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Hot Melt Extrusion: Continuous Process of Preparation of Sustained Released Matrix Tablet by Using Hydroxypropylcellulose

Divakar R. Jaiswar[1]*, Jaywant N. Pawar[1], Purnima D. Amin[1]

1.Department of Pharmaceutical Sciences and Technology,
Institute of Chemical Technology, N. P. Marg, Matunga (E), Mumbai 400019, India

ABSTRACT

The objective of the study was preparation of sustained release matrix tablets by hot melt extrusion (HME) and process optimization for continuous manufacturing. Furthermore, HME tablets were evaluated with respect to in vitro release rate, erosion behavior and water uptake study. Hydroxypropylcellulose (HPC) was used as release retarding polymer. The drug chosen for study was first line anti tuberculosis drug rifampicin. 50 % drug loaded HME tablets were prepared. The HME tablets were characterized by DSC, FTIR and SEM. No chemical interaction was found between drug and polymer as per DSC and FTIR. Dispersion of drug particles and internal micro pores was observed by SEM. In vitro release study revealed 50% drug loaded HPC matrix tablets gave sustained release of $101.41\pm1.02\%$ at the end of 24 h. Release rate of rifampicin from HME tablets was found to be dependent on the concentration of polymers and plasticizer. The release rate from the edges and circumference of tablets suggested the hydration of the tablets from the circumference was more significant than at edges of the tablets. Drug release from HME matrix tablets was found to follow Super case-II transport mechanism. HME tablets were stable for six months as per ICH guideline.

Keywords: Hot Melt Extrusion (HME), Hydroxypropylcellulose (HPC), Rifampicin, Sustained release, Korsmeyer–Peppas model

INTRODUCTION

Tablets is one of the most suitable and conventional dosage form with respect to patient compliance.[1,2] Tablets providing sustained release effect improve theraputic activity by minimizing the fluctuation of drug plasma concentration, reduce side effect, increase safety and reduction in dosing frequecncy makes it patient compliance. It become patient non- compliance when multiple daily admistartion of immediate release dosge form given for long therapy.[3] Various methods have been developed to formulate sustained released dosage form namely wet granulation method, dry granulation method and direct compaction method.[2] Recently few new approches were reported for sustained release formulation like osmotic release formulation, pulsatile drug delivery system, pH sensitive, colonic and programmable release and compress coated tablets. A compression-coated tablet is a system in which the entire surface of an inner core is coated by hydrophillic polymers, the drug release from the tablets follow diffusion and erosion mechanism.[4, 5] Conventional methods involved number of unit operations like mixing, granulation, drying, mixing with tabletting excipients and compaction. These processes are batch processes and associated with many tabletting problems which is overcome by novel technology, hot melt exxtrusion technology.[6]

HME is scalable, dust free, solvent free and continuous process convert raw materials into uniform shape and density by extruding through a die under specified temperature and pressure[7]. HME enables to formulate various dosage form namely granules, powder, tablets, implant, stent, ophthalmic insert. HME is also used to prepare sustained release and transdermal drug delivery system.[6, 8, 9] T_g of polymers and melting point of active pharmaceutical ingredients (API) plays an importanat role in HME process. When glass transition temperature (T_g) of polymer is very close to melting temperature of API, then possibilty of solid solution formation is more. Solid dispersion is obtained if T_g of polymer seems to be very far from melting temperature of API. Processing temperatrure depends on T_g and degradation temperature of polymres and melting temperature of API.[10, 11] Improving the bioavailability of poorly water soluble drugs via molecular dispersions is other major advantage over conventional techniques of continuous manufacturing technology like HME.[12] Sustained release dosage form prepared by HME showed slower release than those prepared by conventional method because of low porosity and high tortuosity.[13] Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery system because of their flexibility to obtain a sustained drug release profile, cost effectiveness, and broad regulatory acceptance of the polymers.[14,15] Hydroxypropyl methylcellulose HPMC) is widely used hydrophilic matrix system for sustained release formulation by conventional method.[16] Eudragit®

RLPO, Eudragit® RSPO[17], Kollidone SR[18, 19] are polymres suitable for sustained release by HME. Hydroxy propyl cellulose (HPC) has been used as pharmaceutical excipent for various purposes, like binder, film coating materials, controlled release materials, matrix and bioadhesive materials.[4] There are very few reported studies on sustained release potential of HPC, prepared by hot melt extrusion technique.

Rifampicin is poorly soluble and high permeable active pharmaceutical ingredients (API). Rifampicin is first line broad spectrum Anti-TB and Antileprotic drug. It has molecular formula $C_{43}H_{58}N_4O_{12}$ and molecular weight 822.95. It is solid and crystalline in nature having melting point of 183°C -188°C. It shows two pK; pKa_1 1.7 for the 4-hydroxy and pKa_2 7.9 for the 3-piperazine nitrogen (Amphoteric).[20, 21]

The objective of the study was to prepare sustained release matrix tablets using HPC as the functional polymer by hot melt extrusion technology as contineous process. The in vitro performance of the different formulations was assessed. Factors affecting release of API were assesed and the formula was optimized. Water upatake and erosion study was conducted to understand the mechanism of release behaviour. The solid state of rifampicin in the formulations was characterized using differential scanning calorimetry (DSC), Fourier transform infrared (FTIR) and Scanning electron microscope (SEM).

