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Review Article

A review on gastroretentive floating tablets of Quinapril HCl

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Abstract

Quinapril HCl is a prodrug that belongs to the angiotensin-converting enzyme (ACE) inhibitor class of medications. It is metabolized to quinaprilat (quinapril diacid) following oral administration. Quinaprilat is a competitive inhibitor of ACE, the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII). ATII regulates blood pressure and is a key component of the Renin-Angiotensin-Aldosterone System (RAAS). Quinapril hcl has a short biological half-life of 2 hrs with a prolonged terminal phase of 25 hours. So the floating tablet formulations are needed for Quinapril hcl to prolong its duration of action, to increase its oral bioavailability and to improve patient compliance. Many methods are used for preparing floating tablet preparations of Quinapril hcl by using various grades of Hydroxypropyl methyl celluloses (HPMC K4M, K15M, K100M) at various concentrations 10%, 20% and 30%. This review article comprises of the research materialized in the field of formulation and evaluation of floating tablets of Quinapril HCl.

1. Introduction

Oral route is the most oldest and convenient route for the administration of therapeutic agents because of low cost of therapy and ease of administration leads to higher level of patient compliance. Approximately 50% of the drug products available in the market are administered orally and historically, oral drug administration has been the predominant route for drug delivery. Tablets are the most commonly and widely used dosage form. This type of drug delivery system is called conventional drug delivery system and is known to provide an immediate release of drug. Such immediate release (IR) products results in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. However, after absorption of drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetics profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached another dose is usually given if a floating longer therapeutic effect is desired. Conventional formulations are required to be administered in multiple doses and therefore have several disadvantages [1,2].

Gastro retentive floating system release dosage forms have been demonstrated to improve therapeutic efficiency by maintenance of a steady drug plasma concentration. Floating gastro retentive prolonged release, modified release, extended release or depot formulations are terms used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The goal in designing floating gastro retentive system delivery system is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug

delivery. So, Gastro retentive floating dosage form is a dosage form that release one or more drugs continuously in a predetermined pattern for a fixed period of time, either systemically or to a specified target organ. Gastro retentive floating system release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment. To formulate a successful stomach specific or gastro retentive drug delivery system, several techniques are currently used such as hydrodynamically balanced systems (HBS) / floating drug delivery system [3], low density system [4-6], raft systems incorporating alginate gels [7-9], bioadhesive or mucoadhesive systems [10], high density systems [11-13], super porous hydro gels [14] and magnetic systems [15-17].

Quinapril HCl (marketed under the brand name Accupril by Pfizer) is an angiotensin-converting enzyme inhibitor (ACE inhibitor) used in the treatment of hypertension and congestive heart failure. A prodrug, it is converted to its active metabolite, quinaprilat, in the liver. Quinapril HCl inhibits angiotensin converting enzyme, an enzyme which catalyses the formation of angiotensin II from its precursor, angiotensin I. Angiotensin II is a powerful vasoconstrictor and increases blood pressure through a variety of mechanisms. Due to reduced angiotensin production, plasma concentrations of aldosterone are also reduced, resulting in increased excretion of sodium in the urine and increased concentrations of potassium in the blood. Quinapril HCl is indicated for the treatment of high blood pressure (hypertension) and as adjunctive therapy in the management of heart failure. It may be used for the treatment of hypertension by itself or in combination with thiazide diuretics, and with diuretics and digoxin for heart failure. Quinapril HCl has short half life (2 hrs).

To reduce the frequency of administration and to improve patient compliance, gastro retentive floating system formulation is desirable. Quinapril HCl is a nonpeptide, non-sulfhydryl prodrug that is deesterified to quinaprilat (quinapril diacid), its major active metabolite following oral administration. Quinaprilat lowers blood pressure by antagonizing the effect of the Renin-Angiotensin-Aldosterone System (RAAS). The RAAS is a homeostatic mechanism for regulating hemodynamics, water and electrolyte balance.

