A REVIEW - TYPES OF NATURAL EXCIPIENTS

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ABSTRACT

Medical science is becoming advance due to their developments and researches for discovered the various formulations those are used in treatment for various types of diseases. In pharmaceutical word ‘Excipients’ are major part of formulations because these are used in combination with active pharmaceutical ingredients in formulation of dosage forms. Any dosage forms cannot be formulated without the use of excipients. In pharmaceutical industries mostly natural excipients are preferred because they are safe and non toxic as compare to synthetic. Natural excipients are plant or plant based substances obtained from different parts of plants with the help of different extraction methods. Due to origin from plants or natural source they don’t provide any side effects and the excipients are not provided any therapeutic effects when use in formulations of dosage form. Natural excipients are used in pharmaceutical formulation as binders, diluents, lubricants, glidants, Disintegrants, coatings agents, coloring, flavorings, sweetners and preservatives etc.

KEYWORDS: Natural excipients, Active pharmaceutical ingredients, Pharmaceutical formulation, Disintegrants, Binders, Diluents.

INTRODUCTION

Excipients: - The substances which are used as a medium for giving a medicament known as Excipients. The excipients play role for determining quality of drug/formulation and bioavailability of drugs from tablets.[1] Few years later, excipients mainly used to form bulk formulations as it restrain potent drugs which could not be taken alone and to assure uniformity of drug in dosage form. Now due to advancement of techniques wide varieties of excipients are used in formulation of dosage forms. With corresponds to various route of administration, state of formulation, strength of formulation excipients are added in different
concentrations. Excipients are used as stabilizing agent for active ingredient in formulation of drug; make sure active compound like “active” and stable essentially till the shelf-life of the product.\(^2\) The amount of excipients which is used in pharmaceutical formulation that is probably 3 times more than therapeutically active compound.\(^3\)

These are usually added along with the API (Active Pharmaceutical ingredients) in order to.
1. Protect, support or enhance stability of the formulation.
2. Help improve bioavailability of active drug.
3. Improve patient acceptance.
4. Enhance overall safety and effectiveness of the formulation during its storage and use.\(^4\)

**Characteristics of ideal excipients**
Excipients should have some certain characteristics. These are as follows:
1. Ease of handling
2. Nontoxic and non-irritant.
3. No interaction with drug substances present in the formulation and packaging.
4. Pharmacologically inert but pharmaceutically active
5. Feasible.
6. Cost effective and readily available.\(^5\)

**Pharmaceutical excipients**: - The non active ingredients that are mixed with therapeutically active compound(s) to form medicines are known as Pharmaceutical Excipients. These ingredients which are not an active compound are regarded as excipients. Excipients also influence the behavior and effectiveness of the drug product more and more functionality and significantly.\(^6\) Excipients used in the pharmaceutical formulations provided variety of functions like\(^7\) bulk and durability of active compounds, to enhance the stability, absorption\(^3\), make up the volume of the dosage form and others.\(^7\)

Origin of Pharmaceutical excipients: - various origins of Pharmaceutical excipients are like: Animal, Plant, Mineral and by synthesis. Examples of various pharmaceutical excipients from different origins are.\(^8\)
Table 1: Different origins of excipients.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Origins of Excipients</th>
<th>Examples of Excipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Animal origin</td>
<td>Lactose, Gelatin, Stearic Acid, Bees Wax, Honey Musk, Lanoline</td>
</tr>
<tr>
<td>2.</td>
<td>Plant origin</td>
<td>Starches, Sugars, Cellulose, Agar, Alginates, Guar Gum, Xanthan Gum, Gelatin, Pectin, Acacia, Tragacanth</td>
</tr>
<tr>
<td>3.</td>
<td>Mineral origin</td>
<td>Talc, Calcium Phosphate, Silicon Dioxide</td>
</tr>
<tr>
<td>4.</td>
<td>Synthetic origin</td>
<td>Povidone, Polysorbates, Polyethylene Glycol</td>
</tr>
</tbody>
</table>