MATERIALS AND METHOD

Materials

Rifampicin was supplied by Lupin Pharmaceuticals, as gift sample. Hydroxypropylcellulose (HPC H); 3800 mPas, HPC LM, HPC M; 350 mPa s, were gift samples from (Nippon Soda co. Ltd, Japan), Propylene glycol was purchased from (S.D. Fine-Chem Limited) and all other chemicals used were of analytical grade.

Preparation of HME tablets

The formulations used in this study are shown in Table 1. 50 g of powder sample containing 50% rifampicin and functional polymers were blended in a mixing poly bag for 2 mins and then plasticizers was blended in a mortar and pestle for 5 min. The premixed blended powder was fed into hopper of a Single-Screw Lab Hot Melt Extruder (SB Panchal & company, Mumbai) equipped with a stainless steel Single Screw with diameter of 24.5mm and length of 5.8 inch. The barrels have feeder, conveyer, mixing sections, and carrier zone with internal diameter 25.5mm and length of 6 inch attached with a round shaped die (4 mm in diameter). The extrusion process was carried out at 50 rpm and temperature was kept at 85±1°C. The extrudate was manually cut by cutter into

cylindrical tablets, equivalent to 150 mg of rifampicin (Theoretically calculated) i.e. 300±5 mg. The tablets were stored at room temperature for at least 48 h and then further evaluation was done.

Table 1: HME tablets compositions used in the present study

| | Composition (%) | | | | | |
	Formulation 1	Formulation 2	Formulation 3	Formulation 4	Formulation 5	Formulation 6
Rifampicin	50	60	50	50	50	50
HPC-H	45	35	--	--	--	--
HPC-M	--	--	45	--	31.5	22.5
HPC-LM	--	--	--	45	13.5	22.5
Propylene Glycol	5	5	5	5	5	5
Total	100	100	100	100	100	100

In-vitro release study

In vitro release testing of tablets containing 150 mg rifampicin was carried out in the USP apparatus 2 (Electrolab, Mumbai, India). The dissolution medium was 900 ml of 0.1N HCl for initial 2 hours and then medium was changed to phosphate buffer pH 6.8 till 24 hours.[22] Both the dissolution mediums contained 0.02% ascorbic acid to prevent oxidation of rifampicin.[23] During dissolution testing, the media were maintained at 37±0.5°C and agitated at 50 rpm. A sample volume of 5 ml was withdrawn at each sampling time point (1h, 2h, 4h, 8h, 12h, 16h, and 24h). All dissolution tests were performed for 24 h. Samples were analyzed using a UV spectrometer (Shimadzu 1600, Japan) at 475 nm. All dissolution tests were performed in triplicate.

Release from circumference and edges of tablets

In vitro release behavior from the circumference and both ends of the HME tablet were studied to understand the effect of site on dissolution rate of HME tablets. The tablets were glued with PVC coated aluminum foil at both the ends in order to block release from these ends of the tablet and allowed the release from circumference of HME tablets and release from circumference was blocked by gluing PVC coated aluminum foil to circumference of tablets which allow release from both ends as showed in Figure 4. The study was done in triplicate for each type.

Effects of concentration of plasticizer

HME SR matrix tablets were prepared with propylene glycol containing 3% 5% and 7%. The concentration of plasticizer and its effect on release profile were also investigated. Effects of concentration of plasticizer on dissolution profile were showed in figure 5.

Water uptake and erosion studies

The uptake and erosion studies of formulations were performed according to Efentakis et al.[24] gravimetrically. The samples were placed in dissolution basket, containing 500 ml of pH 7.4

phosphate buffer solutions at a temperature of 37±0.5˚C and stirring conditions maintained as specified in the dissolution studies section above. At predetermined time points, swollen samples were withdrawn from the dissolution vessel, gently water was removed from the tablets with the help of tissue paper, weighed and dried at 50˚C until constant weight was reached. Fresh tablets were used for each individual time point and the study was performed in triplicate.

The erosion (E) was determined from the equation given below:

$$E\ (\%) = \frac{(W_s - W_f) \times 100}{W_s} \qquad \text{Equation 1}$$

Where as Ws and W_f are the original weight and final dry weight of the same dried and partially eroded tablet, respectively. The increase in weight (uptake) due to absorbed liquid (A) was calculated at each time point from:

$$A\ (\%) = \frac{(W_W - W_f) \times 100}{W_f} \qquad \text{Equation 2}$$

where W_w is the mass of the wet samples before drying.

Model fitting for the mechanism

The mechanism of the drug release was evaluated using Korsmeyer–Peppas model. The release data were fitted to the following exponential equation given by Ritger and Peppas.

$$\frac{M_t}{M_\infty} = kt^n \qquad \text{Equation 3}$$

Where M_t is the amount of drug released at time t, M_∞ is the amount of drug released at infinity, k is a dissolution rate constant and n is the release exponent indicator of the release mechanism of drug through the polymer. The values of n were obtained by regression analysis.

The release exponent n=0.45 is defined by fickian diffusion, whereas anomalous (non fickian) transport is indicated when $0.45 < n < 0.89$ and n=0.89 is characteristic value of Case-II transport.[25]

Differential scanning calorimetry (DSC)

Impact of hot melt extrusion on thermal property, miscibility of API with polymer and nature of API were investigated by DSC. This analysis was conducted by Perkin Elmer Pyris 6 DSC equipped with nitrogen cooling accessory. Sample was prepared by weighing 6±2 mg of polymer, drug polymer blend, extrudates powder in aluminum pan (Pyris 6 DSC, Perkin Elmer, USA) and crimped with an aluminum lid and placed into furnace of DSC. Samples were exposed to heating rates of 10°C/min over a temperature range of 35°C-300°C under continuous nitrogen purging (20 ml/min). The melting point (T_m) and the glass transition temperature (T_g) were determined by the Pyris Software.

