Original Research Article

Oral buccoadhesive films of ondansetron: Development and evaluation

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Abstract

Introduction: Difficulty or inability in swallowing tablets/capsules during or after chemotherapy is common due to chemotherapy induced nausea and vomiting in patients. Buccoadhesive films of ondansetron hydrochloride were prepared for the prevention and treatment of chemotherapy-induced emesis. Films of varying polymeric composition were prepared in order to facilitate initial as well as prolonged drug release that could take care of acute as well as delayed emesis. **Materials and Methods:** Mucoadhesive films were prepared using polymers such as hydroxypropyl methylcellulose (HPMC) E5, HPMC K100, and Eudragit® NE 30 D. The effect of concentration of these polymers on physical properties and drug release were studied. All the films were prepared by solvent casting method. In another part of the study, the effect of drug concentration on physical and mucoadhesive properties of film were assessed, keeping the polymer concentration fixed. **Results:** Films containing HPMC showed good mucoadhesion. Increasing the concentration of Eudragit® NE 30 D in the films retarded drug release and increased residence time, however, reduced mucoadhesion. At a fixed polymer concentration and ratio, films prepared using an increased drug content showed an increased mucoadhesion. **Conclusion:** Films prepared using HPMC E5 (1000 mg), HPMC K100 (500 mg), and Eudragit® NE 30 D (750 mg) provided initial rapid followed by sustained drug release over a period of 6 h. Given the promising results, the study concluded that the developed buccal films have the potential to release ondansetron required for chemotherapy induced acute and delayed emesis.

Key words: Buccoadhesive, Eudragit®, hydroxypropyl methylcellulose, mucoadhesion, ondansetron, permeation

INTRODUCTION

Oral route of drug delivery remains most popular route in drug delivery. Most of the dosage forms are swallowed from oral cavity. However, once swallowed enzymatic degradation and significant first pass effect may limit the bioavailability. Consequently, the nasal route, pharynx, oral cavity, and urogenital regions have been explored for local and systemic drug delivery. There is a need for an alternative route of drug delivery in case of nausea or vomiting. Several intraoral dosage forms have been developed including sublingual and rapid-melt tablets, buccoadhesive, wafers, patches, bioerodible disks, and microparticles. According to dissolution/disintegration, the films may be quick dissolving, slow dissolving, or non-dissolving.

Cancer is a common health issue and is reported to affect over 24.6 million of the world population. Every year almost 11 million people are diagnosed with cancer and mortality rate is extremely alarming. The current choice of treatment for this disorder is chemotherapy, which has been proven to be effective in treatment of all types of cancer.[1] In current anticancer therapy, the drugs are administered using intravenous route or oral route using conventional formulations. Episodes of acute and delayed emesis are common in patients receiving chemotherapy and this affects the quality of life of cancer patients.[2]

Ondansetron hydrochloride belongs to the class of 5-HT_3 antagonists which are approved by United States Food and Drug Administration (US FDA) to control chemotherapy-induced nausea and vomiting.[3] It has been reported that this drug delays the time of onset of nausea significantly in patients on high dose of cisplatin.[4] The present modes of administration of ondansetron are oral, parenteral, and intraoral. The oral bioavailability of ondansetron is approximately 60%, indicating

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first pass metabolism. The plasma half-life of ondansetron on oral administration has been found to be ~4 h with peak plasma level occurring within 1.5 h following oral delivery.[5] Parenteral route although has better bioavailability but this route has its own intrinsic limitations. Intraoral buccal films available for delivery of ondansetron provide drug delivery directly into the systemic circulation; show a better bioavailability and a faster onset of action. These strips can be administered in a situation wherein the patient is unable to swallow (especially in pediatrics/geriatric patients). However, these strips provide only an immediate relief from emesis and do not take care of the delayed emesis. So, it was proposed to develop films that could provide immediate as well as delayed support from emesis. Recently, a number of fast dissolving and sustained released oral strips have been formulated for various categories of drug moieties.[6-11] Polymers such as alginate, sodium carboxymethylcellulose, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose, polyvinyl pyrrolidone, Eudragit® NE, microcrystalline cellulose, etc., have been widely investigated for formulating oral strips/films.[8-11] The objective of the present study was to use a combination of polymers to constitute films that have buccoadhesion and can provide drug release for an extended period of time. Hydrophilic polymers, HPMC E5, and HPMC K100 were used to provide buccoadhesion. Water insoluble polymer Eudragit® NE 30 D was incorporated into the films to retard drug release. The effect of varying the concentration of HPMC and Eudragit® NE 30 D on the physical properties of the films as well as on drug release was also studied.

