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CHEMICALLY MODIFIED STARCHES AND THEIR APPLICATIONS IN PHARMACY

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ABSTRACT

Native starch granules are insoluble at room temperature, highly resistant to enzymatic hydrolysis and lack specific functional properties. Native starches were well explored as binder and disintegrant in solid dosage form. Native starch irrespective of their source are undesirable for many applications, because of their inability to withstand processing conditions such as extreme temperature, diverse pH, high shear rate, and freeze thaw variation. To overcome this, modifications are usually done to enhance or repress the inherent property of these native starches or to impact new properties to meet the requirements for specific applications. The modifications alter the properties of starch, including solution viscosity, association behavior, and shelf life stability in final products. Modified starches were established as multifunctional excipient in the pharmaceutical and food industry. Common modes of modifications useful in pharmaceuticals are chemical, physical and enzymatic with, a much development already seen in chemical modification. This review aims to summarize the latest developments and recent knowledge regarding chemically modified starches. Recently new research works are done to modify starches such as corn (normal and waxy), wheat, potato and tapioca, sago, icacina starch etc were found to act as a multifuctional excipient like disintegrant, super disintegrant, polymer for controlled release, carrier for solid dispersion.

KEYWORDS

Modified Starches and Application in Pharmaceutical and Food Industry.

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INTRODUCTION

Starch is a natural, cheap, available, renewable, and biodegradable polymer produced by many plants as a source of stored energy. It is the second most abundant biomass material in nature. It is found in plant leaves, stems, roots, bulbs, nuts, stalks, crop seeds, and staple crops such as rice, corn, wheat, cassava, and potato. It has found wide use in the food, textiles, cosmetics, plastics, adhesives, paper,

and pharmaceutical industries. In the food industry, starch has a wide range of applications ranging from being a thickener, gelling agent, to being a stabilizer for making snacks, meat products, fruit juices[1]. Starch, which is the major dietary source of carbohydrates, is the most abundant storage polysaccharide in plants, and occurs as granules in the chloroplast of green leaves and the amyloplast of seeds, pulses, and tubers[1]. Chemically, starches are polysaccharides, composed of a number of monosaccharides or sugar (glucose) molecules linked together with α-D-(1-4) and/or α -D-(1-6) linkages. The starch consists of 2 main structural components, the amylose, which is essentially a linear polymer in which glucose residues are α -D-(1-4) linked typically constituting 15% to 20% of starch, and amylopectin, which is a larger branched molecule with α -D-(1-4) and α -D-(1-6) linkages and is a major component of starch. Amylose is linear or slightly branched, has a degree of polymerization up to 6000, and has a molecular mass of 105 to 106 g/mol. The chains can easily form single or double helices. Amylopectin on the other hand has a molecular mass of 107 to 109 g/mol. It is highly branched and has an average degree of polymerization of 2 million, making it one of the largest molecules in nature. Chain lengths of 20 to 25 glucose units between branch points are typical. About 70% of the mass of starch granule is regarded as amorphous and about 30% as crystalline. The amorphous regions contain the main amount of amylose but also a considerable part of the amylopectin. The crystalline region consists primarily of the amylopectin[2]. During recent years, starch has been taken as a new potential biomaterial for pharmaceutical applications because of the unique physicochemical and functional characteristics.

Native starches were well explored as binder and disintegrant in solid dosage form, butdue to poor flowability their utilization is restricted. Most common form of modified starch i.e. Pre-gelatinized starch marketed under the name of starch 1500 is now a day's most preferred directly compressible excipients in pharmaceutical industry. Recently modified rice starch, starch acetate and acid hydrolyzed dioscorea starch were established as multifunctional excipient in the pharmaceutical industry[3, 4].

STARCH MODIFICATION

Native starch irrespective of their source are undesirable for many applications, because of their inability to withstand processing conditions such as extreme temperature, diverse pH, high shear rate, and freeze thaw variation. To overcome this, modifications are usually done to enhance or repress the inherent property of these native starches or to impact new properties to meet the requirements for specific applications. The modifications alter the properties of starch, including solution viscosity, association behavior and shelf life stability in final products. Another purpose of starch modification is to stabilize starch granules during processing and make starch suitable for many food and industrial applications. The process of starch modification involves the destructurisation of the semi-crystalline starch granules and the effective dispersion of the component polymers. In this way, the reactive sites (hydroxyl groups) of the amylopectin polymers become accessible to electrophilic reactants[5].

