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Effect of different polymers on *in vitro* and *ex vivo* permeability of Ofloxacin from its mucoadhesive suspensions

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Abstract   Considering the importance of drug permeation from formulations, *in vitro* and *ex vivo* drug permeation characteristics of three oral mucoadhesive suspensions of Ofloxacin were designed and compared. Three suspensions of Ofloxacin were prepared by taking two grades of Carbopol polymer such as Carbopol 934 (C934) and Carbopol 940 (C940); and Hydroxypropyl methylcellulose. The permeability study was performed by using a Franz diffusion cell through both synthetic cellulose acetate membrane and excised goat gastrointestinal membranes in acidic as well as alkaline pH. To know the permeability of the drug from control/formulations through different membranes in acidic/alkaline pH, cumulative percentage drug permeation, apparent permeability (Papp) and flux (*J*) were calculated. In addition, enhancement ratio (ER) of each formulation was also determined. From our results, it is evident that formulation containing C940 was the best suspension considering Papp and *J* values of all formulations. Moreover, it was the most beneficial formulation for improving permeation and diffusivity of Ofloxacin even after 16 h. Hence, this suspension was probably the most suitable formulation to obtain prolonged release action of the drug. The ER values of all formulations through the excised goat intestinal mucus membrane in alkaline pH were higher than those formulations through the goat stomach mucosal membrane in acidic pH. ER values of those formulations indicate that the permeability of the drug was more enhanced by the polymers in the intestinal part, leading to more bioavailability and prolonged action in that portion of the gastrointestinal tract. It may also be concluded from our results that in addition to formulation containing C940, other formulations may also show effective controlled release action.

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1. Introduction

Ofloxacin (Oflox) is a second generation fluoroquinolone antibacterial. It shows low solubility in aqueous solution and a high rate of absorption in the stomach. It is likely to be precipitated out of solution upon entry into the small intestine where the pH is alkaline. Oflox is considered to be a BCS Class III

drug (highly soluble and low permeable) with permeability properties approaching the border to BCS Class I (highly soluble and high permeable). Controlled release formulations of Oflox would be effective in overcoming the dissolution/permeation limitations by slowing the drug supply from the intact matrix base so that more drug should be soluble and permeable in the small intestine. Thus, it is expected to increase controlled release action and to improve patient compliance with fewer side effects (Chavanpatil et al., 2005; Gangurde et al., 2011; Hosny, 2009; Sakore et al., 2010).

Taking into consideration of the above-mentioned factors, polymeric suspensions of Oflox were prepared by using two grades of mucoadhesive biodegradable environmentally responsive Carbopol polymer i.e., Carbopol934 (C934) and Carbopol940 (C940) (Bettini et al., 1995; Qiu and Park, 2001). Carbopol polymers have recently attracted considerable interest in the field of drug delivery (Galaev and Mattiasso, 1999; Jeong and Gutowska, 2001). The polymer can protect the drug from the physiological environment by improving its stability in vivo (Guo, 2003). Moreover, the gelling and mucoadhesive properties of Carbopol polymers, which are largely defined by their crosslinker levels, are also very important for drug permeation enhancement from different formulations. In addition to Carbopol polymers, polymeric suspension of Oflox was also prepared by using a hydrophilic polymer like Hydroxypropyl methylcellulose (HPMC). Due to nonionic, gelling and mucoadhesive properties of hydrophillic polymeric matrix systems, these are used in formulations to obtain desirable drug permeation and controlled release action (Shoaib et al., 2006).

Since the qualitative and quantitative changes in a formulation may alter drug permeation and in vivo performance, several bio-studies are usually carried out. In this regard, the use of in vitro and ex vivo drug permeation data to predict in vivo bio-performance can be considered as the rational development of controlled release formulations. As we know, in vitro permeabilities can also be used to predict in vivo bioavailability of a given drug substance. Moreover, this method is also suitable for verifying the mechanism of various penetration enhancers like polymers, or their interaction with the gastric mucosa (Singh et al., 2010). So, permeability study of the drug is having tremendous importance.