MATERIALS AND METHODS

HPMC E5 and HPMC K100 were obtained ex-gratis from Corel Pharm Ltd. (Ahmedabad, India). Eudragit® NE 30 D was obtained from Röhm Gmbh, Germany. Ondansetron hydrochloride was obtained as a gift sample from Ind Swift Ltd., Parwanoo. All other reagents and solvents were of analytical grade and commercially purchased from S. D Fine Chemicals, Mumbai, India.

Preparation of mucoadhesive films

A series of buccal films composed of different proportions and combinations of HPMC E5 (1000-1250 mg), HPMC K100 (500-1000 mg), and Eudragit® NE 30 D (150-1000 mg) containing ondansetron hydrochloride (150 mg) were prepared by solvent casting technique All films were plasticized with similar amount of propylene glycol (100 mg). Backing membrane was casted by pouring 4%w/v aqueous solution of polyvinyl alcohol (PVA) on aluminium foil in Petri dish at 42°C and left for 10 h.

Weighed quantities of HPMC were suspended in 10 ml of ethanol with constant stirring and small amount of water (2 ml) was added to it. This solution was mixed with Eudragit® NE 30 D and homogenized. Plasticizer was added to the blend and mixed. In case of drug loaded films, weighed amount of ondansetron was dissolved in propylene glycol before addition into the polymer blend. The above mix was stirred gently until a clear solution was obtained. The solution was sonicated to remove any entrapped air. The clear solution was then casted on the PVA-aluminium foil backing membrane and dried in an oven at 37°C for 16 h. The prepared films were then removed from the Petri dish and stored in vacuum desiccators. Table 1 summarizes the composition of different buccal films prepared in the study. Table 2 shows the composition of buccal films prepared using a fixed polymer blend with an increasing amount of ondansetron HCl.

Measurement of film thickness

Thickness of each film was measured using thickness gauze (Mitutoyo, Japan). The measurement of thickness of each film was done at six different locations (two in middle part and four

Table 1: Composition of the polymeric ondansetron films

Formulation code	HPMC E5 (mg)	HPMC K100 (mg)	Eudragit NE 30 D (mg)	Ondansetron HCl (mg)	Propylene glycol
F1	1,000	500	-	-	100
F2	1,000	1000	-	-	100
F3	1,000	500	250	150	100
F4	1,000	500	500	150	100
F5	1,000	750	500	150	100
F6	1,250	500	500	150	100
F7	1,000	750	750	150	100
F8	1,000	500	750	150	100
F9	1,000	500	1000	150	100
F10	1,250	500	1000	150	100
F5[a]	1,000	750	500	-	100
F8[a]	1,000	500	750	-	100

[a]Denotes placebo films, HPMC: Hydroxypropyl methylcellulose

Table 2: Composition of polymeric films with varying drug concentration

Formulation code	HPMC E5 (mg)	HPMC K100 (mg)	Eudragit NE 30 D (mg)	Ondansetron HCl (mg)	Propylene glycol
F1	1,000	500	-	-	100
F11	1,000	500	-	78	100
F12	1,000	500	-	115	100
F13	1,000	500	-	150	100

HPMC: Hydroxypropyl methylcellulose

corners). For each formulation, three randomly selected films were used. Films of size (3 × 3 cm^2) were cut and all the measurements were done in triplicate. Mean value of film thickness at six different locations was taken as the film thickness.[12]

Determination of drug content in the films

To ensure the uniformity of distribution of ondansetron in the film, a content uniformity test was done. Films (1 × 1 cm^2 equivalent to 2 mg of ondansetron) were cut at three different locations and dissolved in 10 ml of phosphate buffer saline (pH 6.8) by continuous shaking on a water bath at room temperature for 8 h.[13] The solution was filtered through Whatman filter paper and the samples were diluted suitably and analyzed using UV spectrophotometer at a λ_{max} 310 nm against a blank (UV-1800, Double Beam spectrophotometer, SHIMADZU, Japan). A calibration curve was constructed and the drug content was estimated from the curve (2.5-20 μg/ml). The method validation was done for linearity, precision, and accuracy. The regression equation for the calibration curve was Y = 0.041X + 0.006; R^2 = 0.9990.

