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## ADVANTAGES AND APPLICATIONS OF NATURE EXCIPIENTS – A REVIEW

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### ABSTRACT

It is well known that none of dosage forms either for internal use or external use can be manufactured without excipients. However, bio-availability and stability of the dosage forms are fully dependent on the type of excipients used, their concentration in the product and interaction with the active material. The detailed study of physical and chemical properties of the excipients along with their safety and the precautions to handle them must be known to the technologists undertaking the manufacture and development of dosage forms. This review focused on nature excipients, advantages and applications of nature excipients.

**Keywords:** Nature excipients, Advantages, Application.

### INTRODUCTION

Excipients are pharmaceutical additives, the inactive ingredients used to make up a medication. They include dyes, flavors, binders, emollients, fillers, lubricants, preservatives, and many more classifications. Common excipients include cornstarch, lactose, talc, magnesium stearate, sucrose, gelatin, calcium stearate, silicon dioxide, shellac [1].

#### Role of Excipients in Formulations

Binders are used in the formulation of solid oral dosage forms to hold the active pharmaceutical ingredient and inactive ingredients together in a cohesive mix. Binder products are usually differentiated based on the manufacturing process to be used. Dry binders used for direct compaction must exhibit cohesive and adhesive forces so that when compacted the particles agglomerate. Binders used for wet granulation are hydrophilic and soluble in water and are usually dissolved in water to form a wet mass that is then granulated. Binders function as binder for both direct compression and wet granulation. As a dry binder, it compresses well, predominately deforming plastically. It has been shown to produce cohesive dry

blends due to its granular morphology and superior adhesive characteristics. As a result of its partial cold water solubility, it functions exceptionally well in wet granulation applications and performs dual functions of both a disintegrant and a binder. In capsule filling processes, Starch and Star Cap Co-Processed Starch Excipients function as effective binders improving the uniformity of the capsule fill as well as forming a stable capsule plug. Cellulose Ethers can be used as binders in the wet granulation of tablets to produce hard tablets with low friability and consistent disintegration rates. They are extremely versatile and can be used in both aqueous and solvent systems [2].

#### Film Coating Functions

Film coatings offer many advantages for all phases of pharmaceutical and nutritional solid oral dose development as well as benefits for the consumer. Some of these benefits include reducing operation costs, drug protection, modifying drug release, creating a strong recognizable brand, and ensuring product safety and effectiveness [3].

### ***Immediate Release Film Coating Systems for Tablets***

The innovator and industry standard for complete film coating systems, offers a range of custom pigmented and non-pigmented film coatings for immediate release solid dose applications. Our film coating formulas produce attractive, elegant coatings on even the most challenging tablet surfaces and can be used in both aqueous and organic coating procedures.

An extensive selection of polymer blend formulations provides the user with the ability to impart many beneficial features to a solid oral dosage formulation. Benefits include:

Reduced coating process time

- Superior adhesion on difficult to coat cores
- Less stressful processing conditions for heat sensitive, friable or high drug content cores
- Sharper logo definition, even at higher weight gains
- Better gloss and smoothness compared to conventional film coatings
- Improved color stability

Aqueous film coating is the quickest and least expensive method for enhancing your tablet appearance and, unlike other methods, will not affect dissolution or disintegration profiles. Our custom formulated, dry-blend systems consist of polymers, plasticizers and pigments, combined in one, easy-to-use, dry powder system which is rehydrated quickly and simply with water. It also offers customized color selection and color matching of our immediate release tablet film coating products. Film coating polymers has produced many enhanced polymer combinations resulting in new tablet coating options for our customers. Our newly developed, dry coating technology provides benefits such as improved adhesion, reduced processing times, and application of the tablet coating at wider process parameters. Additional advances in our immediate release tablet film coating technology include high gloss and pearlescence, which not only give a more elegant appearance to your solid oral dosage form, but provide unique opportunities for branding and tablet identification [4].