Common modes of modifications useful in pharmaceuticals are chemical, physical and enzymatic with, a much development already seen in chemical modification[6]. Starch can be physically modified to improve water solubility and to change particle size. The physical modification methods involve the treatment of native starch granules under different temperature/moisture combinations, pressure, shear, and irradiation. Physical modification alsoincludes mechanical attrition to alter the physical size of starch granules[7].

Starch modification through chemical derivation such as etherification, esterification, crosslinking, and grafting when used as carrier for controlled release of drugs and other bioactive agents. It has been shown that, chemically modified starches have more reactive sites to carry biologically active compounds, they become more effective biocompatible carriers and can easily be metabolized in the human body[8]. Enzymatic modification of

starch is hydrolysis of some part of starch into a low molecular weight of starch called maltodextrin, or dextrin using amylolytic enzymes. They are widely used for food and pharmaceutical industries.

Chemical modification of starch

Chemical modification can be carried out on three starch states:

1. In suspension, where the starch is dispersed in water, the chemical reaction is carried out in water medium until desired properties are achieved. The suspension is then filtered, washed, and air dried.
2. In a paste, where the starch is gelatinized with chemicals in a small amount of water, the paste is stirred, and when the reaction is completed, the starch is air dried.
3. In the solid state, where dry starch is moisturized with chemicals in a water solution, air dried, and finally reacted at a high temperature (i.e., $\geq 100^{\circ}C$).

There are a number of chemical modifications made to starch to produce many different functional characteristics. The chemical reactivity of starch is controlled by the reactivity of its glucose residues. Modification is generally achieved through etherification, esterification, crosslinking, oxidation, cationization and grafting of starch. However, because of the dearth of new methods in chemical modifications, there has been a trend to combine different kinds of chemical treatments to create new kinds of modifications. The chemical and functional properties achieved following chemical modification of starch, depends largely on the botanical or biological source of the starch,, reaction conditions (reactant concentration, reaction time, pH and the presence of catalyst), type of substituent, extent of substitution (degree of substitution, or molar substitution), and the distribution of the substituent in the starch molecule[9]. Chemical modification involves the introduction of functional groups into the starch molecule, resulting in markedly altered physico-chemical properties. Such modification of native granular starches profoundly alters their gelatinization, pasting and retrogradation behavior[10,11]. The rate and efficiency of the chemical modification process depends on the reagent type, botanical origin of the starch and on the size and structure of its granules[12]. This also includes the surface structure of the starch granules, which encompasses the outer and inner surface, depending on the pores and channels.

Hydroxy propylated starch

Hydroxypropyl groups introduced into starch chains are said to be capable of disrupting inter- and intra-molecular hydrogen bonds, thereby weakening the granular structure of starch leading to an increase in motional freedom of starch chains in amorphous regions Such chemical modification involving the introduction of hydrophilic groups into starch molecules improves the solubility of starch and the functional properties of starch pastes, such as its shelf life, freeze/thaw stability, cold storage stability, cold water swelling, and yields reduced gelatinization temperature, as well as retarded retrogradation. Owing to these properties, hydroxypropylated starches is gaining interest in medicine. Hydroxypropylated starches are prepared by reacting starch slurry with propylene oxide under highly alkaline conditions at a temperature of approximately 30-50°C (86-122°F). A recent application of hydroxypropylated starch in pharmaceuticals is summarized in Table No.1, Figure No.1.

Carboxymethylated starch (CMS)

Starches can have hydrogen replaced by something else, such as a carboxymethyl group, making carboxymethyl starch (CMS). Adding bulky functional groups like carboxymethyl and carboxyethyl groups reduces the tendency of the starch to recrystallize and makes the starch less prone to damage by heat and bacteria. Carboxymethyl starch is synthesized by reacting starch with monochloroacetic acid or its sodium salt after activation of the polymer with aqueous NaOH in a slurry of an aqueous organic solvent, mostly an alcohol. The total degree of substitution (DS), that is the average number of functional groups introduced in the polymer, mainly determines the properties of the carboxymethylated products[13, 14]. The functionalization influences the properties of the

starch. For example, CMS have been shown to absorb an amount of water 23 times its initial weight. This high swelling capacity combined with a high rate of water permeation is said to be responsible for a high rate of tablet disintegration and drug release from CMS based tablets. A recent application of carboxymethylated starch in pharmaceuticals is summarized in Table No.2.

