FORMULATION AND *IN VITRO* EVALUATION OF OFLOXACIN-ETHOCEL CONTROLLED RELEASE MATRIX TABLETS PREPARED BY WET GRANULATION METHOD: INFLUENCE OF CO-EXCIPIENTS ON DRUG RELEASE RATES

SHEFAAT ULLAH SHAH[1], KIFAYAT ULLAH SHAH[1], SYED UMER JAN[2]*, KAMRAN AHMAD[1], ASIM-UR-REHMAN[1], ABID HUSSAIN[1] AND GUL MAJID KHAN[1]

[1]*Drug Delivery Research center, Department of Pharmaceutics, Faculty of Pharmacy, Gomal University, Dera Ismail Khan, Pakistan*

[2]*Department of Pharmacy, University of Balochistan, Quetta, Pakistan*

ABSTRACT

Being controlled release dosage forms, tablets allow an improved absorption and release profiles of Ofloxacin. The fact that drugs with fine particles size can be compressed well after wetting, so in our research studies Ofloxacin controlled release matrix tablets were prepared by wet granulation technique. In order to investigate the potential of Ethyl cellulose ether derivatives as a matrix material, Ofloxacin formulations with different types and grades of Ethocel were prepared at several drug-to-polymer ratios. The method adopted for *in vitro* drug release studies was USP Method-1 (rotating Basket Method) by Pharma test dissolution apparatus using phosphate buffer 7.4 pH as a dissolution medium. Various Kinetic models were employed to the formulations for the purpose of determination of release mechanism. A comparative study was performed between the tested Ofloxacin-Ethocel formulations and a standard reference obtained from the local market. F_1 dissimilarity factor and f_2 similarity factor were applied to the formulations for the checking of dissimilarities and similarities between the tested formulations and reference standard.

Keywords: Ofloxacin, Ethocel standard 7, 10 and 100 premium and FP premium, wet granulation, controlled release matrices, release kinetics and patterns, effect of co-excipients.

INTRODUCTION

In recent years, the number of patients with acute to moderate diseases is increasing day by day. In these chronic situations the patients are treated for a longer period of time with a lot of medicines which can lead to patient non-compliance. These problems are mainly associated with drugs having short biological half lives because they must be taken several times a day. These problems can be solved by controlled release drug delivery systems (Yamunda *et al*., 2001). Recently the development of oral controlled release drug delivery systems has attracted much attention. These dosage forms are capable of delivering the drug in a predetermined time and rate thus maintaining the peak plasma level in therapeutic level for a long time period. These dosage forms increases the patient compliance by reducing the dosage frequency (Hamza *et al*., 2010). Controlled release drug delivery systems are used successfully to achieve a nearly constant drug release profile to maintain a high drug-plasma level for a long period of time. In control drug delivery systems, polymers are used to control the release rate of drug to a longer period of time from a single controlled release tablet thus reduce the dosage frequency. The release of drug from such type of matrix tablet occurs by degradation, diffusion and swelling immediately followed by diffusion (Cleary, 1991).

**Corresponding author:* e-mail: suj55@yahoo.com

Ethocel (Ethyl Cellulose Ether derivative) is a polymer used to control the release rate of drug from the dosage form. It is used in oral dosage forms i.e. tablets and capsules etc as an excipients ((Jan *et al*., 2011) and is also used as a coating material. Ethocel is available in different viscosity grades i.e. Ethocel standard 7, 10 and 100 Premium etc which are granular in nature and is also available in fine particle size (Khan and Zhu, 2001). Co-excipients are used in oral dosage forms for various purposes such as diluents, binders, disintegrates etc. CMC, HPMC and Starch are the most commonly used co-excipients mainly used as disintegrates in oral dosage forms to enhance the release of drug from its dosage form by various mechanisms (Tablet Ingredients, 2008; CMC, 2008; Methocel, 2008).