Considering the above-mentioned information, the aim of this study is to investigate Oflox permeation and diffusion (from control solution/formulations) **using a Franz diffusion cell through synthetic cellulose acetate membrane, and excised goat stomach and intestinal mucosal membranes** in both acidic and alkaline pH. This was done to examine the effect of different polymers on drug permeation. To know the in vitro and ex vivo permeability of the drug from control/formulations in the presence of different membranes and pH values, cumulative percentage drug permeation (%CDP), permeability coefficient or apparent permeability (Papp) and flux (J) were calculated. In addition, enhancement ratio (ER) of each formulation was also determined.

2. Materials and methods

2.1. Materials

The following materials were used: Oflox was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. C934,

C940, Pluronic F 68 and Soya lecithin were purchased from Himedia Laboratories Pvt. Ltd., India. HPMC (HPMC E15 LV Premium) was supplied by Loba Chemie Pvt. Ltd., India. Glycerol, Methyl paraben sodium, Propyl paraben sodium, Sorbitol solution I.P. and Sucrose were obtained from Cosmo Chem. Laboratory, Pune, India.

2.2. Methods

2.2.1. Preparation of control
Oflox was dissolved in distilled water to prepare a control solution for the present study. The final concentration of the control solution was 10 mg/ml.

2.2.2. Preparation of formulations
Mucoadhesive formulations of Oflox were prepared as per the method described by Chakraborti et al. (2012). Moreover, mucoadhesive property of those suspensions was confirmed subsequently by Mukherjee et al. (2014).

2.2.3. Permeability study
In the present investigation, the permeability study of separately used optimized mucoadhesive formulations of Oflox was conducted using a static Franz diffusion cell (Hanson Research Corporation, USA). The Franz cell is a diffusion chamber, made of glass comprising of an upper donor compartment, which is open from above and a lower receptor (acceptor) compartment, which is closed from the bottom side. Between the compartments, the tissue was clamped with the mucosal side oriented upwards (Singh et al., 2010). The capacity of the receptor compartment was 22 ml. The area available for diffusion was about 3.90 cm^2. The lower chamber, containing a sampling port, had a Teflon-coated needle at the base. The junction between the two compartments was designed to hold the mucosa in such a manner that the mucosa did not shift from its place once the dosage form was incorporated into it. The hooks were secured with rubber bands on the sides of both compartments. In this manner, the two compartments formed one single unit without leakage. The donor compartment of diffusion cell was filled separately with each formulation containing 250 µl of Oflox. The donor cell was covered with an aluminium foil to prevent evaporation of vehicle. The fluid, in the receptor compartment, was maintained at $37 \pm 0.5\,°C$ and stirred continuously at a very low speed (30 rpm), using thermostatically controlled magnetic stirrer with Teflon coated bead. The external jacket of Franz diffusion cell was connected to a water bath so as to maintain temperature in cell. The excised goat stomach mucosal membrane was mounted between the half cells, keeping contact with the receptor fluid at pH 1.2 acidic buffer. However, the excised goat intestinal mucosal membrane was mounted similarly with the receptor fluid at pH 7.2 phosphate buffer. Care was taken to make sure that no air bubbles were present inside the receptor compartment.

Aliquot (500 µl each time) was withdrawn periodically at preset time from the above mentioned receiver cell, which was 20 times diluted and filtered through 0.2 µm filter. Oflox content was determined by UV spectrophotometer at 294 nm. The diffusion fluid of same volume was prewarmed at 37 °C. The volume of withdrawn sample was replaced by prewarmed diffusion fluid into the diffusion cell to keep the

volume constant so that sink condition could be maintained. Experiment was carried out up to 16 h with the excised stomach/intestinal mucosal membranes. The rates of drug permeation at different time points were calculated in each case.

2.2.3.1. Data analysis. Data, obtained from the permeability study for each formulation (such as F_1 - Oflox and C934, F_2 - Oflox and C940, and F_3 - Oflox and HPMC; and solution of the pure drug, F_o - control) were used to calculate cumulative drug permeation (CDP), %CDP (mean ± standard deviation), Papp, J, and ER. Papp, J, and ER were calculated by following the standard formulae (Haigh and Smith, 1994; Patel et al., 2010; Singh et al., 2010).

