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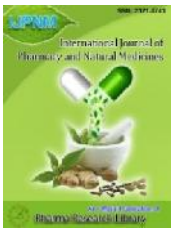

Research Article Open Access

Bioadhesive Buccal Tablets of Ondansetron Hydrochloride: III an *In-vitro* and *Ex-vivo* study

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A B S T R A C T

The purpose of this research was to study bioadhesive bilayer buccal tablets of Ondansetron HCl using the bioadhesive polymers Hydroxypropyl cellulose (HPC) and Carbopol 934P (CP) along with ethyl cellulose as an impermeable backing layer. The tablets were evaluated for weight variation, thickness, hardness, friability, surface pH, bioadhesive strength, swelling index, in vitro drug release, ex vivo drug permeation, ex vivo mucoadhesion, and stability studies. Tablets containing Hydroxypropyl cellulose and CP in the ratio of 1:3 (F32) had the maximum percentage of in vitro drug release without disintegration in 8 hours. The swelling index was proportional to Hydroxypropyl cellulose content and inversely Ondansetron HCl to CP content. The surface pH of all tablets was found to be satisfactory (6.83), close to neutral pH; hence, buccal cavity irritation should not occur with these tablets. The tablets were evaluated for in vitro release in pH 6.6 phosphate buffer for 8 hr in standard dissolution apparatus. In order to improve the permeation of the drug, tauroglycholate (permeation enhancer) added in the optimized formulation at 10mM concentration. The mechanism of drug release was found to be non-Fickian diffusion and followed zero-order kinetics. The formulation F32 was optimized based on good biodhesive strength (34.8 g) and sustained in vitro drug permeation (99.6% for 8 hours). The behavior of formulation F32 was examined in human saliva, and both the drug and the buccal tablet were found to be stable.

Keywords: Bioadhesion, bilayer device, buccal drug delivery, Ondansetron HCl, Hydroxypropyl cellulose, Carbopol 934

A R T I C L E I N F O

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1. Introduction

Ondansetron is a 1,2,3,9-tetrahydro – 9 – methyl – (2 - methyl – 1-H- imidazol – 1- yl) methyl - 4H – carbazol – 4 – One, mono hydrochloride[1]. Ondansetron is a short acting drug for management of nausea and vomiting. Chemotherapeutic agents and radiotherapy cause release of 5HT in the small intestine initiating the vomiting reflux by activating vagal afferents via 5HT3 receptor. It blocks the initiation of these reflexes. It is short biological half life 3.1 h. Buccal delivery of drug provides an attractive alternative to the oral route of drug administration. In recent years, delivery of therapeutic agents through various transmucosal routes gained significant attention owing to their presystemic metabolism or instability in the acidic environment associated with oral administration[2]. Buccal delivery provides direct entry into the systemic circulation, thus avoiding the hepatic first-pass effect, ensuring ease of administration, and making it possible to terminate delivery when required. Attempts have been made to formulate various buccal bioadhesive dosage forms, including tablets, films, patches, disks, and gels. A suitable buccal drug delivery system should possess good bioadhesive properties, so that it can be retained in the oral cavity for the desired duration. In addition, it should release the drug in a unidirectional way toward the mucosa, in a controlled and predictable manner, to elicit the required therapeutic response. This unidirectional drug release can be achieved using bilayer devices[3].

Direct compression is simplest method of tablet manufacture as it required less equipments, has minimum processing steps, reduced labor cost. It is a dry process hence deterioration of active ingredient has been prevented. Further advantage of direct compression is that tablets disintegrate into their primary particles rather than granular aggregates. The resultant increase in surface area available for dissolution results in faster drug release. The direct-compression process is highly influenced by powder characteristics such as flowability, compressibility, and dilution potential. Difficulty in getting suitable excipients with high functionality creates opportunities for the formulation scientists to develop newer grades of existing excipients. Developing newer grades of existing excipients with varying physicochemical properties has been carried out by using techniques referred as “Coprocessing” or “Particle Engineering” of excipients. Co-processing is a novel phenomenon of developing a new single-bodied excipient by interacting two or more excipients at sub-particle level with an objective to provide a synergy of functionality improve[4].