### ***Extended/Controlled Release Coatings***

It offers advanced film coating systems for extended/controlled release dosage forms. While there are multiple solutions available for barrier membrane extended/controlled release technologies. best-in-class polymer products are complemented by our value-added services which support all phases of product design and development. Extended/controlled release technologies from Col use unique combinations of polymers to encapsulate active drug compounds and control release of the drug at varying rates. Through advanced technology, our extended/controlled release products simplify the development and production process for tablets and

capsules while providing consistent rates of drug release [5].

### ***Extended/controlled release barrier membranes***

Designed for extended/controlled release multiparticulate, tablet and taste masking applications, Surelease is an easy-to-use, totally aqueous coating system using ethylcellulose as the release rate controlling polymer. The dispersion provides the pharmaceutical formulator with flexibility to adjust drug release rates in the design of extended/controlled release technologies. Surelease NG is latest system addition, offering enhanced stability over time, improved reproducibility and extended shelf life (24 months). Ethylcellulose Polymers Available in a range of viscosity grades, premium ethylcellulose polymers have ideal properties for use in a variety of pharmaceutical applications. (Ethylcellulose) polymers are most frequently used as barrier membranes to achieve extended/controlled release in multiparticulate formulations. Ethyl cellulose is among only a very small number of water-insoluble polymers that are approved and accepted globally for pharmaceutical applications. Global technical service infrastructure and applications expertise complements the product line and is available for servicing your formulation needs at every step of the drug development process [6].

### ***Diluents***

Diluents are fillers used to increase the bulk volume of a tablet or capsule. By combining a diluent with the active pharmaceutical ingredients, the final product is given adequate weight and size to assist in production and handling [7].

To provide satisfactory performance in a tablet dosage form, a diluent should be:

- Inert so as not to cause pharmacological activity of its own.
- Compatible with the drug substance and other excipients used in the formulation.
- Non-hygroscopic so the formulation does not absorb significant amounts of moisture from its surroundings.
- Compactable and of similar particle size to the active ingredient.

Diluents may serve multiple functions in addition to being filler. Multifunctional starch excipients, such as Starch 1500<sup>®</sup> partially pregelatinized maize starch and StarCap 1500<sup>®</sup> co-processed starch excipient can serve as binders, disintegrants, flow aids, lubricants and/or taste masking. They also promote formulation flexibility by complementing and enhancing the functionality of other excipients [8].

### ***Starch***

Starch is a unique pharmaceutical excipient

which provides good binding and granulation properties, yet retains effective tablet disintegrant properties. The physical structure of Starch1500 also imparts good compactability, flow and lubrication capabilities. It is extremely versatile as a diluent, being effective in a variety of processing methods for solid oral dosage forms [9].

### **StarCap**

StarCap is a unique co-processed mixture of globally accepted excipients designed for use in capsules and tablets. StarCap1500 is an inert free flowing, low dust excipient with disintegration and dissolution properties that are independent of media pH. StarCap1500 exhibits good physical, chemical, and microbiological stability and its multi-functionality make it an excellent choice for use as a diluent in either capsules or tablets.

### **Enteric/Delayed Release Coatings**

Enteric/delayed release coatings consist of pH sensitive polymer, which means the coating remains intact in the acidic environment of the stomach and then solubilizes in the more alkaline environment of the small intestine. Enteric protection for solid oral dosage forms is required to prevent gastric mucosal irritation, to protect a drug which is unstable in gastric fluids or to delay release for local delivery in the intestine. Coating systems are based on a range of enteric polymers to suit the needs of the pharmaceutical formulator. Enteric/delayed release products are compatible with a broad range of active drug substances in several therapeutic categories, including low and high dose drugs, water soluble or insoluble drugs and drugs with a short half-life or a narrow therapeutic window [10].

### **Disintegration of Capsules and Tablets**

The efficacy of a drug mixture can be dependent on the rate at which the tablet or capsule disintegrates in the patient's gastrointestinal tract. For all solid oral dosages, disintegrant may be added to a drug formulation as functional fillers. These excipients assist in the disintegration of the capsule or tablet when it is introduced to moisture.

### **Disintegrants**

Functional starch excipients bring multi-functional benefits to tablets and capsule formulations through binding capability, improved disintegration properties, and enhanced flow and lubricity.