Folding endurance

Folding endurance value was calculated by folding the film of suitable size at the same place and counting the number of time the film could be folded without breaking.[14]

Swelling study: Percentage of hydration and matrix erosion

Film swelling properties and erosion characteristics were determined by calculating the percentage of hydration and matrix erosion of the films. Films of definite size (1 × 1 cm^2) were cut and weighed (W_1). Film was placed on a weighed stainless steel wire mesh. The wire mesh and the film were immersed in phosphate buffer saline (pH 6.8) for predetermined time periods (5, 10, 20, 40, 60, 90, 120 min). At these time intervals the wire mesh was withdrawn from the buffer, the films were wiped off using filter paper and weighed (W_2). Percentage hydration of the films was determined using the following relation:[15]

$$\text{Percentage of hydration} = W_2 - W_1/W_2 \times 100$$

After complete hydration, films were dried at 60°C for 24 h and placed in desiccators for 48 h. The dried films were taken and weight was noted (W_3). Matrix erosion was calculated using the following relation:[16]

$$\text{Matrix erosion} = W_1 - W_3/W_1 \times 100$$

Surface pH

Films (1 × 1 cm^2) were allowed to swell in distilled water for 15 min. The film was taken out, drained, and the pH of the film was noted using litmus paper. The color developed was compared with the standard colors.[17]

Preparation of porcine buccal mucosa

The porcine buccal mucosa excised from porcine cheek pouch was obtained within 2 h of its death from the slaughter house and immediately transported to the laboratory in phosphate buffer solution. The buccal mucosa was separated from full thickness of the tissue after immersion in distilled water and then in isotonic phosphate buffer, pH 6.8 at 37°C. The fatty layers were removed by scalpel and buccal mucosa was isolated from the underlying tissue. Finally, the mucosa was washed with isotonic phosphate buffer, pH 6.8.

Mucoadhesive strength

The mucoadhesive strength of the films was measured by using TA-XTi, Texture Analyzer (Stable Micro systems, Surrey, UK). Porcine cheek pouch was used as substrate for determining the force.[9] The cheek pouch was checked for its biological integrity before mounting onto the holding assembly made of pyrex glass. The film of definite size was cut and adhered to the probe of texture analyzer using double sided adhesive tape. The Perspex glass assembly containing the porcine cheek muscle was filled with 2 ml of buffer solution to keep the muscle wet during contact period.[18] The probe speed was maintained at 0.5 cm/s towards the muscle and a contact time of 20 s was provided.

Ex vivo mucoadhesion time/retention time studies

Mucoadhesion time (*ex vivo*) was noted by applying the films on freshly cut porcine cheek pouch.[10] Porcine cheek pouch (2 × 2 cm^2) was cut and pasted on the inner side of the beaker using a suitable adhesive material. The film of size 1 × 2 cm^2 was cut and surface was made wet using a few drops of phosphate buffer saline (PBS). Films were pasted on the surface of porcine muscle by applying a gentle force for 10 s. PBS pH 6.8 was poured into the beaker and after 2 min, medium was rotated at 150 rpm to simulate buccal conditions. During the study, temperature was maintained at 37 ± 2°C. The film retention time was noted visually in minutes. All the experiments were done in triplicate and average was reported.

In vivo mucoadhesion time

In vivo mucoadhesion time study was carried out using placebo films F1, F2, F5* and F8* (*denotes placebo films). Written consent from the Institutional Ethical committee (M. M. University, Mullana) was taken before carrying out the study. A written consent was also taken from all the volunteers who took part in the study. Films were applied on the cheek pouch of healthy human volunteers (n = 6) and the mucoadhesion time was noted.

In vitro drug release study

Modified paddle apparatus was used to carry out the drug release studies. The film of size 2 × 1 cm^2 was cut and pasted onto the inner side of the dissolution beaker using double sided adhesive tape.[19] Dissolution medium maintained at 37 ± 1°C was poured into the beaker and provided with a stirring rate of 50 rpm. During the study, temperature of dissolution medium was maintained at 37 ± 1°C. Electrolab TDC 50 was used to carry out dissolution experiments. The samples were withdrawn at predetermined time intervals and analyzed using double beam UV spectrophotometer (UV 1800 Shimadzu, Japan) at λ_{max} 310 nm.