Permeability coefficient (apparent permeability) -
$$Papp = (V_A/Area \times time) \times ([drug]_{acceptor}/[drug]_{donor});$$
where, V_A = volume in acceptor compartment
Area = surface area of the intestinal membrane
Time = total transport time

Flux -
$$J = Papp \times CD;$$
where, CD = concentration of donor solution.

Enhancement ratio -
$$ER = Papp \text{ of formulation/Papp of control}$$

3. Results

In vitro permeability study of different formulations of Oflox, such as F_1 (Oflox and C934), F_2 (Oflox and C940), and F_3 (Oflox and HPMC); and solution of the pure drug, F_o (control), was done by Franz diffusion cell, using cellulose acetate membrane and acidic buffer of pH 1.2 as diffusional fluid at different time points up to 6 h. The results of this investigation have been shown in Table 1. The values of %CDP, Papp, and J were also calculated after 6 h in cases of all samples. These values were found to be least/minimum in case of the formulation F_3, while F_1 showed maximum values. However, in

phosphate buffer, formulation F_1 displayed minimum values, whereas they were maximum in case of F_3 (Tables 1 and 2). The above-mentioned results have also been depicted in different graphs by taking %CDP at different time points versus time (Figs. 1 and 2). In addition, bar diagrams (by taking Papp of different samples of Oflox) also indicate the results of the present investigation (Figs. 3 and 4).

The *ex vivo* permeability study of the above-mentioned samples was also performed in a similar manner, using the excised goat stomach mucosal membrane and acidic buffer at different time points up to 16 h. The results of this experiment have been mentioned in Table 3. The values of %CDP, Papp, and J were calculated after 16 h in cases of all samples. These values were minimum in case of the formulation F_2, while F_3 showed maximum values. However, by using the excised goat intestinal mucosa in presence of phosphate buffer, the formulation F_1 displayed minimum values, whereas they were maximum in case of F_2 after 16 h. The Papp values of different formulations of Oflox were more than the control when the goat intestinal membrane was used, while those values of these samples were less than the control in presence of the goat stomach mucosal membrane (Tables 3 and 4). The above-mentioned results have also been depicted in different graphs by taking the %CDP at different time points versus time (Figs. 5 and 6). In addition, bar diagrams of Papp values of different samples of Oflox also indicate the results of the present investigation (Figs. 7 and 8).

The Papp value of F_3 was maximum, while F_2 showed minimum value when the excised goat stomach mucosal membrane was used. On the other hand, in the excised goat intestinal mucosal membrane, just the opposite trend was found. However, in both cases Papp value of F_1 was in between F_2 and F_3 (Table 4). The effect of polymers on diffusion and permeation of Oflox was evaluated in terms of the ER values of different Oflox containing formulations by separately taking both buffers and different diffusional membranes. The ER values of Oflox containing formulations were more in the intestinal mucosa and the value was found to be highest in case of F_2 (Tables 2 and 4).

Table 1 %CDP ± SD of Oflox from control and three suspensions of Oflox using synthetic membrane.

