Research article

Effect of polymers on release pattern of Ondansetron Hydrochloride bioadhisive sustained release matrix tablets

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Abstract

The objective of this research was to conclude the effect of bioadhesive polymers on the release pattern of Ondansetron from bioadhesive matrix tablets. To observe this effect bioadhesive sustained release tablets having ondansetron hydrochloride as active ingredient were formulated using bioadhesive polymers like CMC in concentration of 10%, 17%, 25%, 33% and 40% HPMC in concentration of 10%, 26%, 45%, 64% and 80% and Carbopol with concentration of 5%, 11%, 18%, 24% and 30%. Direct compression method was used to compress the tablets,then these tablets were analyzed for physical and chemical testing. For dissolution 12 hours study was performed by using USP type II apparatus. The order of bioadhesion with relative to polymers was as Carbopol 934P > HPMC > CMC. Formulations A-5, A-10 and A-12 showed the optimum level of results as they followed zero order and Higuchi kinetic model presenting sustained release pattern as there R^2 values are 0.960, 0.985 and 0.984 respectively. All formulations followed the equation of Korsmeyer and Peppas drug release profiles as the values of N is all formulations were above 0.5 except A6 and A13, that shows it follows non-fickian diffusion. According to the results it was concluded that CMC with concentration of 35% to 45%, carbopol 934P with concentration of 20 to 30% and HPMC with concentration of 70% to 80% can be used with Ondansetron to make bio-adhesive sustained release matrix tablets with optimum release over the period of 12 hours.

Introduction

The most popular route of drug administration is oral due to ease in administration and flexibility with this dosage form. Prolonged release, modified release and extended release terms are used to identify the, prolonged therapeutic effect with improvement in safety and convenience of patient [1]. These system also give many pharmacokinetic advantages like minimizing the risk of resistance of drug, maintain the constant therapeutic level for a long period of time and also reduces fluctuation in therapeutic level [2].

In the present study estimation of drug release was investigated from bio-adhesive matrix sustained release tablets containing Ondansetron HCl as drug, by using different bio-adhesive polymers like HPMC, CMC, and carbopol.

Bio-adhesion

The process in which synthetic and natural macromolecules attach to mucosal surfaces and biological membranes is called Bio-adhesion or Mucoadhesion [3]. Because of the extended time of contact of dosage form with the absorbing membrane versus a standard dosage form, a higher drug bioavailability is predictable [4].

Bio-adhesion involves the attachment of a drug dosage system to a specific biological location [5]. The drug bioavailability and duration of action may be increased by delaying the gastrointestinal transit that is brought about by the intimate and extended interaction between bio-adhesive system and mucosal lining [6]. In pharmaceutical development the combination of control release dosage forms and bio-adhesion techniques can result a high performance drug delivery system [7]. To attain muco-adhesion various bio-adhesive polymers are used. The naturally occurring polymers include acacia, tragacanth, xanthan gum, sodium alginate and gelatin although the synthetic polymers include Hydroxy propyl methyl cellulose (HPMC), Carbopol934, Sodium carboxymethyl cellulose, Hydroxy ethyl cellulose (HEC), polycarbophil and Polymethyl methacrylates [8]. The important aspects leading to the release of drug molecules from bio-adhesive dosage forms comprised of, concentration, molecular weight, chemical functional groups present on its surface, hydrophilicity of polymers

used, degree of contact between the two surfaces and degree of cross-linking produced [9].

Effect of pH on Bio-adhesion

The Polymers that commonly form anionic bonds are used in bio-adhesive formulations as they have high bio-adhesion or mucoadhesion capacity and have low toxicity. Such polymers give special characteristics and they have carboxyl and sulphate as functional group which give rise to negative charge at pH values that exceeds the pKa values of the polymers as a result.[10] The conditions like pH of the medium and characteristics of drug like pKa of the drug can also disturb the release profile concerned drug [11].

