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A review on polymers in natural or modified form used in sustained release tablet

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ABSTRACT

Tablet is a solid dosage form which is used to deliver the drug to the body to make pharmacological action. The oral dosage form should disperse into small particles to deliver active ingredients in the body, the disperse time of the dosage form depends on the ingredients which are used in the tablet. To make the tablet disintegrate slow usually sustained release agents are used. The sustained release tablets helps in maintaining the drug concentration in the body for the higher time. In this review article various polymers of natural origin and their modified forms are studied, which can be used in the sustained release tablet. In this review article the polymers studied were, Psyllium husk, HPMC K100M, Cellulose polymers, Cellulose ether polymers, Xanthan gum, Guar gum, Eudragit RLPO, Eudragit RSPO, Eudragit RL 100, Eudragit RS 100, Kollidone SR and Carnauba wax. Now a day the sustained release tablets are used more than the conventional tablets because of the patient incompliance. The main part of the sustained release tablets are the polymers. In the study it was found that the modified forms of natural polymers works better than in their natural form. In the study it was found that the hydrophilic polymers also work better like Xanthan gum and Guar gum, they are effecting and non-toxic in nature. The cellulose derivatives were studied and it was found that Substituted cellulose-methylcellulose, hydroxypropylcellulose and hydroxypropylmethylcellulose works better in the combination form.

Keywords: Sustained release, Xanthan gum, Guar gum, Eudragit, Kollidone, HPMC

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INTRODUCTION

Tablet has always been the most widely used dosage form since the ancient time. Now a days different tablet dosage forms are available in the markets. The tablets are very easy to administer and also they can be taken anywhere, people can take the tablets even during travelling [1,3,5]. Most of the people forget to take the tablet which results in the incomplete action of the drug for a particular disease, so now- days the sustained release tablets are used which are very convenient to use and also it maintains the drug level in the body for a longer time. Hence it can easily use in the patient incompliance. The main mechanism of the sustained release tablet is that it releases the drug at the slower rate. In other words we usually use the polymers that can retard the drug release till the certain period of time [7]. So now we can say that the actual time of drug is changed or delayed. In the review it is studied that sustained-release dosage forms have made significant progress in terms of clinical efficacy and patient compliance in past two decades.In the present work Preparation of drug-embedded matrix tablet that involves the direct compression of a blend of drug, retardant material and additives is one of the least complicated approaches for delivering drug in a temporal pattern into the systemic circulation. The matrix tablet is commonly used for manufacturing sustained release dosage forms because it makes such manufacturing easy [13]. In the wide array of polymers has been employed as drug retarding agents each of which presents a different approach to the matrix concept. Polymers forming insoluble or skeleton matrices constitute the first category of retarding materials, also classed as plastic matrix systems.

There are two classes of polymers hydrophilic and hydrophobic in which, the second class represents hydrophobic and water-insoluble materials, which is usually potentially erodable, while the first group includes polymers those form hydrophilic matrices. The matrix systems, due to their chemical inertness and drug embedding ability, have been widely used for sustaining the release of drug [15]. The

liquid penetration into the matrix is the rate-limiting step in such systems unless joining agents are used and it can be a reason for sustains release property. The hydrophobic and waxy materials, on the other hand, are potentially erodable and control the release of drug through pore diffusion and erosion [16].The hydrophilic matrix systems, when exposed to an aqueous medium, does not disintegrate, but immediately after hydration develops a highly viscous gelatinous surface barrier which controls the drug release from and the liquid penetration into the centre of the matrix system [18], The purpose work is to evaluate the comparative efficiency of abovementioned classes of polymers on sustaining the release of active ingredients having different physical and chemical properties.