### **Rate Controlling Polymers**

Through our global Controlled Release Alliance with the Dow Wolff Cellulosic, It offers an enhanced portfolio of extended/controlled release application expertise to find ideal solutions to our customers' needs and help speed their products to market [11].

The alliance includes the exclusive global distribution rights for Dow Wolf cellulose' products, including ETHOCEL™ premium ethylcellulose polymers, METHOCEL™ premium hydroxypropyl methylcellulose (HPMC), and POLYOX™ water-soluble resins. Dow Wolf cellulose offers more than 50 years of experience in HPMC production, which is the most trusted polymer available for use in extended/controlled release drug delivery systems. ETHOCEL™, METHOCEL™ and POLYOX™ polymers offer an outstanding range of extended/controlled release properties for a wide variety of dosage forms and processing methods. Many variations in molecular weights and chemical substitutions give you multiple ways to optimize formulation performance. Each range has fundamentally different hydrophilicity, swelling and erosion characteristics, to provide flexibility in control of the main mechanisms of release [12].

### **Enteric/Delayed Release Coatings**

Organic and aqueous options for the manufacture of enteric coated tablets or multiparticulates, combined with the expertise and infrastructure to support your every step of development – from initial technology development through final commercialization and product delivery. Enteric/delayed release coatings consist of pH sensitive polymers, which means the coating remains intact in the acidic environment of the stomach and then solubilizes in the more alkaline environment of the small intestine. Enteric protection for solid oral dosage forms is required to prevent gastric mucosal irritation, to protect a drug which is unstable in gastric fluids or to delay release for local delivery in the intestine. Coating systems are based on a range of enteric polymers to suit the needs of the pharmaceutical formulator. Enteric/delayed release products are compatible with a broad range of active drug substances in several therapeutic categories, including low and high dose drugs, water soluble or insoluble drugs and drugs with a short half-life or a narrow therapeutic window. Use of our fully-formulated technologies can help you deliver a final product that saves you development, scale-up and production time while assuring the integrity of the enteric/delayed release coating to the safety and efficacy of your finished dosage form [13].

### **Sources of Excipients**

Excipients are of various origins: animal (e.g. lactose, gelatin, and stearic acid), plant (e.g. starches, sugars, cellulose, and alginates), mineral (e.g. calcium phosphate, silica) and synthesis (e.g. PEGs, polysorbates, povidone, etc.) and they often lack a trade name. Their origin and use do not often guarantee the quality required by the pharmaceutical industry, which must therefore submit them to more thorough-going analytical controls. In order to carry out the numerous functions required, new classes of excipients have now become available, derived from old and new materials, alone or in

combination, adapted to the manufacture of high-performance pharmaceutical dosage forms. Looking at the matter from this angle, excipients can no longer be considered mere inert supports for the active principles, but essential functional components of a modern pharmaceutical formulation. It is also to be borne in mind that the ratio of their weight to that of the active principles is usually very high in a formulation, and such as to cause possible action due to their mass [14].

Like pharmaceutical drugs, they too have their own thermo-dynamic activity which, though generally low, can contribute to reactions leading to degradation or to interactions between the drug and the excipients. Today it is reckoned that over one thousand different materials are used in the pharmaceutical industry to fulfil its various requirements such as diluents, bulking agents, disintegrants, lubricants, colouring agents, sweeteners, etc. They are chemically heterogeneous compounds that go from simple molecules (water) to complex mixtures of natural, semisynthetic or synthetic substances which, from the regulatory point of view, may be subdivided into three categories. In the first category (approved excipients) we find the compounds originating from the food industry (generally recognized as safe: GRAS) or that have been present in pharmaceutical products for a very long time. The intermediate category (essentially new excipients) covers compounds obtained by means of the structural modification of the excipients already approved or those already used in the food or cosmetic industries. The third category covers new compounds, never previously used in the pharmaceutical field and it is growing rapidly due to the present interest in modified-release formulations and the requirements of the modern high-productivity compressing/tabletting machines [15].

#### CLASSIFICATION OF NATURAL EXCIPIENTS

- Excipients are obtained from various natural sources, they are used in the preparation of wide range of dosage forms.
- Their large number and varied occurrence, several uses make them difficult to put them in uniform pattern [16].