As higher pH fluids that penetrate into the drug can convert more ionizable drug to less soluble base. Due to which the formulations that have weakly basic drugs used as oral dosage form can have result of variable and abnormal release rate with the change in pH of surrounding fluids [12]. As weakly basic drugs with pH-dependent solubility like Ondansetron hydrochloride can have problem on release from controlled release dosage forms [11].

Advantages of Bio-adhesion

1. Availability of high drug flux at absorbing site due to intimate contact between dosage form and the absorptive mucosa [13].
2. Increase in bioavailability due to Prolongation of residence time of the dosage form at the site of absorption.
3. Excellent accessibility, rapid onset of action.
4. Rapid absorption because of enormous blood supply and good blood flow rates
5. Drug is protected from degradation in the acidic environment in the GIT
6. Improved patient compliance

Disadvantages of Bio-adhesive drug delivery systems

1. Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property
2. One of the major limitations in the development of oral mucosal delivery is the lack of a good model for in vitro screening to identify drugs suitable for such administration.
3. Patient acceptability in terms to taste, irritancy and mouth feel is to be checked [14].

Polymers

Mucoadhesive polymers that stick to the mucin-epithelial surface can be divided into three main classes:
1. One class that becomes sticky when placed in water and owes their mucoadhesion to stickiness.

2. Second class that adhere through nonspecific, non-covalent exchanges which are primarily electrostatic
3. Third class that bind to specific receptor site on tile self-surface.

An ideal mucoadhesive polymer has the following characteristic:
1. Non-absorbable and nontoxic at gastrointestinal tract.
2. Nonirritant to the mucous membrane.
3. Form a strong non-covalent bond with the mucin-epithelial cell surfaces.
4. Adhere quickly to most tissue and possess some site-specificity.
5. Easy incorporation to the drug and offer no hindrance to its release.
6. Do not decompose on storage or during the shelf life of the dosage form.
7. Cost of polymer should not be so high [15].

Ondansetron

Cancer that is a common health concern and is stated to affect more than 24.6 million of the world people. In present, anticancer therapy, the drugs are administered using intravenous route or oral route using conventional formulations. Incidents of acute and delayed emesis are common in patients receiving chemotherapy and this affects the quality of life of cancer patients [16].

The patients who receive chemotherapy may have a severe side effect of nausea and vomiting also called Chemotherapy-induced nausea and vomiting (CINV). So to prevent this type of symptoms antiemetic therapy is first choice for the compliance of patient condition. Ondansetron an antiemetic drug used to prevent vomiting and nausea during and after chemotherapy medication or radiation therapy or after surgery. Ondansetron hydrochloride has a short biological half-life (3.5 ± 1.2 hours) and 62 % absolute bioavailability. Ondansetron is well absorbed from the gastrointestinal tract and undergoes some first-pass metabolism. Mean bioavailability in healthy subjects, following administration of a single 8 mg tablet, is approximately 56%. Oral bioavailability of Ondansetron hydrochloride is almost 59%, and peak plasma about 0.03–0.04µg/ml is obtained after 1.5 to 2 h of administration [17].

Indications and Usage for Ondansetron

Prevention of nausea and vomiting associated with highly emetogenic cancer chemotherapy, radiotherapy in patients receiving either total or singal body irradiation, postoperative incidences.

Chemotherapy

Recommended adult oral dosage of Ondansetron tablet is 24 mg given as three 8 mg tablets administered 30 minutes before the start of single-day highly emetogenic chemotherapy [18].

Materials and Methods

Materials

All materials used for the formulation were of Analytical grade, gifted by Pharmedic Laboratories Lahore Pakistan. All materials were from Merck, Germany. The materials used in different formulations used are, Ondansetron Hydrochloride (OND HCl) Hydroxypropyl methyl cellulose, Carbopol 934 (Merck, Germany), Carboxy Methyl Cellulose (CMC), Magnesium Stearate, Microcrystalline Cellulose Grade200.

Method of Tablet Preparation

The method employed for tablet preparation was direct compression.

