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A REVIEW ARTICLE ON THE COMBINATION OF HPC AND HPMC TO STUDY THE EFFECT ON MODIFIED RELEASE TABLETS

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ABSTRACT

The aim of this review work was to study the effect of the combination of HPC and HPMC on modified release tablets. Modified release dosage and its variants are mechanisms used in tablets and capsules to dissolve a drug over time in order to be released slower and steadier into the bloodstream while having the advantage of being taken at less frequent intervals than immediate release formulation of the same drug. The polymers have significant role in modified release formulations. The main role of polymer is to protect the drug from physiological environment and prolong release of drug to improve its stability. The drug release from polymer is takes place by diffusion, degradation and swelling. Hydroxypropyl cellulose and Hydroxypropyl methyl cellulose are the examples for such type of polymers. HPMC, also known an hydromellose, is one of the best known cellulose polymer. It is available in various grades. It act as an excellent hydrophilic gel forming polymer. HPMC is used as a matrix that swells and expands after absorbing water. Hydroxypropyl cellulose[HPC] is a cellulosic derivative which has characters such as non-polar, water solubility and highly pH sensitive. It acts as a thickening agent by altering the viscosity. It can be used for the binding of tablet dosage forms. It serves as a film coating agent. In this work, the properties of polymers are considered at various level.

KEYWORDS: Hydroxypropyl methyl cellulose, Hydroxypropyl cellulose, Carbopol, Cellulose etc.

INTRODUCTION

IMPORTANCE OF POLYMERS IN MODIFIED RELEASE TABLETS

Polymers have important roles in the formulation of pharmaceutical products specially in modified release formulations as the modified release tablets have following advantages.

a) Decreased local and systemic side effects: - Reduced gastrointestinal irritation.

b) Better drug utilization.

- Reduction in total amount of drug used.
- Minimum drug accumulation on chronic dosing.

c) Improved efficiency in treatment.

- Optimized therapy and reduction in fluctuation in drug level and hence more uniform pharmacological response.
- Special effects e.g. sustained release aspirin provides sufficient drug so that on awakening the arthritic patient gets symptomatic relief.
- Cure or control of condition more promptly.
- Less reduction in drug activity with chronic use.

Method by which sustained release is achieved can improve the bioavailability of some drugs e. g. drugs susceptible to enzymatic inactivation can be protected by encapsulation in polymer systems suitable for sustained release.

d) Improved patient compliance

- Less frequent dosing
- Reduced night-time dosing
- Reduced patient care time.

e) Economy

CLASSIFICATION OF THE MODIFIED RELEASE TABLETS

Modified-release delivery systems may be divided conveniently into three categories.

a. Delayed release

b. Sustained release

- Controlled release
- Prolonged release

c. Site-specific and Receptor release

Sustained-release systems include any drug-delivery system that achieves slow release of drug over an extended period of time. If the systems can provide some

control, whether this be of a temporal or spatial nature, or both, of drug release in the body, or in other words, the system is successful at maintaining constant drug levels in the target tissue or cells, it is considered a controlled-release system.

Delayed release systems are those systems that use repetitive, intermittent dosing of a drug from one or more immediate release units incorporated into a single dosage form.

Examples of delayed release system include repeat action tablets and capsules. A delayed release dosage form does not produce or maintain uniform drug blood levels within the therapeutic range.

Site -specific and preceptor release systems are those where a drug is targeted for a particular biological action at a specific site, where as receptor release targets the particular receptor within a organ or tissue.

DRUG RELEASE

It is a process in which a drug product is subjected to following processes such as absorption, distribution, metabolism, and excretion, then the product gives the pharmacological actions.

Modified release

a) delayed release: indicates the drug release is not being immediately, release takes place at later time.
b) prolonged release: it indicates the drug get absorbed over a long time period compared to conventional dosage forms.
c) extended release: it indicates drug release is very slow and concentration of drug in plasma maintained for an extended time period.
d) controlled release: drug release follows a zero order kinetics. There is no variation in plasma concentration with time.
e) sustained release: drug release retardation takes place and slower the first order release in blood circulation.[1]

POLYMERS WIDELY USED IN MODIFIED RELEASE DRUG DELIVERY SYSTEMS

Ammonium methacrylate copolymers.
Cellulose derivative ethyl cellulose.
Cellulose acetate.
Polyvinyl derivatives and Polyvinyl acetate.

