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A REVIEW ON APPLICATIONS OF MALTODEXTRIN IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

Since in a formulation excipient affects the critical properties of formulation such as stability and bioavailability it was mandatory to evaluate a safe and inert excipient for its versatility. Maltodextrin which is obtained bypartial hydrolysis of starch is water soluble, non-sweetproduct due to which it is used as diluents in tablets and coating material in microencapsulation of various sensitive nutraceuticals like vitamins has other applications in pharmaceutical industry as well. Maltodextrin's use as a carrier in proniosomes which are novel drug delivery systems stabilize the drug material by forming dehydrated , free flowing powder and incorporation of Maltodextrin as a film forming water soluble polymer in fast dissolving oral films overviewed . The use of Maltodextrin to facilitate direct compression of incompatible active pharmaceutical drugs is described in terse.

KEY WORDS

Maltodextrin, microencapsulation, proniosomes, diluent.

1. INTRODUCTION:

Maltodextrin is a polysaccharide produced from starch by partial enzymatic hydrolysis of starch. Starch (amylum) is a carbohydrate consisting of a large number of glucose units linked by glycosidic bonds and is present in a large quantities in corn, potatoes, wheat etc Maltodextrin has a dextrose equivalence less than 20 which indicates that it has long carbohydrate chains along with 2-3% glucose and 5-7% maltose and is available in white hygroscopic spray-dried powder which is slightly sweet almost flavourless. It is soluble and readily dispersible in water and slightly soluble to almost insoluble in alcohol.

The body digests Maltodextrin as a simple carbohydrate and thus can be easily converted to instant energy. Due to this quality it is used in sports drinks and quick energy satchels for endurance athletes. Use of Maltodextrin is also dependant on the grade that is the DE value for instance MD with low DE value are stickier and thus is used in gelatinous products like syrups and jams whereas high DE value MD freeze better and is used as a bulking agent in ice creams.

Maltodextrin like starch consists of a particular ratio of amylose and amylopectin, different ratios. Amylose is made up of α (1→4) bound glucose units whereas amylopectin has glucose units linked in a linear way with α (1→4) glyosidic bonds with α (1→6) bonds occurring every 24 to 30 glucose units.

Brief overview of uses of Maltodextrin:

1. **Proniosomes**:

The main aim of novel drug delivery is to achieve targeted and controlled drug release. The encapsulation of drug in a vesicle sustains drug action at a sustained rate and maintains an effective drug concentration level at the same time reduces the number of undesirable effect[1]. Encapsulation of drug also enables to prolong the duration of drug release in systemic circulation and reduce toxicity by increasing the selectivity. One of the major advantages of vesicular drug delivery is the ability to deliver drug into the deeper layer of the skin in this way it bypasses hepatic first-pass effect and provides better compliance[1]. The vesicles passes through skin layer mainly because bilayer act on stratum corneum in the skin which is the rate limiting. Liposomes which are bilayered lipid vesicles constituting cholesterol and phospholipids have shown potential in overcoming the stratum corneum layer in the skin. But the major drawback associated with aqueous dispersions of liposomes is the tendency to aggregate or fuse and susceptibility to hydrolysis and oxidation.

Non-ionic surfactant based vesicles known as niosomes are viewed as an alternative potential drugs delivery system to conventional liposomes. Niosomes or non-ionic surfactant vesicles are microscopic lamellar structure which can administer both hydrophilic and hydrophobic drugs[2, 3]. Proniosomes are dry, free flowing, water soluble carrier particles which are coated with surfactant and can from niosomal dispersion on subsequent hydration with hot water. This avoids the problems related to aqueous niosomal dispersion especially leaking, aggregation and fusion. Moreover proniosomes are stable during sterilization as well as storage .Thus distribution, ease of transfer and storage stability make proniosomes a promising novel delivery system[4-6].

Table 2: Materials used for preparation of proniosomes [4, 7]

Ingredient	Role	Example
Surfactant	Increases drug influx across skin	Span 20 ,40 ,60
Penetration enhancer	Better penetration of the drug	Lecithin
Stabilizer	Prevents drug leakage	Cholesterol
Carrier	Drug entrapment	Maltodextrin

METHODS OF PREPARATION

1. Slurry method:

Slurry is formed by addition of the carrier such as Maltodextrin and solution of surfactant such as span 20 or 40 in a round bottomed flask. Solvent is evaporated using rotary flash evaporator at decreased pressure of and vacuum to form a free flowing dry powder. Powder which is obtained is stored in a sealed container at 4°C [8].