The drug, polymer and other ingredients were separately weighed on analytical balance (Schimadzu Japan). Formulations A1-A5 contain Carboxy Methyl Cellulose (CMC) in various concentrations (10%, 16.76%, 25%, 33.24%, 40%), Formulations A6-A10 contain Hydroxy Propyl Methyl Cellulose (HPMC) in various concentrations (10%, 25.77%, 45%, 64.23%, 80%) and formulations A11-A15 contain Carbopol in various concentrations (5%, 10.63%, 17.50%, 24.37%, 30%) as mentioned in table 1. All ingredients were passed through sieve no. 80, separately and mixed for 20 min then lubricated with magnesium stearate 2%. The mixed material again passed through sieve no.80 and then compressed using 5 mm round punches on ZP 18 (STH, China) compression machine to get tablets of 200 mg weight. The practical weight of tablet was calculated based on the drug content.

Evaluation of tablets

Hardness testing

Automatic hardness tester (YD-35, Xian Yima, China) is used to determine the hardness. In this method, the tablets are generally placed between two platens, one of which moves to apply sufficient force to the tablet to cause fracture. 10 tablets of each formulation A-1 to A-15 were taken and the hardness was determined. After which the standard deviation was determined by using MS-Excel [19].

Thickness testing

Thickness and diameter is of vital importance since the compression of the tablet is directly dependent on it. For this the thickness were observed by using Vernier caliper (530 series, USA) [19].

Tablet friability

Friability of the tablets was determined in a Friabilator (Agilant-250, USA). In this method 20 tablets from each formulation were taken weighed and placed in the Friabilator. The rotation speed was set to be 25 rpm for 4 minutes. After that the tablets were removed from friabilator and de-dusted and then final weight was observed. By the help of the following formula friability was determined [17].

% friability = (initial weight- final weight/Initial weight) x 100

Weight Variation

To determine the weight variation, weight 20 tablets of each formulation one by one and then average weight of tablets were observed by using standard physical balance (Shimadzu, Japan). The tablets must be in the official limits of British Pharmacopoeia to ensure that the die filling the tablet production is uniform for all formulations [17].

Table 1. Formulations having polymers in various concentrations

Formulation No.	Ondansetron %	CMC %	HPMC %	Carbopol %	Magnesium Stearate %	Avicel (200) %
A1	3.8	10	-	-	2	84.2
A2	3.8	17	-	-	2	77.2
A3	3.8	25	-	-	2	69.2
A4	3.8	33	-	-	2	61.2
A5	3.8	40	-	-	2	54.2
A6	3.8	-	10	-	2	84.2
A7	3.8	-	26	-	2	68.2
A8	3.8	-	45	-	2	49.2
A9	3.8	-	64	-	2	30.2
A10	3.8	-	80	-	2	14.2
A11	3.8	-	-	5	2	89.2
A12	3.8	-	-	11	2	83.2
A13	3.8	-	-	18	2	76.2
A14	3.8	-	-	24	2	70.2
A15	3.8	-	-	30	2	64.2

Content Uniformity

For the determination of content uniformity pure drug Ondansetron HCl (16mg) was taken and make different concentrations in 0.1N HCl pH 1.2. It was then observed in spectrophotometer (UV-VIS-1800 Shimadzu, Japan) at 216nm. The observed value will be standard value. Then ten tablets from each formulations from A1- A15 were taken, crushed and then accurately weight was taken according to the 16mg of pure drug and dissolved in the suitable solvent and the values were observed in spectrophotometer (UV-VIS-1800 Shimadzu, Japan)at 216nm, these will be the values of sample, after that with the help of the following formula content uniformity was calculated [17].

Content Uniformity = (Absorbance of sample / Absorbance of standard) x 100

Ex-vivo Bio-adhesion studies

For the determination of bio-adhesive strength of the formulations, a simulated apparatus of physical balance and two vials was used. The complete assembly was set in such a way that weights were added to the right hand side pan of the balance and on the left side of the balance two empty vials covered with rabbit inverted intestine were used. A bio-adhesive core tablet was placed between the hanging vials and the other vials just below it and place a drop of water. Then both intestine fitted vials were joined together by bio-adhesive tablets, these vials were hanged to modified physical balance. Bio-adhesive test was conducted by adding weight in the form of water droplets through pipette into small beaker placed in the right side of the balance. The weight at which the two vials detach from each other was noted. For each formulation triplicate reading were taken and the following formula was used to calculate bio-adhesive force.