These pharmaceutical excipients are provided some other properties in pharmaceutical industry like binding agents, disintegrates, sustaining agents, protective’s, colloids, thickening agents, gelling agents, bases in suppositories, stabilizers, and coating materials. These plant based excipients are also known as herbal or natural excipients and originated from various parts of plants mainly by extraction process. Due to plant origin source these excipients are easily available, less expensive, stable, non toxic, eco-friendly, easily biodegradable and overcome the toxicity of synthetic excipients in various drug delivery systems. Plants are renewable and can be cultivated or harvested in sustainable manner, can supply constant availability of raw material. Waste from food industry can also be achieved as a raw material to extract herbal excipients. These are some reasons for increasing the demand of herbal material as excipients in the market.

Some excipients are used in drug delivery system to fulfill the multi-functional role like affecting release pattern, improvement of bioavailability and stability, enhancement of patient acceptability.

According to WHO describes excipients as non-active ingredients that have been proficiently analyzed for safety and included in a drug delivery system to:

- Processing assistance during development of drug delivery system.
- Protect aid and improve stability, bioavailability and acceptability of patients.
- Helps in the identification of substance
- Strengthen any other feature of the drug’s overall safety and effectiveness during processing or use.

Natural Excipients
These are those substances that are obtained from various natural sources like Animals, Plants, and Minerals and used in various pharmaceutical formulations. Natural excipients are
generally used because of its some properties like: - low expanses, less side effect and less toxicity.\[^3\]

**CLASSIFICATION OF EXCIPIENTS**

- Excipients are commonly classified according to their application and function in the drug products.
  - Binders,
  - Filler and Diluents
  - Lubricants, Disintegrants
  - Sweeteners, Coatings agents
  - Flavorings, Colorings
  - Antioxidants, Preservatives\[^{10}\]

**Advantage of herbal excipients**

- Natural polymers produced due to living organism so that herbal excipients are biodegradable and show no adverse effects on human being and environment.
- These are non-toxic and biocompatible because all plant materials are carbohydrates in nature and composed of repeating monosaccharide units.
- They are cheaper and their production cost is less than synthetic material.
- Herbal excipients are safe without showing any side effects because they are formed from natural source.
• Due to their advantages many countries produced herbal excipients because they are used in many industries.\[10\]

**Disadvantages of herbal excipients**

• During the manufacturing of natural excipients they come in contact with the external environment, so that there are some possibilities of microbial contamination.

• Production of different natural excipients depends on number of different factors like:- environmental, regional and climatic conditions, that cannot be changed. So that Natural excipients have a very slow rate of manufacturing.\[9\]

• The productions of Natural polymers are not under control because it depends upon environment and various other factors as compared to synthetic manufacturing is controlled with fixed quantities of ingredients.\[10\]

**Pharmaceutical Application of Herbal excipients:** Natural polymers are most commonly used as adjuvant in pharmaceutical preparations such as: thickener, binder, emulsifier, stabilizer, Disintegrants, gelling agents and others. These natural polymers obtained from various sources can be used in development of sustained release and controlled release formulations.\[11\]

1. **Binders**

The name (binder) suggests that these are used as excipients to bind and hold the components used in formulation. These are also used in mixture to enhance the potential of binding between the formulated particles.\[9\] Different natural polymers used like binding agents in different pharmaceutical formulations.\[11\] Natural binders like starches, gums and mucilages having binding capacity and also have various other properties like disintegrants, filler and these are much safer. Gums, which are used as binders but these, are also used as thickeners, suspending agents, emulsifying agents and film formers in pharmaceutical industries. Some examples of natural binders are: - Guar gum, Locust bean gum (Carob Gum), Tamarind Gum, Aegle Marmelos Gum, Gum Cordial, Okra Gum, Starches like rice, potato, maize, corn, wheat and Mucilages like Aloe mucilage shows good potency as a binding agent.\[1][6]\n
1.1. **Gums and Mucilages:** - Gums are usually pathological products and are produced when plant is injured or grows under unfavorable conditions. This is produced by the breakdown of cell wall and this process known as Gummosis.
Mucilages are physiological products. These are also natural products of plant metabolism, and formed within the cell (intracellular formation). These are produced without injury to the plant. Mucilages form slimy masses with water, but do not dissolve and Gums readily dissolve in water.[12]

- **Tamarind Gum:** It is obtained from endosperm of the seed of the tamarind tree. Tamarind Gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds Microspheres formed was in the size range of 230 - 460μm.