Fourier transform infrared (FT-IR)

Fourier transform infrared (FT-IR) spectral studies were conducted on an IRAffinity-1 Shimazdu Spectrophotometer (Shimadzu, Japan) to investigate possible interactions between the polymers and drug before and after hot melt extrusion. All samples were crushed with potassium bromide. The weighed ratio of a sample and potassium bromide was 1:9. Crushed powders were compressed using a hydraulic compactor at approximately 20,000 pounds under vacuum for 1 min to make pellets. Spectral scanning was conducted from 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1}.

Scanning electron microscope (SEM)

The morphology of plain rifampicin, surface of HME tablets, cross section of HME tablets and HME tablet image after dissolution were taken by using scanning electron microscope (Philips XL-30 SEM, Netherlands) operating at an accelerating voltage of 15 kV. Samples were mounted on aluminum stubs using double-sided adhesive carbon tape and coated with 2 nm gold-palladium beam for 20 min using a gold-palladium sputter coater Polaron Model SC7640.

Stability

The HME tablets prepared from formulation 6 containing both HPC -M and HPC -LM were stored at accelerated condition in induction sealed PVC coated aluminum packet for six months at 30˚C/65% RH and 40˚C/75% RH as per ICH guideline. Release profile and assay of stability samples were investigated.

RESULTS AND DISCUSSION

Effects of temperature

The glass temperature of polymers and melting point of drug was evaluated by differential scanning calorimeter (DSC) which was important parameter with respect to HME processing temperature. The DSC thermograms of polymers, drug, physical mixture and hot-melt extrudate of formulation 6 are shown in Figure 1. The glass transition of HPC M and HPC LM was found to be 70˚C and 63˚C respectively. Generally amorphous polymers show glass transition temperature. It is the temperature where a polymer exhibits rubbery and flexible nature and because of this behavior of polymers at this temperature, dispersion of drug into the polymer matrix becomes easy and uniform. The endothermic peak of pure rifampicin was observed at 193.5˚C which indicate melting point and crystalline nature of rifampicin. Exothermic peak was observed at 256.43˚C indicates oxidation of rifampicin. An endothermic peak was observed at approximately 52.80˚C for physical mixture, this peak was characteristic peak of both the polymers of HPC LM and HPC M, which indicate the T_g of polymer. There was no change in melting temperature of rifampicin.

The processing temperature was set 15°C above the T_g of polymers. DSC of thermogram of formulation 6 exhibit two melting endotherms one at 71.51°C indicates T_g of polymers blend and second melting endotherm at 190.19°C suggest melting point of rifampicin and exotherm at 253.73°C indicate oxidation of rifampicin. It concluded that there was no chemical interaction between polymers and drug.
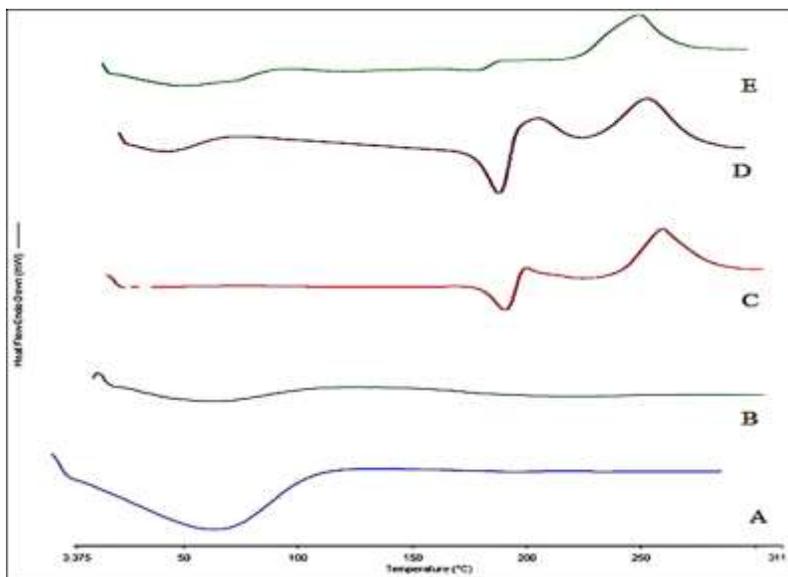

Figure 1. **DSC of (A) HPC M, (B) HPC LM, (C) Rifampicin, (D) Physical mixture, (E) Formulation 6**

Scanning electron microscope (SEM)

The surface morphology of pure drug and HME matrix tablets before and after dissolution were studied by SEM, the image is shown in Figure 2. Long rod like crystal habit was observed in case of pure rifampicin. The surface of HME tablets was smooth with the striated appearance on the tablets (Figure 2B). Shearing of the molten mass on the die wall upon exit from the extruder generally resulted in striated appearance which is termed as "rifling"[26]**.** The thin cross section of HME matrix tablet was analyzed for its internal morphology. A clear uniform distribution of rifampicin crystal into polymer matrix with some micro pores was seen (Figure 2C). The micro pores would have been developed due to evaporation of moisture present in polymers during melt extrusion. The pore size was characterized in image which was in the range of 24.5 μ -32.9μ. There are some crevices near embedded rifampicin particles in matrix tablets. The particle size of rifampicin was reduced during HME process due to torque generated between screw and barrel. The uneven and rough surface was seen on HEM sustained release matrix tablet after 4h dissolution. It may be developed due to evaporation of water from gel layer after drying. Release