Force of Adhesion (N) = Bio-adhesion strength (gms)* 9.81
                                               100

Figure 1. Physical balance for Bio-adhesion study

FTIR (Fourier Transform Infra-red Spectroscopy) Studies

FTIR spectroscopy was performed for prepared formulations to evaluate any possible interaction between ingredients used in formulation by using FTIR (Agilant Technologies USA) with ATR Technology. All the samples were put in assembly of apparatus and then knob of assembly was rotated to form the compact of sample. The range of wavelength used for sample was 650 to 4000 cm1 [20].

In-Vitro Dissolution:

In-Vitro drug release studies were also conducted by using USP Dissolution (type II Paddle) apparatus. Dissolution studies were carried at 50 rpm, in 0.1N HCl pH 1.2 for 12 hours. Absorbance was taken on UV Spectrophotometer (Schimadzu, Japan) at wavelength of 216nm [21]. The obtained data graphs were plotted for Zero order, First order, Korsmeyer-peppas model, Higuch and Hixon-Crowell kinetic models.

By these models the R-square values will be determined which will reflect the release mechanism and patterns. N value was observed to check whether the release pattern was Fickian or Non-Fickian [22].

Results and Discussion

For physical testing weight variation, hardness, thickness, friability and content uniformity were performed (Table 2). The results of weight variation showed the standard deviation within the range of ±2. Standard deviation of hardness of all formulations were not more than +0.50 and the average hardness of all formulations was above 3 Kg. During tableting process the force of compression was constant that can be observed from the resulted standard deviation that is not more than + 0.1 and the thickness was in the range of 3.06mm to 3.13mm. Friability of all formulation was within range that is less than 1%. The standard deviation of all formulations were also within the range of + 0.1. The content uniformity of all resulted formulations were in the range of 95% to 100%, and the resulted standard deviation was in the range of + 0.31. The ex-vivo bio-adhesive strength was determined by the force of adhesion in Newtons (N)for formulations A-1 to A-15. It was observed that the formulations possessing Carbopol 934P have the greatest bio-adhesion followed by HPMC and lastly CMC in the order Carbopol 934P > HPMC > CMC. In addition to this bio-adhesion was directly related with the polymer concentration. By the increase of polymer an increase in bio-adhesion was observed. Figure 2 reflects the bio-adhesion of all formulations in a form of bar chart. FTIR studies showed that there is no major shifting in the frequencies of ondansetron, which indicated that there is no chemical interaction between ondansetron and other polymers. The pure ondansetron FTIR spectra (figure 3)

showed intense band at 1215cm[1] to 3479.5cm[1] with reference to the functional group. The peak at 3479.5cm[1] revealed stretching vibration of OH, peak at 2946.5cm[1] indicates stretching vibration of C-H, 1634.4cm[1] showed the stretching vibration of C=O, and at 1531.9cm[1] points the stretching vibration of N-H. The average peaks observed in FTIR for formulations (A-5,A-10,A-10) were 3460.8cm[1], 2916.6cm[1], 1636cm[1], and 1533cm[1] respectively from the functional group (figure 4,5,6), showed no major shifting in frequencies of Ondansetron which indicated that there is no interaction between drug and polymers.