For many years, pharmacists have been employing polymers in every aspect of their work; polystyrene vials, rubber closures, rubber and plastic tubing for injection kits, and flexible polyvinylchloride bags for blood and intravenous solutions are examples of such polymers. Initial use was often limited to packaging instead of drug delivery. Subsequently, the fusion of polymer and pharmaceutical sciences led to the introduction of polymers in the design and development of drug delivery systems.

The delivery of medicines is highly innovative in terms of materials to help delivery, excipients and technology that allows the rapid or slow release of medicines. For example, pain relievers, which often involve upto five or six tablets a day, can be reduced to a single dose by using appropriate excipients, based on carbohydrate polymers. Polymers are classified in several ways; the simplest classification used for pharmaceutical purposes is into natural and synthetic polymers. Polysaccharides, natural polymers, manufactured in hydrophilic matrices remain popular biomaterials for controlled-release dosage forms and the use of a hydrophilic polymer matrix is one of the most popular approaches in formulating extended-release dosage forms. This is due to the fact that these formulations are relatively flexible and a well designed system generally provides reproducible release profiles.[2]

Since drug release is the process by which a drug leaves a drug product and is subjected to absorption, distribution, metabolism, and excretion (ADME), it is eventually available for pharmacologic action, therefore, drug release is described in several ways as follows.
a) Immediate release refers to the instant availability of drug for absorption or pharmacologic action in which drug products allow drugs to dissolve without intent to delay or prolong the dissolution or absorption of the drug.
b) Modified-release dosage forms include both delayed and prolonged release pharmaceuticals. Delayed release is defined as the release of a medication at a time that is not immediately after administration, while prolonged release products are formulated so that the medication is available over for a prolonged period after administration.
c) Controlled release includes extended-release and pulsatile release products. Pulsatile release involves the release of finite amounts (or pulses) of drug at different intervals that are programmed into the drug product.[3]

Cellulose and Cellulosics

Cellulose is the most abundant naturally occurring bio polymer. Cellulose is insoluble in water and most common solvents; the poor solubility is mainly recognized by the strong intra molecular and intermolecular hydrogen bond between the individual chain. Despite its poor solubility characteristics, cellulose is used in a wide range of applications. The chemical modification of cellulose is done to improve the capacity of the process and to produce cellulose derivatives (c that can be adapted for specific industrial applications. Cellulosics are generally strong, reproducible, recyclable and biocompatible, and are used in various biomedical applications, such as blood purification membranes.

Cellulose derivatives
a. Oxycellulose
b. microcrystalline cellulose
c. cellulose ethers

d. cellulose esters.[4]

HPMC [HYDROXY PROPYL METHYL CELLULOSE]

Hydroxypropyl methyl cellulose [HPMC] is used as the best hydrophilic vehicle in drug delivery systems, especially for orally controlled drug delivery systems. Hydroxy propyl methyl cellulose has high swellable character. It influences the release pattern of drug that is incorporated into the polymer. It has characterstics such as swelling in contact with water or any other biological fluids present in the body, diffusion of the drug occurs and the content of the drug is released. The type of the drug, its quantity, addition of polymer, nature and type of polymer, these factors help to design a new drug delivery system as well as drug release profile.[5]

For the design of new controlled delivery systems of released drugs based on HPMC and intended to provide a particular predetermined profile release, it is highly desirable:(i) to know the exact mechanisms involved in the mass transport of the drug release; and (ii) be able to quantitatively predict the release kinetics of the resulting drug. The practical benefit of appropriate mathematical model is the ability to stimulate the effect of the design parameters of drug delivery systems based on HPMC release profiles.[6] In the ideal case, the necessary composition and the geometry of the new controlled drug delivery system designed to achieve a certain drug release profile can be predicted. Therefore, the number of necessary experiments can be minimized and significantly facilitate the development of new pharmaceutical products. Diffusion, swelling and erosion are important mechanisms that control the speed of most commercially available controlled release products.[7]

HPMC; physicochemical characteristics

HPMC is a methylcellulose propylene glycol ether whose physicochemical properties of this polymer are strongly affected by: (i) the content of methoxy group;(ii) the content of the hydroxypropoxy group;and (iii) molecular weight. The USP distinguishes four different types of HPMC which is classified according to its methoxy and propoxy group. Those are HPMC 1828, HPMC 2208, HPMC 2906 and HPMC 2910. The content of the hydroxypropoxy group, varied relatively more than the content of the methoxy group. These variations lead to significant differences in the drug release.[8]