- **Guar gum:** Guar gum obtained from the endosperm of the seed of the Cyamopsis tetragonolobus belonging to Family Leguminosae. In strong conc. alkalies tends to reduce viscosity and acids cause loss of viscosity and hydrolysis. It is insoluble in most hydrocarbon solvents.

- ** 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 belonging to Family Leguminosae.

- **Honey locust gum:** It is known botanically as Gleditsia triacanthos, and belonging to Family Leguminosea. The gum is obtained from the seeds.

- **Khaya gum:** Khaya gum is a polysaccharide obtained from the incised trunk of the tree Khaya grandifoliola belonging to family Meliaceae. Due to natural availability of gum, this is in expensive, non-toxic and fostered the interest in developing the gum for pharmaceutical use.

- **Hakea Gum:** Hakea gum a dried exudates from the plant Hakea gibbosa belonging to family Proteaceae.

- **Aloe mucilage:** It 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.[6]

- **Pectin:** Pectins are non-starch, linear polysaccharides extracted from the plant cell walls.[13] In 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. 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.
**Alginates**: Alginates are natural polysaccharide polymers isolated from the brown sea weed belonging to family Phaeophyceae.\(^{[13]}\) Alginic acid is obtained from sodium salt of sodium alginate. Alginates offer various applications in drug delivery, such as in matrix type alginate gel beads, in liposomes, for local applications and to deliver the bio molecules in tissue engineering applications.\(^{[6]}\)

**Mimosa pudica**: Mimosa pudica, commonly known as sensitive plant belongs to family Mimosaceae. Mucilage is obtained from seeds, which is composed of d-xylose and d-glucuronic acid. When mimosa seed mucilage come in contact with water its rapidly swells and hydrates. This seed mucilage used for binding and disintegrating agent.

**Fenugreek**: Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant belongs to family leguminous. Fenugreek seeds develop high viscosity mucilage at Low concentration level. This mucilage form viscous tacky mass and does not dissolve when come in contact with water.\(^{[12]}\) Fenugreek used to treat Colic flatulence, dysentery, and diarrhea, decrease of appetite dyspepsia, chronic cough, dropsy, swollen kidney, spleen enlargement and diabetes and can also be used in antiurolithic, diuretic, antidandruff, anti-inflammatory and antioxidant agent.\(^{[9]}\)

2. **Fillers or Diluents**

Fillers or Diluents are pharmaceutical components those are used in pharmaceutical preparations without providing any pharmacological effects. These are chemically ineffective, but most of which are used in the formulation to build up the necessary bulk of the dosage form.\(^{[9]}\) Example: Starch, Plant cellulose & Di basic calcium phosphate.\(^{[1]}\)

**Lactose**

Lactose is a disaccharide produced as a byproduct of dairy and is a major component of whey.\(^{[9]}\) The purest form is α-lactose which is widely used in pharmaceutical industry as excipients.\(^{[8]}\) Lactose is one of the most frequently used excipient in pharmaceutical industries as filler, diluents or bulking agent in tablets and capsules, as a sweetener in liquid formulation and as a carrier for dry powder inhalation products due to its properties like: cost effectiveness, low hygroscopicity, low sweetness, compatibility with active ingredients and other excipients availability, bland taste, high chemical and physical stability, and acceptable water solubility.\(^{[8][9]}\) The amorphous form of lactose is highly compatible with many active components in direct compression tablets.\(^{[9]}\)
✓ Gelatin

