Research Article

Formulation and Characterization of Bilayered Mucoadhesive Buccal Patch

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ABSTRACT

Drug delivery through buccal mucosa offers a novel route of controlled drug delivery by mucoadhesivity using mucoadhesive polymer specially natural polymers. Mucoadhesive patch allows maximum drug to reach systemic circulation without first pass effect. In this study, buccal patch comprises of bi-layers i.e., fast releasing layer made of pectin and sustained releasing layer made in combination with pectin & guar gum. The layers were made by solvent casting method. Different concentrations of pectin in fast as well as sustained release layer, and guar gum in sustained release layer, and drug with different excipients were tried in formulations and evaluated. Incorporation of β-cyclodextrin enhanced the drug permeation through buccal mucosa. FT-IR and DSC methods revealed that there is no interaction between Ondansetron Hcl and polymers. The patches were evaluated for weight variation, thickness, drug content uniformity, folding endurance, surface pH, mucoadhesivity, residence time, and in vitro drug release study. Optimized patch (F6) showed satisfactory results in all evaluation parameters as compared to rest of the batches. Data of *in-vitro* release from patches were fit in to different equations and kinetic models to explain release kinetics. The models used were zero and first-order, Hixon-Crowell, Higuchi and Korsemeyer-Peppas models equation. The optimized patch demonstrated well *in-vitro* results with matrix release in immediate as well as sustained release layer. Thus no mucosal irritation is expected.

Keywords: Bilayered buccal patch, first pass effect, immediate release, mucoadhesivity, sustained release

Received 03 July 2014 Received in revised form 30 Sept 2014 Accepted 07 Oct 2014

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INTRODUCTION

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike [1]. When the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion [2]. The buccal route has been preferred due to avoidance of first pass metabolism and possibility of being accessible for controlled and sustained drug release [3]. The effectiveness of a mucoadhesive formulation is greatly determined by the nature of the polymers used [4]. The mucoadhesive ability of a dosage form is dependent upon a variety of factors, including the nature of the mucosal tissue and the physicochemical properties of the polymeric formulation. Polymers usually diffuse into the mucosal layer and thereafter adhere to the layer by forming intermolecular entanglements [5]. Mucoadhesive dosage forms may be designed to enable prolonged retention at the site of application, providing a controlled rate of drug release for improved therapeutic outcome. The research has been focused on targeting a drug or drug delivery system in a particular region of the body for extended period of time not only for local targeting of drugs, but also for the better control of systemic drug delivery [6]. Drug

delivery via buccal mucosa by using bio-adhesive polymers, offers such a novel route of drug administration. It provides direct entry of drug molecules into systemic circulation, thus avoiding hepatic firstpass effect. The ease of administration and ability to terminate drug delivery when required makes it a potential and attractive route of drug delivery [7].

Ondansetron Hcl is the class of antiemetic drugs developed to control cancer chemotherapy induced vomiting and later found to be highly effective in postoperative nausea and vomiting as well. Ondansetron Hcl blocks ematogenic impulses both at their peripheral origin and their central relay. It does not block the dopamine receptors and apomorphine or motion sickness induced vomiting. A weak gastrokinetic action due to 5-HT_3 blockade has been detected. A minor 5-HT_4antagonist has also been shown [8]. Ondansetron selectively blocks 5-HT_3 receptor probably both in the (1) periphery (that is 5-HT_3 receptors of vagal-splanchic nerves which are stimulated by serotonin released as a result of chemotherapy use in the GI mucosa) as well as (2) in the centre nucleus tractus solitarius and chemo receptor trigger zone. Used in against anticancer chemo therapy induced vomiting. It can also be used in postoperative nausea and vomiting. Headache is a common complaint [9].

Design of patch is divided into two types: (1) The buccal patch designed in a matrix configuration contains drug, adhesive, and additives mixed together. (2) The buccal patch designed in a reservoir system contains a cavity for the drug and additives separate from the adhesive. An impermeable backing is applied to control the direction of drug delivery; to reduce patch deformation and disintegration while in the mouth; and to prevent drug loss [10].

MATERIALS: Ondansetron Hydro-chloride was s Gift sample (Alkem laboratories, Mumbai), Guar gum was obtained from Loba Chemie (Mumbai), Pectin was obtained from Himedia Laboratories (Mumbai), Aspartame was obtained from Fisher Scientific (Mumbai), Vanillin was obtained from Loba Chemie (Mumbai), β-Cyclodextrin was obtained from Fisher Scientific (Mumbai). All the reagents and solvents used were of analytical grade.

Instruments used: UV-spectrophoto-meter (Shimadzu), Franz Diffusion Cell, FTIR (Shimadzu), Magnetic Stirrer, Oven, pH meter, Sonicator and Dessicator were the instruments used for this study.

METHODS:

Drug-Polymer Compatibility: Drug-polymer interaction was observed by IR spectrophotometry and DSC. An FTIR study of pure Ondansetron Hcl, and mixture of Ondansetron Hcl - polymers were performed by KBr dispersion method and DSC study of pure Ondansetron Hcl and mixture of Ondansetron Hcl - polymers were performed by using Mettler thermal analyzer.

Preparation of calibaration curve of drug: Stock solution of Ondansetron hydrochloride drug was prepared by dissolving 2 mg of drug in 20 ml salivary fluid to give 100 µg/ml solution. From this solution, 4 ml was pipette out and diluted up to 40 ml with salivary fluid to give 10 µg/ml. From this stock solution, aliquots of 2 ml, 4 ml, 6 ml, 8 ml, and 10 ml were made. Volumes were made up to 10 ml with salivary fluid from 2 to 8 ml aliquot whereas up to 20 ml volume was made for 10 ml aliquot to give 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, 10 µg/ml. Absorbances of final conc. solutions were taken at 309.80 nm against the blank. Graph of absorbance Vs concentration was plotted.