Table 2. Results of Physical Tests.

| F#	Weight variation	Thickness	Friability	Hardness	Content Uniformity
	(mg)	(mm)	(% loss in weight)	(Kg/cm^2)	(%)
	Mean ± St. Dev. n=20	Mean ± St. Dev. n=10	Mean ± St. Dev. n=20	Mean ± St. Dev. n=10	Mean ± St. Dev. n=20
A-1	209 ± 1.1	3.1 ± 0.06	0.29± 0.05	4.76±0.19	98.6±0.25
A-2	207 ± 1.6	3.1 ± 0.08	0.45± 0.02	4.23±0.24	99.7±0.19
A-3	212 ± 1.9	3.1 ± 0.07	0.15± 0.07	3.96±0.25	97.5±0.17
A-4	218 ± 1.8	3.09 ± 0.08	0.45± 0.08	3.82±0.25	98.9±0.29
A-5	217 ± 1.9	3.06 ± 0.07	0.78±0.09	3.98±0.43	99.8±0.15
A-6	212 ± 1.7	3.11 ± 0.06	0.29±0.03	5.59±0.28	97.3±0.31
A-7	209 ± 1.8	3.1 ± 0.06	0.43± 0.04	6.4±0.27	94.59±0.25
A-8	206 ± 2	3.09 ± 0.05	0.45±0.05	6.26±0.37	95.68± 0.15
A-9	211 ± 1.96	3.08 ± 0.06	0.29±0.05	4.23±0.29	94.59±0.31
A-10	203 ± 1.9	3.08 ± 0.04	0.46±0.03	3.98±0.18	97.5±0.17
A-11	208 ± 1.4	3.13 ± 0.04	0.3± 0.02	3.74±0.35	98.6±0.25
A-12	210 ± 1.3	3.1 ± 0.06	0.3± 0.04	3.59±0.38	97.5±0.17
A-13	207 ± 1.5	3.12 ± 0.06	0.3± 0.05	3.85±0.45	97.3±0.31
A-14	210 ±1.3	3.11 ± 0.07	0.34±0.04	3.35±0.27	99.8±0.17
A-15	211 ±1.33	3.09 ± 0.05	0.46±0.05	3.66±0.48	99.8±0.13
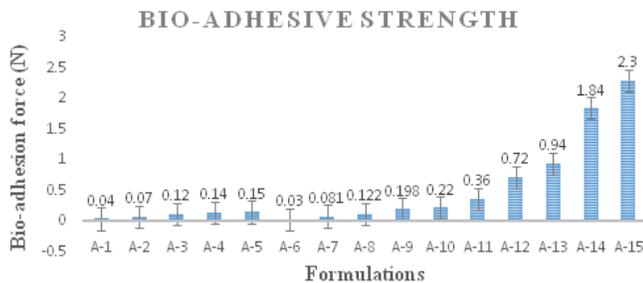
Figure 2. *Ex-vivo* Bio-adhesion results for different formulations of Ondansetron Hcl sustained release bio-adhesive tablets. Triplicate readings were taken (n = 3).
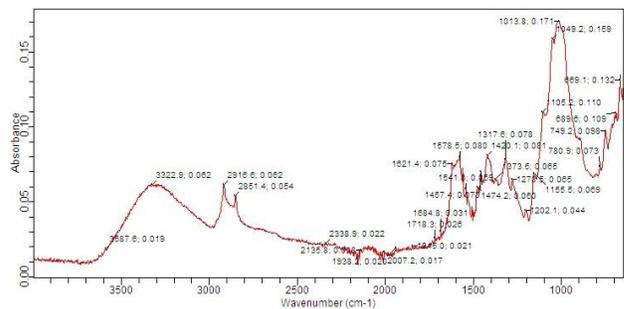
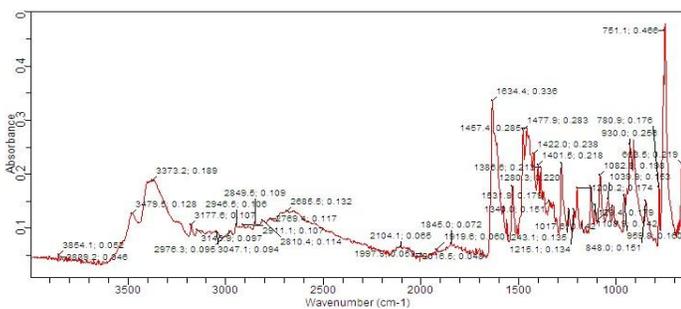