The growing trend to replace synthetic agents with natural ones has increased the use of gelatin in pharmaceutical industry. Gelatin is a soluble protein derived by partial hydrolysis of collagen, the main fibrous protein constituent in bones, cartilages and skins. Source, age of the animal, and type of collagen these all are influence the properties of gelatin. The main sources of gelatin are pig skin, bovine hide and pork and cattle bones. Gelatin is soluble in hot water, insoluble in cold water, most immiscible solvents, volatile and fixed oils. Gelatin is used in pharmaceutical industries as an emulsifier, binder, foaming agent, colloid stabilizer, biodegradable film-forming material and micro-encapsulating agent. Glycerinated gelatin is a combination of gelatin and glycerin, which is used as a vehicle to manufacture suppositories. Gelatin is also used as a shaping material in capsule manufacturing. Both hard and soft gelatin capsules outer covering are made from gelatin. Gelatin is also used to produce lozenges, lyophilizates, pastes and powders.[8]

3. Disintegrants

Disintegrants are substances those are added to the drug formulations, which facilitate dispersion of tablets into smaller particles for rapid dissolution when it comes in contact with water in the GIT. For example starch, Gum karaya, Guar gum.[1]

✓ Gum karaya

Gum karaya is an acid polysaccharide. It is obtained from dry exudates of sterculia urens. It contains galactose sugars, rhamnosis and galactic acid as chemically. Due to high viscosity this gum reduces its application in development of conventional dosage form. Gum karaya can be used as an alternative super-disintegrant with frequently available artificial and organic super-disintegrants, due to its low price, bio-compatibility and easy availability.

✓ Guar gum

Guar gum is extracted from the seeds of the drought tolerant plant tetragonoloba cyamopsis, a member of the Leguminosae family. Guar gum is similar to the locust bean gum mainly composed of the complex polymer of galactose and mannose. Guar gum is used as a colloid, a binding agent and a disintegrating agent in formulations of pills, in bulk laxatives as a depressing appetite, used in peptic ulcer therapy, reduces blood sugar concentrations in diabetic and serum levels in hyperlipidemia patients. This is also useful emulsion stabilizer.[9]
Chitosan

Chitosan is a polysaccharide derivative containing acetyl and amino groups and is most found organic constituent in skeletal invertebrates. Deacetylation of chitin is known as Chitosan. It is found in the exoskeletons of arthropods and crustacean. Due to lowest bulk and tapped density of Chitosan causes excellent flow as well as compression and compaction during tablet processing. Chitosan used as wetting and coating agent, microspheres and micro capsules in drug delivery systems and also used as filler or diluents and add 50% chitosan as a binder in direct compression tablets. Due to its polymeric cationic character and gelling and film forming properties Chitosan is used as good excipient for development of controlled release dosage forms. Grinding of poorly soluble drugs, such as griseofulvin or prednisolone with chitosan showed an enhanced dissolution rate and reduced crystal size in the formulation.[8]

4. Lubricants

A lubricant is an additive and essential component of drug to reduce the friction and provide required lubrication to success of pharmaceutical manufacturing.[1] Lubricants mainly avoid clumping together of components and the adherence to the filling tablet or capsule machine.[1] There are usually two kinds of lubricants: - First is hydrophilic in nature and second is hydrophobic in nature. Hydrophilic lubricants have limited lubrication characteristics and do not exhibit characteristics as anti-adherents. Hydrophobic lubricants providing good lubrication property and act as anti- adhesives and gliders when used in small quantities.[9]

Stearic acid

Stearic acid occurs in nature as mixed triglycerides or fat, with long chain acids (18 carbon chains) and as fatty alcohol ester, obtained from animals and vegetables by extraction process.[8] There are stearic acid and its derivatives, such as magnesium stearate and sodium stearyl fumarates. Magnesium salt of stearic acid is known as Magnesium stearate, which contains one magnesium and two stearic acids. Magnesium stearate is the most common lubricant used in formulations of tablet.[8] Stearic acid is generally used as solubilizing agent, emulsifying agent, tablet and capsule lubricant in dosage formulations.[8] Stearic acid is usually added at around 2.5 % by weight.[9]