Formulation of bilayered mucoadhesive buccal patch [11-13]**:** Bilayered patches were formulated by the combination of two layers i.e. first layer was sustained release layer and second layer was immediate release layer using solvent casting method. For first layer: aqueous solution was made

by dissolving polymers (i.e. guar gum and pectin) in different concentration in required volume of water with stirring to produce a clear solution. To this solution, pure drug, sweetener, flavor, plasticizer were added and stirred to get clear solution. The solution was kept aside for 1 hr. to remove all the air bubbles. Then this solution was casted on 7 cm diameter mould contained in petri dish and dried in oven at 45^{0}C for 24 hrs.

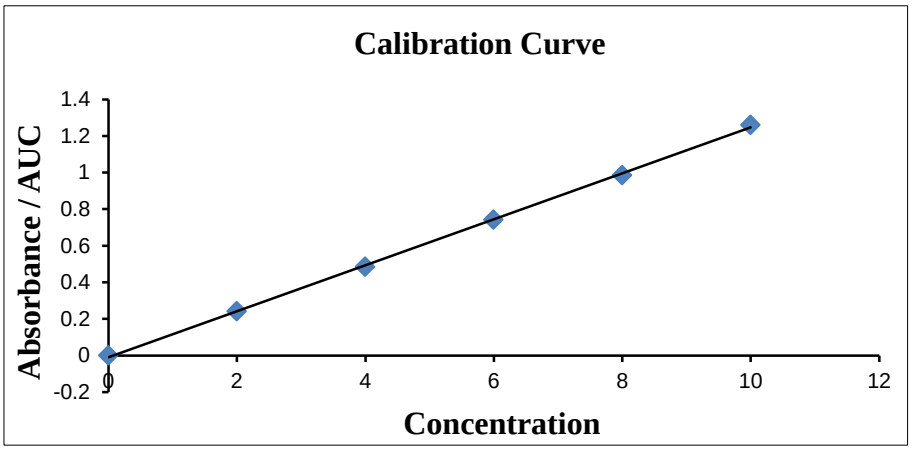

Figure 1: Calibaration curve of Ondansetron Hcl

For second layer: aqueous solution was made by polymer (i.e. pectin) in required volume of water with stirring to produce a clear solution. To this solution, pure drug, sweetener, flavor, plasticizer were added and stirred to get clear solution. This solution was kept aside for 1 hr. to remove air bubbles. Then this solution was poured over previously dried first layer and dried in oven at 45^{0}C for 24 hrs.

The bilayered buccal patch was carefully removed from petridish and checked for any imperfection and cut according to size (rectangle film 1 cm in length and 2 cm in width) so that each patch contained 4 mg of the drug. The samples were stored in vacuumed desicator.

Evaluation of bilayered mucoadhesive buccal patch [14-17]**:** Formulated patches were subjected to the evaluation tests:

Weight uniformity of patch: For weight uniformity determination, 2 × 1 cm^2 film was cut at three places. The weights of each three part of patches were taken using digital balance and the average weight was calculated.

Table 1: Formulation of bilayered buccal patch (F1-F4)

Formulation code	F1		F2		F3		F4	
	IL	SL	IL	SL	IL	SL	IL	SL
Drug (mg)	90	110	90	110	90	110	90	110
Guar gum (mg)	-	400	-	250	-	250	-	200
Pectin (mg)	200	-	150	-	150	150	100	100
Glycerine (ml)	0.48	0.48	0.48	0.48	0.48	0.48	0.24	0.48
Vanillin (mg)	1	1	1	1	1	1	1	1
Aspartame (mg)	1	1	1	1	1	1	1	1
β-CD (mg)	30	-	30	-	30	-	30	-
Water (ml)	10	20	10	20	10	20	10	20

IL- Immediate layer; SL- Sustained layer

Table 2: Formulation of bilayered buccal patch (F5-F8)

Formulation code	F5		F6		F7		F8	
	IL	SL	IL	SL	IL	SL	IL	SL
Drug (mg)	90	110	90	110	90	110	90	110
Guar gum (mg)	-	150	-	150	-	100	-	80
Pectin (mg)	100	-	100	70	70	70	50	60
Glycerine (ml)	0.24	0.48	0.24	0.48	0.24	0.48	0.24	0.48
Vanillin (mg)	1	1	1	1	1	1	1	1
Aspartame (mg)	1	1	1	1	1	1	1	1
β-CD (mg)	30	-	30	-	30	-	30	-
Water (ml)	7	15	7	15	7	15	7	15

IL- Immediate layer; SL- Sustained layer

Thickness of patch: Thickness of the films was measured using digital vernier caliper. The thickness was measured at three different sites of the films and average was taken.

Folding endurance of patch: The flexibility of patches can be measured quantitatively in terms of folding endurance. Folding endurance of the patch was determined by repeatedly folding patch at the same place till it was broken. The number of times patch could be folded at the same place without breaking gave the value of folding endurance.

Tensile strength of patch: Patch strip with dimensions of 10 x 20 mm and without any visual defects are cut and positioned between two clamps separated by a distance of 3 cm. Clamps are designed to secure the patch without crushing it during test, the lower clamp held stationary and strips are pulled apart by upper clamp moving at a rate of 2 mm/sec until the strip breaks. The force of patch at the point when the strip break is recorded. The tensile strength at break values is calculated using the formula.

Tensile strength = Force at breakage (kg) / Strip thickness × Strip width (1 + ΔL/L)

Where,

ΔL = elongation of patch at break point.

L = length of the patch.

Percent Elongation of patch: When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

Percent elongation = Increase in length of strip (mm) × 100 / Initial length of strip (mm) × cross sectional area (mm^2)

Ex-vivo Mucoadhesive strength of patch: Mucoadhesive strength of the patch was measured on a modified physical balance. The fresh goat buccal mucosa was cut in to pieces and washed with phosphate buffer (pH 6.8). A piece of buccal mucosa was tied to the open mouth of a glass vial, which was filled completely with phosphate buffer (pH 6.8). The glass vial was placed and tightly fitted in the centre of glass beaker. The phosphate buffer (pH 6.8, $37^o \pm 10^oC$) was filled in the glass beaker just touching the mucosal surface. The patch was stuck to the lower side of rubber stopper with cyanoacrylate adhesive. Two pans of the balance were balanced with 5 gm weight on the right hand side pan. A weight of 5 gm was removed from the right hand side pan, which lowered the pan along with the patch over the mucosa. The balance was kept in this position for 5 min. contact time. The water (equivalent to weight)

was added slowly with infusion set (100 drops/min.) to the right-hand side pan until the patch detached from the mucosal surface. The weight in grams required to detach the patch from the mucosal surfaces gave the measure of mucoadhesive strength.