Figure 4. FTIR Spectra of Formulation A-5.
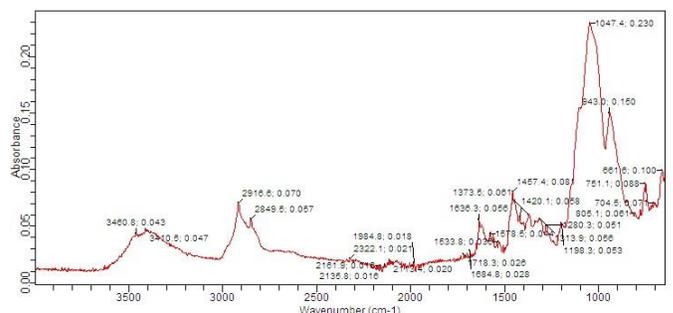

Figure 3. FTIR Spectra of Ondansetron

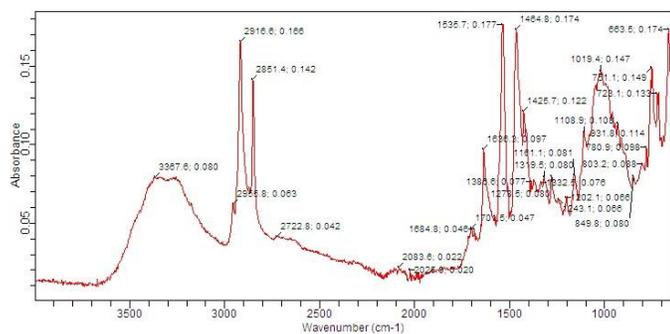Figure 5. FTIR Spectra of Formulation A-10

Figure 6. FTIR Spectra of Formulation A-12

Figure 7 depicts the drug release of formulations A-1 to A-5 having CMC as polymer. Formulations A-1, A-2 and A-3 followed first order kinetics due to low concentration of the polymer. But as the polymer concentration increases about 33-40% in formulations A-4 and A-5, it was observed that the 80% of the drug was released in 6 hours and the remaining drug release was retarded. R-square values for these formulations ranged from 0.879 to 0.9059 for zero order kinetics and N-value ranged from 0.61 to 0.93 presenting Non-Fickian drug release. In this group A-5 formulation revealed best release pattern, as it followed Higuchi kinetic model along with zero order kinetics R-square value of 0.9.

Figure 8 reflects the drug release of formulations A-6 to A-10 which comprises of HPMC E4M as polymer with concentration between 10-80%. Formulation A-6 did not show sustained release effect as more than 50% of the drug was released in 2hrs. Formulation A-7 having 26 % polymer reflected good sustained release effect followed by zero order kinetics. With polymer concentration of 45-64%, it was observed that, in 11hrs almost 50% drug was released in formulation A-8 and less than 50% was released in A-9. Formulation A-10 that showed the optimum sustained release effect with 80% drug release in 12 hours followed by zero order kinetics. N values ranged from 0.44 to 0.93, in which only A-6 presented Fickian drug release. Remaining formulations reflected Non-Fickian drug release. In this group only formulation A-10 followed both higuchi kinetic model along with zero order kinetics.

Figure 9 presents the drug release for the formulations (A-11, A15) comprising of Carbopol 934P. Formulation A-11 reflected the release pattern of first order kinetics with less than 50% of the drug release 11hrs. While formulation A-12 and A-13 showed sustained release effect with 99% drug release in 12 hours. On the other side formulation A-14 and A-15 followed first order kinetics due to higher concentration of polymer. The N-values obtained from KP model ranged from 0.41 to 0.94, out of these formulations A-12 and A-13 drug release patterns were Fickian, whereas, A-11 A-14 and A-15 followed Non-Fickian drug release. Along with that A-11 and A-12 followed Higuchi kinetic model with zero order kinetics.
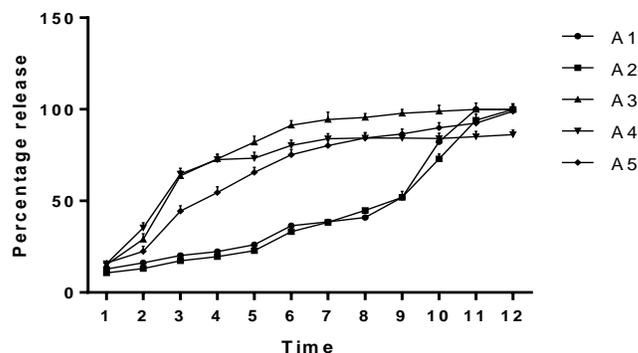