of drug from surface and erosion of gel layer made internal pores exposed to dissolution medium (Figure 2D), which also play important role in release of rifampicin.
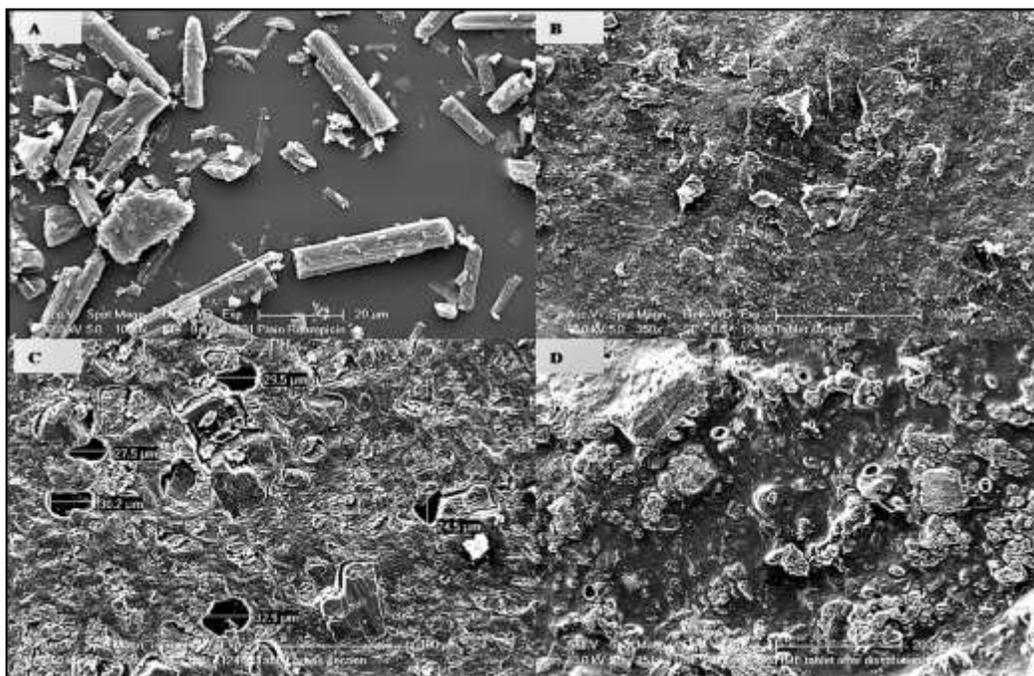

Figure 2. SEM (A) Pure Rifampicin, (B) Surface of HME tablet formulation 6 (C) Cross sectional surfaces of HME tablet formulation 6, (D) Surface of HME tablet formulation 6 after 4 h dissolution

In-vitro release study

Release profile of Formulation 1 was slow and incomplete till 24 h (see Figure 3) the 50% rifampicin loaded formulation 1 contained HPC-H with viscosity of 1,000 ~ 4,000 mPas at 20˚C/2%aq, and molecular weight about 910,000. Higher the viscosity and molecular weight lower the release from the matrix tablets, the hydrogel made by polymer on the surface of HME tablets was thick HPC –H, and hence penetration of dissolution medium to matrix through gel layer and drug diffusion from matrix was slow[27.] Loading of rifampicin was increased to 60% in formulation 2 in order to minimize the release retarding potential of HPC H and increasing the contact of rifampicin with dissolution medium from HME matrix tablet, but even increasing the loading of rifampicin and decreasing HPC-H concentration, the tablets were unable to sustain drug release till 24h. Initially release was similar to formulation 1 because rifampicin released from surface of HME tablets in SGF but rifampicin is a poorly soluble drug, there was decrease in release rate after 12 h. Solubility plays important role in dissolution rate, Drugs are released by diffusion through or erosion of the gel matrix tablets, it depend upon on the solubility of drug. Rifampicin showed pH depended solubility, highly soluble at acidic pH and poor solubility at alkaline pH[(28).] As the