Bioadhesive polymers such as Carbopol 934P, hydroxypropyl cellulose (HPC) are suitable for use in buccal adhesive preparations because when hydrated with water, they can adhere to the oral mucosa and withstand salivation, tongue movements and swallowing for a significant period of time. HPC and Ethyl cellulose (EC) have been used as principal excipients to achieve adhesion to the oral mucous membrane and to control the drug release from the tablet.

The main objective of the present study was to formulate a bioadhesive bilayered buccal tablet of Ondansetron HCl to prolong the residence time of the buccal tablet, which ensures satisfactory drug release in a unidirectional way to the mucosa, thus avoiding loss of drug due to wash out with saliva. The bioadhesive buccal tablets were evaluated by weight uniformity, content uniformity, thickness, hardness, swelling index, in vitro drug release studies, bioadhesive strength, and ex vivo permeation study. The bioadhesive buccal tablet was compared for drug release and bioadhesive study for both ondansetron hydrochloride with non-bitter taste base ondansetron and complexes of ondansetron.

2. Materials and method

Ondansetron HCl and Carbopol 934 P were gift samples from Zydus Cadila, Ahmedabad, India. Hydroxy propyl cellulose obtained from AET laboratories, Hyderabad, India. Ethyl cellulose, Microcrystalline cellulose and Mannitol from Vilin Biomed Ltd, Roorkee, India. Spray dried lactose and Aspartame from Dr Reddy’s laboratories, Hyderabad, India. Sodium taurocholate gift sample from Moly Chem, Mumbai, India.

Preparation of bilayered buccal tablets

Bilayered buccal tablets were prepared by a direct compression method, before going to direct compression all the ingredients were screened through sieve no.40, except lubricant all the ingredients were thoroughly blended in a glass mortar with pestle for 15 min. After sufficient mixing lubricant was added and again mixed for additional 2-3 min. Preparation involves two steps, first the mixture is compressed using 8 mm flat faced punch on 16 stages rotary tablet compress machine. Then upper punch is raised and the backing layer of ethyl cellulose is placed on above compact then two layers are compressed again to get bilayered buccal tablet[4]. Composition of the prepared bioadhesive buccal tablet formulations of Ondansetron HCl were given in Table 1.

Evaluation of buccal tablets[5]

All prepared buccal tablets were evaluated for uniformity of weight and drug content, as per I.P. method. Friability was determined using Roche friabilator. Hardness was measured by using Pfizer hardness tester. Diameter and thickness were measured by Vernier caliper.

a) Disintegration test:

The test was performed for buccal tablets which are not having backing; six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 4 hr and the basket was lift from the fluid, observe whether all of the tablets have disintegrated (USP NF, 2004).

b) Measurement of bioadhesion strength:

Bioadhesive strength of the tablets was measured on a modified physical balance[6].The apparatus consisted of a modified double beam physical balance in which a lighter pan had replaced the right pan and the left pan had been replaced by a glass slide (4 cm length and 2.5 cm width)

with plastic hang suspended by Teflon rings and copper wire. The left-hand side of the balance was exactly 5 g heavier than the right side .The height of the total set up was adjusted to accommodate a glass container of 6.6cm height. All parts of modified physical balance were shown in Figure 1. In order to find out the bioadhesion strength first buccal tablet (n=3) was stacked to the glass slide with the help of knob, which was situated at the base of physical balance. Now five grams weight from the right pan was then removed. This lowered the glass slide along with the tablet over the membrane with a weight of 5.0 g. This was kept undisturbed for 5 min. Then the weights on the right-hand side were slowly added in increments of 0.1 g till the tablet just separated from the membrane surface. The excess weight on the right pan, i.e. total weight minus 5g was taken as a measure of the bioadhesive strength[6].

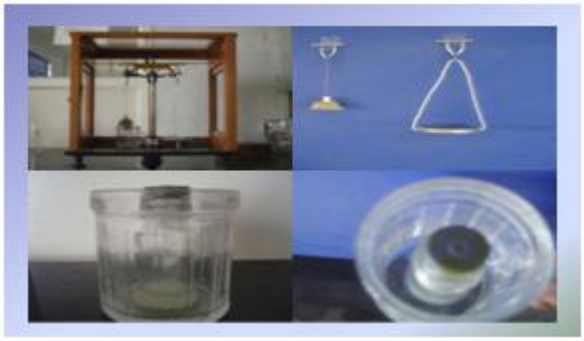

Fig 1: Bioadhesion strength apparatus

c) Determination of the ex vivo residence time:

The ex vivo residence time was determined using a locally modified USP disintegration apparatus[7] as shown in Figure 2. The disintegration medium was composed of 800 mL pH 6.6 phosphate buffer maintained at 37°C. The porcine buccal tissue was glued to the surface of a glass slab, vertically attached to the apparatus. The buccal tablet was hydrated from one surface using 0.5 mL of pH 6.6 phosphate buffer and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to run in such a way that the tablet was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the tablet from the mucosal surface was recorded. The experiments were performed in triplicate (n=3) and mean of triplicate was determined.