General drug release mechanism of HPMC –based systems

The general drug release mechanism of HPMC-based pharmaceutical devices depends greatly on the design of the particular delivery system. The phenomena are involved:(i) At the beginning of the process, steep water concentration gradients are formed on the polymer / water interface that resulting in the imbibitions of water in the matrix. To describe this procedure correctly, it is important to take into account (i) the exact geometry of the device;(ii) in the case of cylinders, both the radial direction of axial mass transport and; and (iii) the significant dependence on the water coefficient of diffusion in the swelling ratio of the matrix. (ii) Due to the imbibition of water, HPMCs swells and produces dramatic changes in polymer and drug concentrations, and increases the dimensions of the system. (iii) Upon contact with water, the drug dissolves and diffuses outside the device (iv)With the increase in water content the diffusion coefficient of the drug increases substantially. (v) In the case of high initial drug loads, the internal structure of the matrix changes significantly during drug release, becoming more porous and less destructive for diffusion when the drug is depleted. (vii) Depending on the chain length and the degree of substitution of the type of HPMC used, the polymer itself dissolves more or less rapidly.[9]

Swelling and release mechanisms from HPMC

Matrices containing swellable polymers are called hydrogel matrices, polymeric matrices that imply hydrocolloid matrices, inflatable controlled release moving boundary systems or hydrophilic matrix tablets. In pharmaceutical science moldable matrices for oral administration are commonly manufactured as tablets by the compression of hydrophilic microparticulate powders. Therefore, the most suitable classification are swellable matrix tablets.[10] Its composition comprises resistance at a high level of loading (60-80% w/w) together with a hydrophilic polymer at a moderate level (10-30% w/w). Hydroxypropyl methylcellulose (HPMC) of different grades and sugars are the most commonly used as polymers and fillers. In general, release of drug from the swellable matrix tablets is based on glassy-rubbery transition of polymer as a result of water penetration into the matrix, While the interactions between water, the polymer and the drug (or filler) are the primary factors for release control, various formulations variables, such as polymer grade, drug/polymer ratio, drug solubility, filler solubility, drug and polymer particle size and compaction pressure, can influence the release rate of drug to greater or lesser degree. However the central element of the drug release mechanism is the gel layer (gummy polymer) that forms around the matrix, capable of preventing disintegration of the matrix and faster water penetration.

Water penetration, polymer swelling, drug dissolution and diffusion and matrix erosion are the phenomena that determining the thickness of the gel layer. Finally, the drug release is controlled by drug diffusion through the gel layer and/or by erosion of the gel layer. To follow the dynamics of the gel layer during the release of drug in swellable matrices, the limits of such layer must be defined. It is well known that a gel layer is physically delimited by two sharp fronts that separate different states of matrix, i.e. the boundaries that separate the swollen matrix from the solvent and glassy from rubbery polymer. However, the possibility of the presence of a third front within the gel layer was described in matrices containing diclofenac, due to the precipitation of the drug

dissolved in the gel layer. This additional front was called the undissolved drug front or diffusion front and proved to be a function of the solubility and loading of the drug. Its presence can create conditions such that the release will be more controlled by dissolution of the drug than by the polymer swelling. Therefore, in swellable matrix tablet three fronts can be expected.

a) the swelling front, the limit between the still glassy polymer and its rubbery state,

b) the diffusion front, the boundary in the gel layer between the solid, as yet undissolved, drug and the dissolved drug and.

c) the erosion front, the boundary between the matrix and the measurement of front positions offers the possibility to determine three important parameters related to the behavior of the matrix, i. e. the water absorption rate, the dissolution rate of the drug and the erosion rate of matrix, associated with the movements of swelling front, diffusion front and erosion front respectively.