Kollidone SR

Kollidone is a chemical substance that is used as a pharmaceutical agent to work in a tablet as a sustained release agent. Kollidon SR (Polyvinyl acetate and polyvinyl pyrrolidone based matrix forming agent), Carnauba wax is a waxy material that is obtained from the plant source. It is maily found in the South American region. Carnauba wax and Hydroxypropyl methyl cellulose (HPMC-15cps) worked as hydrophobic and hydrophilic matrix systems respectively. Three drugs e.g. atenolol as a soluble neutral drug, diclofenac sodium as an acidic drug with pH dependant solubility and diltiazem HCl as basic drug of acidic salt works very well with these types of polymers. The present study is aimed to evaluate the influence of polymer content and polymer type on the release profile of drug as well as to establish a relationship between drug retaining efficacy of the polymer and physic chemical nature of the drug [20].In the study it was found that the Carnauba wax causes the strongest retardation of drug. On the other hand, highest drug release was from matrices however the Kollidon SR gave an intermediate release profile between these two polymers. The release rate was also found to be the function of physico-chemical nature of drug molecule. Theophylline and diltiazem HCl, being soluble in nature, released faster than diclofenac sodium from all matrix systems. The release mechanism was explored and explained with bi-exponential equation Reza S *et al*.

HPMC

Hydroxypropylmethylcellulose, is derived from the cellulose family and it is used to control drug release from several pharmaceutical systems because of its non-toxic nature, easy compression, swelling properties and accommodation to high levels of drug. This cellulose derivative excipient has been widely investigated in our laboratory [21]. There are lots of research that has been done on HPMC and it always says that drug-release processes from both methylcellulose and hydroxypropylcellulose better than the other agents in case of sustained release dosage form. The sole purpose of the present study is to evaluate the effect of polymers on the kinetics of the drug release, using distinct formulations, in order to understand how they rule this process. It will also hopefully allow the design of more suitable cellulose matrices. The main part of the diluent is also examined [22].

Guar gum

Guar gum is a natural non-ionic polysaccharide derived from the seeds of *Cyamopsis tetragonolobus* (Family Leguminosae) gummy substance. In pharmaceutical products, Guar gum is used in solid dosage forms as a binder and disintegrant. The naturally occurring guar seed extract which usually contains about 80% of galactomannan (guaran), 10% moisture, 5-7% protein and trace amounts of heavy metals and ash. It is free flowing in nature, completely soluble, neutral polymer and is approved for use in food [24]. It is not so sensitive to pH, moisture contents or solubility of the tablet matrix. As a binding agent, guar gum has been found to be superior to some common disintegrants such as corn starch, celluloses, alginates and magnesium aluminium silicate. Particle size can affect binding properties, with finer particle sizes having greater disintegrating capabilities. Guar gum alone could not efficiently control the drug release, while Xanthan gum and all combinations of natural gums with HPMC could retard drug release.The guar gum has shown in Fig. 1.

Fig. 1: Guar gum

Xanthan Gum

Xanthan gum is natural, biosynthetic, edible gum and an extracellular polysaccharide produced by the bacterium *Xanthomonas campestris*. Xanthan gum consists of glucose, mannose, and glucuronic acid [26] and is used in different foods as thickener and stabilizer. The main purpose of this study was to review matrix sustained-release tablets with natural gums (xanthan and guar gum) as suitable hydrophilic matrix systems compared with the extensively investigated hydrophilic matrices. The Xanthan gum has shown in Fig. 2.

Fig. 2: Xanthan gum

GUMS IN COMBINATION FORM OR MODIFIED FORM

It was studied that Different combinations of natural gums (guar or xanthan) and also a triple mixture of these polymers were used to provide matrix tablets for sustained release of water-soluble tramadol HCl. The total 64% of release retardant polymer(s) was used in the formulations. It was studied that the combination of the gums retained the drug release up to 70% than the used alone (Varshosaz *et al*.)

Plantago ovata

*Plantago ovata*is also known as the *isapghula,* it is a husk that is commonly used as a husk for treating the constipation, due to its swelling properties. When it comes in contact with the water it get swell. Mucilage of *Plantago ovata* has various properties like binding, disintegrating and sustaining properties. The mucilage of the *isapghula* is used as a super-disintegrating agent and it's a very unique technique. To use as a super-disintegrant the extraction of the gummy material is an essential part. For the extraction the gum, the *isapghula*

seeds are soaked overnight in a Luke warm water, overnight the seed releases its all mucilage, after that the mucilage is separated from water through muslin cloth. Then it is ready to get dry and then it's sieve under # 40 and placed in desiccators. Then store into a well tight container. The rapid disintegration of the tablet is due to the swelling of the super-disintegrants to create an enough hydrostatic pressure to break the tablet. The gum was studied in the dispersible tablet and the study showed that the natural gums as disintegrants were effective in low (5 %) concentrations [30]. During the study it was found that the plantago husk works best with the combination chitin. The *plantago ovata* has shown in Fig. 3.