MATERIALS AND METHODS

Materials

Sodium hydroxide (NaOH), Monobasic Potassium Phosphate, CMC and Starch (Merck, Germany), Ofloxacin, PVP K-30 (Leeds Pharma Islamabad), Magnesium stearate and Lactose (BDH chemical Ltd, pool England), Ethocel standard 7, 10 and 100 Premium and Ethocel 7, 10 and 100 FP Premium, Methocel K100 M Premium EP (Dow chemical Co., Midland USA), UV-Visible Spectrophotometer (UVIDEC-1601 Shimadzu, Japan), Pharma Test Dissolution Apparatus (D-63512 Hainburg, Germany), Single Punch Tablet Machine

(Erweka AR 400, Germany), Friability Testing Apparatus (Erweka TA3R, Germany), Hardness Testing Apparatus (Erweka Apparatus TB24, Germany).

Ofloxacin CR tablets formulation and preparation

Ofloxacin-Ethocel CR tablets were formulated for wet granulation at two drug to polymer ratios i.e. 10:03 and 10:01. Co-excipients (CMC, HPMC and Starch) were added to some selected formulations to investigate their effects on the drug release enhancement.

Each 200 mg Ofloxacin-Ethocel matrix tablet prepared at D:P ratios of 10:03 and 10:01 contains, 100 mg Ofloxacin (50%), Ethocel Standard 7, 10 and 100 Premium and Ethocel Standard 7, 10 and 100 FP Premium; 30 mg (15%) and 10 mg (5%) respectively, excipient lactose (filler) 69 mg (34.5%) and 89 mg (44.5%) respectively, Magnesium stearate (lubricant) 1 mg (0.5%), and one of the co-excipients (CMC, HPMC or Starch); 20.7 mg (30% of Lactose) to selected formulations.

All the formulations were mixed geometrically with pestle and mortar except Magnesium stearate (lubricant) and were wetted with 10% PVP solution. After wetting, the damp mass was forced through #8 mesh screens for granulation. These granules were placed in trays and were kept in oven for drying. After drying these granules were again passed through #12 mesh screens to prevent it from agglomeration or lump formation. After drying Magnesium stearate was added to the formulations and was finally compressed into tablets by single Punch Machine (Erweka AR 400, Germany).

***In vitro* drug release studies**

For in vitro studies of Ofloxacin CR tablets in laboratory, USP Method-1 (Rotating Basket Method) was used with Pharma Test Dissolution apparatus (D-63512 Hainburg, Germany). The medium used for dissolution was phosphate buffer having a PH of 7.4 kept at constant temperature of 37± 1 C º. Samples of 5 ml each were withdrawn at specific time intervals (0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 10, 12, 18, 24 hours) and were filtered through a membrane filter (0.45µm) in order to remove any impurities or particles present in the samples. Absorbance of the samples was checked by UV-Visible Spectrophotometer (UVIDEC-1601 Shimadzu, Japan) at 293 nm and their % age releases were calculated.

Determination of release kinetics

Several Kinetic models were employed to the data obtained from the dissolution of Ofloxacin-Ethocel CR tablets in order to investigate the release patterns and release mechanism of the drug. These kinetic models include:

Zero order kinetics

$W = K_1 t$

(Xu GJ and Sunada H, 1995) (1)

First order kinetics

$In (100-W) = In 100 – K_2 t$

(Xu GJ and Sunada H, 1995) (2)

Table 1: Parameters of kinetic models applied to release profile of CR tablets of Ofloxacin and Ethocel® standard 7P, 10P and 100P at (D:P ratio 10:3) and Ethocel® standard 7FP, 10FP and 100FP at (D:P ratio 10:3 and 10:1) by Wet Granulation Method in PH 7.4 Phosphate Buffer solution (mean ± SD of three determinations)

