Research Article

Development And Evaluation of Press Coated Tablets of Fexofenadine Hydrochloride as Pulsatile Delivery System

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ABSTRACT

Pulsatile drug delivery systems are developed to deliver drug according to circadian behavior of diseases. The product is characterized by a time period of no release (lag time) followed by a rapid and complete drug release as a pulse after the lag time. Thus drug can be delivered at right time, in right amount and at right site of action by use of such approach. These systems are beneficial for drugs with chronopharmacological behavior, where nocturnal dosing is required. Common symptoms of allergic rhinitis ;sneezing, nasal rhinorrhea, red itchy eyes, nasal pruritus and nasal congestion were found to occur most frequently before breakfast and in the morning and least frequently in the middle of the day. An oral press-coated tablet of Fexofenadine HCl was developed by means of wet granulation and direct compression to achieve time-controlled tablet with a predetermined lag time. The preparation of press coated tablet involved preparation of fast dissolving core tablets by wet granulation method, where 60 mg of Fexofenadine HCl was formulated with different types and concentrations of superdisintegrants, and an outer coat which is formulated with different weight ratios of hydrophobic polymer; Ethyl cellulose (EC) and hydrophilic polymer; Hydroxy propyl methylcellulose (HPMC) using direct compression. The Formulation was evaluated on basis of acceptable physical properties and *in vitro* drug release. The results indicated that press-coated tablet composed of B3 (as core tablet formula) and C2 (as coat formula) gave complete and rapid release of Fexofenadine HCl after 6 hours lag time which is suitable to achieve time-controlled release of Fexofenadine hydrochloride, based on chronopharmaceutical approach for the treatment of morning allergic rhinitis through providing maximum concentration of the drug at time of its maximum need.

Keywords: Fexofenadine HCl, Chronodelivery, Allergic rhinitis, Superdisintegrant, Lag time, Ethyl cellulose, Hydroxypropylmethylcellulose.

INTRODUCTION

Conventional drug dosage forms have been widely used for treatment of various conditions. These drug dosage forms typically provide an immediate or rapid medication release, and supply a given concentration or quantity of the drug to the body's systemic circulatory system without any rate control.[1] Many problems are associated with conventional multiple dosing regimen of long acting therapy, such as systemic accumulation of the drug leading to side effects or toxicities, irregular profile of the plasma drug level, and poor patient compliance. To maintain the effective plasma drug concentration, frequent administration is required. Due to poor drug efficacy, the incidence of side effects, frequency of administration and patient compliance of these conventional drug preparations, many traditional drug dosage forms are undergoing replacement by second-generation, modified drug-release dosage forms. Treatments of numerous diseases using traditional drug products are often inconvenient and impractical if disease symptoms occur during the night or early morning .[2] The target of drug discovery is to obtain maximum drug efficacy and minimum side effect .[3] Second-generation modified release drug preparations achieved continuous and constant rate drug delivery, in which constant or sustained drug output minimize drug concentration "peak and valley" levels in the blood, promoting drug efficacy and reducing adverse effects.[4] Several second-generation modified release preparations present numerous problems such as resistance and drug tolerance, and activation of the physiological system due to long-term constant drug concentrations in the blood and tissues.[5] Controlled-release medications deliver continuous treatment, rather than providing relief of symptoms and protection from adverse events solely when necessary. The development of a third-generation (advanced drug delivery systems) to optimize and create new innovative drug delivery systems which provide a defined dose, in a chosen rate, at a selected time to a targeted site is now a growing challenge.[6] A chronodelivery system (DDS), based on biological rhythms, is a state of art technology for drug delivery chronomodulated] (DDS) not only increase safety and efficacy levels, but also improves overall drug performance. Diseases that follow rhythmic patterns have given rise to the creation of new drug delivery dosage forms, called chronopharmaceuticals chronotropic DDS technology for delivering drugs precisely in a time-controlled fashion in accordance with circadian rhythms may be developed as a chronopharmaceutical product to treat different human diseases.[1] The concept of chronotherapeutics originates from the finding of the major disease conditions such as asthma, cardiac disorders, allergic rhinitis, and arthritis following circadian