Fig. 3: *Plantago ovato*

Chitin or Chitosan

Chitin is a natural product which is a structural polysaccharide. Chitin is widely distributed in nature it supports the tissue crustaceans and insects. The chitosan ia an deacetylation product of the chitin. That compound is non-toxic in nature; recently it has been used in various research projects. S Miyuki *et al*. have utilized the chitosan with lactose in sustained release dosage form. The drug and chitosan with lactose were dissolved in the solvent followed by the distilling off. The dosage form was studied or compared with other sustained release agents and chitosan has shown the better result thus, the mixture of chitosan and lactose can form sustained release preparation in an acidic solution. Since chitosan was gelled to encapsulate the medicaments in an acidic solution. The chemical structure of the chitosan has shown in Fig. 4.

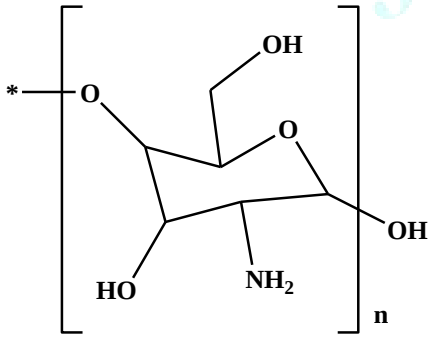

Fig. 4: Chitosan

Eudragit

Eudragit is a polymer which is widely used in the pharmaceutical industries, eudragit available in the differnet grades like eudragit EPO, eudragit RS 100, eudrgit RLPO, eudragit RSPO. Patra NC *et al* has studied the bilayer tablet eudrgit RLPO and eudragit RSPO, which were evaluated for various physical properties. In the study the bulk densities for the granules of various formulations ranged between 0.87 ± 0.14 and 2.42 ± 0.42 g mL–1, as determined by the tap method. It was found that this value of bulk density indicates of good packing character. The compressibility index (CI) for all the formulations was found to be below 15%, indicating desirable flow properties [34]. It was studied that the flow properties of granules were quite good; it ranged between 21.32 ± 0.58 to 25.03 ± 0.23°. The value indicates good flow property of granules with Eudragit RLPO and Eudragit RSPO as matrix material. Thus, we can say that eudragit works quite well in two different grades.

CONCLUSON

Form the above observations it is observed that the natural and modified forms has their own working capacity in the dosage form. The natural compounds always works the best since the natural compounds devoid of the toxicity and irritation sensation. But to increase the working capability of the product the modified forms are usually used. It was studied that the Guar gum alone cannot efficiently control drug release, and Xanthan gum has higher drug retarding ability than Guar gum. The combination of each natural gum with HPMC leads to a greater retarding effect compared with a mixture of these natural gums. No synergistic effect has been seen for these mixtures of polymers. All combinations of guar gum and xanthan with HPMC or xanthan alone can retard drug release. It was also concluded that during the study the HPMC was studied for the DSC studies as well and it was found out that the DSC thermograms alone, it is possible to conclude that the selected excipients are likely to be suitable for the preparation of tablet formulations, since no significative incompatibilities were detected. Even the drug: excipient interactions were detected, it was not found to affect the drug bioavailability.

The swelling experiments, shows that the water uptake increases with the polymer viscosity, which is a very important factor to consider when preparing hydrophilic matrix tablets according to the release studies, polymer HPMC are not appropriate for the preparation of modified ketoprofen hydrophilic matrix tablets, in the conditions under study, while HPMC K15M and K100M may be advantageous, because it holds the drug for longer time.

The present research was carried out to study the different polymers for the sustained release tablet in the bilayer tablet of propranolol hydrochloride using superdisintegrant sodium starch glycolate for the fast release layer and ethylcellulose, Eudragit RLPO and Eudragit RSPO for the sustaining layer it was studied that, Bilayer tablets showed an initial burst effect to provide the loading dose of the drug, followed by sustained release for 12 h, which indicats that the potential of the propranolol hydrochloride bilayer tablet as an alternative to the conventional dosage form.

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