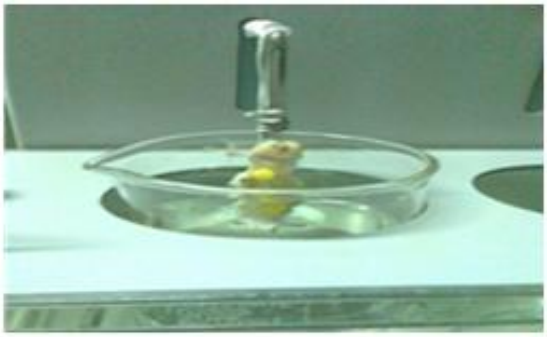

Fig 2: Ex vivo residence time measurement apparatus

d) Swelling Studies:

Buccal tablets were weighed individually 8 (designated as W1) and placed separately in Petri dishes containing 15 mL of phosphate buffer (pH 6.6) solution. At regular intervals (1, 2, 3, 4, 5, 6, 7 and 8 hr), the buccal tablets were removed from the Petri dishes and excess surface water was removed carefully using the filter paper. The swollen tablets were then reweighed (W2). This experiment was performed in triplicate. The swelling index (water uptake) calculated according to the following equation.

Swelling index(%)= (W2-W1)/W1×100

e) Surface pH Study:

The bioadhesive tablet was allowed to swell by keeping it in contact with 1 mL of distilled water for 2 hr at room temperature[9]. The pH was measured by bringing the pH-meter electrode, in contact with the surface of the tablet and allowing it to equilibrate for 1 min.

f) In vitro drug release of buccal tablets:

The United States Pharmacopeia (USP) XXIII rotating paddle method was used to study the drug release from the buccal tablets. The dissolution medium consisted of 200 mL of phosphate buffer pH 6.6. The release was performed at 37°C ± 0.5°C, with a rotation speed of 50 rpm[10]. The backing layer of buccal tablet was attached to the glass slide with instant adhesive (cyanoacrylate adhesive). The slide was placed in to the bottom of the dissolution vessel. Samples (5 mL) were withdrawn at predetermined time intervals and replaced with fresh medium. Dissolution for the conventional marketed product was conducted without glass slide. The samples were filtered through filter paper and analyzed after appropriate dilution by UV spectrophotometer at 310 nm.

g) Ex vivo permeation of buccal tablets:

Ex vivo permeation study of buccal tablets through the porcine buccal mucosa was performed using Franz-type diffusion cell at 37°C ± 0.2°C and 50rpm. This temperature and rpm was maintained by using magnetic stirrer. Porcine buccal mucosa was obtained from a local slaughterhouse and used within 2 hr of slaughter. The tissue was stored in Krebs buffer at 4°C upon collection. The epithelium was separated from underlying connective tissues with surgical scissors and clamped between donor and receiver chambers of the Franz-type diffusion cell. After the buccal membrane was equilibrated for 30 min with Krebs buffer solution between both the chambers, the receiver chamber was filled with fresh pH 7.4 buffer solution[11]. The buccal tablet was placed in donor chamber and 1mL of buffer solution (pH 6.6) was added 12 . Aliquots (5 mL) were collected at predetermined time intervals and filtered through a filter paper, and the amount of drug permeated through the buccal mucosa was then determined by measuring the absorbance at 310 nm using a UV spectrophotometer. The medium of the same volume (5 mL), which was prewarmed at 37°C, was then replaced into the receiver chamber. The experiments were performed in triplicate (n = 3) and mean value was used to calculate the flux, permeability coefficient. Due to the low permeability of drug from the formulation, permeation enhancer (Sodium taurocholate) was added in the concentration of 10 mM to the optimized formulation to increase the permeability. The enhancement

ratio for flux was determined by dividing the cumulative amount permeated of ondansetron HCl in the presence of sodium taurocholate (Qenh) by the amount of ondansetron HCl alone (Q control).