**Based on Origin:** It is of three kinds,

**A. From animal:** Beeswax, Cochineal, Gelatin, Honey, Lactose, Lanolin, Spermaciti, Musk, Suet etc.

**B. From Vegetable:** Kokum, butter, Bentonite, Kieselghur, Kaolin, Paraffins, Talc, alamine, Fuller's, earth, Asbestos etc.

**C. From Minerals:** Pectin, Starch, Peppermint, Cardamon, Vanilla, Tumeric, Saffron, Guargum etc

#### DESCRIPTION OF EXCIPIENTS

##### *Antiadherents*

Antiadherents are used to reduce the adhesion between the powder (granules) and the punch faces and thus prevent sticking to tablet punches. They are also used to help protect tablets from sticking. Most commonly used is magnesium stearate.

##### *Binders*

Binders hold the ingredients in a tablet together. Binders ensure that tablets and granules can be formed with required mechanical strength, and give volume to low active dose tablets. Binders are usually:

Saccharides and their derivatives:

Disaccharides: sucrose, lactose; Polysaccharides and their derivatives: starches, cellulose or modified cellulose such as microcrystalline cellulose and cellulose ethers such as hydroxypropyl cellulose (HPC); Sugar alcohols such as xylitol, sorbitol or maltitol; Protein: gelatin; Synthetic polymers: polyvinylpyrrolidone (PVP), Polyethylene glycol (PEG) [17].

##### *Classification of Binders According to Their Application*

- Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose and polyethylene glycol.
- Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose, polyvinylpyrrolidone and polyethylene glycol.

##### *Coatings*

Tablet coatings protect tablet ingredients from deterioration by moisture in the air and make large or unpleasant-tasting tablets easier to swallow. For most coated tablets, a cellulose ether hydroxypropyl methylcellulose (HPMC) film coating is used which is free of sugar and potential allergens. Occasionally, other coating materials are used, for example synthetic polymers, shellac, corn protein zein or other polysaccharides. Capsules are coated with gelatin [18].

##### *Changing the Dissolution Rates of Active Species*

###### *Enterics*

Control the rate of drug release and determine where the drug will be released in the digestive tract.

###### *Disintegrants*

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. Disintegrant types include:

- Water uptake facilitators
- Tablet rupture promoters

They ensure that when the tablet is in contact with water, it rapidly breaks down into smaller fragments, facilitating dissolution.

**Disintegrants include**

- Crosslinked polymers: crosslinked polyvinylpyrrolidone (crospovidone), crosslinked sodium carboxymethyl cellulose (croscarmellose sodium).
- The modified starch sodium starch glycolate.

**Fillers and Diluents**

Fillers fill out the size of a tablet or capsule, making it practical to produce and convenient for the consumer to use. By increasing the bulk volume, the fillers make it possible for the final product to have the proper volume for patient handling. Good filler must be inert, compatible with the other components of the formulation, non-hygroscopic, relatively cheap, compactible, and preferably tasteless or pleasant tasting. Plant cellulose (pure plant filler) is a popular filler in tablets or hard gelatin capsules. Dibasic calcium phosphate is popular tablet filler. A range of vegetable fats and oils can be used in soft gelatin capsules. Other examples of fillers include: lactose, sucrose, glucose, mannitol, sorbitol, calcium carbonate, and magnesium stearate [19].

**Flavours**

Flavours can be used to mask unpleasant tasting active ingredients and improve the likelihood that the patient will complete a course of medication. Flavourings may be natural (e.g. fruit extract) or artificial.

For example, to improve:

- a bitter product - mint, cherry or anise may be used
- a salty product - peach, apricot or liquorice may be used
- as our product - raspberry or liquorice may be used
- an excessively sweet product - vanilla may be used

**Colors**

Colours are added to improve the appearance of a formulation. Colour consistency is important as it allows easy identification of a medication.

**Lubricants**

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall. Common minerals like talc or silica, and fats, e.g. vegetable stearin, magnesium stearate or stearic acid are the most frequently used lubricants in tablets or hard gelatin capsules. Lubricants are agents added in small quantities to tablet and capsule formulations to improve certain processing characteristics.