Time (h)	Acidic buffer (pH 1.2)				Phosphate buffer (pH 7.2)			
	$^a F_o$	$^b F_1$	$^c F_2$	$^d F_3$	F_o	F_1	F_2	F_3
0.25	19.34 ± 0.01	16.30 ± 0.05	18.03 ± 0.03	18.47 ± 0.01	01.30 ± 0.02	1.30 ± 0.05	1.52 ± 0.04	1.73 ± 0.01
0.50	35.42 ± 0.03	20.21 ± 0.01	25.20 ± 0.01	22.38 ± 0.02	01.95 ± 0.03	2.60 ± 0.04	3.25 ± 0.02	3.04 ± 0.03
0.75	47.80 ± 0.01	28.13 ± 0.02	29.12 ± 0.04	27.16 ± 0.05	02.17 ± 0.01	4.78 ± 0.01	5.43 ± 0.01	4.12 ± 0.02
1.00	55.84 ± 0.04	44.33 ± 0.04	48.67 ± 0.02	45.41 ± 0.03	03.04 ± 0.01	6.51 ± 0.02	6.95 ± 0.03	6.30 ± 0.01
1.25	60.41 ± 0.05	50.19 ± 0.03	56.05 ± 0.01	54.97 ± 0.01	03.91 ± 0.04	8.25 ± 0.01	8.69 ± 0.01	8.69 ± 0.04
1.50	65.40 ± 0.02	53.67 ± 0.01	59.97 ± 0.03	56.49 ± 0.04	04.78 ± 0.01	9.34 ± 0.03	10.21 ± 0.01	10.42 ± 0.01
1.75	68.66 ± 0.01	55.19 ± 0.05	63.01 ± 0.04	58.23 ± 0.01	05.64 ± 0.02	10.64 ± 0.04	11.73 ± 0.03	12.60 ± 0.05
2.00	71.49 ± 0.04	60.84 ± 0.01	66.27 ± 0.02	61.49 ± 0.02	06.08 ± 0.01	12.38 ± 0.01	13.25 ± 0.01	14.34 ± 0.01
3.00	75.62 ± 0.03	62.36 ± 0.03	68.44 ± 0.01	64.75 ± 0.03	06.95 ± 0.03	13.68 ± 0.01	15.42 ± 0.05	17.60 ± 0.01
4.00	82.35 ± 0.01	68.44 ± 0.04	71.26 ± 0.05	65.18 ± 0.01	08.04 ± 0.04	14.77 ± 0.02	17.60 ± 0.03	20.42 ± 0.02
5.00	86.48 ± 0.05	74.75 ± 0.01	76.48 ± 0.02	68.66 ± 0.01	08.90 ± 0.01	14.99 ± 0.01	18.90 ± 0.01	22.81 ± 0.01
6.00	90.17 ± 0.04	81.48 ± 0.02	80.17 ± 0.04	78.87 ± 0.02	09.56 ± 0.01	16.29 ± 0.02	19.99 ± 0.01	24.98 ± 0.01

[a] Pure solution of Oflox.
[b] Oflox and C934.
[c] Oflox and C940.
[d] Oflox and HPMC.

Table 2 *In vitro* permeability profiles of the samples of Oflox through synthetic membrane up to 6 h.

| Samples	%CDP[e]	[f]Papp (cm s^{-1}) × 10^{-7}	[g]J (µg cm^{-2} s^{-1}) × 10^{-3}	[h]ER
(a) Acidic buffer (pH 1.2)				
[a]F_o	90.17	26.76	26.76	–
[b]F_1	81.48	24.18	24.18	0.904
[c]F_2	80.17	23.79	23.79	0.889
[d]F_3	78.87	23.41	23.41	
(b) Phosphate buffer (pH 7.2)				
F_o	09.56	2.84	2.84	–
F_1	16.29	4.84	4.84	1.704
F_2	19.99	5.92	5.92	2.085
F_3	24.98	7.42	7.42	2.613