Acetylated starch

Acetylated starch has also been known for more than a century. Starches can be esterified by modifications with an acid. When starch reacts with an acid, it loses a hydroxyl group, and the acid loses hydrogen. An ester is the result of this reaction. Acetylation of cassava starch has been reported to impart two very important pharmaceutical characters to it; increased swelling power and enhanced water solubility of the starch granules. Starch acetates and other esters can be made very efficiently on a micro scale without addition of catalyst or water simply by heating dry starch with acetic acid and anhydride at 180°C for 2-10 min. At this temperature, starch will melt in acetic acid and thus, a homogeneous acetylation would be expected to occur. Using acetic acid, starch acetates are formed, which are used as film-forming polymers for pharmaceutical products. Slurry of starch is prepared at pH 8 and 25 to 30°C, the acid anhydride is added slowly to the starch slurry while maintaining pH 8 and temperatures of 25 to 30°C. After addition of reagents, the mixture is stirred for 20 to 30 min, and then adjusted to pH 6 to 7. The modified starch is isolated by washing and drying. Recent application Acetylated starches in pharmaceuticals are summarized in Table No.3, Figure No.2.

Succinylated starch

Modification of starch by Succinylation has also been found to modify its physicochemical properties, thereby widening its applications in food and non-food industries like pharmaceuticals, paper and textile industries. Modification of native starch to its succinate derivatives reduces its gelatinisation temperature and the retrogradation, improves the freeze-thaw stability as well as the stability in acidic and salt containing medium. Generally, succinylated starch can be prepared by treating starches with different alkenyl succinic anhydride, for example, dodecenyl succinic anhydride, octadecenyl succinic anhydride or octenyl succinic anhydride. The incorporation of bulky octadecenyl succinic anhydride grouping to hydrophilic starch molecules has been found to confer surface active properties to the modified starch. Unlike typical surfactants, octadecenyl succinic anhydride starch, forms strong films at the oil–water interface giving emulsions that are resistant to reagglomeration. Recent applications of succinylated starch in pharmaceuticals are summarized in Table No.4.

Phosphorylated starch

Phosphorylation was the earliest method of starch modification. The reaction gives rise to either monostarch phosphate or distarch phosphate (cross-linked derivative), depending upon the reactants and subsequent reaction conditions. Phosphate crosslinked starches show resistance to high temperature, low pH, high shear, and leads to increased stability of the swollen starch granule. The presence of a phosphate group in starch increases the hydration capacity of starch pastes after gelatinization and results in the correlation of the starch phosphate content to starch paste peak viscosity, prevents crystallization and gel-forming capacity. These new properties conferred on starch by phosphorylation, makes them useful as disintegrants in solid dosage formulations and as matrixing agents. Interestingly, it has been documented that, the only naturally occurring covalent modification of starch is phosphorylation. Traditionally, starch phosphorylation is carried out by the reaction of starch dispersion in water with reagents like mono- or di sodium orthophosphates, sodium hexametaphosphate, sodium tripolyphosphate (STPP), sodium trimetaphosphate (STMP) or phosphorus oxychloride. Alternative synthetic methods such as extrusion cooking, microwave irradiation and vacuum heating have been. Some of the recent uses of phosphorylated starch in pharmaceuticals are summarized in Table No.4.

Co-polymerized starch

Chemical modification of natural polymers by grafting has received considerable attention in recent years because of the wide variety of monomers available. Graft copolymerization is considered to be one of the routes used to gain combinatorial and new properties of natural and synthetic polymers. In graft copolymerization the guest monomer benefits the host polymer with some novel and desired properties in which the resultant copolymer gains characteristic properties and applications (Fares, et al., 2003). As a rule, graft copolymerization produces derivatives of significantly increased molecular weight. Starch grafting usually entails etherification, acetylation, or esterification of the starch with vinyl monomers to introduce a reaction site for further formation of a copolymeric chain. Such a chain would typically consist of either identical or different vinyl monomers (block polymers), or it may be grafted onto another polymer altogether. Graft copolymers find application in the design of various stimuli-responsive controlled release systems such as transdermal films, buccal tablets, matrix tablets, microsphers/hydrogel bead system and nanoparticulate system (Sabyasachi Maiti, 2010). Some of the recent uses of graft copolymerized starch in pharmaceuticals is summarized in Table No.5.