viscosity of HPC decreases to 150 - 400 mPas in HPC-M, Gel layer around the HME matrix tablets was weak in comparison of gel layer of HPC-H, but still incomplete release for 24 h and 100 % release of rifampicin was observed in 12 hr in case of formulation 4 where viscosity of HPC LM was lower than HPC-M. Hence rate of release of rifampicin was found to be in this order HPC LM >HPC-M > HPC H. Lower viscosity grade HPC gelled rapidly and form weak gel layer, and showed rapid release. With the understanding of release behavior of rifampicin from above HME matrix tablets made with individual HPC polymer and in order to have sustained release of rifampicin, the combination of HPC M and HPC LM was used. Formulation 5 showed sustained release for 24 h but unable to release 100 % drug. Hence HPC LM concentration was increased to 50% of total polymer concentration in formulation 6, which showed sustained and complete release till 24 h. Thus many mechanisms seemed to be involved in release of rifampicin from the HME matrix tablets which includes hydration of polymer matrix, swelling of polymers, diffusion of drug through gel layer, erosion of gel layer.
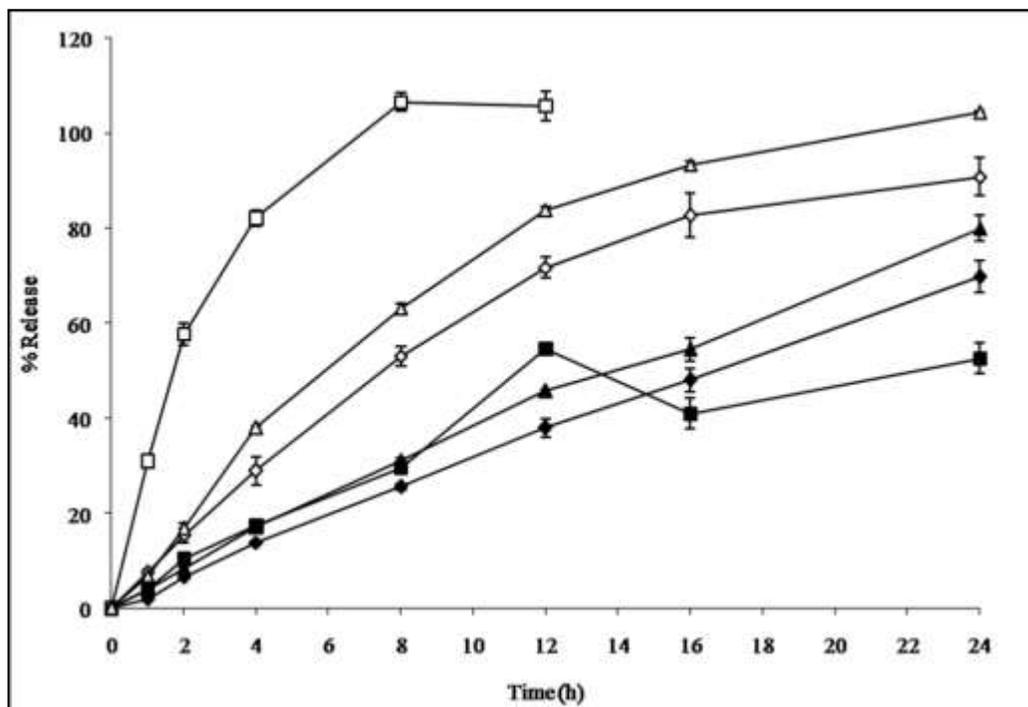

Figure 3. Dissolution release of (♦) Formulation 1, (■) Formulation 2, (▲) Formulation 3, (□) Formulation 4, (◊) Formulation 5 and (Δ) Formulation 6

Release from circumference and edges of tablets

Release of rifampicin form the circumference and edges of the HME matrix tablets was investigated to understand which side played a major role in penetration of dissolution medium and release of drug with respect to sides of HME matrix tablets as shown in Figure 4. Penetration

of dissolution medium was much higher through circumference than penetration through edges due to more surfaces (Figure 4). Hence increase in release was seen from the circumference where as slow release of rifampicin from the edges was observed, at the end of 24 h. Release rate was found to be more in case of unblocked complete HME matrix tablets than cumulative release from circumference and edges. It suggest penetration of dissolution medium from all directions in unblock tablets resulted in increased hydration & swelling, hence increase in dissolution rate.
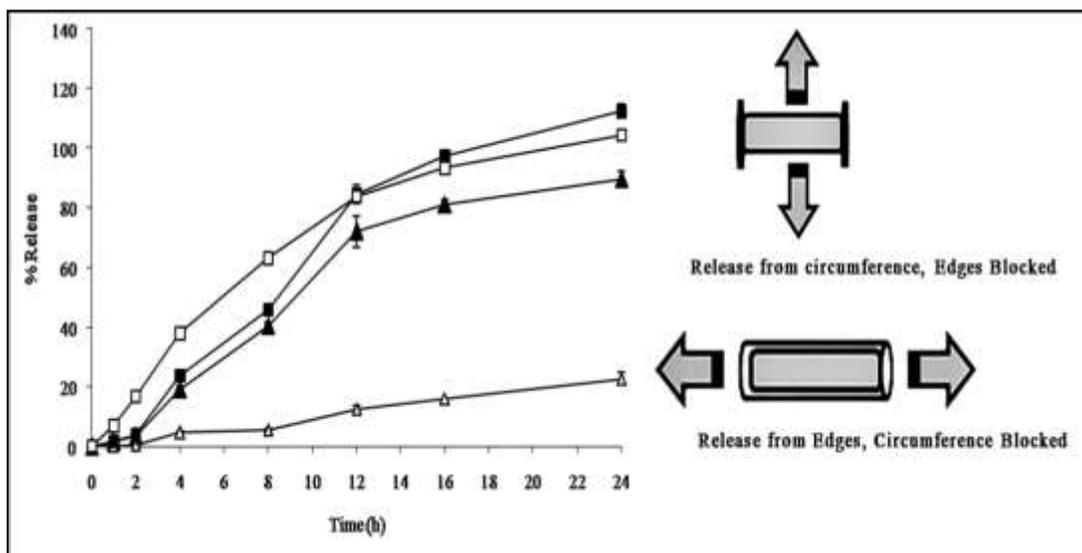
Figure 4. Release profile of HME tablets includes release from (▲) circumference, blocked from edges (Δ) both edges blocked from circumference, (■) cumulative release from circumference and edges and (□) unblocked complete tablets