**Roles Identified With Lubricants**

True Lubricant Role:

- To decrease friction at the interface between a tablet's surface and the die wall during ejection and reduce wear on punches & dies.

Anti-adherent Role:

- Prevent sticking to punch faces or in the case of encapsulation, lubricants
- Prevent sticking to machine dosators, tamping pins, etc

Glidant Role:

- Enhance product flow by reducing interparticulate friction.

**Major Types of Lubricants****1. Hydrophilic**

- Generally poor lubricants, no glidant or anti-adherent properties.

**2. Hydrophobic**

- Most widely used lubricants in use today are of the hydrophobic category. Hydrophobic lubricants are generally good lubricants and are usually effective at relatively low concentrations.
- Many also have both anti-adherent and glidant properties. For these reasons, hydrophobic lubricants are used much more frequently than hydrophilic compounds.
- Examples include magnesium stearate [20].

**Glidants**

Glidants are used to promote powder flow by reducing interparticle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce die wall friction. Examples include fumed silica, talc, and magnesium carbonate.

**Preservatives**

Some typical preservatives used in pharmaceutical formulations are

- Antioxidants like vitamin A, vitamin E, vitamin C, retinyl palmitate, and selenium
- The amino acids cysteine and methionine
- Citric acid and sodium citrate
- Synthetic preservatives like the parabens: methyl paraben and propyl paraben.

**Significance of 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 nonionic polysaccharides. On hydrolysis gums yield sugar and salts of uronic acid [21].

**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  $\beta$ -D-mannopyranose joined by  $\beta$ -(1-4) linkage with  $\alpha$ -D-galactopyranosyl units attached by 1, 6-links in the ratio of 1:22. 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-aminosalicylic 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 core.

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 [22].

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 trimetazidine dihydrochloride. 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 [23].

#### **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 FeSO<sub>4</sub> 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 [24].

#### **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. Parket al. showed 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 extracellular 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 ( $\beta$ -D-glucose residues) and a trisaccharide side chain of  $\beta$ -D-mannose- $\beta$ -D-glucuronic acid- $\alpha$ -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 glucuronic acid and pyruvic acid groups in the side chain. In one of the trials, xanthan gum showed a higher ability to retard the drug release than synthetic hydroxypropyl methylcellulose. Xanthan gum and hydroxypropylmethylcellulose were used as hydrophilic matrixing agents for preparing modified release tablets of diltiazem HCl. The amount of hydroxypropylmethylcellulose and xanthan gum exhibited significant effect on drug release from the tablets prepared by direct compression technique. It was concluded that by using a suitable blend of hydroxypropylmethylcellulose and xanthan gum desired modified drug release could be achieved. 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. Laser profilometry analysis and scanning electron microscopy of the upper surface and the surface of fracture of tablets revealed that particles remained as coherent individual units after compression process. 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. By utilizing retention properties of xanthan gum and releasing properties of galactomannan, desired release profile was achieved in delivery of theophylline. Hydrophilic galactomannan is obtained from the seeds of the Brazilian tree *Mimosa scabrella* (Family Leguminosae). The matrices made alone with xanthan gum (X) showed higher drug retention for all concentrations, compared with galactomannan (G) matrices that released the drug too fast. The matrices prepared by combination of both gums were able to produce near zero-order drug release. The XG (conc 8%) tablets provided the required release rate (about 90% at the end of 8 h), with zero-order release kinetics [25].

### **Tragacanth**

This gum is obtained from the branches of *Astragalus gummifer*, Family Leguminosae. Tragacanth when used as the carrier in the formulation of 1- and 3-layer matrices produced satisfactory release prolongation

### **Volatile Oils**

Volatile oils are generally mixtures of hydrocarbons and oxygenated compounds derived from these hydrocarbons. Many oils are terpenoid in origin; some of them are aromatic derivatives mixed with terpenes (e.g. cinnamon and clove). A few compounds (e.g. thymol and carvacrol) although aromatic in structure, are terpenoid in origin.