[a] Pure solution of Oflox.
[b] Oflox and C934.
[c] Oflox and C940.
[d] Oflox and HPMC.
[e] Cumulative percentage drug permeation.
[f] Apparent permeability.
[g] Flux.
[h] Enhancement ratio.
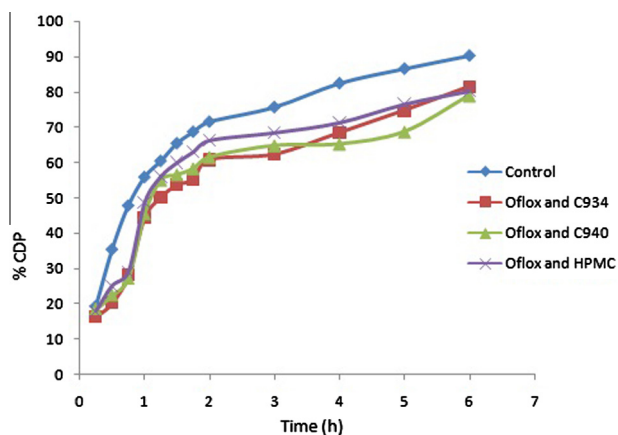
Figure 1 Comparative %CDP ± SD of different samples of Oflox versus time through synthetic membrane in acidic buffer up to 6 h.
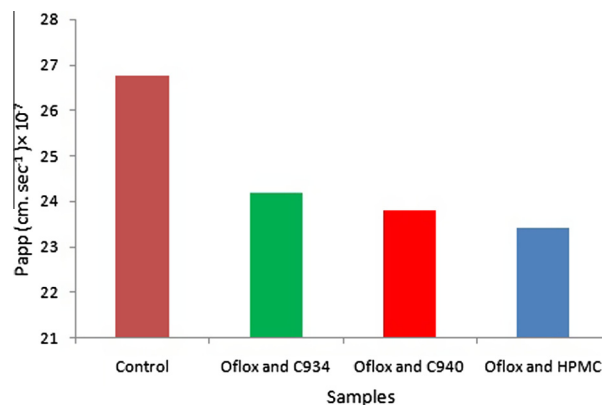
Figure 3 Comparative Papp values of different samples of Oflox through synthetic membrane in acidic buffer up to 6 h.
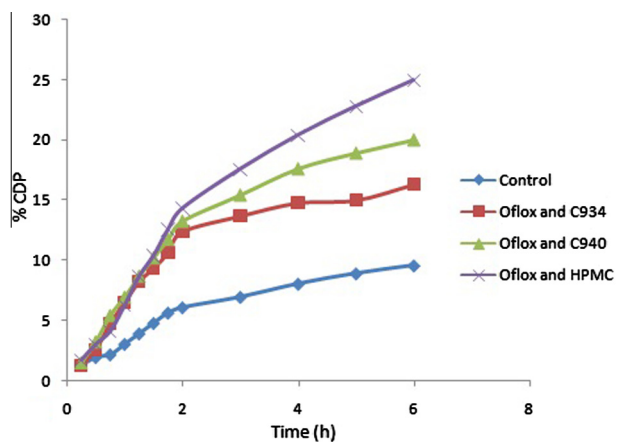
Figure 2 Comparative %CDP ± SD of different samples of Oflox versus time through synthetic membrane in phosphate buffer up to 6 h.
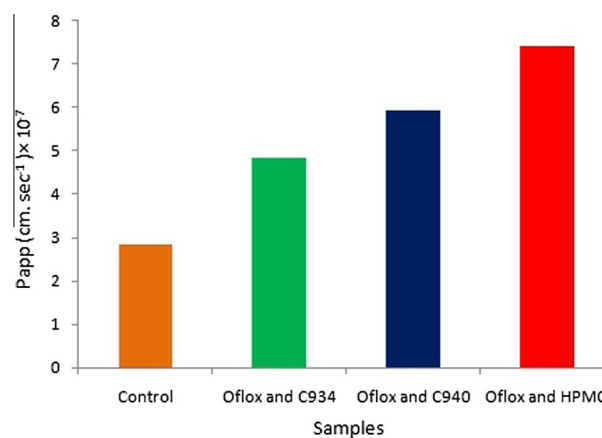
Figure 4 Comparative Papp values of different samples of Oflox through synthetic membrane in phosphate buffer up to 6 h.

Table 3 %CDP ± SD of Oflox from control and three suspensions of Oflox using biological membranes.