Ex vivo drug permeation studies

Drug permeation studies were carried out using porcine cheek pouch as permeation barrier on a standard two chambered Franz diffusion cell[19] to determine the rate and extent of mucosal permeation of ondansetron. The water jacket was maintained at 37 ± 1°C. The receptor compartment was filled with PBS (pH 6.8). Film of size 1 × 1 cm^2 was cut and weighed. The film was mounted in donor compartment which was filled with 7 ml of dissolution medium. The dissolution media was stirred at 50 rpm making use of a magnetic bead. Samples were withdrawn at predetermined time intervals from the receptor compartment, suitably diluted, and analyzed using UV spectrophotometer at λ_{max} 310 nm against a blank (UV 1800, Shimadzu, Japan).

Scanning electron microscopy

Selected films (F13, F6, and F9) were taken for SEM studies. All the films selected had 150 mg of drug loading. Films were fixed in place by means of a double sided silver electrical tape and gold coated in SCD005 Baltek Sputter Coater in neutral environment of argon maintained at a low pressure. SEM images were obtained using a Jeol 457V, Japan at intensity of 15 kV.

RESULTS AND DISCUSSION

The main purpose of the study was to develop and evaluate new buccal films comprising a drug containing mucoadhesive polymeric blend consisting of HPMC E5, HPMC K 100, and Eudragit® NE 30 D. The physicomechanical evaluation [Table 3] of the film indicates that the thickness of films varied from 0.19 ± 0.015 to 1.30 ± 0.044 mm. The film F1 was thinnest and film F10 was thickest. Presence of Eudragit® NE 30 D in the film increased the thickness of film considerably. The drug content in all the formulations varied between 93 and 99%. This indicates a uniform distribution of drug throughout the polymeric film [Table 3].

Highest folding endurance was shown by film F13 (372 ± 12) and the lowest was found to be for film F12 (162 ± 12).[20] All the films formed were flexible and showed good tensile strength [Table 3]. Film F1 and F2 showed a folding endurance of 182 ± 10 and 162 ± 12, respectively. Keeping the polymer concentration constant, an increase in drug concentration in the HPMC film increased folding endurance to 276 ± 21, 347 ± 21, and 372 ± 12 in films F11, F12, and F13, respectively. This increase in folding endurance value indicates that the incorporation of drug provided mechanical strength to the film and also provided plasticizing effect to the film. HPMC alone as a film former is known to form brittle films.[20] There have been studies where ingredients added to the film have shown to act as plasticizer in the film. In studies carried out by Llabot *et al.*,[21] it was found that the addition of ascorbyl palmitate to nystatin film increased plasticization in films.

The swelling and hydration studies showed that the percent hydration varied from 48 to 74 between films F9 to F2, respectively [Table 3, Figure 1]. In most of the films the hydration was found to be proportional to the content of the hydrophilic polymer. Presence of hydrophilic drug increased the hydration (Film F12). This could be explained on the basis that an increase in drug content increased hydration due to hydrophilic nature of drug. The salt form of drug imbibes more amount of water and that too quickly. This imbibed water is retained by polymer which swells. Similar results have been reported with drug loaded films of chitosan.[22] Further increase in drug content in film (F13), decreased hydration. It was also observed that Eudragit® NE 30 D had a significant influence on hydration. As the concentration of Eudragit® NE 30 D in the film (F9) was increased, the hydration was decreased to 48. Drug loading was not found to have a significant effect on matrix erosion. The surface pH of the films varied from 6.8-7.2.

In the current study, placebo films F1 and F2 prepared using HPMC blends (mucoadhesive polymers), showed mucoadhesive

Table 3: Mucoadhesive time/retention time of the films and the mucoadhesive strength of the different films