Specific category of starches are resistant starches (RS), which are nowadays intensively researched, due to their impact on human health and properties of products and starch-based edible films. Recently new research works are done on native starches such as corn (normal and waxy), wheat, potato and tapioca, sago, icacina starch etc. Chowdhary k p r et al has reported calcium starch, cross linked starch urea etc as a novel disintegrant agent and as a carrier in the solid dispersion of in the tablet formulations. And calcium starch, cross linked starch urea as a new starch based polymer controlled release formulations (Table No.5).

Starch citrate

Starch citrate prepared by reacting native starchs such as potato, tacca, sago, icacina etc with citric acid at elevated temperatures was crystalline, non-hygroscopic and was insoluble in water and aqueous fluids of acidic and alkaline pHs. It also exhibited good swelling (1500%) in water. It has no pasting or gelling property when heated at 100^0C in water for 30 min. As starch citrate exhibited good swelling in water it is considered as a promising disintegrant in tablet formulations and was evaluated as disintegrant in tablet formulations. Citric acid (40g) was dissolved in 100 ml of water and pH of the solution was then adjusted to 3.5 with 10 M sodium hydroxide. Starch citrate was prepared based on the method of Klaushfer et al with some modifications. Citric acid (20g) was dissolved in 20 ml of water, the pH of the solution was adjusted to 3.5 with 10 M sodium hydroxide and finally the volume was made upto 50 ml by adding water. The citric acid solution (50 ml) was mixed with 50g of potato starch in a stainless steel tray and conditioned for 16 h at room temperature (28^0C). The tray was then placed in forced air oven and dried at 60^0C for 6 h. The mixture obtained was ground and further dried in a forced air oven at 130^0C for 2 h. The dry mixture was repeatedly washed with water to remove unreacted citric acid. The washed starch citrate was further dried at 50^0C to remove the water/moisture completely. The product obtained was ground and sized in Figure No.3[24].

Cross linked starch urea

Cross linked starch - urea, a new starch based polymer has been synthesized and its application in controlled release Cross-linked starch-urea polymer was synthesized by gelatinization of starch in the presence of urea and crosslinking by treatment with calcium chloride. Starch (9 parts) was dispersed in purified water (10 parts) to form starch slurry. Urea (1 part) and calcium chloride (1 part) were dissolved in purified water (40 parts) and the solution was heated to boiling. While boiling, the starch slurry was added and mixed. Mixing while heating was continued for 20 minutes to form cross-linked starch-urea polymer. The mass formed was spread on to a stainless steel plate and dried at 85^0C for 6-8h. The dried polymer was powdered and passed through mesh No.100.

Calcium starch

Calcium starch, a new starch based polymer and to evaluate its application in controlled release (CR). Calcium starch polymer was synthesized by gelatinization of starch in the presence of sodium hydroxide and cross linking by treatment with calcium chloride. Potato starch (5 parts) was dispersed in purified water (50 parts) to form starch slurry. Sodium hydroxide (3 parts) was dissolved in water (30 parts) and the solution was added to starch slurry, while mixing. Mixing was continued for 30 minutes to form a thick gelatinized mass. The mass formed was added to 300 mL of calcium chloride (20 % w/v) solution contained in a vessel while stirring at 1000 rpm with a medium duty stirrer. The stirring was continued for 1 hour to precipitate calcium starch formed. The calcium starch formed was collected by vacuum filtration, washed repeatedly with water and dried at 80ºC. The dried polymer was powdered and passed through mesh No.100.

Starch phosphate

Starch phosphate is one of the modified starches used in the frozen food industry. It is produced by phosphorification of free hydroxyl groups of anhydroglucose units of starch molecule. They are esterified with phosphate reagents. Phosphate reagents for starch phosphate monoester are orthophosphate salts. Starch phosphate production is normally by using wet process 2. No reports are available on its use as pharmaceutical excipient. Starch phosphate (Figure No.4) was prepared based on the method of Choi et al. with some modifications. Potato starch (100 g) and di-sodium hydrogen orthophosphate anhydrous (30g) were suspended in 100 mL of water and continuously stirred for 20 min. This starch slurry was then filtered and the wet starch mixture was conditioned for 12 h at room temperature (28^0C). To enhance phosphorylation, this mixture was heated in a forced air oven at 130^0C for 3 h. The product obtained was grounded and sized. Starch phosphate was insoluble in water and aqueous fluids of acidic and alkaline pHs. It also exhibited good swelling (400%) in water. It has no pasting or gelling property when heated at 100^0C in water for 30 min. As starch phosphate exhibited good swelling in water, it is considered as a promising disintegrant in tablet formulations. Some of the newly developed modified starches used in the pharmaceuticals are given in the Table No.6[25].