example of symptom outburst .[7] In chronopharmacotherapy, drug administration is synchronized with circadian rhythms. If the peak of symptoms occurs at daytime, a conventional dosage form can be administrated just before the symptoms are worsening. If symptoms of the disease became worse during the night or in the early morning, the timing of drug administration and nature of the drug delivery system needs careful consideration. The treatment of the disease to the fullest not only depends on the medicine but it also depends on the time, release of drug at the site needed require maintaining the utilization of drug at that site. Release of drug by biological rhythm in body at specific time is proposed development of pulsatile formulation because disease active at the specific time so action of drug must show at that particular time .[8]Pulsatile drug delivery is defined as the rapid and transient release of certain amount of molecules within a short time period immediately after predetermined off-released period, i.e., lag time.[9] Common symptoms of allergic rhinitis are sneezing, nasal rhinorrhea, red itchy eyes, nasal pruritus and nasal congestion. Each of the symptoms was found to occur most frequently before breakfast and in the morning and least frequently in the middle of the day. There are two phases of occurrence of allergic rhinitis i.e. early phase (developing within minutes) and late phase (manifesting after 12-16 h). The early phase happens due to release of histamine, prostaglandins, cytokines, TNF-α, chemotactic factors etc. resulting in sneezing, nasal itch, rhinorrhea. On the other hand late phase is shown due to elaboration, adhesion and infiltration of circulating leukocytes, T cells and eosinophil evoking nasal congestion, obstruction due to the exacerbation of inflammation of the nasal, sinus and other tissue of the upper airway .[10] Time controlled drug delivery systems are considered to be potential therapeutic options. These dosage forms are designed to mimic the circadian rhythm of the disease by releasing the drug at the appropriate time, by means of an internal pre-programmed clock that is initiated when the dosage forms come in contact with gastrointestinal fluids. Time controlled delivery systems have been formulated as pellets, capsules or tablets designed to release drug only after a defined lag time. Tablet formulations generally consist of a rapid release core tablet encased in a barrier layer either formed by press-coating or liquid coating or a combination of both .[11] Press-coating, also known as compression coating, is relatively simple and cheap, and may involve direct compression of both the core and the coat. Press-coated device in which the inner core contains the drug and the outer coat is made of different types of polymers. The outer barrier, which controls drug release, can be either swellable or erodible. Lag times can be varied by changing the barrier formulation or the coating thickness .[12] Delivery system with soluble or erodible membranes is a type of time controlled pulsatile release system in which the core containing drug is coated with erodible or soluble polymers and drug release is controlled by dissolution or erosion of outer coat .Time dependent release of drug can be obtained by optimizing the thickness of outer coat .[13] The press coated tablet investigated in the current study consists of a rapidly disintegrating core tablet press coated by a barrier layer consisting of varying concentrations of Hydroxypropylmethylcellulose (HPMC) and Ethyl cellulose (EC). HPMC is a disintegrant and had been used to cause rapid disintegration of tablets. The other component of the barrier layer, Ethyl cellulose (EC) is a well-known water-insoluble polymer that has long been used as a rate-controlling membrane in medication dosage forms to regulate drug release. EC has been added in tablet formulations to act as a retarding material and used as a directly compressible Excipient. When the barrier layer was exposed to dissolution media, the HPMC particles swell and erode, a process which was retarded to varying degrees depending upon the quantity of EC present, demonstrating that manipulation of both components controls the erosion rate.[14] Fexofenadine HCl is a second-generation non-sedating histamine H1 receptor antagonist widely used in seasonal allergic rhinitis. Fexofenadine HCl is a white to off-white crystalline powder. It is freely soluble in methanol and ethanol; slightly soluble in chloroform and water.[15] Fexofenadine HCl is a selectively peripheral H1 blocker of the GI tract, large blood vessels, and bronchial smooth muscle. Blockage prevents the activation of the H1 receptors, preventing the symptoms associated with allergies .[16] The main aim of the present study is to develop, design, and evaluate Fexofenadine hydrochloride as a pulsatile release tablet intended for chronotherapy of allergic conditions using press-coating technology to provide maximum drug plasma concentrations at time of its maximum need in early morning.