Formulation code	Drug content (%)	*In vivo* mucoadhesion (min)	*Ex vivo* mucoadhesion time (min)	Mucoadhesive strength (g)	Folding endurance	Film thickness (mm)	Percent hydration
F1	-	76.6±7	93±7	94.214±2.34	182±10	0.19±0.015	64±4.5
F2	-	140±8	122±7	140.221±3.21	162±12	0.22±0.022	74±3.4
F3	98.34±1.61	-	184±5	94.213±3.54	252±12	0.41±0.067	60±2.2
F4	97.82±2.02	-	243±8	92.781±3.88	245±8	0.69±0.032	58±3.1
F5	95.42±2.65	-	300±9	245.221±2.98	255±8	0.86±0.025	65±2.8
F6	97.23±1.53	-	291±7	252.221±4.12	242±11	0.80±0.034	62±3.4
F7	95.82±1.30	-	353±8	225.043±3.12	239±8	0.92±0.056	60±2.4
F8	92.92±1.25	-	378±9	122.940±1.45	220±11	1.12±0.055	55±2.0
F9	95.31±1.75	-	447±14	101.55±2.56	190±13	1.23±0.034	48±3.6
F10	93.86±1.93	-	452±12	131.54±1.98	185±9	1.30±0.044	52±2.2
F11	95.68±2.12	-	103.3±7	137.68±2.56	276±21	0.40±0.037	68±4.6
F12	96.23±1.98	-	115±5	216.41±1.78	347±21	0.41±0.025	82±3.2
F13	97.53±1.66	-	120±8	343.10±2.12	372±12	0.39±0.005	73±3.0
F5[a]	-	170±20	-	-	-	-	-
F8[a]	-	240±8	-	-	-	-	-

[a]Denotes placebo films

strength of 94.214 and 140.221 g, respectively. The mucoadhesive strength was found to increase with an increase in HPMC content [Table 3]. These results were in agreement with results obtained by Goudanavar *et al.*[23] Films with a higher HPMC content forms a stronger bond between polymer and mucin than corresponding film with lower HPMC content. Similar results have been reported by Kumar and Shivakumar,[24] wherein the mucoadhesion strength of terbutaline loaded films were found to increase with an increase in HPMC content.

In the case of drug loaded HPMC films (F11, F12, and F13), mucoadhesive strength was found to increase with an increase in drug concentration. Film prepared using HPMC blend and loaded with highest concentration of the drug (150 mg in F13), showed mucoadhesive strength of 354.35 g [Table 3]. Further, it was also observed that an increase in concentration of hydrophobic polymer (Eudragit® NE 30 D) in the film enhance the mucoadhesion time/retention time. Presence of hydrophobic polymer in films decreases rate of solubilization of film matrix and retention time increases. As the concentration of Eudragit® NE 30 D was increased from film F3 to F4 and then F8 to F9, the mucoadhesion time increased from 184 to 243 min and from 378 to 447 min, respectively [Table 3].

In vivo mucoadhesion time was determined making use of placebo films. All the films were found to be nonirritating. It was found that film F1 prepared using HPMC blend showed a mucoadhesion time of 76.6 ± 7.6 min. As the content of HPMC was increased in the film F2, mucoadhesion time was found to increase to 140 ± 8 min. Presence of Eudragit® NE 30 D in the film (F5*) increased mucoadhesion time to 170 ± 20 min [Table 3]. Increase in concentration of Eudragit® NE 30 D in the film (F8*) enhanced the mucoadhesion time to 240 ± 8.

The *in vitro* drug profile indicated release of ~30-38% of drug (loading dose) within the first 10 min from prepared buccal films. This initial drug release could be from surface of the film.

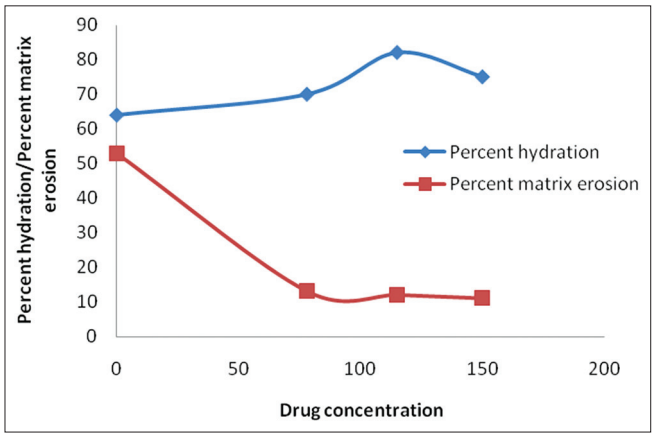

Figure 1: Effect of drug content on percentage hydration and percentage erosion of formulated films (t = 120 min). The data represents the mean of three determinations

Further, release from buccal film varied with respect to polymer concentration and type. An increase in drug release from buccal films was observed with an increase in concentration of polymers that are hydrophilic in nature. HPMC film (F13) released the entire drug in first 120 min. On the other hand, as concentration of Eudragit® NE 30 D in films was increased, the drug release was found to be retarded. As the penetration of dissolution medium into film matrix is limited upon addition of hydrophobic polymer into the matrix, drug release from the film is retarded. These findings are similar to the data reported by others.[25,26]

Film F8 releases nearly 30% of drug in first 10 min. This was followed by a slower release and 65% drug release was observed in 180 min (3 h). Over a period of 360 min, drug release was shown to be minimal in film F9 amounting to 72%. Film F8 showed a drug release of 82% in 360 min [Figure 2].