Effects of concentration of plasticizer

The concentration of plasticizer and its effect on release profile were also investigated. The release rate of active depended on concentration of plasticizer in HME matrix tablets. Propylene glycol (PG) was used as plasticizer for extrusion of HPC. The release rate was slow, when the concentration of PG was 3%. As the concentration of PG increased the release rate also increased (Figure 5). Plasticizers allow mobility of rifampicin into the matrix and flexibility of HME matrix tablets. As the concentration of plasticizers increased the bonding between particles in matrix became loose and interparticulate volumes increased. This allowed increase in the rate of penetration of dissolution medium into HME matrix tablets which enhance release rate.
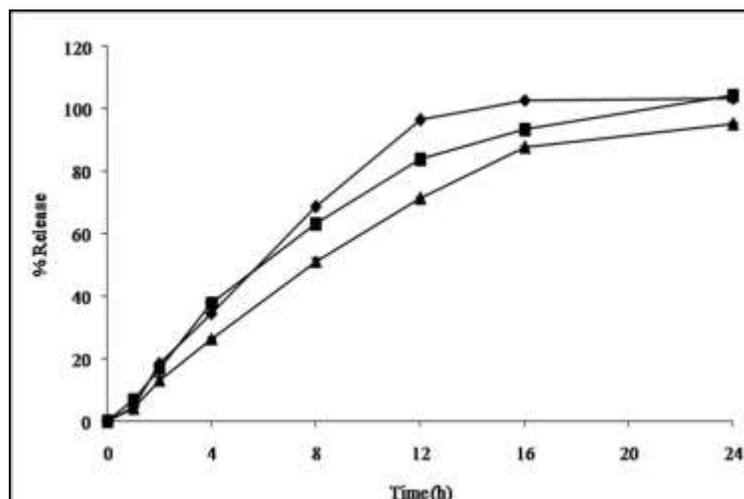
Figure 5. Drug release profile on varying concentrations of plasticizer: (▲) Propylene glycol 3%, (■) Propylene Glycol 5 %, (♦) Propylene Glycol 7%

Water uptake and erosion studies

Figure 6 and Figure 7 showed the results of erosion and uptake studies for the HME matrix tablets. Matrix hydration and erosion was evaluated by gravimetrical analysis. This is vital approach to know release mechanism and the related parameter which affect directly on dissolution profile.[29] The penetration rate of dissolution medium in placebo HME tablets was faster than drug loaded HME matrix tablets. Increased water uptake and retention time was observed in case of placebo HME tablets due to absence of drug. When erosion of placebo tablets was compared with drug loaded HME matrix tablets. The erosion of placebo HME tablet was 61% at the end of 12h and it was slow due to absence of release of drug from the matrices and strong gel barriers. The water uptake of drug loaded HME matrix tablets was slow due to presence of insoluble drug in matrix and 50% less polymer as compared with placebo tablets. 95% of tablet erosion was observed in drug loaded HME matrix tablets at the end of 12h. The erosion of drug loaded HME matrix tablets was faster due to release of drug from the tablets by diffusion as well as erosion of gel barriers. The penetration of water took place into matrix, solubilized the drug present into matrix which further causes release of drug. The gel layer of the tablets eroded due to interaction between polymers present in drug loaded HME matrix tablets and aqueous medium. The release of drug from the drug loaded HME matrix tablets was due to erosion and diffusion mechanism.
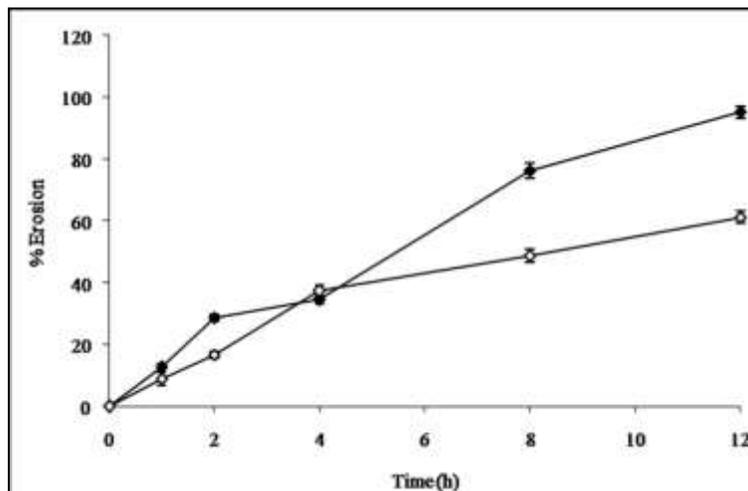
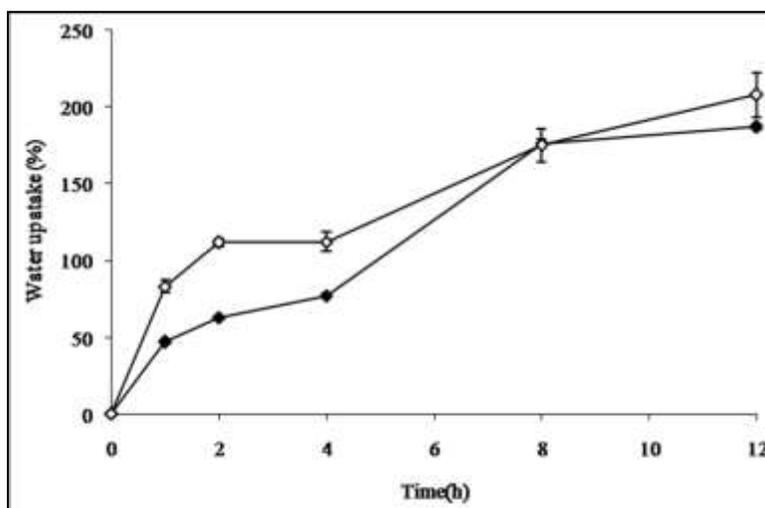**Figure 6**. Erosion study of (♦) formulation 6 and (◊) placebo tablets

Figure 7. Water uptake (%) study of (♦) formulation 6 and (◊) placebo tablets

Model fitting for the mechanism

The values of n were obtained by regression analysis. The drug release from a swellable cylindrical device was characterized by release exponent n value in cylindrical HME tablets containing HPC as hydrophilic polymers. The release exponent n value for the HME matrix tablets was listed in Table 2, formulation 4 and formulation 2 was found to follow Anomalous (non-fickian) diffusion which means drug release through diffusion and erosion mechanism. Formulation 2 has HPC H but it have increased loading. As the viscosity of HPC increased drug release shifted towards Super case-II transport mechanism (i.e. swelling, disentanglement and system erosion) as indicated by an increasing exponent *n* more than 0.89.