Time (h)	Excised goat stomach mucosal membrane at pH 1.2				Excised goat intestinal mucosal membrane at pH 7.2			
	[a]F_o	[b]F_1	[c]F_2	[d]F_3	F_o	F_1	F_2	F_3
0.25	04.99 ± 0.02	03.05 ± 0.01	02.82 ± 0.02	03.04 ± 0.01	01.73 ± 0.02	03.69 ± 0.02	03.69 ± 0.04	03.04 ± 0.04
0.50	13.47 ± 0.01	10.21 ± 0.02	10.21 ± 0.03	11.08 ± 0.03	03.47 ± 0.03	11.08 ± 0.01	11.08 ± 0.01	10.21 ± 0.01
0.75	18.68 ± 0.01	13.68 ± 0.04	14.12 ± 0.01	16.29 ± 0.01	05.43 ± 0.01	14.99 ± 0.01	15.43 ± 0.03	14.99 ± 0.03
1.00	21.94 ± 0.03	17.81 ± 0.03	18.46 ± 0.01	20.20 ± 0.01	07.17 ± 0.02	19.33 ± 0.04	19.56 ± 0.01	19.34 ± 0.01
1.25	26.72 ± 0.04	22.38 ± 0.05	22.59 ± 0.04	24.98 ± 0.04	09.34 ± 0.04	23.03 ± 0.01	23.25 ± 0.02	22.16 ± 0.01
1.50	29.98 ± 0.01	25.85 ± 0.01	26.72 ± 0.05	29.11 ± 0.05	11.08 ± 0.01	26.29 ± 0.02	26.51 ± 0.01	25.20 ± 0.03
1.75	35.20 ± 0.01	31.28 ± 0.01	30.85 ± 0.01	33.46 ± 0.02	13.25 ± 0.02	29.98 ± 0.03	30.42 ± 0.05	29.55 ± 0.01
2.00	39.76 ± 0.02	34.76 ± 0.03	34.98 ± 0.01	37.59 ± 0.01	16.07 ± 0.03	35.20 ± 0.01	35.20 ± 0.01	34.11 ± 0.02
3.00	44.97 ± 0.05	40.19 ± 0.01	41.06 ± 0.01	43.23 ± 0.02	19.12 ± 0.04	39.98 ± 0.05	40.42 ± 0.01	39.76 ± 0.01
4.00	51.49 ± 0.01	47.15 ± 0.02	47.36 ± 0.02	48.88 ± 0.01	22.16 ± 0.01	46.93 ± 0.01	47.15 ± 0.03	46.06 ± 0.01
5.00	56.71 ± 0.03	53.01 ± 0.01	53.23 ± 0.03	53.88 ± 0.03	25.63 ± 0.02	53.01 ± 0.01	53.67 ± 0.01	52.37 ± 0.04
6.00	62.36 ± 0.02	58.01 ± 0.05	59.31 ± 0.05	59.97 ± 0.01	28.24 ± 0.01	58.90 ± 0.01	59.10 ± 0.04	58.45 ± 0.01
8.00	66.48 ± 0.01	62.14 ± 0.01	62.14 ± 0.01	64.09 ± 0.01	29.33 ± 0.01	62.36 ± 0.03	63.66 ± 0.05	62.40 ± 0.02
10.0	70.61 ± 0.03	64.75 ± 0.04	65.18 ± 0.02	68.00 ± 0.03	31.07 ± 0.03	65.18 ± 0.04	67.14 ± 0.01	66.05 ± 0.01
12.0	74.09 ± 0.01	68.87 ± 0.02	68.22 ± 0.03	72.35 ± 0.04	32.59 ± 0.01	68.44 ± 0.01	70.40 ± 0.01	68.80 ± 0.02
14.0	78.22 ± 0.02	72.79 ± 0.03	71.48 ± 0.01	76.26 ± 0.01	34.54 ± 0.04	71.05 ± 0.02	74.09 ± 0.03	71.27 ± 0.03
16.0	83.43 ± 0.01	76.04 ± 0.01	75.61 ± 0.02	80.82 ± 0.01	36.06 ± 0.01	74.96 ± 0.01	78.00 ± 0.02	73.44 ± 0.01

[a] Pure solution of Oflox.
[b] Oflox and C934.
[c] Oflox and C940.
[d] Oflox and HPMC.

Table 4 *Ex vivo* permeability profiles of the samples of Oflox through biological membranes up to 16 h.

| Samples	%CDP[e]	[f]P_{app} (cm s^{-1}) × 10^{-7}	[g]J (µg cm^{-2} sec^{-1}) × 10^{-3}	[h]ER
(a) Excised goat stomach mucosal membrane at pH 1.2				
[a]F_o	83.43	9.27	9.27	–
[b]F_1	76.04	8.45	8.45	0.912
[c]F_2	75.61	8.40	8.40	0.906
[d]F_3	80.43	8.98	8.98	0.969
(b) Excised goat intestinal mucosal membrane at pH 7.2				
F_o	36.06	4.01	4.01	–
F_1	74.96	8.33	8.33	2.077
F_2	78.00	8.67	8.67	2.162
F_3	73.44	8.16	8.16	2.035

[a] Pure solution of Oflox.
[b] Oflox and C934.
[c] Oflox and C940.
[d] Oflox and HPMC
[e] Cumulative percentage drug permeation.
[f] Apparent permeability.
[g] Flux.
[h] Enhancement ratio.