Formulation Ofloxacin-Ethocel	$W = k_1 t$		$(100-w) = \ln 100-k_2 t$		$(100-w)^{1/3} = 100^{1/3}-k_3 t$		$W = k_4 t^{1/2}$		$M_t / M_{\infty} = k5\, t^n$		
	$k_{1 \pm SD}$	r_1	$k_2 \pm$ SD	r_2	$k_{3 \pm SD}$	r_3	$k_4 \pm$ SD	r_4	$k_5 \pm$ SD	r_5	n
Ofloxacin-Ethocel® standard 7 Premium Matrix Tablets											
10:03	4.25 ± 1.73	0.873	0.076 ± 0.17	0.617	0.107 ± 0.20	0.721	5.15 ± 1.09	0.873	0.246 ± 0.98	0.981	0.741
Ofloxacin-Ethocel® standard 7 FP Premium Matrix Tablets											
10:03	3.57±1.08	0.959	0.058 ± 0.09	0.910	0.085 ± 0.13	0.929	3.9 ± 0.184	0.959	0.74 ±1.45	0.993	0.752
10:01	4.37 ± 1.63	0.853	0.076 ± 0.27	0.637	0.107 ± 0.21	0.751	5.15 ± 1.19	0.853	0.246 ± 0.98	0.971	0.753
Ofloxacin-Ethocel® standard 10 Premium Matrix Tablets											
10:03	5.07 ± 1.36	0.929	0.09 ± 0.20	0.587	0.13 ± 0.23	0.737	5.69 ± 0.93	0.929	0.15 ± 0.28	0.98	0.73
Ofloxacin-Ethocel® standard 10 FP Premium Matrix Tablets											
10:03	3.57 ± 0.99	0.952	0.060 ± 0.97	0.877	0.089 ± 0.14	0.906	3.98 ± 0.71	0.952	0.50 ± 0.97	0.998	0.708
10:01	4.17±1.08	0.959	0.058 ± 0.09	0.911	0.085 ± 0.13	0.921	3.9 ± 0.184	0.959	0.75 ±1.45	0.988	0.744
Ofloxacin-Ethocel® standard 100 Premium Matrix Tablets											
10:03	5.004 ± 1.58	0.936	0.09 ± 0.21	0.624	0.127 ± 0.23	0.765	5.66 ± 1.12	0.936	0.185 ± 0.39	0.999	0.750
Ofloxacin-Ethocel® standard 100 FP Premium Matrix Tablets											
10:03	3.63 ± 0.95	0.95	0.06 ± 0.10	0.881	0.09 ± 0.138	0.910	3.97 ± 0.71	0.954	0.38 ± 0.76	0.998	0.686
10:01	5.21 ± 1.37	0.933	0.09 ± 0.21	0.577	0.13 ± 0.22	0.737	5.69 ± 0.93	0.933	0.15 ± 0.28	0.982	0.739

Higuchi kinetics

$W = K_4 t^{1/2}$ (3)

(Higuchi T, 1963)

Hixson Crowell kinetics

$(100 - W)^{1/3} = 100^{1/3} - K_3 t$ (4)

(Xu GJ and Sunada H, 1995)

Korsmeyer Peppas equations

$M_t / M\infty = K_5 t^n$ (5)

(Ritger RL and Peppas NS, 1987)

Table 1 shows Ofloxacin-Ethocel CR tablets formulated at (D:P ratios of 10:03 and 10:01) with out co-excipients and tables 2, 3 and 4 show Ofloxacin-Ethocel CR tablets having co-excipients CMC, HPMC and Starch respectively.