A co relation was found in dissolution profile, erosion study, water uptake and n values of HME hydroxypropylcellulose matrix tablets. As formulation 1 contained low viscosity grade HPC, it exhibited complete release within 12 h due to erosion of weak gel layer and diffusion. But

formulation 4 contained high viscosity grade of HPC with 60% drug loading, it also followed Anomalous diffusion with incomplete release. The combination of polymers were used to achieve sustained release profile, the viscosities of these polymers were more than the viscosity of HPC L grade. Formulation 1, 3, 5 and formulation 6 exhibited higher n value more than 0.89 followed Super case-II transport mechanism.

Table 2: Assay, release exponent (n) and regression coefficient (r^2)

Formulations	Assay (%) (mean±SD, n=3)	Korsmeyer–Peppas model n (mean±SD, n=3)	r^2
Formulation 1	102.12±0.15	1.083±0.012	0.981
Formulation 2	99.89±0.12	0.831±0.007	0.969
Formulation 3	100.71±0.21	0.946±0.001	0.996
Formulation 4	100.62±0.34	0.704±0.321	0.998
Formulation 5	101.11±0.71	0.922±0.003	0.998
Formulation 6	100.89±0.24	1.033±0.097	0.999

Fourier transform infrared (FT-IR)

Interactions between drug and polymers in extrudate were investigated by FTIR shown in Figure 8. The FTIR spectra of rifampicin indicated by characteristic peaks at 3412.08 cm^{-1} (-OH group), 1267 cm^{-1}, 1288 cm^{-1} of -C-O-C stretching of –OCH$_3$. Peaks at 1732 cm^{-1}, 1710 cm^{-1} is indicates -C=O stretching, 1654 cm^{-1} (Amide –C=O Stretch), 2970 cm^{-1}, 2932 cm^{-1} (Aliphatic –C-H stretch) and 1566 cm^{-1}, 1450 cm^{-1}, 1429 cm^{-1} (Aromatic C=C stretching).

The FTIR spectra of HME tablet showed broaden peaks at 3448.51 cm^{-1} characteristics of (-OH group), 1246 cm^{-1} (-C-O-C stretching of –OCH$_3$), 2970 cm^{-1}, 2932 cm^{-1} Aliphatic –C-H stretch) and 1433 cm^{-1}, 1568 cm^{-1} (Aromatic C=C stretching). It was found that there were no chemical interactions between polymer and rifampicin. These spectral observations in broadening of peaks indicate intermolecular hydrogen bonding between rifampicin and the polymers used in the hot melt extrusion.
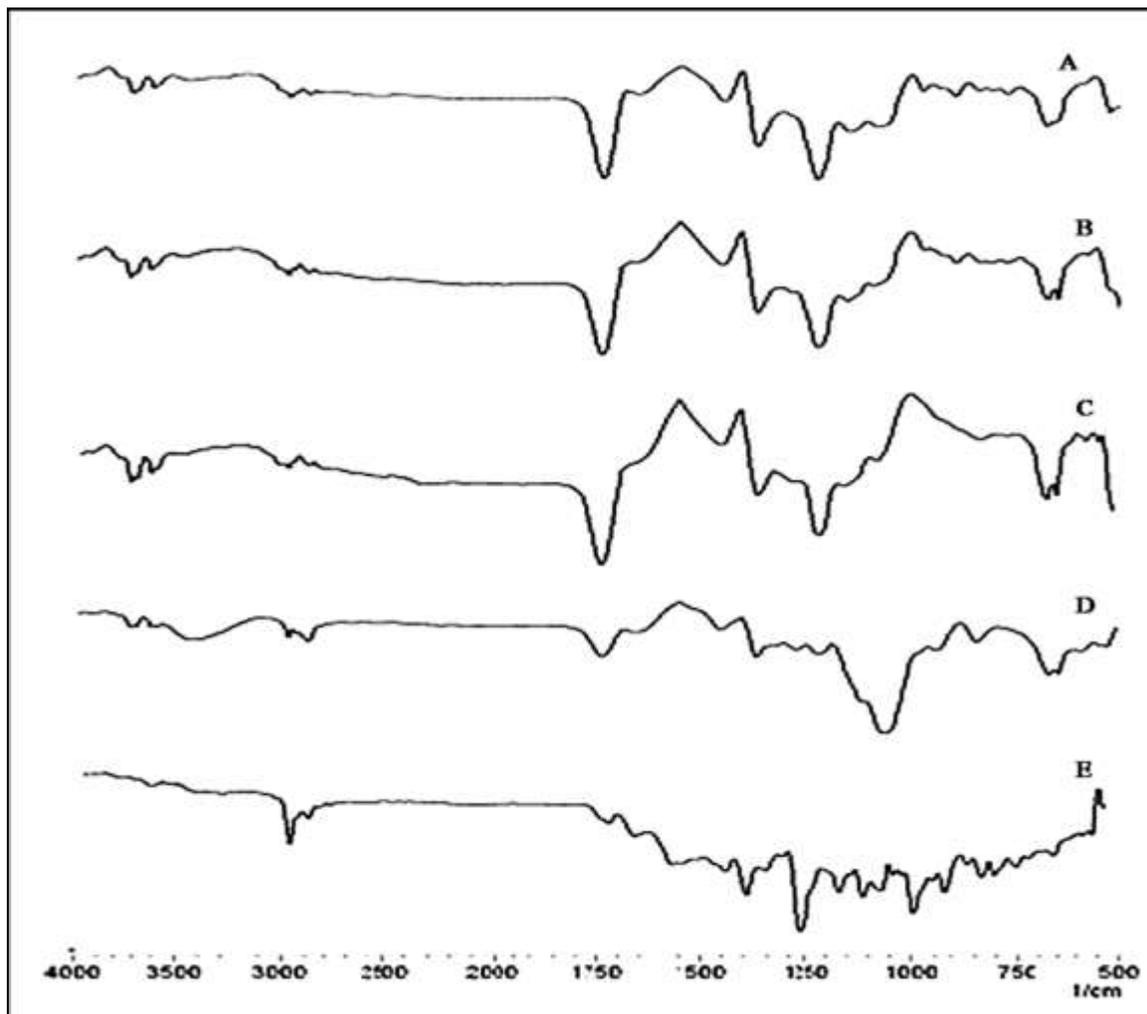
Figure 8. FTIR (A) Formulation 6 (B) Physical Mixture of Rifampicin, HPC LM and HPC M (C) HPC M (D) HPC LM and (E) Pure Rifampicin