2. Slow spray coating

A solution of cholesterol and surfactant is prepared and sprayed into a round bottom flask containing carrier which is attached to a rotary evaporator. The evaporator has to be completely emptied and rotating flask can be rotated in water bath under vacuum at 65-70 ^{0}C for 15 – 20 min. The evaporation should be continued until a completely dry powder is obtained [4, 9].

Role of Maltodextrin:

The use of Maltodextrin as a carrier in proniosomes imparts flexibility in the ratio of surfactant used and other excipients which are incorporated. Maltodextrin although a polysaccharide has minimal solubility in organic solvents and thus it is possible to coat the Maltodextrin particles by simply adding surfactant in organic solvent. For drugs where encapsulation efficiency is affected negatively by Maltodextrin , the concentration can be minimized for producing proniosomes with greater surface loading[4][10]. Optimum entrapment efficiency can be obtained by using Maltodextrin and surfactant in the equal ratios[5].

Maltodextrin does not interfere with the drug and thus is comparatively less tedious as compared to other carriers such as sorbitol. In addition low solubility of Maltodextrin in organic solvents an additional advantage because when carriers are soluble in organic solvents it is mandatory to repeat the process until desired surface loading has been achieved. The circular Maltodextrin particles proves to be a vital plus point because circular shape means higher surface area which results in a thin layer of surfactant thereby making the process of rehydration all the more efficient[7] . The maximum loading limit which permits efficient hydration of the surfactant coating is 3.3 grams surfactant per gram of carrier or 8 mmol/L surfactant per gram of carrier[2].

1. **Microencapsulation:**

Microencapsulation is a process in which tiny particles or droplets are surrounded by a coating to give small capsules. A microcapsule is a small sphere with a uniform wall around it and the material inside the microcapsule is referred to as the core or internal phase whereas the wall is sometimes called a shell or coating [11] .

Reasons for microencapsulation[12, 13]:

1. Taste the mask of bitter core
2. Reduce reactivity of core with environment
3. Controlled release of core drug material
4. Improved processing and texture
5. Enhanced solubility

Manufacturing techniques [14]:

The application of spray-drying process in microencapsulation involves few basic steps: preparation of the dispersion or emulsion to be processed, homogenization of the dispersion, atomization of the mass into the drying chamber and separation using cyclone bags.

1. Concentration: Feedstock is concentrated prior to introduction into the spray dryer. It consists of carrier material (Maltodextrin) and the material to be encapsulated (e.g.: nutraceuticals such as vitamins) along with an emulsifying agent. The ratio of encapsulant to carrier is 1:4 but this can be optimized for each individual ingredient.

2. Atomization: The oil-in-water emulsion which is obtained is then atomized into a heated air stream which is supplied to the drying chamber and the evaporation of the solvent, usually water, consequently leads to the formation of microcapsules. As the sprayed particles fall through the gaseous medium, they form a spherical shape with the oil encased in the aqueous phase.

3. Separation: Electrostatic precipitators, cyclones and bag filters may be used for the

final separation stage. Wet Scrubbers are often used to purify and cool the air so that it can be released to atmosphere.

Maltodextrin as encapsulating material

Maltodextrin is considered as good coating material because it exhibits low viscosity at high solids contents and also shows good water solubility. In addition, it is known that polysaccharides having gelling properties and stabilizes emulsions towards flocculation as well as coalescence. Maltodextrin samples show the highest retention of flavour because they could be dispersed in water up to 35.5% of the solution without haze formation.