MATERIALS AND METHODS

Materials

Fexofenadine HCl**,** Avicel PH 102, Sodium starch glycolate**,** Croscarmellose sodium and Ethylcellulose 100 mPa•s were from Hangzhou Hyper Chemicals Ltd./China, PVP K30, Talc and Magnesium stearate were from Samara Drug Industry/Iraq, HPMC K4M was from Indian Fine Chemicals/India.

Methods

Preparation of fast dissolving core tablets

Fast dissolving tablets of Fexofenadine HCl were prepared by using different superdisintegrants; Sodium starch glycolate, and Croscarmellose sodium by wet granulation method. For preparation of tablets previously sieved (Sieve no. 50) ingredients were mixed according to formula specified in formulation as shown in table 1. Polyvinyl pyrrolidine (PVP) was dissolved in isopropyl alcohol (IPA) to prepare 5% alcoholic solution and added to above mixture to form lump like mass. This was passed through (Sieve no. 16) for preparation of granules. The granules were dried at 60 ^{0}C for 15-20 minutes and then passed through (Sieve no. 20) for regranulation.

Superdisintegrant was added as intragranular. Finally magnesium stearate and talc were added to above mixture and mixed well. Then 100mg of the granules were punched to form tablets .[17]

Formulation of coating mixed blend for press – coated tablet

Coat layer blend for coating the core tablet was prepared by using different ratios of the EC100 mPa·s and HPMC K4M as shown in table 2. These powders were weighted; dry blended at about 10 min. and used as press-coating material for coating the core tablet to prepare press-coated pulsatile tablets by direct compression method .[18]

Preparation of press-coated pulsatile release tablets

The core tablets were press-coated with coat blend where 40% of the coating material was weighed and placed in 11-mm die of the tablet machine, the core tablet was placed centrally in the die cavity, and the remaining quantity 60% of coating material was poured into the die cavity over the core tablet and finally compressed using single punch machine .[19]

Table 1: Composition of core powder blend

Ingredients (mg)	A1	A2	A3	B1	B2	B3
Fexofenadine HCl	60	60	60	60	60	60
Sodium Starch Glycolate	1	3	5	-	-	-
Crosscarmellose Sodium	-	-	-	1	3	5
Avicel PH 102	34	32	30	34	32	30
PVP K30 (alcoholic binder solution 5%)	2	2	2	2	2	2
Magnesium Stearate	1	1	1	1	1	1
Talc	2	2	2	2	2	2
Total weight	100	100	100	100	100	100

Table 2: Composition of coat powder blend

Coat mixture formula	Total weight (mg)	EC100 mPa·s (%)	HPMC K4M (%)
C1	200	80	20
C2	200	60	40
C3	200	50	50
C4	200	40	60
C5	200	20	80

Pre-compression parameters of core powder blend

Micromeritic properties of pre-compressional powder blend for core and coat powders blends were measured. These properties include:[20]

Angle of repose

Angle of repose was performed using funnel method by keeping a funnel vertically in a stand at a specified height above a paper placed on a horizontal surface. The funnel bottom was closed and powder was filled in the funnel. Then the funnel was opened to release the powder on the paper to form a smooth conical heap. The radius (r) and the height of the heap (h) were measured. The $\tan^{-1}$ of the height of the pile / radius of its base gave the angle of repose .[21]

Apparent bulk density and tapped density

The bulk density was determined by transferring the accurately weighed amount of blend (2gm) to the graduated cylinder (10 ml) with the aid of a funnel. The volume was noted. The ratio of weight of the sample to the volume occupied was calculated. To measure tapped density, the cylinder was tapped manually for a fixed number of taps (100) and the volume was noted. Average of three determinations was taken. The tapped density was determined as the ratio of weight of sample to tapped volume .[20]

Carr's index and Hausner ratio

Carr's Index, the compressibility of sample blend is the simplest way for measurement of free flow of powder. An indication of the ease with which a material can be induced to flow is given by compressibility index(I) which is calculated as follows :

Percentage Compressibility = (Tapped density – Bulk density)/ Tapped density × 100

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula:

Hausner's ratio = tapped density / bulk density .[22]

Physical evaluation of the prepared core tablets

Weight variation

Twenty randomly selected tablets were weighed individually and the average weight was calculated .[23]