### **Menthol**

Menthol is obtained by steam distillation of the flowering tops of *Mentha piperita* belonging to the family Labiatae. A membrane-moderated transdermal therapeutic system (TTS) of nimodipine using 2% w/w hydroxypropylmethylcellulose (HPMC) gel as a reservoir system containing menthol as penetration enhancer and 60% v/v ethanol-water as solvent system was prepared. The in vivo evaluation of nimodipine TTS patch was carried out to find the ability of the fabricated menthol-based TTS patch in providing the predetermined plasma concentration of the drug in human volunteers. The results showed that the menthol-based TTS patch of nimodipine provided steady plasma concentration of the drug with minimal fluctuations with improved bioavailability in comparison with the immediate release tablet dosage form.

Menthol was tested for improving the bioavailability of poorly water-soluble ibuprofen in the rectum with poloxamer. The effects of menthol and poloxamer 188 on the aqueous solubility of ibuprofen were investigated. The poloxamer gel with poloxamer 188 and menthol was found to be a more effective rectal dosage form for ibuprofen [36]. Terpenes such as menthol (fig. 5a), cineole and propylene glycol (PG) were tested as chemical enhancers to improve the skin penetration of propranolol. Release and skin permeation kinetics of

propranolol from film preparations were examined in in vitro studies using a Franz-type diffusion cell [20,22].

### **Caraway**

Caraway fruit consists of the dried, ripe fruits of *Carum carvi* (Umbelliferae). The volatile oil consists of the ketone carvone and the terpene limonene<sup>15</sup>. In another attempt, a limonene-based transdermal therapeutic system (TTS) was prepared to study its ability to provide the desired steady-state plasma concentration of nicorandil in human volunteers.

It was concluded that the limonene-based TTS of nicorandil provided the desired plasma concentration of the drug for the predetermined period of time with minimal fluctuations and improved bioavailability. In a similar manner a carvone based and nerodilol based transdermal therapeutic systems were prepared using nicorandil as a model drug. It was concluded that both TTS of nicorandil provided the desired in vivo controlled-release profile of the drug for the predetermined period of time.

### **Synthetic Excipients**

Synthetic excipients have become commonplace in today's pharmaceutical dosage forms. Both synthetic and semisynthetic products have enjoyed a long history of use, frequently offering unique properties and advantages over all-naturally derived compounds, including a low sensitivity to various ingredients or moisture, resulting in more efficient and effective pharmaceutical products. But despite the many potential benefits of synthetics, manufacturers must still address a number of challenges before their current universe of implementation can be expanded synthetic excipients have become commonplace in today's pharmaceutical dosage forms. Both synthetic and semisynthetic products have enjoyed a long history of use, frequently offering unique properties and advantages over all-naturally derived compounds, including a low sensitivity to various ingredients or moisture, resulting in more efficient and effective pharmaceutical products. But despite the many potential benefits of synthetics, manufacturers must still address a number of challenges before their current universe of implementation can be expanded.

Eg. Magnesium stearate - a cheap lubricating agent; research shows it to be immune-compromising. Methyl paraben - a benzoate family member; a known cancer-causing agent. Microcrystalline cellulose - cheap filler. Silicon dioxide - a cheap flowing agent (common sand). Natural flavors - an AKA for MSG (monosodium glutamate), a well known neurotoxic agent. Methacrylic copolymer - methacrylic acid, a component of the methacrylic acid copolymer, has been reported to act as a

teratogen in rat embryo cultures. PVP-poly vinyl propylene. Corn starch - typically from cheap GMO corn; can invoke allergic responses. Talcum Powder - a common excipient not listed on product labels; a suspected carcinogen [21,-24].

### **Advantages of Natural Excipients over Synthetic Excipients**

Synthetic excipients have become commonplace in today's pharmaceutical dosage forms. Both synthetic and semisynthetic products have enjoyed a long history of use, frequently offering unique properties and advantages over all-naturally derived compounds, including a low sensitivity to various ingredients or moisture, resulting in more efficient and effective pharmaceutical products. But despite the many potential benefits of synthetics, manufacturers must still address a number of challenges before their current universe of implementation can be expanded.