Water absorption capacity test of patch: Patches are allowed to swell on the surface of agar plates prepared in simulated saliva (2.38 g Na_2HPO_4, 0.19 g KH_2PO_4, and 8 g NaCl per liter of distilled water adjusted with phosphoric acid to pH 6.8), and kept in an incubator maintained at 37°C ± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hours), samples are weighed (wet weight) and then left to dry for 7 days in a desicator over anhydrous calcium chloride at room temperature till constant weight is recorded. Water uptake (%) is calculated using the following equation:

$$\text{Water uptake (\%)} = (Ww - Wf) / Wf \times 100$$

Where, Ww is the wet weight and Wf is the final weight.

Characterization of Drug Release of patch: *In-vitro* drug release studies were carried out by attaching buccal mucosa to one end of the Franz diffusion cell which acted as donor compartment. The buccal patch containing drug was placed inside donor compartment which is agitated continuously using magnetic stirrer and then temperature was maintained at 37 ± 1ºC. The receptor compartment consisted of 100 ml of phosphate buffer (pH 6.8). 1 ml of sample was withdrawn at periodic intervals from receptor compartment and replaced with fresh phosphate buffer (pH 6.8) immediately. The absorbance of samples was analyzed spectrophotometrically at 309.8 nm. The percent drug release was then analyzed and the release kinetics was also determined by various release kinetic models with the value of n (diffusion coefficient) for each batches.

Organoleptic test of patch: Formulated patches were tested for colour, odour, shape and size.

Swelling study of patch: Buccal patches were weighed individually (W1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1-hour time intervals until 3 hours, patches were removed from gel plates and excess surface water is removed carefully using filter paper. The swollen patches were then reweighed (W2) and swelling index (SI) is calculated using the following formula.

$$S1 = (W2-W1) / W1 \times 100$$

Surface pH of patch: Surface pH of the films was determined by bringing a combined glass electrode or pH paper near the surface of patch previously wetted with 1ml distilled water for 2 hrs and allowing equilibration for 1 min.

Drug content uniformity study of patch: The patches were tested for drug content uniformity by UV-Spectrophotometric method. Three randomly selected patches from each batch were taken. Each patch was placed in 50 ml volumetric flask and dissolved in phosphate buffer (pH 6.8) and 1.25 ml was taken and diluted with phosphate buffer (pH 6.8) up to 10 ml. The absorbance of the solution was measured at 308.9 nm using UV spectrophotometer. The concentration of Ondansetron Hcl was calculated.

Percentage moisture loss of patch: Percentage moisture loss was carried to check the integrity of patches at dry condition. Three 1 × 2 cm^2 diameter patches were weighed accurately and kept in desicator containing fused anhydrous calcium chloride. After 3 days the patches were removed, weighed. Average percentage moisture loss of three patches was calculated.

$$\text{\% Moisture loss} = \frac{\text{Final weight - Initial weight}}{\text{Final weight}} \times 100$$

Ex-vivo residence time of patch: The ex vivo mucoadhesion time was studied (n = 3) after application of patches on freshly cut goat buccal mucosa which

was fixed on the inner side of a beaker, about 2.5 cm from bottom, with cyanoacrylate glue. One side of each patch was wetted with 1 drop of phosphate buffer (pH 6.8) and pasted to the goat buccal mucosa by applying a light force with a fingertip for 30 seconds. The beaker was filled with 200 ml of phosphate buffer (pH 6.8) and is kept at 37°C ± 1. After 2 minutes, at 50-rpm stirring rate was applied to simulate the buccal cavity environment, and patch adhesion was monitored. Time requires for the patch to detach from goat buccal mucosa was recorded as the mucoadhesion time.

Stability studies: The formulated buccal patches were wrapped in aluminum foil and stored at 2 – 8 ± 0.5 ºC and 40 ± 0.5ºC for period of one month for stability studies. After an interval of 7, 15, and 30 days the patches were tested for physical appearance, weight uniformity, thickness, drug content and drug release.

RESULTS AND DISCUSSION:

Drug Estimation: Calibration curves of Ondansetron Hcl in phosphate buffer (pH 6.8) solutions were constructed at λmax 309.8 nm with a UV-VIS spectrometer (Shimadzu, Japan). Beer's law obeyed to construct the calibration curve was in the concentration range of 2 – 10 µg/ml. Analysis was done in triplicate.

Drug-Polymer Compatibility: IR spectra and DSC of Ondansetron Hcl alone and its combination with polymers are shown in (**Fig. 2, 3 and 4**). An IR spectrum of pure Ondansetron Hcl shows the peaks 2980.02 cm^{-1}, 2131.34 cm^{-1}, 1842.02 cm^{-1}, 1409 cm^{-1} and 923 cm^{-1} in (**Fig. 2**). These peaks can be considered as characteristic peaks of Ondansetron Hcl and were not affected and prominently observed in IR spectra of Ondansetron Hcl along with polymers as shown in the (**Fig. 3 and 4**), which indicated that there was no interaction between Ondansetron Hcl and polymers. DSC spectrum of pure Ondansetron Hcl shows the characteristic peaks at 189.25^{0}C in (**Fig 5**). These peaks can be considered as characteristic peaks of Ondansetron Hcl and were not affected and prominently observed in DSC spectra of Ondansetron Hcl along with polymers at 95.93^{0}C as shown in the (**Fig. 6**), which indicated that there was no interaction between Ondansetron Hcl and polymers. The shortening of peak was due to the dissolution state of pectin.