Thickness and diameter

Thickness and diameters were measured by using digital Vernier caliper in mm. Ten tablets from each formula were used, and the average values were calculated .[20]

Hardness test

Hardness test was performed using Monsanto hardness tester in which five tablets from each formula were tested randomly and the average reading ± SD was recorded as kg/cm^2 .[24]

Friability test

Preweighed sample of twenty tablets were placed in the friabilator, which was then operated for 100 revolutions, then tablets were dusted and reweighed. Percentage friability was calculated from the following equation:[25]

$$\text{Percentage Friability} = \frac{(\text{Initial Weight} - \text{Final Weight})}{\text{Initial Weight}} \times 100$$

Content uniformity

Ten tablets from each formula were weighed and powdered. The powder equivalent to 60 mg of Fexofenadine hydrochloride was extracted into methanol and liquid was filtered (Whatman No. 1 filter paper). The drug content in the filtrate was determined by measuring the absorbance at 259 nm after appropriate dilution with methanol. The drug content was determined using the standard calibration curve. The mean percent drug content was calculated as an average of three determinations .[26]

In- vitro disintegration time for core tablet

The test for disintegration was carried out in disintegration test apparatus. It consists of 6 glass tubes which are 3 inches long, open at the top, and held against a 10 mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tablets, one tablet was placed in each tube with a disc and the basket rack was positioned in a 1 liter beaker containing 900 ml of phosphate buffer of pH 6.8 and temperature was 37±0.5°C such that the tablet remains 2.5 cm below the surface of the liquid. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.[27, 28]

In-vitro release (dissolution) studies of core tablets

Dissolution test was performed using a USP apparatus type-II (paddle type) at 37 ^{0}C ± 0.5 in 900 ml of phosphate buffer pH 6.8 at speed of 50 rpm. At 1 minute time intervals 5 ml of aliquot of sample was withdraw and replaced with fresh phosphate buffer pH 6.8. The samples were filtered through a 0.45 µm cellulose acetate filter and analyzed at λ max of 259 nm to determine the percentage drug release using a double beam UV spectrophotometer. One tablet was used for each determination and the experiment was performed in triplicates.[29]

Pre-compression parameters of coat powder blend

The coat powder blend was evaluated for angle of repose, apparent bulk density, tapped density, Carr's index and Hausner ratio as in case of core powder blend.

Physical evaluation of the prepared coated tablets

The prepared coated tablets were evaluated for weight variation, thickness and diameter, hardness and friability in the same way mentioned for core tablets.

In-vitro release studies of press-coated pulsatile tablets

The prepared press coated tablets were subjected to in vitro drug release sequentially in two different suitable dissolution media to assess their ability to provide the desired lag time before drug release. USP type II dissolution apparatus was used. The dissolution medium for the first 2 hrs was 900 ml of 0.1 N HCl (pH 1.2) and continued in phosphate buffer pH 6.8) for the next 10 hrs. The temperature of dissolution medium was maintained at 37 ± 0.5 °C and the paddle was rotated at 50 rpm. An aliquot of 5 ml was withdrawn at predetermined time intervals and replaced with an equal volume of the fresh dissolution medium to maintain sink conditions. The samples were filtered through a 0.45 µm cellulose acetate filter and analyzed at 259 nm for the percentage drug release using a double beam UV spectrophotometer. One tablet was used for each determination and the experiment was performed in triplicates.[29]

Comparison with marketed product

The selected press coated tablet was compared with Telfast®, the brand product of Fexofenadine HCl. This comparison was carried out by performing the in-vitro release study for the marketed product. As recommended in the FDA dissolution guidelines for about 45 minutes, and the aliquot of 5 ml was withdrawn at 5, 10, 20, 30, and 45 minutes.

Drug – excipients compatibility studies

The physicochemical compatibilities of the drug and excipients were tested by FTIR. The FTIR spectra of Fexofenadine hydrochloride, Avicel PH 102, physical mixture of drug and Avicel in 1:1 ratio, selected core and press coated tablets after grinding were recorded using FTIR spectrometer "Spectrum One" in a spectral region between 4000 and 400 and analyzed by transmittance technique. Sample was mixed in a mortar with potassium bromide KBr (1:100) and pressed in a hydraulic press (14 tons) to small tablet .[30]

RESULTS AND DISSCUSION

Pre-compression parameters of core powder blend

The values of micromeritic properties for the prepared core powder blend of each formula were shown in table 3. These results were estimated according to USP. The results show that the prepared core mixtures have acceptable flow properties and compressibility.