The analysis of swelling and erosion front movement of these matrices explained the release behavior: in the case of poly vinyl acetate matrices immediate synchronization of the movement of the swelling and the erosion fronts (constant gel layer thickness) was observed, while for the CMC matrices, synchronization was reached after more than 120 min. In the case of the HPMC matrices synchronization had not been achieved at the end of experiment. Evidently PVA had sufficient solubility to allow the movement of erosion front in synchronization with swelling front. In these matrices the movement of the swelling and the erosion fronts showed a rapid synchronization. Due to the synchronization, the release rate was the same, despite the different solubility of the drug. It should be stressed that as the solubility of the drug was increased, the matrices revealed a thicker gel layer and shorter time to achieve complete drug release. In conclusion, in synchronizable systems, the release behavior is determined by the properties of the polymer, which encompasses the solubility effect on drug release. A detailed analysis of the swelling behavior of the matrices could be based on the movement of the three fronts. Therefore, the position of the fronts and the amount of drug released were measured. The erosion front exhibited rapid initial outward movement that approached almost constant values. The diffusion and swelling fronts exhibited a sudden internal displacement then followed by a linear movement. These last two fronts were divergent, the movement of diffusion front was slower than swelling front. A comparison of the relative movement of the erosion and swelling fronts, or the erosion and diffusion fronts, indicated that they had not yet synchronized. The internal fronts showed an increase and increased rate of movement. The result of the relative movement of the external and internal fronts was a thinner gel layer, so explaining the faster release on these systems revealed that the increase in the porosity of the matrix increased the amount of drug released. This was to be expected, because tablets of constant weight with greater porosity were thicker and, since the dissolution experiments were carried out with the device that allowed water to enter only the thicker radially tablets had a larger releasing area. In fact, by normalizing the transport through HPC films. The films with high molecular weight were approximately three times more permeable than the film with lower molecular weight, although these films shows comparable weight reduction after leaching.[11]

HPC [HYDROXYPROPYL CELLULOSE]

Hydroxypropyl cellulose[HPC] is a cellulosic derivative which has characters such as non-polar, water solubility and highly pH sensitive. It acts as a thickening agent by altering the viscosity. It can be used for the binding of tablet dosage forms. It serves as a film coating agent. Also it has influence on modified drug release.

HPC charecteristics

Pore characterization developed was applied to ethylcellulose (EC) and hydroxypropyl cellulose(HPC) blended films, often used as pharmaceutical coatings, It was studied how two different HPC viscosity grades influence the pore structure and, hence, mass transport through the respective films. The film with higher HPC viscosity grade had been observed to be more permeable than the other in a previous study; however, experiments had failed to show a difference between their pore structures. By instead characterizing the pore structures using tools from image analysis, statistically significant differences in pore area fraction and pore shape were identified. More specifically, it was found that the more permeable film with higher HPC viscosity grade seemed to have more extended and complex pore shapes than the film with lower HPC viscosity grade. Porous polymer blended films are often used as pharmaceutical coatings since they can provide a wide range of structures with different properties favorable for controlled drug release. In order to understand and control mass transport properties like permeability, it is essential to characterize the pore structure within such films. The pore shape, in turn, can be related to pore tortuousity and connectivity, which have previously been identified as important factors affecting mass transport and overall releasability of a drug.

On comparing pore characteristics of blended films of two of the most common cellulosic polymers used in controlled release formulations, namely ethyl cellulose (EC) and hydroxypropyl cellulose (HPC). Such bio-based films are non-toxic, non-allergenic and have good film forming properties and stability. Whereas EC is water insoluble, HPC is generally soluble in water or in the gastrointestinal tract at room temperature (0-solvent at about 41 °C) and can be used as a pore former. The two polymers are dissolved in a common solvent, which evaporates during film spraying resulting in phase separation. In this way the film structure forms and the pores result from subsequent HPC leaching. Hence, the HPC-rich domains serve as a template for pores and determine their size and shape. There are several factors

influencing the formation of the pore structure of EC/HPC films such as film processing parameters, polymer blend composition and polymer viscosity grade.

Two different HPC viscosity grades were used to produce two types of films. A fixed polymer blend composition with 30%w/w HPC is used. The polymer blend ratio was chosen to ensure that a percolating pore systems forms, where the main release mechanism is diffusion through pores. For films with HPC concentrations below the percolation threshold, micro-structural characteristics may be of less importance for drug release due to the possibility of a convective release process occurring through cracks in the film. Experiments on leakage of HPC indicates no prominent differences between the films, whereas a great differences in permeability was measured, The leaching experiments showed an expected high release of almost all HPC from both films confirming that the percolation threshold had been exceeded and that the porosities were familiar. It is suggested that pore shape is responsible for differences in permeability of films. The pore characterization of two films with different HPC molecular weight was used to study how HPC viscosity grades may affect the pore structure and hence, the mass transport through HPC films.