Evaluation of Patches:

Weight variation: Drug loaded patches (1 × 2 cm^2) were tested for uniformity of weight. The patches were found uniform. All the prepared patches using different concentration of guar gum and pectin were weighed between 54.21 ± 1.11 to 134.03 ± 2.13 mg.

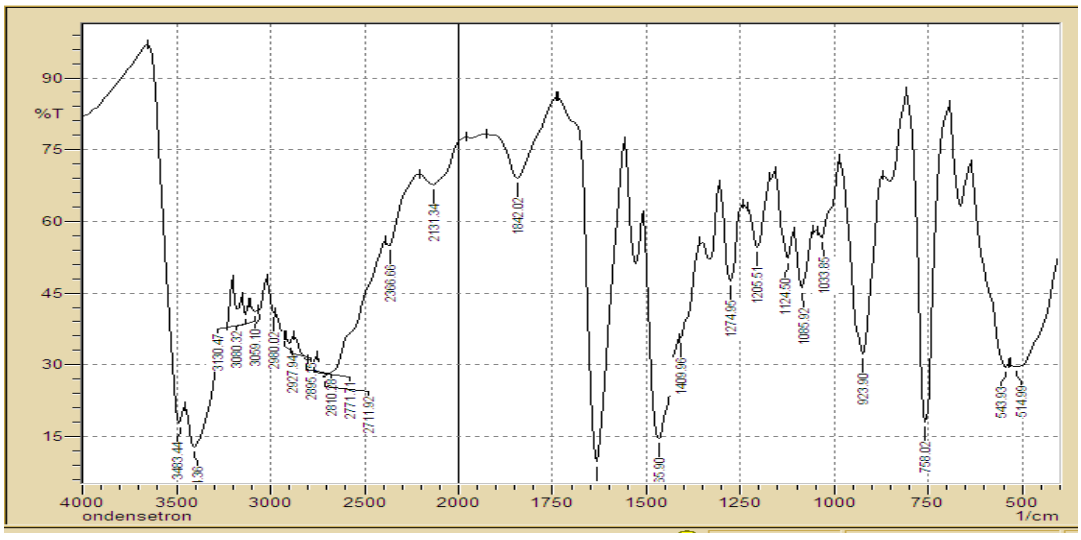

Figure 2: FT-IR of Ondansetron Hcl

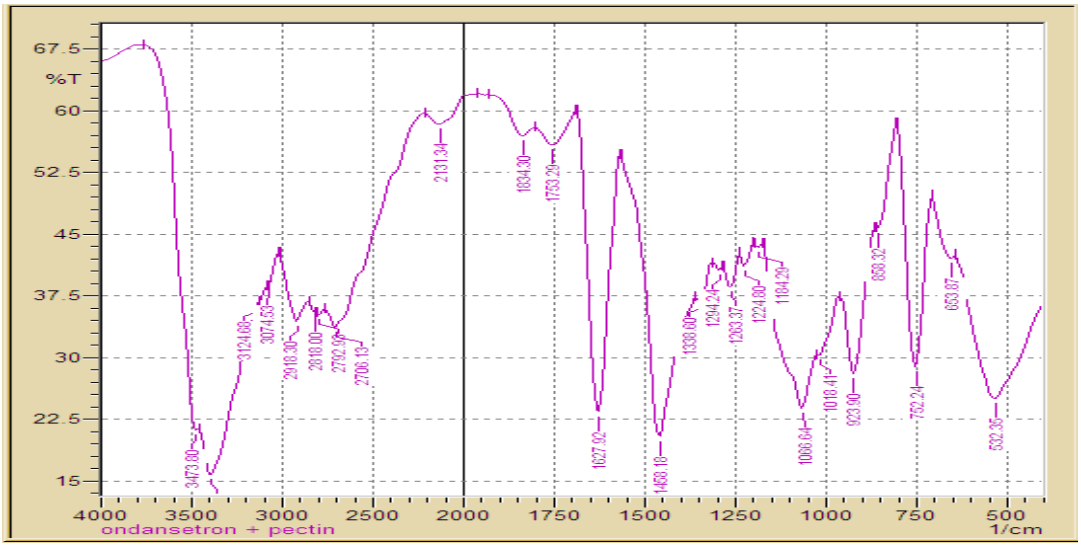

Figure 3: FTIR Spectrum of drug-pectin

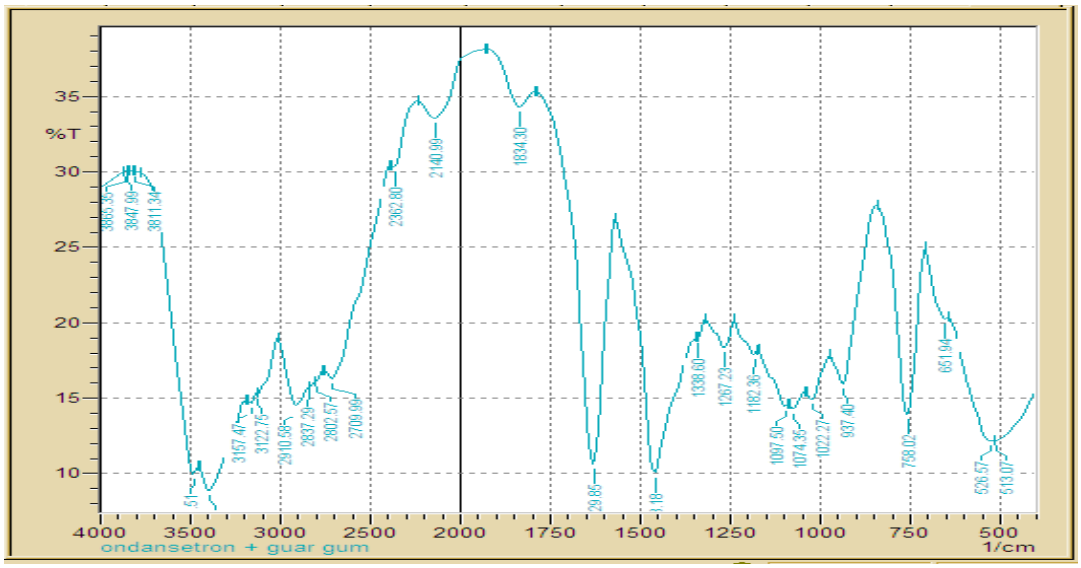

Figure 4: FTIR Spectrum of drug-guar gum

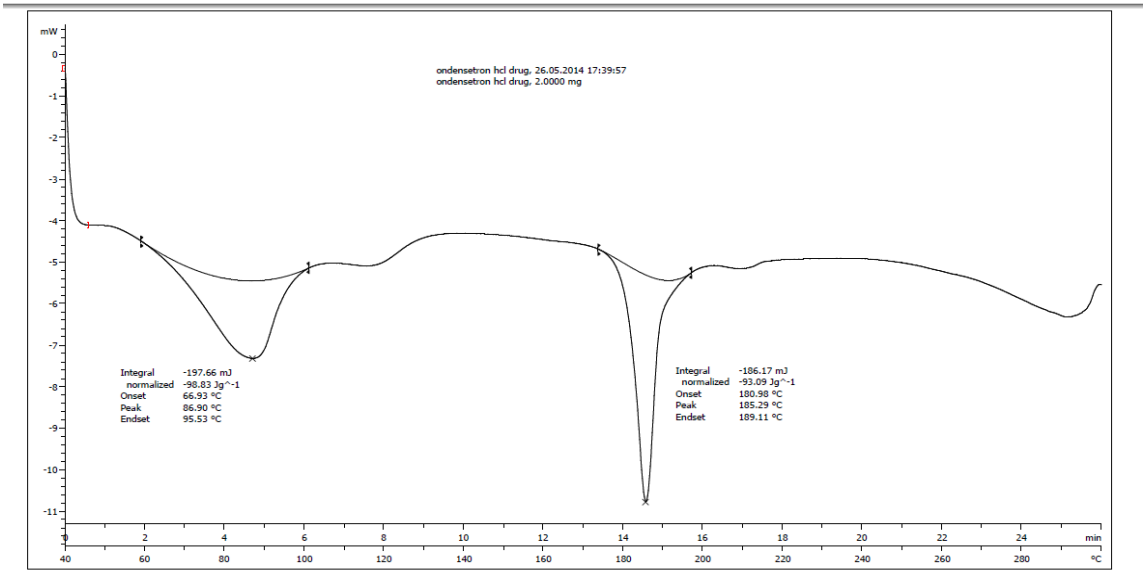

Figure 5: DSC Thermogram of Ondansetron Hcl

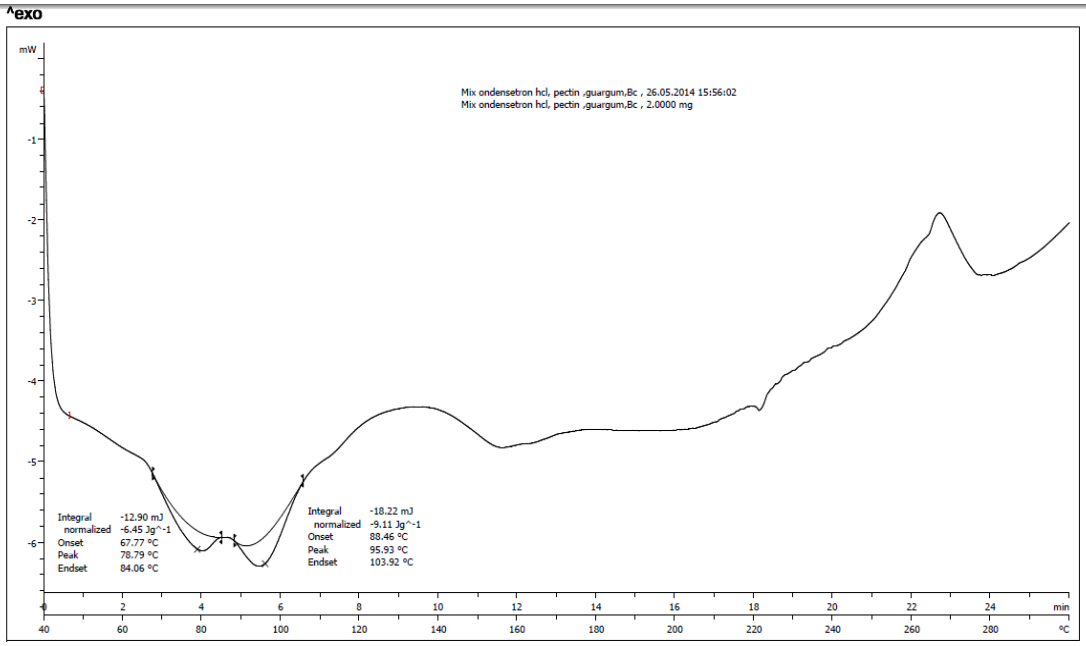

Figure 6: DSC thermogram of Drug-Pectin-Guar gum-β-CD

Thickness: All the patches have uniform thickness throughout. The patches showed thickness values in between 0.32 ± 0.03 to 0.56 ± 0.03 mm.

Swelling index: The swelling of the patches were observed in phosphate buffer solution (pH 6.8). Swelling was more pronounced in patch F1 which contains highest concentration of guar gum. Patch F8 showed least swelling (due to least concentration of guar gum). The patches showed swelling index values in between 34.11 ± 1.12 to 62.11 ± 0.85 %.

Surface pH: All the batches of patch were subjected to pH determination. All the batches were in the range of 6.2-7.2. Surface pH of all the patches prepared was ranging in between 6.43 ± 0.11 to 7.21 ± 0.17 pH.