Enhancement ratioflux=Qenh/Qcon

h) Stability of buccal tablets:

Stability studies of buccal tablets were performed for optimized formulation in normal human saliva. The human saliva was collected from humans and filtered through filter paper. Buccal tablets were placed in separate Petri dishes containing 5 mL of human saliva and placed in a temperature-controlled oven for 8 hr at 37°C ± 0.2°C. At regular time intervals (0, 2, 4, 6 and 8 hr), the buccal tablets were examined for change in color, surface area and integrity[13]. The experiments were repeated in triplicate (n = 3) in a similar manner.

3. Results and Discussion

HPC and CP were selected as the bioadhesive polymers because of their excellent bioadhesive properties. EC has recently been reported to be an excellent backing material, given its low water permeability, hydrophobicity, and moderate flexibility, so it was chosen as an impermeable backing layer[14]. Spray dried lactose, Mannitol and MCC were used to improve the release of drug from polymer matrices, and the concentration was optimized during the preliminary trial to find the best formulation of bilayer buccal tablets (Table 1). Tablets were found to be satisfactory when evaluated for weight variation (151±0.60 to 159.8±0.25 mg), thickness (2.33±0.020 to 2.67±0.090 mm), hardness (4.3±0.15 to 7.6±0.08 kg/cm^2), friability (0.02 to 0.47%), and drug content (99.16 to 101.39%). The surface pH of all the tablets was within a range of 6.14 to 6.92 (Table 2), close to neutral pH.

Measurement of bioadhesion strength

This evaluation test was conducted for all formulations; there is a gradual increase in bioadhesion strength from F1to F4. The maximum bioadhesion strength (41.1 g, 40.85 g) was found for formulations F8, F4 and low bioadhesion strength was found for F33, F34 (17 g). Bioadhesion is defined as the attachment of a synthetic or natural macromolecule to mucus and/or an epithelial surface[15].Bioadhesion strength is depends on molecular weight and swelling behavior of the polymers, contact time with mucus[16].

The bilayered tablets containing higher proportions of carbopol showed good bioadhesion strength for 5min contact time. Bioadhesion characteristics were found to be affected by the nature and proportion of bioadhesive polymers used. As the concentration of carbopol increased the bioadhesive strength was also increased, the reason for such findings might be ionization of CP at salivary pH, which leads to the formation of secondary bioadhesion bonds with mucin and interpenetration of the polymer chains in the interfacial region, while other polymers undergo superficial bioadhesion[17]. The optimized tablet (F32) showed 34.8±0.08 g of bioadhesion strength. Bioadhesion strength values of all the formulations represented in Table 3.

***Ex vivo* residence time**

Ex vivo residence time for all the formulations varied from 3-11 hr. The optimized formulation (F32) showed 9.05±0.25 hr. The difference could be due to the combination of various amounts of polymers, which affects the mucoadhesion. In fact with bilayered tablets containing higher proportion of carbopol the mucoadhesion time was found to be increased. This is because of the high mucoadhesive nature of the carbopol and inter penetration of polymeric chains in to the mucus membrane. *Exvivo* residence time and bioadhesion strength values were given in Table 3.

Swelling Studies of buccal tablets

Swelling behavior of a buccal adhesive system is essential for uniform and prolonged release of the drug and effective mucoadhesion. The swelling study indicated that the rate of swelling was proportional to the HPC content and inversely proportional to the CP content of the tablets in the initial study up to 6 hour. In formulations containing HPC, (F28) shows swelling index of 3.39; within the formulations containing HPC, (F32) shows high swelling index of 3.56; The swelling state of the polymer in the formulation was reported to be crucial for its bioadhesive behavior. This finding may have been because of the fast-swelling property of HPC compared with CP. Adhesion occurs shortly after the beginning of swelling but the bond formed between mucosal layer and polymer is not very strong. The adhesion will increase with the degree of hydration until a point where over-hydration leads to an abrupt drop in adhesive strength due to disentanglement at the polymer/tissue interface. Results indicate that as the concentration of Carbopol 934P increases the swelling index increases. Swelling index values of all the formulations were given in Table 4. Swelling behavior of buccal tablets of all formulations as a function of time is shown in Figure 3a-3c.