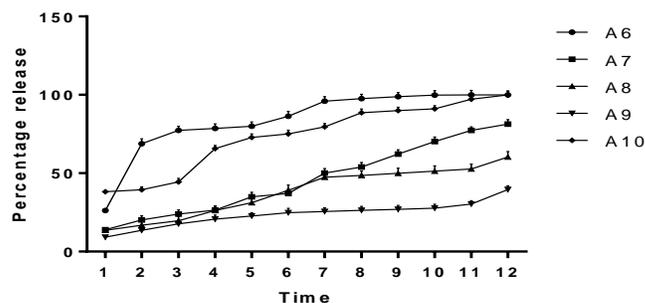**Figure 7. Dissolution profile of formulations A-1 – A5.**

Figure 8. Dissolution profile of formulations A-6 – A10.
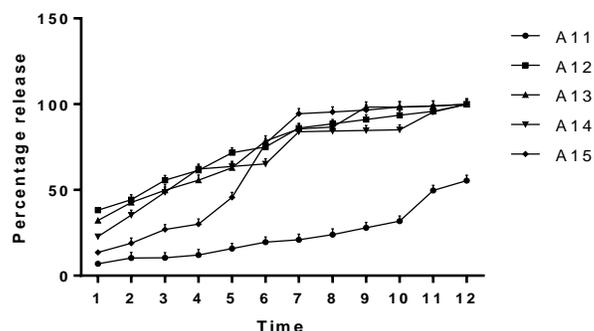

Figure 9. Dissolution profile of formulations A-11– A15.

Conclusion

In present study, an effort was done to deliver ondansetron via an oral mucoadhesive drug delivery system to the absorption site by prolonging the gastric residence time of the dosage form. For the formulation of the oral bio-adhesive tablet, various formulations were prepared by using variable concentrations of matrix forming polymers particularly with bio-adhesive and sustained release properties by direct compression. All of the formulations were divided in three groups according to the specific polymer used. These formulations were subjected to Physical tests including weight variation, Hardness, Friability, Thickness, content uniformity testing, bio-adhesive strength and *in-vitro* dissolution studies.

For ex-vivo bio-adhesion studies, the formulation A-5 presented best results for group 1 that have CMC as polymer with concentration of about 40% in the formulation , in group two formulation A-10 showed best results as compared to other formulations of this group that have HPMC as polymer with concentration of about 80% and in group three the results of formulations A-12, A-13, A-14 and A-15 are excellent, as in these formulations the bio-adhesion was good as compared to other formulations of this group that contains Carbopol 934P as polymer with concentrations of 24% to 30%.

FTIR studies was also done on formulation and it was concluded from FTIR results that there was no major shifting in the frequencies of Ondansetron which indicated that there is no chemical interaction between ondansetron and other polymers.

During *in-vitro* dissolution studies it was observed that formulations A-5, A-10 and A-12 were the optimum in this regard as they followed zero order and Higuchi kinetic model presenting sustained release mechanisms as there R2 values are 0.960, 0.985 and 0.984 respectively. It was also observed that formulations of all groups followed the equation of Korsmeyer and Peppas drug release profiles as the values of N is all formulations were abore 0.5 except A6 and A13, that shows it follows non-fickian diffusion.

So the present study reveals that CMC with concentration of 35% to 45%, carbopol 934P with concentration of 20 to 30% and HPMC with concentration of 70% to 80% can be used with Ondansetron to make bio-adhesive sustained release matrix tablets and at above concentrations the release of drug from polymers is optimum over the period of 12 hours.