Table No.1: Application of carboxymethylated starch in pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Hydroxy propylated starches of varying amylose contents as sustained release matrices in tablets[13].	Propanolol hydrochloride	Improved the sustained release ability of amylose containing starch matrices, and conferred additional resistance to the hydrolytic action of pancreatic under simulated gastrointestinal condition.

Table No.2: Applications of carboxymethylated starch in pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Synthesis and *in vitro* evaluation of carboxymethyl starch-chitosan nanoparticals as drug delivery system to the colon.	5 - aminosalicylic acid	Chitosan-carboxymethyl starch nanoparticals developed based on the modulation of ratio show promise as a system for controlled delivery of drugs to the colon[15].
2	An Aqueous Film coating formulations based on sodium carboxymethyl mungbean starch.	Material science	Carboxy methylated mungbean starch exhibited the ability to form clear, thin film with greater flexibility and strength that of the native starch. This study reports the potential of Carboxy methylated mungbean starch as a tablet film coating agent[16].
3	High amylose sodium carboxymethylated starch matrices for oral, sustained drug release: Formulation aspects invitro drug release evaluation.	Acetaminophen	The results proved that the spray drying process for high amylose sodium carboxymethyl starch is suitable for obtaining similar quality in terms of drug release compression performences[17].

Table No.3: Applications of Acetylated starch in pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Acetylated starch based biodegradable materials with potential biomedical applications as drug delivery systems	Bovine serum albumin	Drug release studies shown that the starch acetate tablets could deliver the drug to the colon suggesting that it can be a potential drug delivery carrier for colon targeting [18].

2	Optimization and characterization of controlled release multiparticulate beads coated with starch acetate	Dyphylline	Starch acetate coated tablets provide controlled release of dyphylline[19].
3	Starch acetate microparticals for drug delivery into retinal pigment in vitro study	Calcein	The study indicates that the natural enzyme sensitive starch acetate is suitable for drug delivery into retinal pigment epithelium (RPE). The starch acetate microparticals were easily taken up by cultured human RPE cells without significant toxicity[20].

Table No.4: Applications of phosphorylared starch in pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Starch Phosphate: A Novel Pharmaceutical Excipient For Tablet Formulation	Ziprasidone	At low concentration, starch phosphate proved to be a better disintegrant than native starch in Tablet formulation[21].
2	Starch phosphates prepared by reactive extrusion as a sustained release agent	Metoprolol Tartrate	Starch phosphate prepared by reactive extrusion produced Stronger hydrogels with sustained release properties as compared with native starch[22].

Table No.5: Application of graft copolymerized starch in pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Characterization and *in vitro* evaluation of starch based hydrogels as carriers for colon drug delivery systems	Ketoprofen	Hydrogels prepared showed pH responsive property[23].
2	Hydrophobic grafted and cross linked starch nanopaticals for drug delivery	Indomethacin	Fatty acid grafted atrch nanopaticals with high swelling power was obtained and found to bea a good vehicle for oral controlled drug delivery[8].

Table No.6: Applications of newly developed modified starches in the pharmaceuticals

S.No	Study Title	Drug used	Summary
1	Formulation and Development of Aceclofenac Solid dispersion Tablets Employing Starch Phosphate -A New Modified Starch	Aceclofenac	Starch phosphate acts as a carrier in solid dispersions for enhancing the dissolution rate of aceclofenac[26].
2	Evaluation of Complexed Starch-Urea-Citrate as A Novel Super Disintegrant	Ofloxacin	The disintegration time of all the formulations was less than one minute. Thus it was made evident that the starch-urea-citrate could be used as an excellent super disintegrant[27].
3	Preparation and Evaluation of Cross Linked Starch Urea- A New Polymer for Controlled Release of drug	Aceclofenac	Cross-linked starch-urea was more suitable than starch-urea for controlled release application. Aceclofenac release from the matrix tablets formulated employing cross-linked starch-urea was slow, spread over 24h and the release was diffusion controlled[28].
4	Enhancement of Dissolution Rate and Formulation Development of Efavirenz Tablets Employing Starch Citrate-A New Modified Starch	Efavirenz	Starch citrate acts as a carrier in solid dispersions for enhancing the dissolution rate of aceclofenac[29].
5	Preparation, characterization and evaluation of starch citrate-a new Modified starch as a disintegrant in tablet formulations	Sulfamethoxazole, Paracetamol, ibuprofen	Starch citrate prepared exhibited excellent flow characteristics. It also exhibited good swelling (1500%) in water. It has no pasting or gelling property when heated at100^0C in water for 30 min. As starch citrate exhibited good swelling in water it is considered as a promising disintegrant in tablet formulations[24].