Maltodextrin based micro particles containing up to 1% iodine were stable for periods up to 12 months under a temperature of 40 ^{0}C. The use of a 10:1 Maltodextrin /Pectin weight ratio (11% w/v) led to encapsulate 3% w/v polyphenol-rich extracts and formed stable powders. This combination with pectin may be a useful replacement of the Maltodextrins-alone carrier. Even under harsh storage conditions, neither the bioactive polyphenols nor moisture content of the particles or the antioxidant activity appeared significantly modified. The maltodextrin/pectin matrix is able to mask the unpleasant smell of the extracts and the product is rapidly soluble in water. Maltodextrins were found to be effective in protecting the carotenoids of paprika oleoresin as well. Maltodextrins along with whey proteins were reported as effective wall materials for microencapsulation of ethyl caprylate. Moreover its combination with emulsifier Tween 80 encapsulated a higher amount of bixin than only maltodextrin[15-17] .

2. **Fast dissolving films:**

Research is continuously going on for providing a viable alternative dosage form for paediatrics, geriatrics and bedridden people for a more patient complaint dosage form. For this purpose oral disintegrating dosage has been developed especially tablets dispersible in water has been widely used. However some of the disintegrants which are a part of tablets may remain on the tongue and may prove to be a problem to swallow for patients suffering from aphagia or dysphagia[18, 19] .

Mouth dissolving thin oral films which has been gaining prominence in the pharmaceutical field consists of thin film of thickness (approximately 320µm) which disintegrates in less than a minute with the help of saliva without drinking or chewing [20]. The unique feature about the film is that it is extremely thin, elegant and is available in various shapes and sizes. There is no water needed to administer since it wets with the help of saliva and thus it a convenient way of administering drug without the need for a trained personnel thereby increasing patient compliance. Besides that due to excellent mucoadhesion of the thin film there is no danger of choking as observed in the case of tablets. These films are also cheaper to manufacture as compared to normal orally disintegrating tablets which are manufactured by expensive lyophilisation process .Thus above qualities along with taste masking , enhanced drug stability, fast disintegration followed by rapid release and cheaper cost of manufacturing as compared to OD tablets makes it one of the most promising way to administer drug[19, 21].

Though there are many advantages there are a certain drawbacks related to the films.

The major disadvantage of the films is that high doses cannot be incorporated as well as the drugs unstable at buccal pH have to be avoided. Moreover the drugs which irritate oral mucosa cannot be administered by this route. Special attention has to be given to the masking of taste of bitter drug as well as to the packaging of the films because the films have to be protected from water contact [22].

Table 1 : Typical composition of a thin fast dissolving film[19, 22, 23]

Ingredient	Concentration (%w/v)	Examples
API	1-25 %	Nicotine
Water soluble polymer	40-50 %	Maltodextrin
Plasticizer	0-20 %	Glycerine
Saliva Stimulant	2-6%	Citric Acid
Flavouring agent	0-40%	Peppermint , Menthol

Methods of Film preparation:

1. **Hot melt extrusion :**
   In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the mixture is melted by the extruder having heaters which causes complete evaporation of solvent. Finally the melt is shaped in to films by the dies. There are a few benefits of this technique over others such mainly because of fewer unit operations, better content uniformity and anhydrous process, low air entrapment and easy scale up. There is also improved bioavailability of poorly soluble drugs and also better content uniformity. However there are a certain drawbacks such as use of high temperatures may degrade drugs which are thermo labile and high temperature needs high power input. [24]
2. **Solvent Casting[25] :**
   In this method water soluble polymer is dissolved in water along with other water soluble excipients. The solution is mixed with a suitable solvent used to solubilize drug and the resulting solution is then mixed, stirred and casted on to a petri plate followed by drying.

Role of Maltodextrin:

Maltodextrin acts as a film forming water soluble polymer and is the most vital and major component in the formulation (40 – 50 % w/v). It imparts tensile strength and good mouth feel to the film and the amount of polymer used decides the robustness of the film. The major advantage of using maltodextrin is its cost and availability as compared to other polymers especially Pullulan, a glucan consisting of maltotrioseunits, which was first used to make edible films[26]. Maltodextrin with low DE value has shown to impart flexibility and reduce cracking of the films[27]. Maltodextrin with DE value 12 along with 16-20%w/w has been proposed to produce fast dissolving films. However it has been found that certain taste masking agents have negative impact on the tensile strength of the film especially mint which causes an increase in stiffness in maltodextrin films. But this effect can be reversed by varying the

amount of glycerine content or by using maltodextrin of different molecular weight[28]. Moreover high drug loading capacity can be achieved in films made by maltodextrin using hot melt extrusion as the manufacturing technique[20].