The terms synthetic and semisynthetic are both broadly used to distinguish this family of excipients from those extracted from natural sources (plants/animals) such as starch, lactose, and microcrystalline cellulose (MCC). There are, however, also shades of gray and subtle nuances between two types. Semisynthetic typically refers to a substance that is naturally derived but that has been chemically modified. Most excipients in use today fall into this category. In contrast, synthetic is usually defined as a pure synthetic organic chemical that is derived from oil or rock. Excipient manufacturers easily disagree with these definitions when describing their products because so much chemistry is involved in the manufacturing process. As a result, the term synthetic is frequently used to encompass both types.

Synthetic excipients are used in the manufacture of tablets to bind the tablet together, reduce die-wall friction between the tablet and the tableting press, control pH balance, and to disintegrate the tablet in the stomach once it has been ingested. They're used for just about every function of an inactive ingredient except as bulking agents, which are usually natural products. In parenteral, synthetics are used as solubilization agents to make actives more soluble, and therefore, more deliverable. Synthetics also offer other benefits over natural excipients. Because they're not extracted from animal materials, they're free of transmissible diseases--a characteristic that may be of increased importance among manufacturers and regulators in light of the recent case of a BSE-infected cow found in the United States last year. The absence of plant or animal material in synthetics also eliminates concerns posed by genetically modified organisms (GMOs), which can also interfere with the safety and acceptability of a drug formulation.



Another benefit of synthetics compared with natural excipients is that they can be produced to a certain specification because there is more control over the manufacturing process. Most natural-based polymers aren't chemically identical because of the variability that exists in nature. For example, depending on changes in weather from one year to the next, the structure and properties of natural materials can also vary slightly--an effect avoided with synthetics, which are synthesized in chemical reaction. Synthetic excipients are used in the manufacture of tablets to bind the tablet together, reduce die wall friction between the tablet and the tableting press, control pH balance, and to disintegrate the tablet in the stomach once it has been ingested.

They're used for just about every function of an inactive ingredient except as bulking agents, which are usually natural products. In parenterals, synthetics are used as solubilization agents to make actives more soluble, and therefore, more deliverable. Synthetics also offer other benefits over natural excipients. Because they are not extracted from animal materials, they are free of transmissible diseases—a characteristic that may be of increased importance among manufacturers and regulators in light of the recent case of a BSE infected cow found in the United States last year. The absence of plant or animal material in synthetics also eliminates concerns posed by genetically modified organisms (GMOs), which can also interfere with the safety and acceptability for drug formulation [25].

## APPLICATIONS

The use of natural excipients to deliver the bioactive agents has been hampered by the synthetic materials. 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. Excipients are any component other than the active substance(s) intentionally added to formulation of a dosage form. This article gives an overview of herbal excipients which are used in conventional dosage forms as well as novel drug delivery systems.

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.

The traditional view that excipients are inert and do not exert any therapeutic or biological action or modify the biological action of the drug substance has changed and it is now recognized that excipients can potentially influence the rate and/or extent of absorption of a drug. As herbal excipients are non toxic and compatible, they have a major role to play in pharmaceutical formulation. Hence, this paper is an attempt to review herbal excipients used in NDDS.

Natural polysaccharides are extensively used for the development of solid dosage forms. These polymers of monosaccharides (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. Pectins, starch, guar gum, amylase and karaya gum are a few polysaccharides commonly used in dosage forms. Non-starch, linear polysaccharides remain intact in the physiological environment of the stomach and the small intestine, but are degraded by the bacterial inhabitants of the human colon which make them potentially useful in targeted delivery systems to the colon [20,24].

## CONCLUSION

As the herbal excipients are promising biodegradable materials, these can be chemically compatible with the excipients in drug delivery systems. In addition herbal excipients are non-toxic, freely available, and less expensive compared to their synthetic counterparts. They have a major role to play in pharmaceutical industry. Therefore, in the years to come, there is going to be continued interest in the natural excipients to have better materials for drug delivery systems. To deliver the bioactive agents has been hampered by the synthetic materials. The drawback proposed 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. Natural polysaccharides are extensively used for the development of solid dosage forms. These polymers of monosaccharides (sugars) are inexpensive and available in a variety of structures with a variety of properties.

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