During sympathetic stimulation or when renal blood pressure or blood flow is reduced, renin is released from the granular cells of the juxtaglomerular apparatus in the kidneys. In the blood stream, renin cleaves circulating angiotensinogen to ATI, which is subsequently cleaved to ATII by Angiotensin-Converting Enzyme (ACE). ATII increases blood pressure using a number of mechanisms. First, it stimulates the secretion of aldosterone from the adrenal cortex. Aldosterone travels to the Distal Convolute Tubule (DCT) and collecting tubule of nephrons where it increases sodium and water reabsorption by increasing the number of sodium channels and sodium-potassium ATPases on cell membranes. Second, ATII stimulates the secretion of vasopressin (also known as Ant Diuretic Hormone or ADH) from the posterior pituitary gland. ADH stimulates further water reabsorption from the kidneys via insertion of aquaporin-2 channels on the apical surface of cells of the DCT and collecting tubules. Third, ATII increases blood pressure through direct arterial vasoconstriction. Stimulation of the Type 1 ATII receptor on vascular smooth muscle cells leads to a cascade of events resulting in myocyte contraction and vasoconstriction. In addition to these major effects, ATII induces the thirst response via stimulation of hypothalamic neurons. ACE inhibitors inhibit the rapid conversion of ATI to ATII and antagonize RAAS-induced increases in blood pressure. ACE (also known as kininase II) is also involved in the enzymatic deactivation of bradykinin, a vasodilator. Inhibiting the deactivation of bradykinin increases bradykinin levels and may sustain the effects of quinaprilat by causing increased vasodilation and decreased blood pressure. Peak plasma concentrations of quinapril HCl occur within one hour following oral administration. The extent of absorption is at least 60%. The rate and extent of quinapril HCl absorption are diminished moderately (approximately 25-30%) when Quinapril HCl tablets are administered during a high-fat meal. [18]

The most commonly method of modulating the drug release is to include it in a matrix system. Because of their flexibility, hydrophilic polymer matrix systems are widely used in oral controlled drug delivery to obtain a desirable drug release profile, cost effectiveness and broad regulatory acceptance. Hence in the present work an attempt has been made to develop prolong release matrix tablets of Quinapril HCl using hydrophilic matrix materials like HPMC K100, K15M, and K4M .

Several gastro retentive floating formulation has been prepared for Quinapril HCl by different polymers and techniques. A few are described as mentioned below:

Vasanth *et al* 2013 designed the bilayer floating of tablets Quinapril Hydrochloride by direct compression method. The type and the concentration of the polymer are optimized to show the maximum retentive effect with good drug release profile. The tablets were prepared by polymers like HPMC k 100, carbopol, xanthangum, guar gum. Sodium bicarbonate acts as gas generating agent with a view to deliver the drug at sustained manner in GIT & consequently in to systemic circulation. Formulations were prepared and evaluated for physical parameters & were found within prescribed limits. The in-vitro drug release studies were performed using USP apparatus type II. The drug release was dependent on the type and concentration of the polymer. Drug release was faster from tablets prepared with carbopol, xanthan gum and HPMC alone. However, in combination tablets sustained drug release effectively. The rate and mechanism of release of tablets were analysed by fitting the dissolution data into kinetic models. The in-vitro drug release followed zero order Kinetics and drug release was found to be diffusion controlled & it follows Higuchi diffusion mechanism model. It can be concluded that the optimized batch F6 selected as best formulation, shown buoyancy lag time of 17 sec, total floating time of 12 hrs and drug release of 99.636% by adopting biphasic drug release pattern in a single dosage could improve patient compliance by increasing the gastric retention time and give better disease management. [19]

Himabindu *et al* designed bilayer tablets of Quinapril Hydrochloride. The tablets were formulated using direct compression technology by employing polymers like Sodium alginate, Cekol 30000 and Kollidon SR in sustained release layer and crospovidone was used as super disintegrant along with other excipients. The drug-excipient compatible studies were performed by FTIR. The study revealed that there is no drug- excipient interaction. The prepared bilayered tablets were evaluated for various physicochemical parameters including in-vitro drug release studies of all formulations. Out of all formulations the one prepared with combination of sodium alginate and Kollidon SR has the release of drug over 12 hrs. The in-vitro release data was fitted to different kinetic models which showed highest regression for zero order kinetics with higuchi mechanism. [20]

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Ghorpade *et al* designed the gastro-retentive floating drug delivery system containing antihypertensive drug. The floating drug delivery system can remain in the gastric region for several hours via float on the gastric contents and hence significantly prolong the gastric residence time of drugs. In the recent years, scientific and technological advancement have been made in the research and developed of novel drug delivery system. By overcoming physiological troubles such as short gastric residence time and unpredictable gastric emptying times, oral route is the most preferable route of administration but it has certain limitation for those drugs which absorb from upper part of GI tract or having narrow absorption window. The bioavailability of these drugs by increasing the residence of the dosage form in the stomach. The gastric residence time of the dosage form can be improved by formulating them as floating drug delivery system. The current and recent development of stomach specific antihypertensive drug formulated as floating drug delivery system is discussed in this review. [22]

2. Conclusion

To achieve the prolong effect in hypertension i.e. antihypertensive, the drug availability must be ensured in the body. The gastro retentive floating system prolongs release formulations attempted with different investigators mentioned above may be used commercially. Quinapril HCl gastro retentive floating tablets may be formulated with different polymers at various concentrations. With gastro retentive floating prolong release drug delivery system reduced frequency of dosing or increase effectiveness of the drug by localization at the site of action or enhanced bioavailability and uniform drug release may be achieved. Hence it also improves the patient convenience and compliance.

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