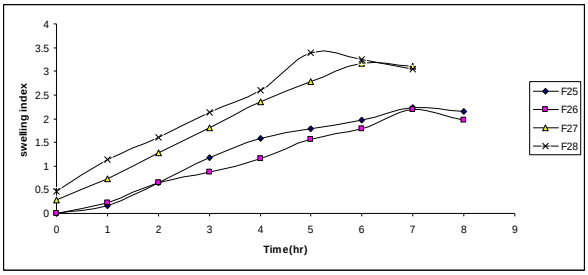

Fig 3a: Swelling index profile of Ondansetron HCl buccal tablets formulated with mannitol as diluent

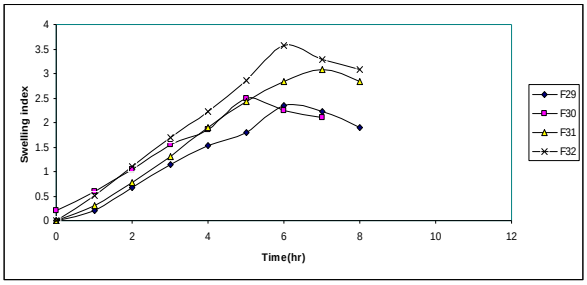

Fig 3b: Swelling index profile of Ondansetron HCl buccal tablets formulated with spray dried lactose as diluent

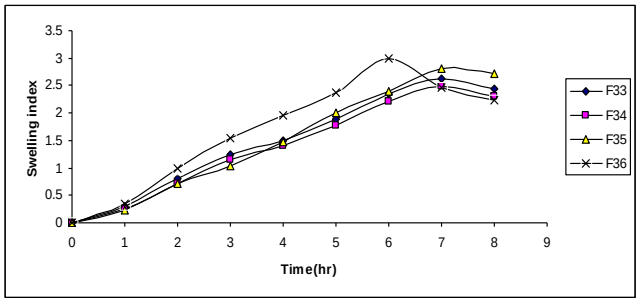

Fig 3c: Swelling index profile of Ondansetron HCl buccal tablets formulated with MCC as diluent

***In vitro* drug release of buccal tablets**

An ideal controlled release system should be able to release the drug immediately to attain the therapeutic level at a faster rate and maintain this drug level for a prolonged period of time[17, 18].*In vitro* drug release studies revealed that the release of ondansetron HCl from different formulations varies with characteristics and composition of matrix forming polymers as shown in graphs. The release rate of ondansetron HCl decreased with increasing concentration of HPC. These findings are in compliance with the ability of these cellulose derivatives to form complex matrix network which leads to delay in release of drug from the device. Drug release rate was increased with increasing amount of hydrophilic polymer.

The maximum cumulative percent release of ondansetron HCl (99.6±0.2%) from formulation F32 and F28 found to release (90.3±0.4%) could be attributed to ionization of carbopol at pH environment of the dissolution medium. Carbopol is more hydrophilic, it can swell rapidly, and therefore decrease of carbopol content delays the drug release[19]. Formulations with spray dried lactose and mannitol showed higher percentage drug release values compared to MCC, this is because of the water soluble diluents (spray dried lactose and mannitol) can absorb more water and swell and then release the drug rapidly compared to that of water insoluble diluent (MCC) that retards the release. Data of the in vitro release was fit into different equations and kinetic models to explain the release kinetics of ondansetron HCl from buccal tablets. The kinetic models used were zero-order equation, first-order equation, Higuchi and Korsemeyer-Peppas models[20]. The results indicate that as the concentration of each polymer increases in the respective series, peppas mechanism turns to zero-order release profile.

Drug release rate was increased with increasing amount of hydrophilic polymer. The maximum cumulative percent release of ondansetron HCl (89.1±0.4%) from formulation F16 and F20 found to release (83.2±0.6%) could be attributed to ionization of carbopol at pH environment of the dissolution medium. Ionization of carbopol leads to the development of negative charges along the backbone of the polymer. Repulsion of like charges uncoils the polymer into an extended structure. This is because as the proportion of these polymers in the matrix increased, there was an increase in the amount of water uptake and proportionally greater swelling leading to a thicker gel layer. Zero-order release from swellable hydrophilic matrices occurs as a result of constant diffusional pathlengths. When the thickness of the gelled layer and thus the diffusional pathlengths remain constant, zero-order release can be expected. Moreover, the hydrophilic polymers would leach out and hence, create more pores and channels for the drug to diffuse out of the device.All the results were shown in the in the Table 5.The comparison of cumulative percent drug release of all formulations was shown in Figure 4a-4c.