Physical evaluation of core tablets

The results of weight variation, thickness, diameter, hardness, friability content uniformity and disintegration time of all the prepared core tablets are shown in table 4. These results show that all the prepared core tablet formula agree with the requirements of USP.

Table 3: Micromeritic Properties of Pre-Compressional Core Powder Blend

Formula	Angle of repose (Degree) Mean ± SD, n=3	Bulk density (g/cm^3) Mean ± SD, n=3	Tapped density (g/cm^3) Mean ± SD, n=3	Carr's index Mean ± SD, n=3	Hausner ratio Mean ± SD, n=3	Type of flow
A1	26.46±1.057	0.34±0.006	0.37±0.004	7.59±2.517	1.08±0.029	Excellent
A2	25.45±1.074	0.35±0.009	0.38±0.007	11.59±0.095	1.11±0.006	Excellent
A3	24.45±1.044	0.34±0.003	0.38±0.004	10.39±0.041	1.11±0.005	Excellent
B1	25.63±0.359	0.36±0.003	0.38±0.004	6.63±1.024	1.07±0.011	Excellent
B2	24.16±1.250	0.34±0.003	0.38±0.004	10.65±0.473	1.12±0.011	Excellent
B3	26.13±0.633	0.33±0.002	0.36±0.004	8.97±0.911	1.09±0.011	Excellent

Table 4: Physical Evaluation of Core Tablets

Formula	Weight variation (mg) Mean ± SD, n=20	Thickness (mm) Mean ± SD, n=10	Diameter (mm) Mean ± SD, n=10	Hardness (kg) Mean ± SD, n=5	Friability	Content uniformity % Mean ± SD, n=3	Disintegration time in seconds Mean ± SD, n=6
A1	99.36±1.424	3.94±0.007	6.03±0.004	4.42±0.319	0.339%	99.71±1.077	97.50±4.487
A2	98.05±2.502	3.95±0.008	6.04±0.006	4.10±0.141	0.583%	99.51±1.173	55.83±4.622
A3	98.45±2.564	3.95±0.008	6.04±0.009	4.28±0.432	0.476%	99.97±0.628	41.50±5.009
B1	99.85±1.694	3.93±0.012	6.04±0.011	4.20±0.463	0.413%	99.99±0.570	45.50±4.969
B2	98.35±1.598	3.95±0.014	6.04±0.009	4.30±0.234	0.452%	99.67±0.327	31.83±7.467
B3	99.10±1.447	3.94±0.006	6.04±0.005	4.49±0.181	0.330%	99.95±1.441	20.00±2.898

In-vitro release studies of core tablets

The results of drug release from all core formula were shown in figure 1. As the concentration of superdisintegrant increases; the disintegration time decreases and the drug release increases because the superdisintegrant accelerates disintegration of tablets by virtue of its ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration occurs. This disintegration is reported to have an effect on dissolution characteristics as well .[31]

It was found that the formula containing Crosscarmellose sodium as a superdisintegrant have lower disintegration time and rapid release rate than that composed of sodium starch glycolate and as a superdisintegrant which may be due to that Crosscarmellose sodium is a cross linked polymer of carboxymethyl cellulose sodium and this cross linking makes it an insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities, so Crosscarmellose sodium provides superior drug dissolution and disintegration characteristics.[32]