6	Preparation and evaluation of starch phosphate- a new modified starch as a disintegrant in tablet formulations	Sulfamethaxazole, paracetamol	As starch phosphate exhibited good swelling in water it is considered as a promising disintegrant in tablet formulations[25].
7	Evaluation of calcium starch: a new starch Based polymer for controlled release formulations	Diclofenac	Diclofenac release from the matrix tablets formulated employing cross-linked starch-urea was slow, spread over 24 h and the release was diffusion controlled[30].

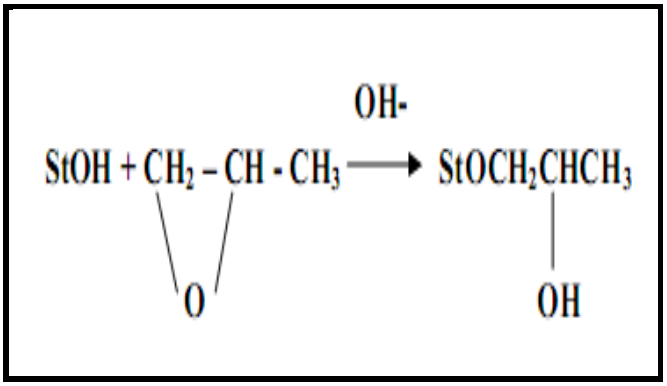

Figure No.1: Chemical reaction for hydroxypropyl substitution of starch. St = starch polymer

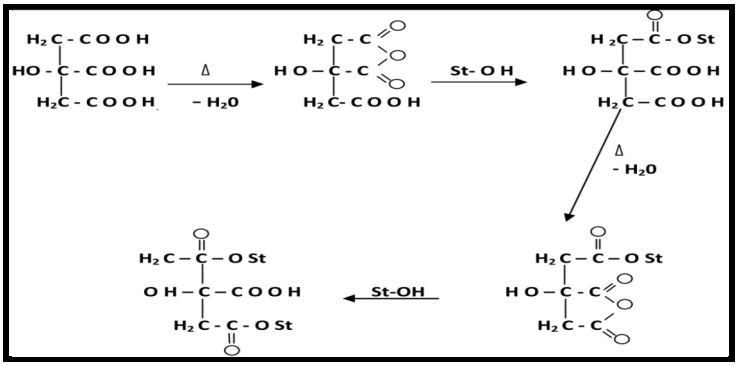

Figure No.3: Chemical reaction involved in the preparation of starch citrate

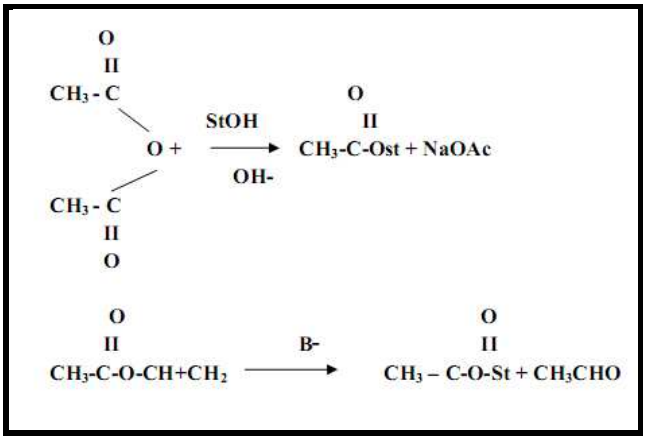

Figure No.2: Chemical reactions for acetate substitution of starch. St = starch polymer