Table 2: Parameters of kinetic models applied to release profile of CR tablets of Ofloxacin and Ethocel® standard 7P; 7FP, 10P, 10FP & 100P, 100FP Premium at (D:P Ratio 10:3) containing CMC as co-excipient in PH 7.4 Phosphate Buffer solution (mean ± SD of three determinations)

Formulation Ofloxacin-Ethocel	$W = k_1 t$		$(100-w) = \ln 100 - k_2 t$		$(100-w)^{1/3} = 100^{1/3} - k_3 t$		$W = k_4 t^{1/2}$		$M_t / M_{\infty = k5}\, t^n$		
	$k_{1 \pm SD}$	r_1	$k_2 \pm$ SD	r_2	$k_{3 \pm SD}$	r_3	$k_4 \pm$ SD	r_4	$k_5 \pm$ SD	r_5	n
Ofloxacin-Ethocel® standard 7 Premium Matrix Tablets											
10:03	10.80 ±3.17	0.720	0.39 ±0.47	0.812	0.44 ±0.48	0.792	8.41 ±1.48	0.720	0.002 ±0.01	0.955	0.541
Ofloxacin-Ethocel® standard 7 FP Premium Matrix Tablets											
10:03	9.45 ±1.27	0.896	0.27 ±0.41	0.917	0.32 ±0.43	0.926	8.01 ±0.25	0.896	0.007 ±0.02	0.950	0.562
Ofloxacin-Ethocel® standard 10 Premium Matrix Tablets											
10:03	10.8 ±2.59	0.788	0.38 ±0.52	0.837	0.42 ±0.50	0.840	8.62 ±1.05	0.788	0.004 ±0.01	0.955	0.511
Ofloxacin-Ethocel® standard 10 FP Premium Matrix Tablets											
10:03	9.28 ±0.87	0.893	0.29 ±0.49	0.911	0.33 ±0.46	0.930	8.01 ±0.03	0.893	0.005 ±0.01	0.974	0.575
Ofloxacin-Ethocel® standard 100 Premium Matrix Tablets											
10:03	10.72 ±2.58	0.769	0.39 ±0.52	0.832	0.42 ±0.50	0.826	8.61 ±1.08	0.769	0.005 ±0.02	0.954	0.511
Ofloxacin-Ethocel® standard 100 FP Premium Matrix Tablets											
10:03	11.21 ±2.50	0.819	0.34 ±0.52	0.893	0.37 ±0.48	0.894	9.02 ±0.94	0.819	0.024 ±0.08	0.955	0.604

Table 3: Parameters of kinetic models applied to release profile of CR tablets of Ofloxacin and Ethocel® standard 7P; 7FP, 10P, 10FP & 100P, 100FP Premium at (D:P Ratio 10:3) containing HPMC as co-excipient in PH 7.4 Phosphate Buffer solution (mean ± SD of three determinations)

Formulation Ofloxacin-Ethocel	$W = k_1 t$		$(100-w) = \ln 100 - k_2 t$		$(100-w)^{1/3} = 100^{1/3} - k_3 t$		$W = k_4 t^{1/2}$		$M_t / M_{\infty = k5}\, t^n$		
	$k_{1 \pm SD}$	r_1	$k_2 \pm$ SD	r_2	$k_{3 \pm SD}$	r_3	$k_4 \pm$ SD	r_4	$k_5 \pm$ SD	r_5	n
Ofloxacin-Ethocel® standard 7 Premium Matrix Tablets											
10:03	10.48 ±2.52	0.771	0.36 ±0.47	0.833	0.41 ±0.47	0.825	8.42 ±1.06	0.771	0.004 ±0.01	0.958	0.502
Ofloxacin-Ethocel® standard 7 FP Premium Matrix Tablets											
10:03	9.19 ±0.95	0.908	0.26 ±0.40	0.908	0.31 ±0.42	0.922	7.87 ±0.02	0.908	0.01 ±0.02	0.960	0.573
Ofloxacin-Ethocel® standard 10 Premium Matrix Tablets											
10:03	10.39 ±2.62	0.724	0.38 ±0.47	0.763	0.43 ±0.48	0.761	8.34 ±1.17	0.724	0.004 ±0.01	0.966	0.533
Ofloxacin-Ethocel® standard 10 FP Premium Matrix Tablets											
10:03	9.42 ±0.84	0.919	0.26 ±0.43	0.900	0.30 ±0.43	0.928	8.12 ±0.08	0.919	0.02 ±0.04	0.960	0.627
Ofloxacin-Ethocel® standard 100 Premium Matrix Tablets											
10:03	10.43 ±1.97	0.851	0.34 ±0.52	0.882	0.37 ±0.49	0.896	8.51 ±0.61	0.851	0.005 ±0.01	0.965	0.545
Ofloxacin-Ethocel® standard 100 FP Premium Matrix Tablets											
10:03	9.70 ±1.03	0.897	0.27 ±0.44	0.912	0.31 ±0.44	0.927	8.30 ±0.04	0.897	0.023 ±0.06	0.952	0.644