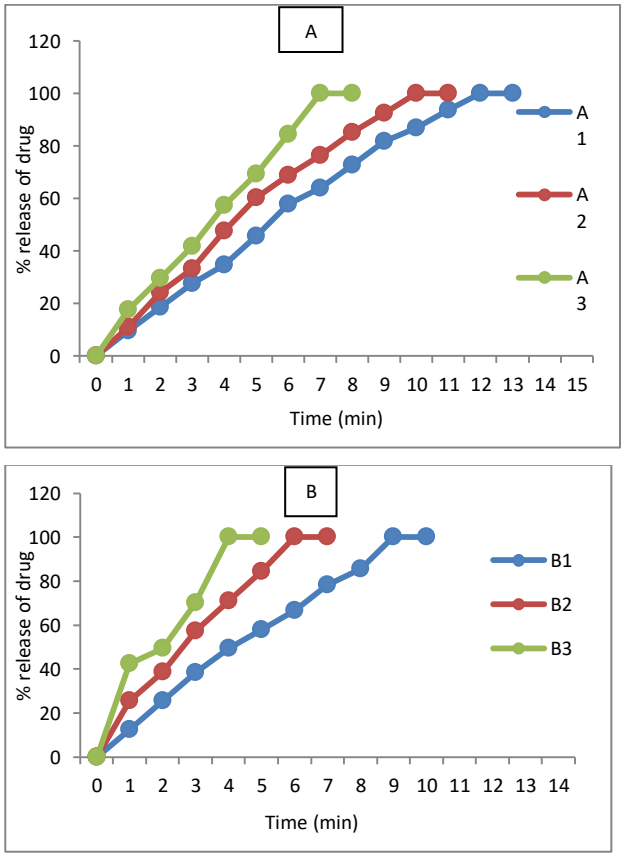

Figure 1-A: Effect of Sodium Starch Glycolate Concentration, **1-B:** Effect of Crosscarmellose Sodium

Concentration on Drug Release from Core Tablet (pH 6.8, Temp. 37°C).

The B3 formula was selected as the best core tablet formula to be coated with different coat blend to prepare pulsatile press coated tablets as it produced the fastest 100% release of fexofenadine hydrochloride within 4 minutes.

Pre-compression parameters of coat powder blend

The resulted values of micromeritic properties of pre-compressional coat powder blend of each formula are illustrated in table 5 and the results were estimated according to USP. The results showed that the prepared coat blends have acceptable flow properties and compressibility.

Table 5: Micromeritic Properties of Pre-Compressional Coat Powder Blend

Formula	Angle of repose (Degree) Mean±SD, n=3	Bulk density (g/cm^3) Mean±SD, n=3	Tapped density (g/cm^3) Mean±SD, n=3	Carr's index Mean±SD, n=3	Hausner ratio Mean±SD, n=3	Type of flow
C1	29.33±1.679	0.33±0.005	0.37±0.007	10.07±1.517	1.11±0.019	Excellent
C2	31.78±2.255	0.33±0.003	0.37±0.007	12.19±0.944	1.13±0.012	Good
C3	32.55±1.899	0.32±0.003	0.38±0.004	13.79±0.907	1.15±0.012	Good
C4	33.66±1.761	0.32±0.008	0.37±0.004	13.08±1.335	1.15±0.017	Good
C5	39.98±0.671	0.31±0.005	0.37±0.004	14.86±0.716	1.17±0.009	Good

Physical Evaluation for the press coated tablets

The results of weight variation, thickness, diameter, hardness, and friability of all the press coated tablets were shown in table 6. These results show that all the prepared core tablet formula agree with the requirements of USP. The hardness of the press coated tablets was slightly decreased as the HPMC concentration was increased because HPMC had lower compressibility than EC .[33]

Table 6: Physical Evaluation of Press Coated Tablets

Formula	Weight variation (mg) Mean ± SD, n=20	Thickness (mm) Mean ± SD, n=10	Diameter (mm) Mean ± SD, n=10	Hardness (kg) Mean ± SD, n=5	Friability
C1	297.45±1.394	5.366±0.034	11.154±0.004	6.693±0.758	0.445
C2	298.55±1.932	5.374±0.008	11.149±0.003	6.200±0.852	0.467
C3	297.997±0.850	5.380±0.012	11.145±0.004	6.104±1.047	0.573
C4	299.659±1.395	5.427±0.009	11.152±0.006	5.742±0.927	0.568
C5	297.742±0.589	5.436±0.008	11.148±0.004	5.063±0.687	0.623

