indigenous Ayurvedic medicine. The chemical composition of Tulsi is highly complex, containing many nutrients and other biological active compounds.

CONCLUSION:

In addition to conventional pharmaceutical excipients as bulking agents, substance used for masking taste/texture or as a substance use to aid during manufacturing process, Novel excipients offer broad range of additional properties suitable to preserve the integrity of active constituents of the formulation and enhances it's self life. The synthetic polymers can be designed or modified as per requirement of the formulation; by altering polymer characteristics and on the other hand herbal pharmaceutical excipients are biocompatible, nontoxic, environment friendly and economical. It seems conceivable that in the near future, kilogramquantities of fusion proteins, fibronectin, poly (lysine), or hemolysin could become available as off-the-shelf excipients or as designer excipient kits. Excipients that have never been used before must pass formidable regulatory requirements before being incorporated into approved dosage forms

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