RESULTS

The main objective of preparing CR Ofloxacin tablets by wet granulation method was to achieve control release profiles of drug and peak plasma level up to desired time. Polymer tablets prepared by wet granulation method were physically suitable. Average hardness of Ofloxacin-Ethocel CR tablets with Premium and FP Premium grades of Ethocel were from 6-7 kg/cm^2 which was with in the USP acceptable range. Average thickness was 2.6 mm ± 0.05 for the CR tablets with Premium grades of Ethocel and 2.5 mm ± 0.06 for CR tablets having FP grades of Ethocel. Average diameter of CR Ofloxacin-Ethocel tablets was 8 mm ± 0.01. Average friability of all the CR formulations of Ofloxacin with both Premium and FP Premium grades of Ethocel were not more than 0.18% ± 0.015.

The *in vitro* drug release mechanism was analyzed by fitting the dissolution data in the five above mentioned kinetic models. All the kinetic models best fits the dissolution data, but the drug release mechanism can be best described by Korsmeyer Pappas kinetic model given in equation (5). From equation 5, an (n) value indicates the drug release mechanism from matrix tablets. The (n) values (n > 0.5) indicates non-Fickian or diffusion mechanism and (n = 1) indicates zero order release mechanism. From the above tables 1, 2, 3 and 4, it could be observed that all the controlled release formulations exhibited non-Fickian release or diffusion mechanism having (n) values (1 < n > 0.5).

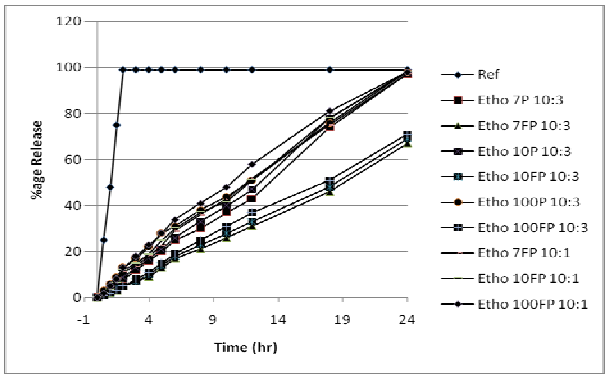

Fig. 1: Release profile of Ofloxacin from Reference conventional formulation, Ethocel Standard 7, 10 and 100 Premium at (D:P ratio 10:3) and Ethocel standard 7, 10 and 100 FP Premium matrices at (D: P ratio of 10:03 and 10:1) by Wet granulation Method

Influence of co-excipients on drug release rates

Co-excipients could be added to controlled release formulations so as to enhance the drug release rate and to obtain tablets with desirable properties. So, the effect of several co-excipients was examined on the CR tablets of Ofloxacin-Ethocel in dissolution studies in phosphate buffer 7.4 PH. The co-excipients used are CMC, HPMC and Starch.