In-vitro release studies of Fexofenadine hydrochloride from press coated tablets

The results of dissolution test for press coated tablet formula shown in figure 2. It was found that lag time decreases with increasing concentration of HPMC K4M. This is probably because of mechanism of producing a lag time of this formulation was based upon the hydration of outer barrier layer or water penetration through outer barrier layer. Ethyl cellulose is semipermeable in nature, although it is naturally insoluble in water. The hydrophobicity of ethyl cellulose retards the hydration of HPMC. Therefore dissolution medium did not penetrate the outer coating layer, but the coating eroded slowly. The active erosion rate of outer barrier layer depends upon the composition of the formulation which determines the lag time of press coated tablets. The HPMC is responsible for active erosion of barrier layer as a characteristic of such disintegrate is absorption of water followed by swelling thus as the weight ratio of HPMC was increased, lag time decreases .[34] Coat formula C2 was selected as the best one to be compressed around B3 core tablet formula to prepare the best pulsatile press coated tablet because it gave 100% release the drug after 6 hours lag time which is required to provide maximum concentration of drug at time of its maximum need.

Comparison with marketed product

The comparison of pulsatile release tablet with marketed product was shown in figure 3.The dissolution study of the market formulation of Fexofenadine HCl (120 mg) showed complete drug release within 30 minutes .[35]

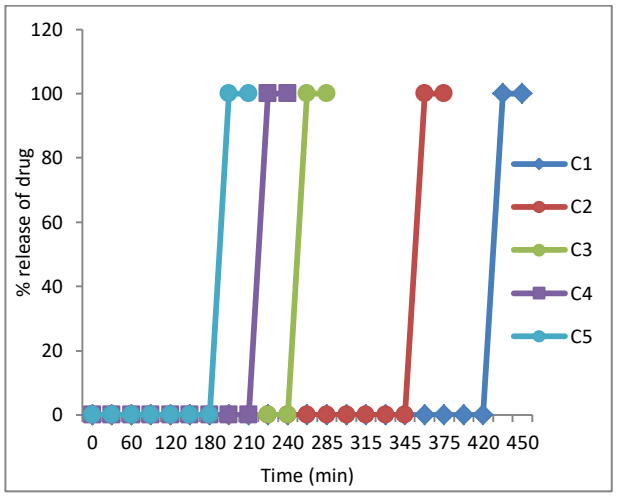

Figure 2: Effect of EC100 mPa•s : HPMC K4M polymers ratio on lag time of press coated tablet (0.1 N HCl for 2 hrs and pH 6.8 for 10 hrs, temp. 37°C)

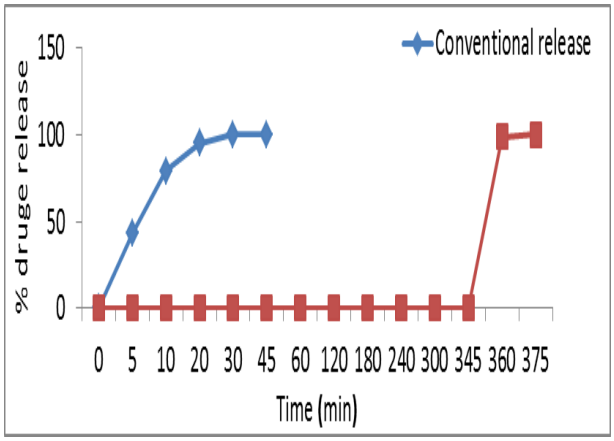

Figure 3: Comparison of the pulsatile release tablet with marketed product (0.1 N HCl for 2 hrs and pH 6.8 for 10 hrs, temp. 37°C)

Drug – excipients compatibility studies

The FTIR spectra for pure drug, Avicel PH 102, pure physical mixture of drug and Avicel PH 102 and for fexofenadine HCl in optimum core and the selected press coated tablets were shown in figure 4.

The FTIR spectrum for the pure fexofenadine HCl powder showed characteristic absorption bands at 3354, 2939, 1701, and 1273 cm^{-1} which are related to the following functional groups: OH stretch of alcohol and acid, CH stretch of CH2, C=O stretch of carboxylic acid, and CN stretch of tertiary amine respectively.