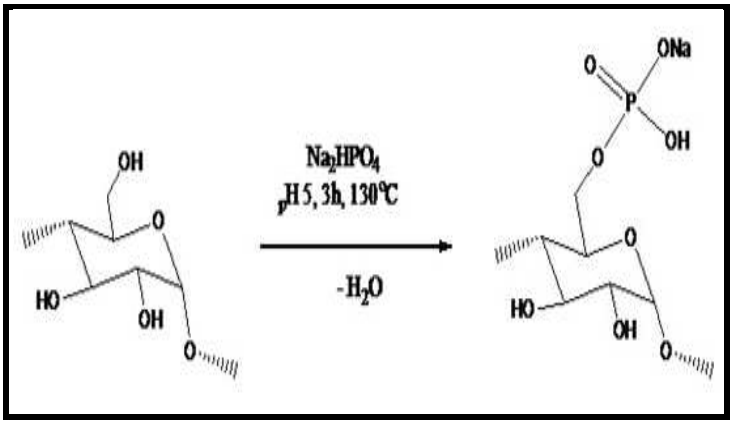

Figure No.4: Reaction involved in the preparation of starch phosphate

CONCLUSION

It is obvious that starch has moved from its traditional role as food to being an indispensable medicine. The wide use of starch in the medicine is based on its adhesive, thickening, gelling, swelling and film-forming properties as well as its ready availability, low cost and controlled quality. Starch has proven to be the formulator's "friend" in that, it can be utilized in the preparation of various drug delivery systems with the potential to achieve the formulator's desire for target or protected delivery of bioactive agents. Native starch irrespective of their source are undesirable for many applications, because of their inability to withstand processing conditions such as extreme temperature, diverse pH, high shear rate, and freeze thaw variation. To overcome this, modifications are usually done to enhance or repress the inherent property of these native starches .Such modification of native granular starches profoundly alters their gelatinization, pasting and retrogradation behavior and thus modified starch plays an important role in food and pharmaceuticals. Recently many researches are made for the development of new modified starches such as Cross linking starch urea and calcium starches are the chemically modified starches which acts as a new polymer in the controlled release formulations. Starch citrate, starch phosphate are the chemically modified starches which exhibit good swelling and excellent flow property than native starches which exhibits as a promoising disintegrant in the tablet formulations.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Manek R V, Kunle O O, Emeje M O, Builders P, Rao G V R, Lopez G P and Kolling W M. Physical, Thermal and Sorption Profile of Starch Obtained from Tacca leontopetaloides, *Starch - Stärke*, 57(2), 2005, 55-61.
2. Sajilata M G, Singhal R S and Kulkarni P Z. Resistant Starch-A Review, *Comprehensive Reviews in Food Science and Food Safety*, 5(1), 2006, 1-17.
3. Freire C, Podczeck F, Veiga F and Sousa J. Starch-based coatings for colon specific delivery. Part II: Physicochemical properties and *in vitro* drug release from high amylose maize starch films, *European Journal of Pharmaceutics and Biopharmaceutics*, 72(3), 2009, 587-594.
4. Serrero A l, Trombotto S P, Cassagnau P, Bayon Y, Gravagna P, Montanari S and David L. Polysaccharide Gels Based on Chitosan and Modified Starch: Structural Characterization and Linear Viscoelastic Behavior, *Biomacromolecules*, 11(6), 1534- 1543.
5. Shangraw R F. International harmonization of compendia standards for pharmaceutical excipients, *D.J.A. Crommelin, K.Midha (Eds.), Topics in Pharmaceutical Sciences*, 8(1), 1992, 205-223.
6. Rajan A, Sudha J D and Abraham T E. Enzymatic modification of cassava starch by fungal lipase, *Industrial Crops and Products*, 27(1), 2008, 50-59.
7. Prochaska K, Konowal E, Sulej-Chojnacka J and Lewandowicz G. Physicochemical properties of cross-linked and acetylated starches and products of their hydrolysis in continuous recycle membrane reactor, *Colloids and Surfaces B:Biointerfaces*, 74(1), 2009, 238-243.
8. Simi C and Emilia Abraham T. Hydrophobic grafted and cross-linked starch nanoparticles for drug delivery, *Bioprocess and Biosystems Engineering*, 30(3), 2009, 173-180.
9. Singh J, Kaur L, and McCarthy O J. Factors influencing the physico-chemical, morphological, thermal and rheological properties of some chemically modified starches