The drug release behavior from prepared films was fitted into suitable mathematic model to predict and correlate drug release behavior. The *in vitro* release data from buccal films was evaluated using mathematic models including zero order, first order, Higuchi, and Korsmeyer-Peppas model equation.

Zero order kinetic equation

$F = K_o t$, where F represents the fraction of drug released in time t, and K_o is the zero order release constant.

First order kinetics equation

$\ln (1- F) = -K_1 t$, where F represents the fraction of drug released in time t, and K_1 is the first order release constant.

Higuchi equation

$F = K_H t^{1/2}$, where F represents the fraction of drug released in time t, and K_H is the Higuchi dissolution constant.

Korsmeyer-Peppas equation

$F = K_p t^n$, where F represents the fraction of drug released in time t, K_p is the Korsmeyer-Peppas release rate constant, and n is the diffusion exponent.

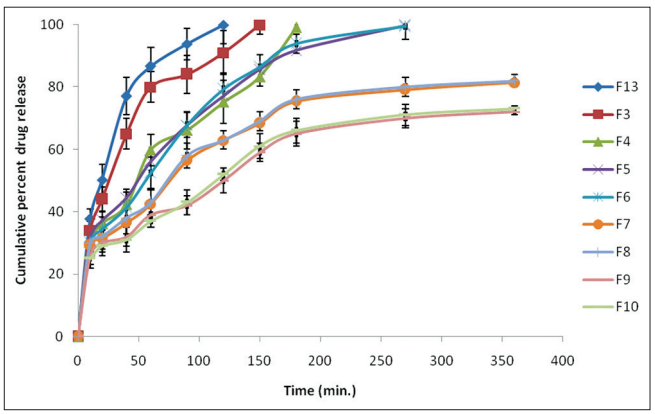

Figure 2: *In vitro* drug release of different films. The data represents mean ± SD (standard deviation) of six determinations

Table 4 illustrates the result of curve fitting drug release into above mathematical drug release kinetic equations. When the drug release rate and correlation coefficients were compared, drug release was found to follow first order release kinetics (R^2 = 0.982-0.995).

The *ex vivo* permeation of ondansetron from the film showed that the drug permeated well across porcine buccal mucosa over a period of 360 min. The *ex vivo* permeation from F13 was found to be 98 ± 3.2% in 180 min. In case of formulation F8, nearly 53% drug permeated in 120 min and drug release was complete in 360 min. Film F9 showed minimum ex *vivo* drug permeation in 360 min [Figure 3].

All films selected for SEM had a constant amount of drug loading. F13 was a HPMC blend film. A comparison of the films clearly shows that films containing Eudragit® NE 30 D had drug in a more crystalline nature as against the film F13 [Figure 4a]. Presence of crystalline drug in films is associated with formation of brittle films.[21] These results can be correlated with folding endurance value which clearly shows that film F13 has a higher folding endurance as compared to films F6 and F9 [Figure 4b and c].

DISCUSSION/CONCLUSIONS

Oral buccoadhesive adhesive films of ondansetron hydrochloride prepared using HPMC E5, HPMC K100, and Eudragit® NE 30 D were found to be nonirritant with good mucoadhesion, uniform drug distribution, neutral surface pH, and desirable mechanical strength. These films could be effectively used to provide faster onset of action, increased bioavailability, and a prolonged drug release for ondansetron. The sustained release that films provide can provide support for delayed emesis. Further, drug release rate from the films can be regulated by increasing either the content of hydrophilic or hydrophobic polymer within