Hydroxypropyl cellulose (HPC) is a familiar solid pharmaceutical adhesive. Frequently, a low molecular weight HPC is used in combination with other materials. It is included as a binder of immediate-release tablet as a concentration of 2% to 8%. These act as hydrophilic matrix formers at polymer levels of 20% to 30%. Adhesion of drug binder is a factor which has an influence in tablet strength. The binders exhibit substantial plastic deformation. By adding the strength of binder, tablet strength increases. Fine particle size grades of function as pressure binders, while regular HPC particle size grades function as solution binders because it has a more water dispersible character. HPC behavior is prior by plastic deformation and high axial recovery. HPC is a visco-elastic substance. Therefore the compactness and plasticity are factors that influence on HPC. Both characters increase with low molecular weight and particle size. Hydroxypropyl cellulose[HPC] is a cellulosic derivative which has characters such as non-polar, water solubility and highly pH sensitive. It acts as a thickening agent by altering the viscosity. It can be used for the binding of tablet dosage forms. It serves as a film coating agent. Also it has influence on modified drug release.[12]

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The formation of hollow granules also exhibited by HPC. A higher concentration of HPC produces a dense network of solid bridges. At low concentrations, the particles cannot be collected by HPC to prevent collapse. It takes place during the drying process. Therefore a minimum concentration of HPC is required. It helps in prevention of granule collapse. The minimum concentration of HPC is different in the case of different powders. There of the theophylline release rate was studied by using HPC. The drug content release decreased in case of high-viscosity grade polymer. Drug release is rapid from low viscosity grade polymers. Hence most of the tablets use the proper mixing ratio of HPC.

Hydrophilic polymers, in contact with the dissolution medium, can swell and form a continuous gel layer, erode or experience a combination of the two. The swelling action of these polymers is controlled by the speed of their hydration in the dissolution medium. The degree of the swelling of the polymer, the relative mobilities of the dissolution medium and the drug, and matrix erosion dictate the kinetics as well as mechanism of drug release from the polymeric matrices.

Hydroxypropyl methyl cellulose and Hydroxypropyl cellulose are the cellulosic derivatives that are involved in the manufacture of hydrophilic matrix tablets. Sustained release drug products release the drug over an extended time periods, and reducing dosing interval. These type of hydrophilic polymers used to control the release pattern of several drugs.

A general approach or the method used to overcome the poor water solubility involves reducing the size and there by improving the solubility by altering the surface area. The polymers such as HPC and HPMC have low molecular weight. It has high water retention capacity. These polymers tend to form aggregates with more wettable drug microparticles.

HPC and HPMC has different molecular weights and different proportion of methoxyl and hydroxypropoxy groups. From this knowledge, manipulation of the matrix – swelling erosion kinetics is possible and mechanism of rate of drug release can also be controlled. The solubility of the drug and the polymer brand have a relative contribution in the drug diffusion. The use of polymeric matrix devices to control the release of a variety of therapeutic agents the case of swellable, monolithic systems, the polymer release of a variety of therapeutic agents has increasingly important in the development and the formation of release dosage forms. A matrix is a drug delivery system in which the drug is dispersed. For a matrix tablet comprising release of the drug takes place in three different stages. First step is the dissolution medium penetrated into the matrix. The swelling or erosion of the matrix takes place in second stage. Then in the final stage the dissolved drug is transported to the medium. The outer layer of the matrix tablet influences on the hydration, swelling and transport of drug particles. It will facilitate the erosion of the matrix.[13]

On oral administration the hydrophilic matrices are hydrated. In the case of sustained- release tablets, a barrier to control the rate of drug release is, gelatinous layer development. Carbopol (CP) polymer is a high molecular weight polymer that has been employed in sustained release formulations. Direct compression is one of the method for the production of tablets. Time consumption for the production is less. Manufacturing is very easy compared to other methods, hence power consumption and cost is less.

In case of HPMC tablets, water content has an influence on the drug diffusion coefficients. HPMC degree substitution and chain length has an influence on drug release. Drug characteristics has influence on drug release. In case of poorly water soluble drugs, drug dissolution is a major factor considerable in drug release. The adjustment of the polymer concentration, excipient amount, excipient concentration and viscosity grade affect the release pattern. There is a presence of diffusion layer, it was illustrated in mathematical models.

Starch is used in the preparation of HPMC tablets sometimes. Starch is swellable in nature by water. Starch content in the HPMC matrix tablet has influence on release rate, there is a disintegration phenomenon which will based on the uptake of the water and followed by swelling of HPMC.

HPMC can be substituted by low-substituted HPC. It acts as a release modifier. It tailor the drug release rate. Hence the preparation of injection moulded matrix tablet can include the mixtures of ethyl cellulose and L-HPC. HPMC is widely used in pharmaceutical preparation because it acts as a hydrophilic gel matrix material and bio-adhesion material. These polymers give rapid formation of gel which control the initial drug release and the strong viscous gel formation further controls the drug release.