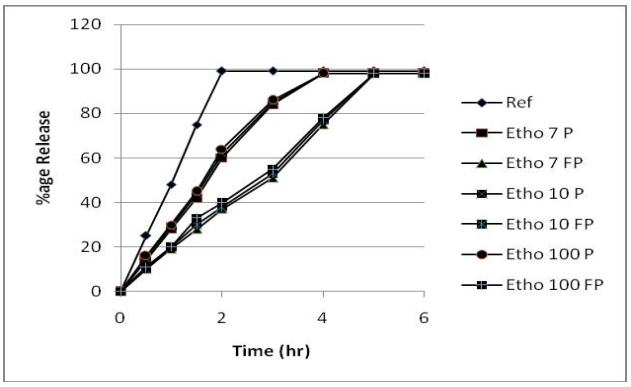

Fig. 2: Release profile of Ofloxacin from Reference conventional formulation, Ethocel Standard 7, 10 and 100 Premium and Ethocel standard 7, 10 and 100 FP Premium matrices at (D: P ratio 10:03) containing CMC as Co-excipient

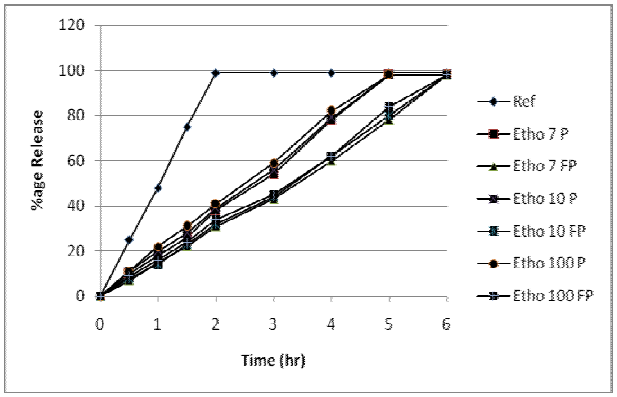

Fig. 3: Release profile of Ofloxacin from Reference conventional formulation, Ethocel Standard 7, 10 and 100 Premium and Ethocel standard 7, 10 and 100 FP Premium matrices at (D: P ratio 10:03) containing HPMC as Co-excipient

Comparative effect of co-excipients

The comparative effect of co-excipients on the drug release profiles from Ofloxacin-Ethocel controlled release matrix tablets in term of the dissolution time is shown in fig 5. It could be seen that the CR formulations containing no co-excipients demonstrated the longest dissolution time, but the formulations with one of the co-excipients demonstrate short dissolution time. CMC was observed to exhibit the shortest dissolution time as compared to HPMC and Starch. The order of co-excipients demonstrating the shortest dissolution time was CMC>HPMC>Starch.

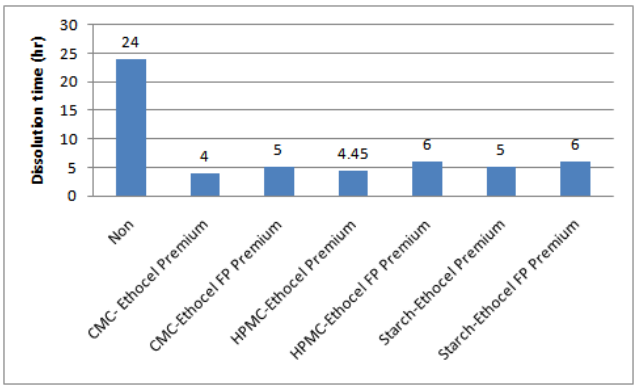

Fig. 5: Effect of co-excipients on the release profile of Ofloxacin from Ethocel Standard Premium and Ethocel Standard FP Premium formulations prepared at (D: P ratio of 10:03)

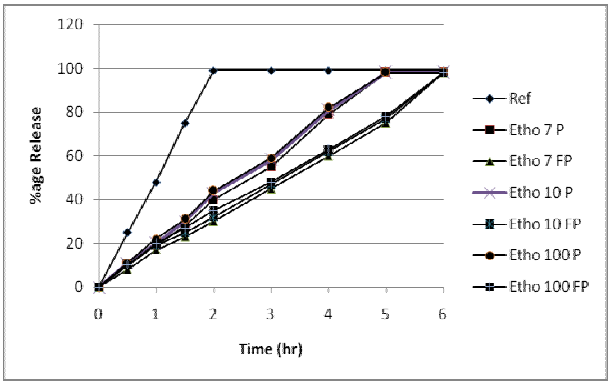

Fig. 4: Release profile of Ofloxacin from Reference conventional formulation, Ethocel Standard 7, 10 and 100 Premium and Ethocel standard 7, 10 and 100 FP Premium matrices at (D: P ratio of 10:03) containing Starch as Co-excipient