4. Discussion

In cases of Oflox containing mucoadhesive suspensions, F_1 and F_2 were found to be more permeable than F_3 in acidic medium, but F_3 showed the highest permeability than others at pH 7.2 when synthetic medium was used. So, in acidic medium, Carbopol polymers may show lesser gelling property and viscosity than HPMC, whereas these properties of Carbopol polymers seem to be relatively more than HPMC at pH 7.2 (Basaran and Bozakir, 2012) (Tables 1 and 2; Figs. 1–4). Moreover, the permeability of formulations containing Carbopol polymers (F_1/F_2) in the excised goat stomach was less than the formulation with HPMC (F_3). However, in case of the goat intestine, the permeability of F_1/F_2 was more than F_3, which may be due to more mucoadhesive property of formulations containing Carbopol polymers at the intestinal part (Barakat, 2010) (Tables 3 and 4; Figs. 5–8). On the basis of the overall results (using both synthetic/biological membranes), it might be mentioned that more controlled release action of Oflox from the formulations containing Carbopol is expected. These overcome the low absorption window of the drug at the intestinal part.
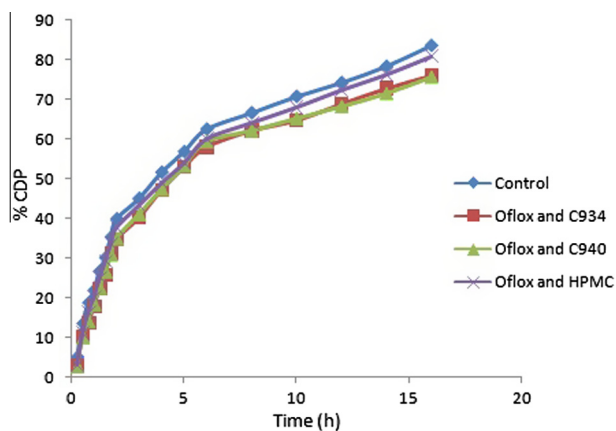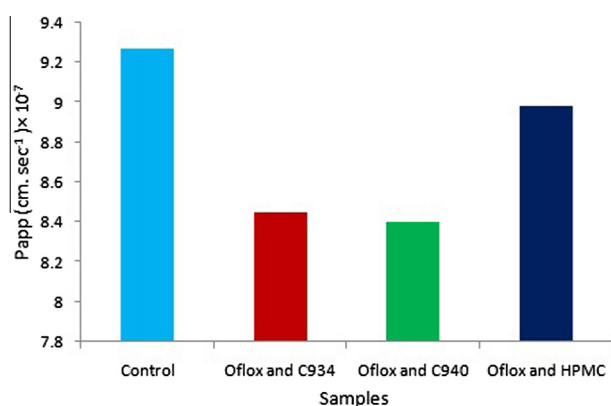
Figure 5   Comparative %CDP ± SD of different samples of Oflox versus time through excised goat stomach mucosal membrane in acidic buffer up to 16 h.
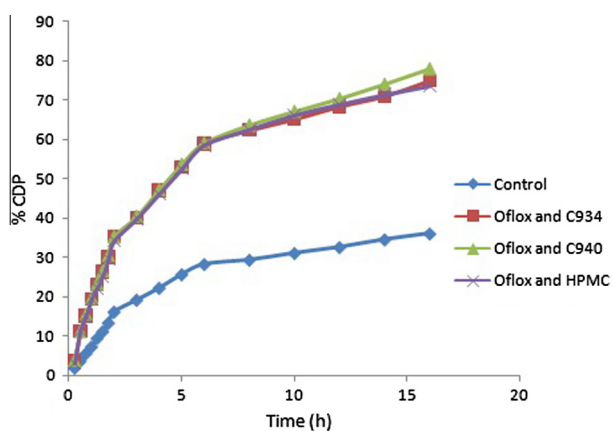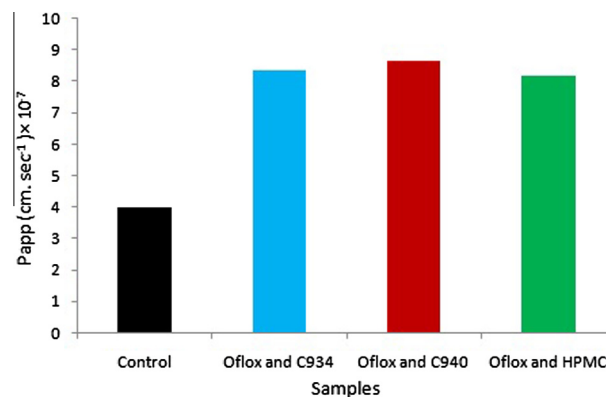