In recent years, hydrophilic cellulose polymer systems has high interest. On a theoretical basis, the drug release controlling is become difficult. Number of factors influencing on it. So the polymers either alone or in mixtures are used in combination for the tablet formulation.

A wide variety of polymers included in the matrix-based controlled release delivery systems. These delivery systems are one of the modified release systems. Methyl cellulose(MC), hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose(HPC), sodium carboxy methyl cellulose (Na CMC) are those derived from the cellulose ether. These polymers are predominantly used for hydrophilic matrices. They have several advantages such as easy to formulate, commercial, easy to operate. They have a better in vitro-in vivo correlation. In addition, HPMC is the material most frequently used in hydrophilic matrix tablets, primarily because of its hydrophilicity and swelling nature, its non-toxicity and its ability to adapt to high levels of drug loading. However, due to the growing need to find suitable polymers to achieve the desired drug release patterns, a wide range of synthetic and natural polymers is examined for their ability to delay the release of specific pharmacological substances. Since the discovery of a new polymeric substance and testing its safety is very expensive and an attractive alternative strategy is to investigate the use of polymeric mixtures of pharmaceutically approved polymeric materials. A powerful approach is to combine a non-ionic polymer with an ionic polymer to provide better water capture by the matrix. As a result the viscosity of the gel layer and the length of the diffusion path of the matrix tablet, which are the critical factors that affect the rate of release of the drug, in turn increase.

One of the most used methods to modulate the release of medications in tablets is to include it in a matrix system. The classification of the matrix system is based on the matrix structure, the release kinetics, controlled release properties and the chemical nature and properties of the materials used. It is generally classified into three main groups; hydrophilic, inert, and lipid.[14] In addition, drug release is a function of factors, including the chemical character of the membrane, the geometry and its thickness, and the surface area of the particles of the pharmacological device, the physicochemical characters of active constituent, and interaction between the

membrane and the permeable fluids are also important. In fact, the mechanism probably varies from one membrane to another, depending on the structure of the membrane and the nature of permeability solution. It is believed that several different mechanisms are involved in drug release through a non-disintegrable polymer layer.

a)permeation through pores filled with water; in this mechanistic model, drug release involves the transfer of dissolved molecules through pores filled with water. The coating is not homogenous. The pores can be treated by incorporating leachable components, such as sugars or incompatible water soluble polymers in the original coating materials or they can be produced by an appropriate production process.

b)permeation through the membrane material; in this mechanism, the release process involves the consecutive process of partition of the drug between the core and membrane formulation. The drug molecules dissolves in the membrane on the inner side of coating, which represents the balance between a saturated solution of drug and the membrane material. The transport of the drug through the layer is driven by the concentration gradient in the membrane, the drug tends to dissolve in an aqueous environment.

c) Osmotic pumping; the release mechanism is due to the difference in osmotic pressure. There is an osmotic pressure gradient developed between the drug solution and the environment outside the formulation.

In addition to the above, the particle size and the type of wetting of the polymer, the hydration of polymer and the dissolution of polymer, and the proportion of the drug's polymer, these are the factors that depends on the controlled release of drug from the matrix. The hydration rate largely depends on the constituent nature, such as molecular structure and degree of substitution. The changes in viscosity may be possible by increasing the average weight of polymer and the concentration of the polymer as well as by reducing the temperature of the solution. Factors related to polymers such as molecular weight, concentration of the polymer, degree of substitution, particle size etc have an influence in release of drug. In case of HPMC contained tablet formulations, release rate is influenced by the rate of formation of partially hydrated gel layer of tablet surface that is formed due to contact with aqueous gastric media. In addition to this process variables affecting on the extended release. Those process variables are the method of granulation, the amount of binder added during the process, the mixer used, the distribution of granule size etc.[15]

CONCLUSION

From various research studies it was concluded that.

The formulations which uses a single HPMC K100M as the polymer can withstand the release of the drug minimum 12hr while the other formulas (the combination of HPMC and HPC) the drug has been off entirely before 8hrs. This happens because the HPMC K100M forming a barrier gel with high viscosity, which is more resistant to the diffusion process, so that the drug release from the matrix tablets to be slow. Tablets which are formulated with HPC cannot resist the drug release. As HPC is easily soluble in water temperatures below 38 °C, in hot water, insoluble and precipitates form a precipitate which expands at a temperature between 40-45 °C. HPC probably could not resist the drug release in dissolution conditions used.

Formulations which were prepared by combination of HPC and carbomer showed controlled released upto 24hrs.

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