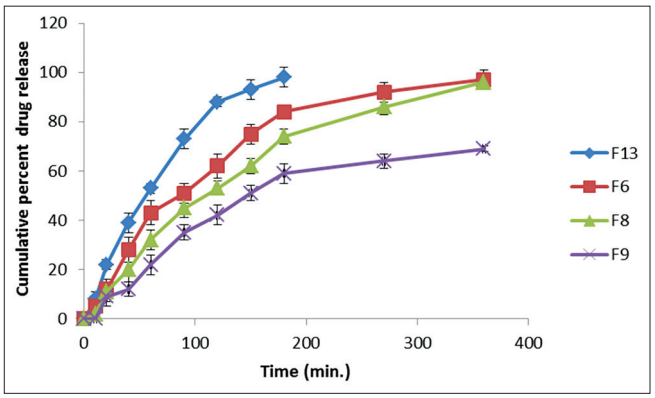

Figure 3: *Ex vivo* drug permeation profile of films F13, F6, F8, and F9 containing ondansetron. The data represents the mean ± SD of six determinations

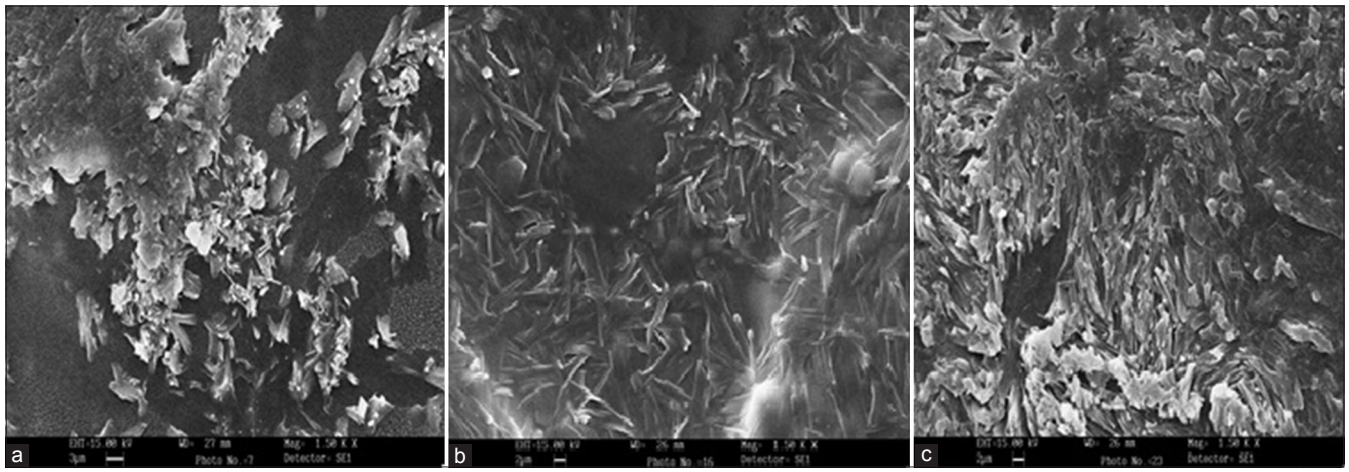

Figure 4: Scanning electron microscope images of prepared films at different magnification (×1500 magnification). (a) film F13, (b) film F6, and (c) film F9

Table 4: Results of curve fitting of the *in vitro* ondansetron HCL release from buccal films

Formulation code	Zero order		First order		Higuchi		Korsmeyer-Peppas		
	K_o	R^2	K_1	R^2	K_H	R^2	K_P	n	R^2
F3	0.560	0.806	0.036	0.990	7.178	0.9589	91.765	0.404	0.977
F4	0.450	0.904	0.035	0.995	6.461	0.9769	91.182	0.407	0.968
F5	0.328	0.834	0.023	0.984	5.467	0.9776	93.981	0.378	0.982
F6	0.341	0.842	0.026	0.985	5.955	0.9687	92.862	0.409	0.967
F7	0.193	0.754	0.036	0.994	3.821	0.9618	93.654	0.345	0.949
F8	0.193	0.749	0.039	0.982	3.806	0.9427	92.452	0.328	0.955
F9	0.169	0.787	0.026	0.992	3.290	0.9577	93.526	0.316	0.949
F10	0.175	0.793	0.029	0.988	3.479	0.9525	94.234	0.338	0.948
F13	0.723	0.781	0.031	0.991	8.142	0.9383	95.234	0.406	0.966

HCL: Hydrochloride

the film matrix. Film F8 prepared using a blend of HPMC E5, HPMC K100, and Eudragit® NE 30 D in concentration of 2:1:1.5, loaded with 2 mg of ondansetron per cm^2 could be used for treatment of chemotherapy-induced emesis.

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