Sodium stearyl fumarate

Sodium stearyl fumarate is frequently given in a pure form, so that it can be preferred to avoid chemical incompatibility due to less pure stearate lubricants (stearic acid and
magnesium stearate). Due to that fact, Sodium stearyl fumarate is used as an alternative lubricant in solid-dosage form in contrast to stearic acid and stearic acid is often supplied as a solid-dose substitute lubricant. In Comparison to magnesium stearate, this stearic acid is less hydrophobic and is less retardant in tablet dissolution.[9]

5. **Flavouring agent**
Flavouring agents are used in formulations to mask an unpleasant taste. These are thermolabile and cannot be added earlier to an operation involving heat. They are often mixed with the granules as an alcohol solution.[1] These flavors are used in many pharmaceutical formulations like: cough syrups, sedatives, anti-malarial and antibiotic.[3] Examples: citric acid, glycerol, orange oil, menthol, vanillin, Peppermint, Raspberry.[1][3]

6. **Colorants**
Colorants or coloring agents are added in formulations to mask off color of drug product and provide more elegant product. These are also used to improve patient compliance. All coloring agents must be approved and certified by FDA. These dyes are applied as solution in the granulating agent. Example: Yellow 6- FD & C sunset yellow yellow 5- FD & C Tartrazine.[1] Examples of few colors of excipients due to some plants like: - Yellow color due to leaf part of Adhato davasica, Brown color due to bark of Azadirachta indica, Red color due to whole plant of Aloe barbadensis.[3]

7. **Sweeteners**
Sweeteners are mainly used in chewable tablet to prohibit the use of sugar in the product. Mainly used sweeteners are: - Mannitol, lactose, sucrose, Dextrose 72% as sweet as sucrose.

8. **Antioxidants**
Antioxidants are added in formulation of tablets because they protect the drug from oxidation. Commonly used anti-oxidants are: - ascorbic acid and their esters, alphatocopherol, ethylene diamine, tetra acetic acid. Chelators may also act as antioxidant.

9. **Coating Agents**
Coating is a process by which an outer layer of material is applied to the surface of a dosage form and agents which is used in this process are called coating agents. These coating agents are provided some properties to the drug like: - Protection, Masking, Elegance, Ease of swallowing, and identification of drug product. Film coating, Sugar coating and Compression
coating these three different types of coating are used in industries.[1] Examples of natural coating agents are: - Gelatin, Xanthan gum, Guar gum, Pectin.[3]

10. Preservatives
Preservatives are chemical substances which are commonly used in various pharmaceutical products in order to prolong their shelf life and also used in Cosmetics and food industries.[1][3] Preservatives do not compromise with product performance and providing vital functions to products like: - avoid the alteration and degradation of microorganisms during storage, particularly in those with greater water content.[9] Examples: Clove oil, Neem oil, Benzoic acid & its salts etc.[1]

✓ Clove oil
Clove oil obtained from buds of Myrtaceae syzygium belong to Family Myrataceae.[3] This plant is contains highest amount of phenolic compounds such as eugenol, eugenol acetate and Gallic acid, while ß-pinene, limonene, benzaldehydes and other volatile compounds that occur in lower levels in clove oil. Clove has strong antioxidant and antimicrobial activities among the others. Clove essential oil is generally accepted as a safe substance at levels below 1500 mg / kg. The world health organization defined that the appropriate intake of clove per day is 25mg/kg of weight in individuals. Eugenol is easily consumed by oral route that reaches quickly plasma and blood.