The FTIR spectrum of Avicel PH 102 shows a broad band at 3357 cm^{-1} due to OH stretch vibration and another band was also visible at 1375 cm^{-1} due to OH bending. Another peak was observed at 1117 cm^{-1} due to stretch vibration of CO for C-OH and at 1066 cm^{-1} due to CO stretch of C-O-C ether group.[36]

The FTIR spectra of physical mixture, and of optimum core and selected coated tablet show that the characteristic peaks of the drug still within the normal values and did not result in disappearance or addition of any peaks. That probably indicated absence of any chemical interaction between the drug and the excipients used.[37] The broadness of the characteristic peak of Fexofenadine HCl (3354cm^{-1}) might be due to formation of hydrogen bonding between the carboxylic group and/or the hydroxyl group of the drug with the hydroxyl group of Avicel and HPMC.[38]

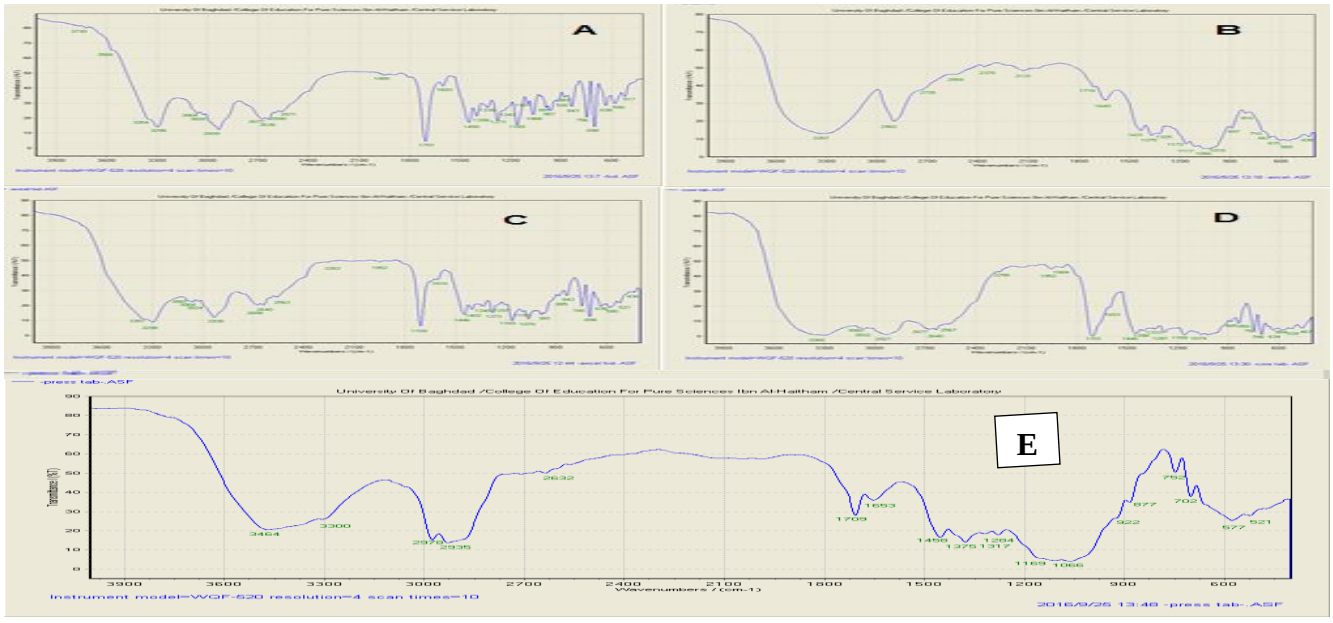

Figure 4: FTIR spectra: A- Fexofenadine HCl, B- Avicel PH 102, C- Physical mixture of Fexofenadine HCl with Avicel PH 102, D- Fexofenadine HCl optimum core tablet, E- Fexofenadine HCl selected press coated tablet

CONCLUSION

A satisfactory attempt was made to develop pulsatile system of Fexofenadine hydrochloride and evaluated it that might be useful as night time antihistamine to overcome the early morning exacerbation of allergic rhinitis symptoms. Hence, it can be concluded that multilayered pulsatile unit of Fexofenadine hydrochloride may be providing a better pharmacological effect, thus can be effectively used in management of allergic conditions.

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