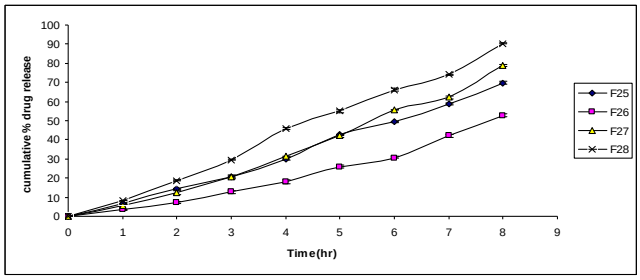

Fig 4a: In-vitro drug release profiles of Ondansetron HCl buccal tablets formulated with mannitol as diluent

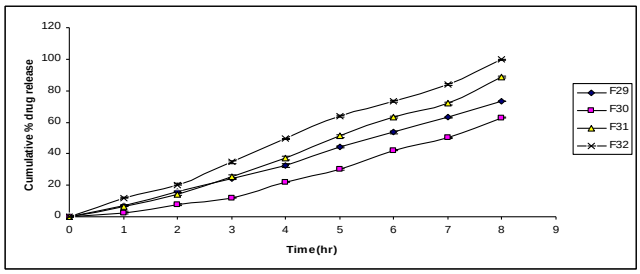

Fig 4b: In-vitro drug release profiles of Ondansetron HCl buccal tablets formulated with spray dried lactose as diluent

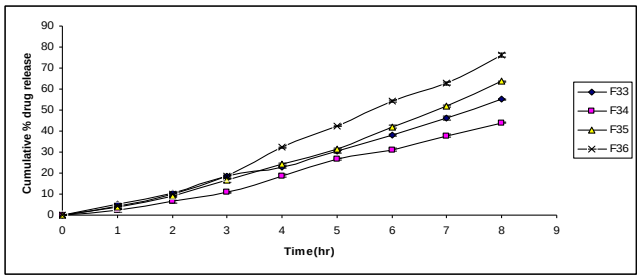

Fig 4c:*In-vitro* drug release profiles of Ondansetron HCl buccal tablets formulated with MCC as diluent

***Ex vivo* permeation of buccal tablets**

Based on the *in vitro* drug release studies, F32 selected for the *ex vivo* permeation study (Figure: 5). The flux, permeation coefficient and cumulative percent drug permeated from formulation F32 were found to be 0.6029 mg/hrs.cm^2, 0.0753cm/h and 58.4% respectively. Due to the low permeability of drug from the formulation, permeation enhancer (sodium taurocholate) was added in the concentration of 10 mM to the optimized formulation to increase the permeability. After addition of permeation enhancer (sodium taurocholate) the flux, permeability coefficient and cumulative percent drug permeated values were found to be 0.8519 mg/hrs.cm^2, 0.1064cm/h and

85.6% respectively, with enhancement ratio of 1.41. Sodium taurocholate can extract lipids from the cell membranes, along with the extraction of mucosal lipid from the intercellular spaces by formation of micelles. This results in enhancing the passive diffusivity of the drug via transcellular (crossing the cell membranes and entering the cell) and paracellular routes[21].It was mentioned that sodium taurocholate could also cause the uncoiling and extension of the protein helices, which leads to opening the polar pathways for diffusion[19]. All these effects may contribute to the enhancing the permeation of the drug.