Applying the dissimilarity factor f_1 and similarity factor f_2

F_1 similarity factor and f_2 dissimilarity factor are used to compare the release profiles of a reference standard and test formulations and are approved by FDA. The value of f_1 is from 1-15, values (>15) shows that the release profiles of reference standard and test formulations are not similar.

$$f_1 = \{ \sum_{t-1}^{n} [Rt - T] \div \sum_{t-1}^{n} Rt \} \times 100$$

The value of f_2 is from 50-100, values (>50) shows similarities and (<50) shows dissimilarities between the drug release profiles of standard reference and test formulations (FDA, 1997; EMEA, 1999).

$$f_2 = 50\text{Log} \{[1+1/n\ W_t \sum_{t=1}^{n} (R_t - T_t)^2]^{-0.5} \times 100\}$$

DISCUSSION

Ethocel effectively control the release of Ofloxacin from the polymeric tablets, but the release of drug from FP formulations were extended desirably and a less amount of drug was released in 24 hours as compared to Ofloxacin CR formulations with Premium grades of Ethocel, the reason behind this could be that Ethocel FP Premium are fine particle polymers which offers more compression and harder tablets are produced from which less drug release occurs (Khan and Median, 2007).

Fig. 1 shows the release profiles of Ofloxacin-Ethocel CR tablets prepared at different drug to polymer ratios. It could be seen that the Ofloxacin-Ethocel FP formulations

Table 4: Parameters of kinetic models applied to release profile of CR tablets of Ofloxacin and Ethocel® standard 7P; 7FP, 10P, 10FP & 100P, 100FP Premium at (D:P Ratio 10:3) containing STARCH as co-excipient in PH 7.4 Phosphate Buffer solution (mean ± SD of three determinations)

Formulation Ofloxacin-Ethocel	$W = k_1 t$		$(100-w) = \ln 100 - k_2 t$		$(100-w)^{1/3} = 100^{1/3} - k_3 t$		$W = k_4 t^{1/2}$		$M_t / M_\infty = k_5 t^n$		
	$k_{1 \pm SD}$	r_1	$k_2 \pm$ SD	r_2	$k_{3 \pm SD}$	r_3	$k_4 \pm$ SD	r_4	$k_5 \pm$ SD	r_5	n
Ofloxacin-Ethocel® standard 7 Premium Matrix Tablets											
10:03	10.71 ±2.42	0.768	0.39 ±0.53	0.829	0.42 ±0.51	0.822	8.63 ±0.95	0.768	0.006 ±0.02	0.975	0.535
Ofloxacin-Ethocel® standard 7 FP Premium Matrix Tablets											
10:03	9.26 ±0.68	0.910	0.30 ±0.55	0.887	0.33 ±0.48	0.927	8.05 ±0.17	0.910	0.006 ±0.02	0.982	0.596
Ofloxacin-Ethocel® standard 10 Premium Matrix Tablets											
10:03	9.86 ±1.25	0.882	0.31 ±0.50	0.865	0.34 ±0.47	0.891	8.32 ±0.17	0.882	0.007 ±0.02	0.979	0.588
Ofloxacin-Ethocel® standard 10 FP Premium Matrix Tablets											
10:03	8.74 ±0.26	0.921	0.26 ±0.46	0.879	0.30 ±0.44	0.911	7.81 ±0.40	0.921	0.008 ±0.02	0.914	0.606
Ofloxacin-Ethocel® standard 100 Premium Matrix Tablets											
10:03	9.83 ±1.39	0.821	0.35 ±0.53	0.823	0.38 ±0.49	0.837	8.24 ± 0.27	0.821	0.004 ±0.01	0.986	0.564
Ofloxacin-Ethocel® standard 100 FP Premium Matrix Tablets											
10:03	9.75 ±1.05	0.908	0.28 ±0.49	0.900	0.32 ± 0.46	0.932	8.34 ±0.05	0.908	0.02 ±0.05	0.974	0.632