for food applications-A review, *Food Hydrocolloids*, 21(1), 2007, 1-22.
10. Choi S G, and Kerr W L. Water mobility and textural properties of native and hydroxypropylated wheat starch gels, *Carbohydrate Polymers*, 51(1), 2003, 1-8.
11. Perera C, Hoover R, and Martin A M. The effect of hydroxypropylation on the structure and physicochemical properties of native defatted and heat-moisture treated potato starches, *Food Research International*, 1997, 30(3-4), 235-247.
12. Huber K C and BeMiller J N. Location of Sites of Reaction within Starch Granules, *Cereal Chemistry*, 78(2), 2001, 173-180.
13. Onofre F O and Wang Y J. Hydroxypropylated starches of varying amylase contents as sustained release matrices in tablets, *International Journal of Pharmaceutics*, 385(1-2), 2010, 104-112.
14. Heinze T. Carboxymethyl ethers of cellulose and starch - a review, *Chemistry of plant raw materials*, 3, 2005, 13-29.
15. Saboktakin M R, Tabatabaie R M, Maharramov A and Ramazanov M A. Synthesis and *in vitro* evaluation of carboxymethyl starch-chitosan nanoparticles as drug delivery system to the colon, *International Journal of Biological Macromolecules*, 48(3), 2010, 381-385.
16. Brouillet F, Bataille B and Cartilier L. High-amylose sodium carboxymethyl starch matrices for oral, sustained drug-release: Formulation aspects and in vitro drug-release evaluation, *International Journal of Pharmaceutics*, 356(1-2), 2008, 52-60.
17. Kittipongpatana O S, Chaichanasak N, Kanchongkittipoan S, Panturat A, Taekanmark T and Kittipongpatana N. An Aqueous Film-coating Formulation based on Sodium Carboxymethyl Mungbean Starch, *Starch – Stärke*, 58(11), 2006, 587-589.
18. Tuovinen L, Peltonen S and Järvinen K. Drug release from starch-acetate films, *Journal of Controlled Release*, 91(3), 2003, 345-354.
19. Nutan M T H, Soliman M S, Taha E I and Khan M A. Optimization and characterization of controlled release multi-particulate beads coated with starch acetate, *International Journal of Pharmaceutics*, 294(1-2), 2007, 89-101.
20. Tuovinen L, Ruhanen E, Kinnarinen T, Ronkko S, Pelkonen J, Urtti A, Peltonen S and Järvinen K. Starch acetate microparticles for drug delivery into retinal pigment epithelium-in vitro study, *Journal of Controlled Release*, 98(3), 2004, 407-413.
21. Prasanthi N L, Rama Rao N. Starch Phosphate: A Novel Pharmaceutical Excipient for Tablet Formulation, Journal of Pharmacy Research, 3(12), 2010, 2919.
22. O Brien S, Wang Y J, Vervaet C. and Remon J P. Starch phosphates prepared by reactive extrusion as a sustained release agent, *Carbohydrate Polymers*, 76(4), 2009, 557- 566.
23. El-Hag Ali A, and AlArifi A. Characterization and *in vitro* evaluation of starch based hydrogels as carriers for colon specific drug delivery systems, *Carbohydrate Polymers*, 78(4), 2009, 725-730.
24. Chowdary K P R, Veeraiah E. Preparation, characterization and evaluation of starch citrate-A new modified starch as a disintegrant in tablet formulations, *International Journal of Pharma Research and Development*, 2(12), 2011, 9-17.
25. Chowdary K P R, Veeraiah E, Sandhya Rani A. Preparation and Evaluation of Starch Phosphate-A New Modified Starch as a disintegrant in tablet formulations, *Int. J. Chem. Sci*, 9(2), 2011, 893.
26. Chowdary K P R, Veeraiah Enturi and A. Sandhya Rani. Formulation Development of Aceclofenac Tablets Employing Starch Phosphate- A New Modified Starch, *International Journal of Pharma Sciences and Research*, 2(3), 2011, 124-129.
27. Bharath S, Raghavendra Naik, Basavaraj B V, Deveswaran R, Madhavan V. Evaluation of Complexed Starch-Urea-Citrate as A Novel Super Disintegrants, *Asian Journal of Biomedical and Pharmaceutical Sciences*, 2(7), 2012, 01-07.

28. Chowdary K P R and Krishna chaithanya K. Preparation and Evaluation of Cross Linked Starch Urea- A New Polymer for Controlled Release of Aceclofenac, *Asian Journal of Chemistr*, 22(6), 2010, 4265-4270.
29. Chowdary K P R, Veeraiah E. Enhancement of Dissolution Rate and Formulation Development of Efavirenz Tablets Employing Starch Citrate - A New Modified Starch, *Journal of Applied Pharmaceutical Science*, 1(5), 2011, 119-123.
30. Chowdary K P R, Tripura Sundari P. Evaluation of calcium starch: A new starch based polymer for controlled release of diclofenac, *Int. J. Chem. Sci*, 6(3), 2008, 1189-1195.

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