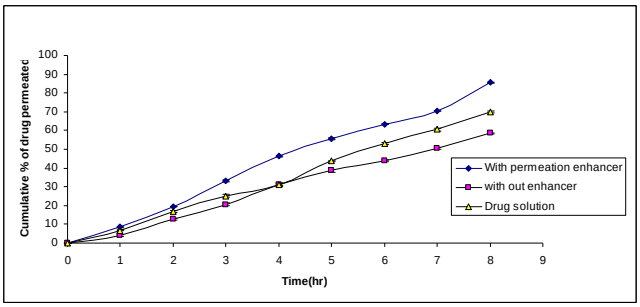

Fig 5: Comparison of cumulative % drug permeation of drug solution, formulation with enhancer and without enhancer

Stability of buccal tablets

Stability study was conducted only for optimized formulation (F32). There was no change in the colour and integrity of the tablets. From the stability results it was known that formulation F32 has stability in human saliva, if it is unstable color would change. It was reported that colour of ondansetron HCl changed to yellow when it was placed in human saliva[22]. Physical properties of the ondansetron HCl buccal tablets such as thickness and diameter slightly changed owing to swelling of the system in human saliva. Buccal tablets maintained their integrity in the human saliva throughout the study, conforming the sufficient strength of the system.

Fourier transform infrared spectroscopic studies

FTIR study revealed that (Figure 6&7), in pure ondansetron HCl the keto group(1638 cm^{-1}), tertiary amine (3411cm^{-1}), C-C stretching (3175cm^{-1}, 2909cm^{-1}, 2721cm^{-1}) gave peaks at respective wave numbers. In optimized formulation (F32) also same groups showed peaks very nearer to those wave numbers. From this it was concluded that there was no interaction between drug and excipients.

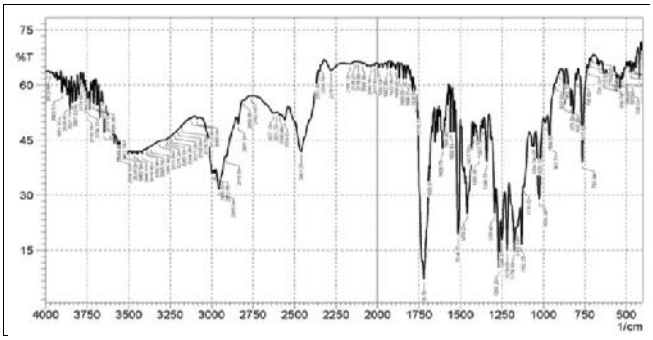

Fig 6:FTIR spectra of Ondansetron HCl

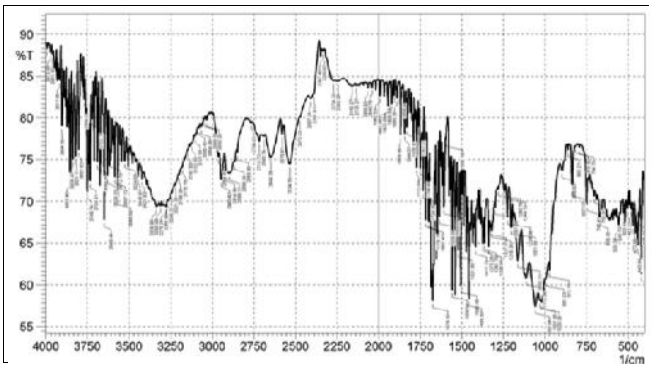

Fig 7:FTIR spectra of optimized formulation

4. Conclusion

The prepared Bioadhesive buccal tablets of Ondansetron HCl can help bypass extensive hepatic first-pass metabolism and improve bioavailability. HPC shows satisfactory buccoadhesive properties. Formulation F32 using this polymer in a drug: polymer: polymer (1:3:1) ratio showed significant bioadhesive properties with an optimum release profile and could be useful for buccal administration of ondansetron HCl. From the results, it was concluded that the in vitro drug release, bioadhesion strength, ex vivo residence time of the optimized formulation (F32) is suitable for buccal delivery. The release pattern followed non-fickian diffusion with Zero order release. FTIR studies concluded that there was no interaction between drug and excipients.

Table 1: Composition of formulations containing CP:HPC with different diluents

Ingredients(mg/tablet)	Formulation code											
	F25	**F26**	**F27**	**F28**	**F29**	**F30**	**F31**	**F32**	**F33**	**F34**	**F35**	**F36**
Ondansetron HCl	8	8	8	8	8	8	8	8	8	8	8	8
Carbopol-934	30	20	40	45	30	20	40	45	30	20	40	45
HPC	30	40	20	15	30	40	20	15	30	40	20	15
Mannitol	30	30	30	30	-	-	-	-	-	-	-	-
Spray dried lactose	-	-	-	-	30	30	30	30	-	-	-	-
MCC	-	-	-	-	-	-	-	-	30	30	30	30
Aspartame	1	1	1	1	1	1	1	1	1	1	1	1
Magnesium stearate	1	1	1	1	1	1	1	1	1	1	1	1
Ethyl	50	50	50	50	50	50	50	50	50	50	50	50

cellulose(backing)												
Total weight(mg)	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Table 2: Physico-chemical parameters of formulations containing HPC