3. **Diluent:**

Tablet is the most widely used dosage form existing today because of its convenience in terms of self-administration and ease in manufacturing. In order to facilitate tablet handling during manufacture and to achieve targeted content uniformity, the size of the tablet should be kept above 2-3 mm and weight of tablet above 50 mg. Many potent drugs have low dose (for e.g. diazepam, clonidine hydrochloride) in such cases diluents provide the required bulk of the tablet when the drug dosage itself is inadequate to produce tablets of adequate weight and size.

Maltodextrins derived from starch are ideal candidate as a diluent in tablets as well as capsules. Due to its colourless and flavourless characteristics they are preferred over others and have been widely used in pharmaceutical industry. Besides acting as diluent Maltodextrin can be co-processed with other excipients to make API direct compression compatible.

4. **Co-spray drying [29]:**

One of the major roles of Maltodextrin is in allowing direct compression of tablets. Direct compression is the preferred method for the preparation of tablets however it has been estimated that not more than 20 % of the active pharmaceutical ingredients (API) can be processed into tablets via direct compression since the majority of API lack the flow ability, cohesion or lubricating properties required for direct compression. Therefore one has to resort to other granulation techniques (dry or wet) to achieve API/excipient agglomerates with desired properties for compression. This involves several processing steps such as drying, mixing, granulation and again drying. Also different equipment is needed and numerous written procedures have to be followed and extensive downstream testing for powder homogeneity / segregation. In addition, wet granulation is a batch process and scaling-up of this technique is a labor-intensive and time-consuming process.

Co-spray drying a mixture of polysaccharide such as Maltodextrin and API along with monosaccharide polyols (eg: erythritol , mannitol) provides an alternative method to obtain a fully continuous process without granulation, milling and blending steps in between spray drying and compaction . Using this technique the number of unit operations is reduced, improving production efficiency and reducing costs, especially since spray drying is a technique which can be easily automated and equipped for in-line product analysis. Initial study which consisted of co-spray drying of drug with a single excipient. Various candidates were chosen for example lactose,xylitol,lactitol but among those promising result were obtained in case of Maltodextrin, mannitol and erythritol. The drug used as reference was acetaminophenol.

According to the statistical prediction the optimal formulation was: Drug (46.5%

w/w) , Mannitol (11.6% w/w) , Erythritol (20.9% w/w) and Maltodextrin (13.9% w/w) . Co-processing API along with Maltodextrin has also shown to prevent capping and lamination. Mannitol and erythritol imparted sweetness and reduced the amount of calories. In addition almost all of the polyols can be consumed by diabetics without any significant increase in body glucose, insulin or lactic acid concentration unlike the conventional saccharides such as sucrose, glucose and lactose. Erythritol crystals are non-hygroscopic, which is suitable in tablets and dry powder aerosol formulations and Maltodextrin imparts tensile strength to the tablets.

Maltodextrin increases the drug compatibility for direct compression and along with erythritol; mannitol blended with 0.3% w/w colloidal silicon dioxide and 0.5% w/w magnesium stearate in addition to glidant and lubricant is a proven strategy to facilitate direct compression.Different grades of Maltodextrin have different effects on the end product since ratio of amylose to amylopectin differs in each grade. Generally grade with higher amylose content (>50 %) has negative effect on disintegration time and thus is not preferred for conventional tablets.

CONCLUSION

Various applications of Maltodextrin are studied. Among all the carriers evaluated for proniosome Maltodextrin was found to provide more entrapment efficiency of drug. Further, Maltodextrin found to be safe and non-toxic, free flowing, poor solubility in the loaded mixture solution and good water solubility for ease of hydration. The film forming capacity and its ability to withstand high temperature it is used in fast dissolving oral films which is a convenient dosage form for paediatrics as well as geriatric. Maltodextrin can be used as a coating material to encapsulate nutraceutics such as vitamins. It being white,tasteless powder without having its own pharmacological activity enables it to be used extensively as a diluent as well as a co-processing excipient to make certain drugs direct compression compatible.

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