Stability

Stability study of HME tablets were performed of formulation 6 which was stored at 30°C/65%RH and 40°C/75%RH for the period of 6 months. No significant change in the release profile and drug content was observed a under specified storage condition (see Table 3 and Figure 9). The result indicate the sustained release matrix of rifampicin tablets prepared by HME were stable under above mentioned storage conditions.
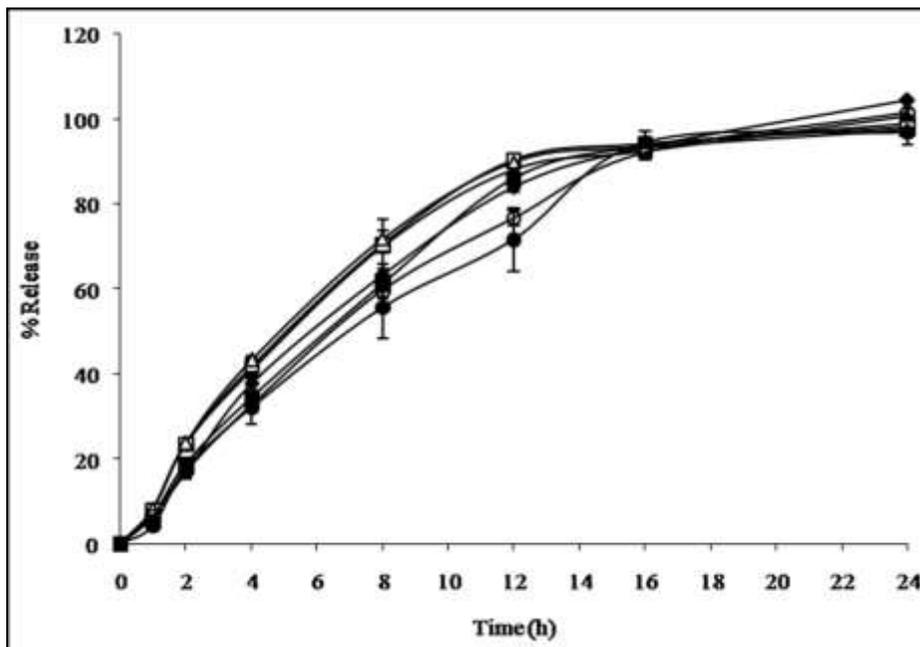
Figure 9. Dissolution release of formulation 6 for (♦) 0 Day, (■) 1st month at 30°C/65% RH, (▲) 1st month at 40°C/75% RH, (□) 3rd month at 30°C/65% RH, (Δ) 3rd month at 40°C/75% RH, (●) 6th month at 30°C/65% RH and (○) 6th month at 40°C/75% RH

Table 3: Assay of the stability samples

0 Day	1st Month		3rd Month		6th Month	
	30°C/65%RH	40°C/75%RH	30°C/65%RH	40°C/75%RH	30°C/65%RH	40°C/75%RH
104.27±0.34	98.89±1.79	100.4±0.34	97.90±0.17	97.40±1.13	96.79± 2.90	101.41±1.02

Assay (%) mean ±SD, n=3

CONCLUSION

Sustained release matrix tablets were successfully prepared by HME using hydroxypropylcellulose as continuous process for preparation of tablets. Sustained release matrix tablets of rifampicin were optimized using HPC M grade and HPC LM grade. The low viscosity of HPC LM grade played vital role in controlling initial release and subsequent release were sustained by high viscosity of HPC M grade. Release of drug from sustained release matrix tablets was dependent upon swelling of hydroxypropylcellulose and erosion behavior of the matrix tablets. The release behavior was also dependent on internal pores, which were observed by SEM study. The values of n were found to be more than 0.89 by regression analysis after subjecting the release data to Korsmeyer–Peppas model which indicates Super case-II transport mechanism. HME tablets were found to be stable for the period of 6 months as per ICH guideline.

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