Formulation code	Thickness (mm)	Weight Variation(mg)	Friability (%)	Hardness (Kg/cm^2)	%Drug content	Surface pH
F25	2.67±0.090	151±0.60	0.47	4.3±0.15	99.81	6.14±0.095
F26	2.40±0.015	153.1±0.55	0.23	4.9±0.04	99.58	6.62±0.040
F27	2.62±0.050	155.0±0.75	0.11	5.4±0.08	99.55	6.71±0.035
F28	2.50±0.035	153.5±0.15	0.04	6.1±0.05	100.43	6.76±0.010
F29	2.40±0.015	152.4±0.20	0.14	5.2±0.24	101.39	6.92±0.055
F30	2.61±0.030	154.7±0.50	0.65	5.5±0.15	99.53	6.87±0.025
F31	2.33±0.020	158.1±0.40	0.02	6.3±0.06	98.54	6.60±0.025
F32	2.49±0.045	150.0±0.55	0.12	7.6±0.08	100.17	6.83±0.015
F33	2.61±0.030	157.2±0.50	0.23	4.5±0.05	99.03	6.83±0.040
F34	2.34±0.060	157.7±0.65	0.18	5.6±0.13	99.56	6.76±0.080
F35	2.54±0.020	159.8±0.25	0.26	6.3±0.05	99.16	6.82±0.070
F36	2.63±0.040	154.2±0.55	0.08	6.7±0.05	99.38	6.87±0.005

Table 3: Bioadhesive strength and ex vivo residence time of Ondansetron HCl buccal tablets with HPC

Formulation Code	Bio adhesion Strength (gm)	*Ex vivo* residence Time (hr)
F25	18.4±0.21	3.62±0.25
F26	18.6±0.18	4.26±0.55
F27	29.5±0.31	6.82±0.05
F28	34.7±0.19	9.45±0.15
F29	17.4±0.43	4.38±0.51
F30	16.3±0.05	4.25±0.35
F31	26.9±0.14	7.35±0.50
F32	34.8±0.08	9.05±0.05
F33	17.6±0.08	3.45±0.16
F34	17.2±0.03	4.53±0.24
F35	24.7±0.15	7.22±0.16
F36	35.3±0.28	8.75±0.31

Table 4: Swelling index profile of Ondansetron HCl buccal tablets containing CP:HPC

Time (hr)	F25	F26	F27	F28	F29	F30	F31	F32	F33	F34	F35	F36
0	0	0	0	0	0	0	0	0	0	0	0	0
1	0.16	0.22	0.27	0.46	0.2	0.20	0.31	0.51	0.29	0.24	0.23	0.33
2	0.65	0.64	0.73	1.13	0.66	0.62	0.77	1.10	0.79	0.72	0.71	0.98
3	1.17	0.86	1.27	1.61	1.13	1.03	1.30	1.69	1.23	1.148	1.03	1.53
4	1.58	1.16	1.81	2.13	1.53	1.53	1.89	2.22	1.50	1.40	1.46	1.96
5	1.78	1.56	2.35	2.60	1.82	1.85	2.42	2.85	1.88	1.77	2.00	2.36
6	1.96	1.78	2.78	3.39	2.35	2.48	2.84	3.56	2.35	2.21	2.39	3.02
7	2.24	2.18	3.17	3.25	2.22	2.24	3.07	3.27	2.62	2.47	2.80	2.46
8	2.16	1.97	3.09	3.03	1.92	2.10	2.83	3.07	2.45	2.31	2.72	2.23

Table 5: In-vitro dissolution kinetics parameters of Ondansetron HCl buccal tablets formulated with HPC

Formulation code	Correlation coefficient (R^2)				'n' value
	Zero order	First order	Higuchi	Peppas model	
F28	0.9667	0.6213	0.7365	0.9426	1.177
F32	0.9987	0.8463	0.8343	0.9956	1.024

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