✓ Neem oil
This herb is tremendous because all parts of this plant like: - seeds, leaves, flowers and bark are all very essential and used to make herbal medicines. It consist of all aerial parts of plant known as Azadirachta indica, belongs to the Meliaceae family. This medicinal herb is used worldwide and is widely used to cure cold, chest pain as well as diabetes.[9]
### Table 2: List of Herbal Excipients.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Types of Excipients</th>
<th>Examples of Excipients</th>
<th>Sources of Excipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Binders Gums and Mucilages</td>
<td>Tamarind gum, Guar gum, Locust bean gum, Honey locust gum, Khaya gum, Hakea gum, Aloe mucilage, Mimosa pudica, Fenugreek, Pectin, Alginates</td>
<td>Tamarindus indica, Cyamopsis tetragonaloba (L), Endosperm of seeds from the carob tree Ceretonia siliqua, Gleditsia triacanthos, From the incised trunk of the tree Khaya grandifoliola, Dried exudates from the plant Hakea gibbosa, From the leaves of Aloe barbadensis, Obtained from seeds, which is composed of d-xylose and d-glucuronic acid, Trigonella foenum graecum, Plant cell walls, Isolated from the brown sea weed</td>
</tr>
<tr>
<td>2.</td>
<td>Fillers and Diluents</td>
<td>Microcrystalline cellulose, Lactose, Gelatin</td>
<td>Plants, Milk, Animals</td>
</tr>
<tr>
<td>3.</td>
<td>Disintegrants</td>
<td>Gum karaya, Guar gum, Chitosan</td>
<td>Trees of the genus Sterculia urens, Cyamopsis tetragonaloba (L), Crab and shrimp shells.</td>
</tr>
<tr>
<td>4.</td>
<td>Lubricants</td>
<td>Stearic acid, Sodium stearyl fumarate, Paraffin oil</td>
<td>Animals, Plants and animal, Paraffin plant</td>
</tr>
<tr>
<td>5.</td>
<td>Flavouring agent</td>
<td>Citric Acid, Glycerol, Orange Oil, Menthol</td>
<td>Citrus fruits, Animal fat, vegetable oil, Citrus aurantium, Mentha piperita</td>
</tr>
<tr>
<td>6.</td>
<td>Colorants</td>
<td>Natural colorants</td>
<td>Yellow color due to leaf part of Adhato davaica, Brown color due to bark of Azadirachta indica, Red color due to whole plant of Aloe barbadensis</td>
</tr>
<tr>
<td>7.</td>
<td>Sweeteners</td>
<td>Mannitol, Lactose, Dextrose</td>
<td>Plants, Fraxinus ornus, Milk and dairy</td>
</tr>
<tr>
<td>8.</td>
<td><strong>Antioxidants</strong></td>
<td>Ascorbic Acid (Vit.C)</td>
<td>Animals and plants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alpha-Tocopherol,</td>
<td>Plant source</td>
</tr>
<tr>
<td>9.</td>
<td><strong>Coating agents</strong></td>
<td>Gelatin</td>
<td>Animals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pectin</td>
<td>Inner portion of citrus fruits and vegetables</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Xanthan gum</td>
<td>Secreted from bacterium Xanthomona scampestris</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Guar gum</td>
<td>Seeds of Cyamopsis tetragonolobus</td>
</tr>
<tr>
<td>10.</td>
<td><strong>Preservatives</strong></td>
<td>Clove oil</td>
<td>Buds of Myrtaceae Syzygium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Neem oil</td>
<td>Fruits of Azadirachta chintanica</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Turmeric</td>
<td>Roots of Curcuma longa</td>
</tr>
</tbody>
</table>

**CONCLUSION**

This review was discussed information about various sources of different herbal pharmaceutical excipients and their use in pharmaceutical formulations as binders, coloring agents, sweeteners, preservatives, diluents, disintegrants and others. These Herbal excipients obtained from various natural sources such as plants, animals, marines, minerals and microbes. The use of Herbal excipients in pharmaceutical industries is gaining a lot of concentration in these days and increase day by day because they are less expensive, biodegradable, eco friendly, non-toxic and freely available. Preference of herbal excipients not only depends upon these qualities but they also provided health benefits as compare to synthetic chemicals. Therefore, in next upcoming years, the natural excipients used as good materials for drug delivery systems.

**REFERENCES**