Figure 6   Comparative %CDP ± SD of different samples of Oflox versus time through excised goat intestinal mucosal membrane in phosphate buffer up to 16 h.

Figure 7   Comparative Papp values of different samples of Oflox through excised goat stomach mucosal membrane in acidic buffer up to 16 h.

As mentioned earlier, from suspensions and aqueous solution of pure drug, the extent of drug permeated up to 16 h was significantly different. The ER values of all suspensions

Figure 8   Comparative Papp values of different samples of Oflox through excised goat intestinal mucosal membrane in phosphate buffer up to 16 h.

showed higher permeation percent than aqueous solution of Oflox in presence of the goat intestinal membrane. Moreover, the ER values of all formulations in the excised goat intestinal mucosal membrane were more than those in presence of the goat stomach mucosal membrane (Table 4). It indicates that the permeability of the drug was more enhanced by the polymers in the intestinal part, leading to more bioavailability and prolonged action in the intestine (Bregni et al., 2008). In this manner, the limitation of BCS Class III drugs (such as Oflox) could be overcome. In this connection, it may be mentioned that an electrostatic attraction force occurs between the negative charge of each formulation and positive charge of GI mucosal membrane. As a result, mucoadhesive property of the gel base might ensure an intimate contact between suspension and GI mucosal membrane, which seems to prolong the retention of the formulation at site of absorption. This is beneficial for enhancing permeation (Hosny, 2009). That is why by taking into consideration of ER values of the present study, it may be concluded that in addition to F_1, and F_2, other formulation (F_3) is also expected to show effective controlled release action (Shojaei, 1998).

It has already been mentioned that both F_1 and F_2 may produce more controlled release action than F_3. Out of two Carbopol containing formulations (F_1 and F_2), F_2 was appeared to be the better formulation than F_1 considering their Papp and flux values. So, it might be mentioned that F_2 was probably the most beneficial for improving in vitro/ex vivo permeation and diffusivity of Oflox even after 16 h. Hence, this preparation may be considered as the best suspension to obtain effective controlled release action of the drug.

In addition, in our laboratory, particle size distribution of Oflox formulations was studied (using SEM), and their values of zeta potential were also determined. From particle size distribution study, it was found that maximum particle size ranges for formulations containing Oflox with C940, Oflox with C934, and Oflox with HPMC were from 2–4 μm, 10–15 μm and 4–6 μm, respectively. So, maximum particle sizes of all formulations were from 2 to 15 μm, i.e., they were pharmaceutically acceptable (Sahoo et al., 2012). Moreover, the values of zeta potential of Oflox formulations were found between -0.205 and -0.431 Mv. So, this study suggested that all formulations showed good flocculation and maximum/strong agglomeration properties, as the value of zeta potential

of each formulation (suspension) was between -5 mV and +5 mV (Sahoo et al., 2014). Thus, all suspensions were pharmaceutically acceptable and stable suspensions.

5. Conclusions

Considering all the above mentioned information, it may be concluded that effective controlled release action seems to be better when mucoadhesive suspensions of Oflox containing Carbopol like F_1 and F_2 would be used. Out of these formulations, F_2 was the best suspension to obtain effective controlled release action of the drug. Moreover, it was pharmaceutically acceptable and stable suspension. The present study is having tremendous importance because modelling, understanding and characterizing the penetration and permeation process of drugs through various biological membrane barriers are essential in order to predict the *in vivo* behaviour of formulation. Relevant *in vivo* studies of the formulations should be carried out in future to finally conclude their importance.

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