Tensile strength: All prepared batches were subjected to tensile strength and showed good result. Optimized batch has satisfactory tensile strength. This shows that patches are capable to bear stress. The values of tensile strength of all the patches prepared was ranging in between 2.17 ± 0.13 to 4.76 ± 0.15 kg/mm^2.

Percent elongation test: All prepared batches were subjected to percent elongation and showed good result. Optimized batch has satisfactory percent elongation. The values of % elongation test of all the patches prepared was ranging in between 21.22 ± 2.35 to 28.87±2.14 %/mm^2.

Percentage moisture loss (PML): The PML of the patches was observed in phosphate buffer solution (pH 6.8). PML was more pronounced in patch F. Patch F showed least PML. The PML values of all the patches prepared was ranging in between 1.01 ± 0.01 to 2.08 ± 0.02 %.

Folding endurance: Films did not show any cracks even after folding for more than 90 times. Hence it was taken as the end point. Higher the plasticizer higher will be folding endurance. The patches showed folding endurance values in between 93 ± 3 to 99 ± 2.

Mucoadhesive strength: All prepared batches were subjected to mucoadhesive strength and showed good result. Optimized batch has satisfactory mucoadhesive strength. The may be due to fact that positive charges on surface of polymer could give rise to strong electrostatic interaction with mucous or negatively charged mucus membrane. The mucoadhesive strength of all the patches prepared was ranging in between 8.010 ± 0.05 to 10.040 ± 0.07 gm.

Water absorption capacity: The water absorption capacity test of all prepared

patches was ranging in between 10.23 ± 0.61 to 26.73 ± 0.26 %. Higher water absorption is due to the higher concentration of guar gum. So F1 shows highest water absorption and F8 shows the least.

Drug content uniformity: The patches were subjected to drug content uniformity study and it is in between 97.34 ± 0.21 to 99.73 ± 0.06 %, which suggested that the drug was uniformly distributed throughout the buccal patch.

In vitro drug release: The in-vitro drug release study was carried out for all the patches (A1 to A8 batches) and release profile were subjected to various kinetic equations like Matrix diffusion equation and Peppas exponential equation. The results showed that F6 mucoadhesive bilayered buccal patch having good mucoadhesive strength, optimum thickness, 99.73% drug content, 98.68% drug release over 12 hrs, having matrix release in both immediate and sustained layer with the value of n = 0.5795 (non-fickian) in immediate layer and n = 0.2908 in sustained layer (fickian), through buccal mucosa without causing any tissue damage. Thus, from above data confirmed the potential of this bilayered buccal patch as a potential/optimized candidate for immediate and sustained buccal delivery.

Table 3: *In vitro* cumulative percentage drug release studies of buccal patch F1 to F8 for immediate release

Time	Formulations							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
15	4.69 ±1.13	6.00 ±2.13	6.60 ±1.87	5.97 ±2.67	4.81 ±1.78	7.16 ±2.67	9.47 ± 3.22	9.55 ±3.77
30	16.19±1.16	19 ±2.87	21.16 ±1.24	20.87 ±2.87	20.08 ±1.48	20.24 ±2.98	22.59 ±2.76	22.25±3.21
45	30.16 ±1.34	34.4 ±1.67	38.21 ±1.98	38.78 ±2.56	38.35 ±2.56	39.40 ±3.57	39.14 ±3.11	38.91±3.51
60	46.94 ±1.78	53.08±1.54	59.91 ±1.33	59.82 ±2.76	59.73 ±2.67	60.85 ±2.87	60.22 ±3.54	60.36±2.76
75	65.41 ±2.12	69.19±1.39	79.97 ±2.76	79.12 ±1.89	79.09 ±2.56	80.91 ±2.39	79.68 ±2.67	80.42±3.98
90	82.01 ±1.67	84.41±2.67	98.42 ±1.09	96.94 ±2.45	96.91 ±2.34	99.60 ±0.09	98.49 ±1.11	98.82±1.01
105	97.20 ±1.62	98.41±1.01						

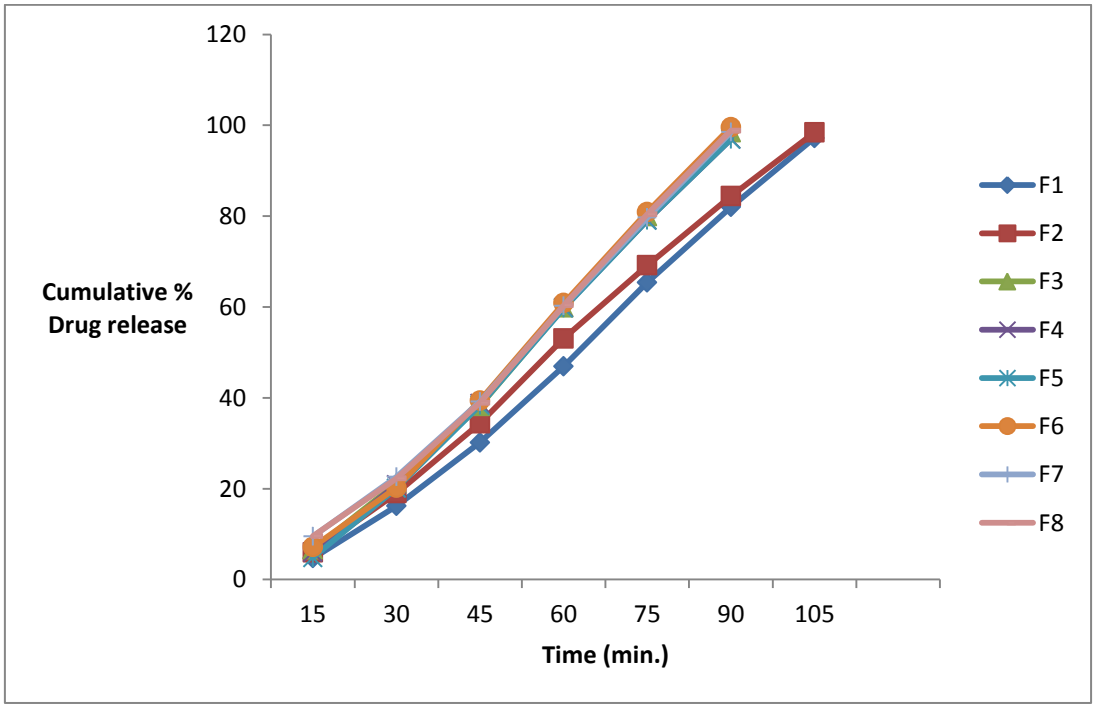

Figure 7: Cumulative percentage drug release studies of buccal patch F1 to F8 for immediate release