show less drug release rates as compared to CR formulations of Ofloxacin with Ethocel Premium grades and releases only 69% of the whole drug, so they were formulated by decreasing the amount of polymer i.e. at drug to polymer ratio of 10:01 which gave the expected results and the drug was released up to 98% in 24 hours. This could be due to the reason that increasing or decreasing the amount of polymer directly effects the release of drug from the CR tablets i.e. by decreasing the amount of polymer ratio increases the drug release profiles (Khan and Zhu, 2001a).

Effect of Carboxy Methyl Cellulose

Carboxy Methyl Cellulose (CMC) is a co-excipient used in tablets as a disintegrating agent. Its formulations with CR tablets enhance the release of drug from the tablet, causing the tablet to rupture in small period of time and release the drug into the surrounding medium; this could be due to its inherent disintegrative properties (Khan and Zhu, 2001a). As shown in fig. 2, in Ofloxacin formulations, the addition of CMC greatly enhanced the disintegration of matrix tablets and releases the whole drug in 4 hours for Ofloxacin CR tablets with Premium grades of Ethocel and 5 hours for Ofloxacin CR formulations with FP Premium grades of Ethocel respectively.

Effect of Hydroxy Propyl Methyl Cellulose

Hydroxy Propyl Methyl Cellulose (HPMC) is a co-excipient as well as release rate controlling polymer. As a co-excipient, it could exhibit faster drug release rates. As shown in fig. 3, its addition to the Ofloxacin controlled release matrix tablets, the time of drug release is increased from the dosage form, which could be due to its water absorbing capacity, because it absorbs sufficient quantity of water and by the intake of water osmotic pressure is produced with in the tablet which ruptures the tablet thus releasing the drug in short period of time (Khan and Zhu, 2001a).

Effect of starch

Fig. 4 shows the release profiles of Ofloxacin-Ethocel CR tablets, formulated at a drug-polymer ratio of 10:3, containing starch as co-exipient. It was observed that the release profiles of Ofloxacin-Ethocel CR tablets containing starch as co-excipient displayed higher release rates. Starch is naturally existing water swellable polymer so it could enhance the drug release from polymeric tablets by absorbing water and swallowing the tablet thus releasing the drug in desirable time (Khan and Zhu, 2001a). It could be seen from the figure that starch increases the release of Ofloxacin from CR matrix tablets and release the drug in 5 hours, while the drug release time was 6 hours in case of Ofloxacin CR tablets with FP grades of Ethocel.

In this study f_1 and f_2 factors were employed to the dissolution profiles of controlled release tablets of Ofloxacin-Ethocel formulated at several drug to polymer ratios and a reference standard (Ofloxacin 200 mg immediate release tablet) obtained from the local market. As given in table 5, a remarkable change was observed between the reference standard and the tested tablets which show the dissimilarities between the dissolution profiles.

CONCLUSION

From this investigative study it was observed that wet granulation method could be used successfully to develop control release matrix tablets of Ofloxacin. The use of Ethyl Cellulose Ether derivatives as matrix material in controlled release drug delivery systems gave a prominent result, by successfully controlling the release of slightly soluble antibiotics like Ofloxacin. Moreover, the use of FP grades of Ethocel in Ofloxacin-Ethocel CR tablets gave more extended drug release profiles. It was also observed that by decreasing the amount of polymer, the drug release rate could be enhanced. Co-excipients were observed to effectively enhance the drug release rates; however, this enhancement effect was more dominant in case of CMC.

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