Table 4: *In vitro* cumulative percentage drug release studies of buccal patch F1 to F8 for sustained release

Time	Formulations							
	F1	F2	F3	F4	F5	F6	F7	F8
1	3.77± 2.31	4.17±3.24	4.37±2.80	4.81 ± 2.76	5.01±3.72	5.61±2.71	4.57 ±2.77	5.81 ±2.97
2	8.00±2.43	8.59±1.41	9.37±2.21	10.32 ±1.97	10.49±2.31	11.47±2.95	10.57±2.09	12.12 ± 2.66
3	12.90± 2.99	13.35±3.67	15.28 ±3.56	16.32± 3.47	16.97±3.32	17.80±2.61	17.73 ±3.81	20.14 ± 3.75
4	18.14±3.35	18.99±2.94	21.60±2.90	22.92±2.74	23.63±3.90	24.80±3.80	25.74±2.28	29.85±3.91
5	23.64±3.23	25.13±3.25	29.33±1.90	30.46± 1.41	30.74±2.96	32.32±3.53	34.44±3.81	39.46±2.70
6	29.37±2.53	31.93±3.87	38.07±2.96	38.81±2.94	38.44±2.47	40.31±2.36	43.75±2.96	49.97±3.49
7	35.44±1.34	39.17±2.19	46.90±3.23	47.64±3.22	46.72±2.87	48.86±2.89	53.28±2.85	61.87±2.14
8	41.39±1.49	46.80±3.49	56.86±1.45	56.90±3.29	55.62±3.88	57.50±13.83	65.04±3.50	74.00±3.14
9	47.57±2.24	54.63±1.94	66.86±2.38	66.28±3.44	64.58±2.94	66.70±3.13	75.48±3.65	86.90±2.30
10	53.61±2.80	62.66±2.24	77.04±3.77	77.28±2.04	74.58±1.23	76.50±2.10	87.28±2.30	98.17±1.13
11	59.34±2.87	70.76±3.39	87.14±2.97	88.28±1.83	85.28±1.59	87.40±2.56	97.18±2.11	
12	64.96±3.10	78.96±1.17	97.12±3.47	98.43±0.49	96.39±2.76	98.67±0.07		
13	70.50±2.44	86.06±1.19						
14	75.68±3.13	92.06±2.94						
15	80.46±2.77	96.98±2.21						
16	84.84±2.45							
17	88.56±2.83							
18	92.32±3.43							

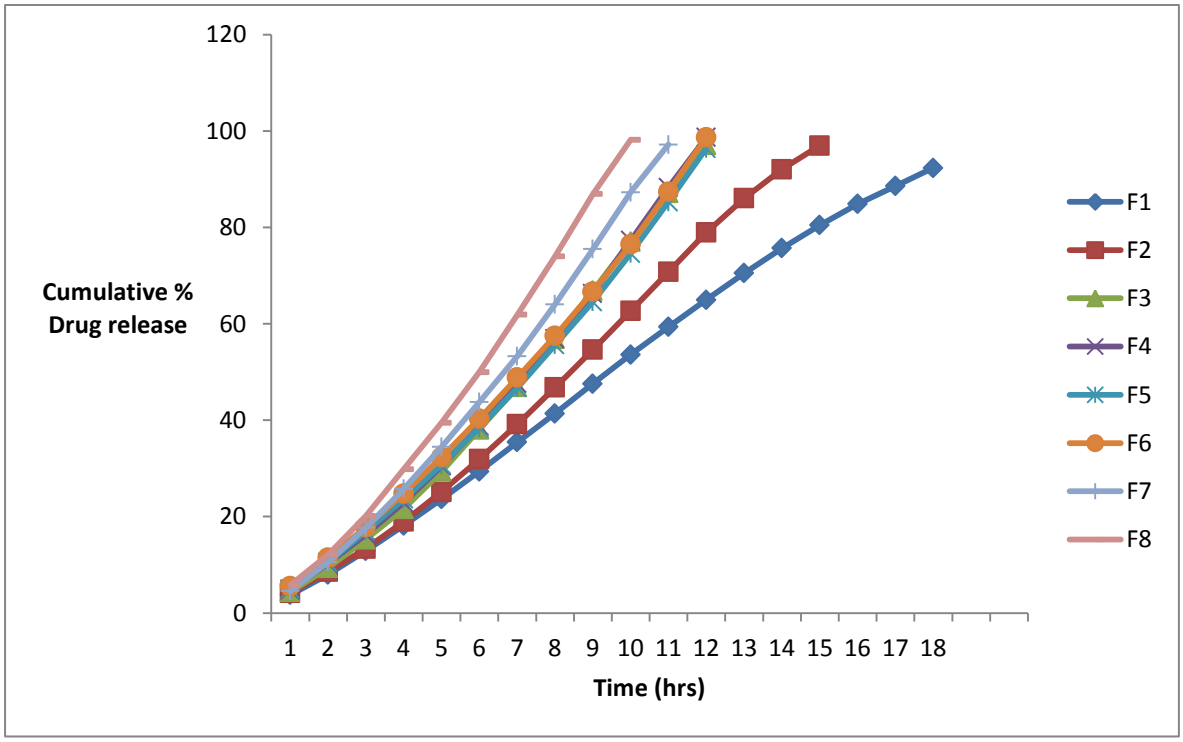

Figure 8: Cumulative percentage drug release studies of buccal patch F1 to F8 for sustained release

Stability studies: The formulated buccal patches were wrapped in aluminum foil and stored at 2 – 8 ± 0.5 ºC and 40 ± 0.5ºC for period of one month for stability studies. After an interval of 7, 15, and 30 days the patches were tested for physical appearance, drug content and drug release. The physical appearance, weight uniformity, thickness, drug content and drug release results suggested that there were no significant changes in the formulations after one month.

Table 5: Physical evaluation of buccal patch (F1-F4)

Sr No	Evaluation parameters	Formulation			
		F1	F2	F3	F4
1	Weight uniformity (mg)	134.03±2.13	118.07±2.17	113.09±1.16	98.17±1.21
2	Thickness (mm)	0.56 ± 0.03	0.48 ± 0.03	0.50 ± 0.02	0.42 ± 0.06
3	Folding endurance	93 ± 3	96 ± 3	95 ± 3	98 ± 1
4	Tensile strength (kg/mm^2)	2.17 ± 0.13	3.46 ± 0.19	4.76 ± 0.15	4.23 ± 0.18
5	Percent Elongation (%mm^{-2})	25.67 ± 1.24	22.35 ± 0.16	28.87 ± 2.14	26.11 ± 2.34
6	Mucoadhesive strength (gm)	8.020 ± 0.05	8.050 ± 0.04	10.040±0.07	8.070 ± 0.06
7	Water absorption capacity test (%)	26.73 ± 0.26	20.19 ±0.77	19.38 ± 0.23	18.61 ± 0.21
8	Physical appearance and surface texture	Smooth & elegant	Smooth & elegant	Smooth & elegant	Smooth & elegant
9	Swelling index (%)	62.11 ± 0.85	54.56 ± 0.55	58.71 ±1.37	49.28 ± 1.02
10	Surface pH	7.21 ± 0.15	6.66 ± 0.12	6.43 ± 0.11	7.21 ± 0.17
11	Drug content uniformity (%)	98.03 ± 0.10	97.83 ± 0.29	98.34 ± 0.13	98.67 ± 0.57
12	PML (%)	1.42 ± 0.05	2.08 ± 0.02	1.21 ± 0.04	1.18 ± 0.03
13	Residence time (hrs.)	18	15	12	12

Table 6: Physical evaluation of buccal patch (F5-F8)

Sr No	Evaluation parameters	Formulation			
		F1	F2	F3	F4
1	Weight uniformity (mg)	76.14 ± 1.19	58.07 ± 1.10	59.16 ± 1.15	54.21 ±1.11
2	Thickness (mm)	0.41 ± 0.04	0.38 ± 0.07	0.35 ± 0.04	0.32 ± 0.03
3	Folding endurance	99 ± 2	98 ± 1	97 ± 2	96 ± 3
4	Tensile strength (kg/mm^2)	3.67 ± 0.21	4.13 ± 0.14	3.83 ± 0.25	3.98 ± 0.17
5	Percent Elongation (%mm^{-2})	21.22 ± 2.35	24.58 ± 2.46	22.65 ± 1.97	23.87 ± 1.67
6	Mucoadhesive strength (gm)	9.060 ± 0.07	9.070 ± 0.04	8.040 ± 0.03	8.170 ± 0.05
7	Water absorption capacity test (%)	16.26 ± 0.73	15.77 ± 0.19	14.21 ±0.38	10.23 ± 0.61
8	Physical appearance and surface texture	Smooth & elegant	Smooth & elegant	Smooth & elegant	Smooth & elegant
9	Swelling index (%)	47.91 ± 1.03	44.81 ± 1.34	39.63 ±1.31	34.11 ± 1.12
10	Surface pH	6.56 ± 0.15	6.92 ± 0.10	7.01 ± 0.17	6.65 ± 0.11
11	Drug content uniformity (%)	99.41 ± 0.08	99.73 ± 0.06	98.56 ± 0.17	97.34 ± 0.21
12	PML (%)	1.31 ± 0.05	1.01 ± 0.01	1.11 ± 0.06	1.27 ± 0.03
13	Residence time (hrs.)	12	12	11	10

Table 7: Stability studies of buccal patch at 2-8^{0}C

Formulation Period (days)	F6			
	0	7	15	30
Physical appearance	No change	No change	No change	No change
Weight uniformity (mg)	58.01 ± 1.10	58.01 ± 1.01	57.91 ± 2.06	57.78 ± 1.08
Thickness (mm)	0.38 ± 0.07	0.38 ± 0.05	0.38 ± 0.08	0.38 ± 0.04
Drug content (%)	99.73 ± 0.06	99.15 ± 0.03	98.97 ± 0.05	98.23 ± 0.06
Drug release (%)	98.68	98.25	98.43	98.71

Table 8: Stability studies of buccal patch at 40^{0}C

Formulation Period (days)	F6			
	0	7	15	30
Physical appearance	No change	No change	No change	No change
Weight uniformity (mg)	58.01 ± 1.10	57.21 ± 2.07	57.56 ± 2.06	57.47 ± 1.04
Thickness (mm)	0.38 ± 0.07	0.38 ± 0.08	0.38 ± 0.03	0.38 ± 0.06
Drug content (%)	99.73 ± 0.06	99.27 ± 0.03	98.75 ± 0.06	98.12 ± 0.08
Drug release (%)	98.68	98.11	98.53	98.29

CONCLUSION

Mucoadhesive drug delivery system shows promising future in enhancing the bioavailability by utilizing the physiochemical characters. The buccal patches obtained by solvent casting technique were found to be of uniform thickness and weight, smooth texture with uniform drug content and good tensile strength and bio-adhesive properties. Good results obtained from *in vitro* release of Ondansetron Hcl bilayered buccal patches. The release of Ondansetron Hcl from patches showed a significant improvement consisting of permeation enhancer. The drug remained intact and stable in the patches during storage with no significant changes. All the patches showed good results when evaluated for different parameters. But optimized batch F6 showed the best result in all the evaluation parameters amongst the rest of the batches.

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