References

1. Kundan P., P.M. An Overview: Extended Release Matrix Technology. International journal of pharmaceutical and chemical sciences 2012; 1(2): 828-843.
2. Gangurde H.H, M.A. Formulation and evaluation of sustained release bioadhesive tablets of ofloxacin using 3 2 factorial design. International journal of pharmaceutical investigation 2011; 1(3):148.
3. Woodley. Bioadhesion. Clinical pharmacokinetics 2001; 40(2):77-84.
4. Sonani S., H.D. Design and evaluation of gastroretentive mucoadhesive cephalexin tablets. Pharmaceutical development and technology 2010; 15(2):178-183.
5. Saraswathi, A.B. Polymers in mucoadhesive drug delivery system-latest updates. Int. J Pharm Pharmaceut Sci 2013; 5:423-30.
6. Chandrakala, M.S. Formulation and Evaluation of Bioadhesive Cyproheptadine Tablets. Tropical Journal of Pharmaceutical Research, 2011; 10(4):365-373.
7. Waleed M. K. et al., Simple Controlled Release Delivery System for an Antihypertensive Drug via Buccal Route. British Journal of Pharmaceutical Research 2014; 4(10):1174-1195.
8. Aditya G., G. Design and evaluation of controlled release mucoadhesive buccal tablets of lisinopril. International journal of current pharmaceutical research 2010; 2(4):24-27.
9. Nayaka A.K., M.S. Mucoadhesive beads of gliclazide: Design, development, and evaluation. Sci. Asia 2010; 36(1):319-25.
10. Peranu A.E, I.T. Formulation of Bioadhesive Hydrophilic Matrix Tablets with Famotidine Using Different Combination of Polymers. FARMACIA 2012; 60(4):457-474.
11. Gutsche, K.M. Strategies to overcome pH-dependent solubility of weakly basic drugs by using different types of alginates. Drug development and industrial pharmacy 2008; 34(12):1277-1284.
12. Squier C.A, W.P. Structure and function of the oral mucosa and implications for drug delivery. Drugs and the pharmaceutical sciences 1996; 74:1-26.
13. Monica R.P Rao, S.S. Design and evaluation of sustained release matrix tablets using sintering technique, International Journal of Pharmacy and Pharmaceutical Sciences 2016; 8(2): 115-121.
14. Tangri P., S.K. Mucoadhesive drug delivery: mechanism and methods of evaluation. Int. J Pharm Biosci 2011; 2(1): 458-467.
15. Patil S.B., R.S. Mucoadhesive polymers: Means of improving drug delivery. Pharma Times, 2006; 38(4):25-28.
16. Korner A., A. L., P. W. Tuning the polymer release from hydrophilic matrix tablets by mixing short and long matrix polymers. Journal of pharmaceutical sciences 2005; 94(4):759-769.
17. Hassan N., R. K. K. A. Development and evaluation of buccal bioadhesive tablet of an anti-emetic agent ondansetron. AAPS PharmSciTech 2009; 10(4):1085.
18. Kotagale N.R. Carbopol 934-sodium alginate-gelatin mucoadhesive ondansetron tablets for buccal delivery: Effect of PH modifiers. Indian journal of pharmaceutical sciences 2010; 72(4):471.
19. Madhu S. S., S. K. D. Effect of excipient and processing variables on adhesive properties and release profile of pentoxifylline from mucoadhesive tablets. Drug development and industrial pharmacy 2006; 32(3):377-387.
20. Venkatesh T., A. K. Formulation optimisation of Ondansetron floating tablets for gastric retention, International journal of advanced pharmaceutics 2011; 11-18.
21. Akbari B.V., D. R. Design, evaluation and study of effect of hydrophilic polymers on release rate of antiulcer floating tablets. Journal of Young Pharmacists 2009; 1(4): 305.
22. Arora S., B. R. Effect of polymers and excipients on the release kinetics, bioadhesion, and floatability of metronidazole tablet. Asian Journal of Pharmaceutics 2014; 5(4): 215-224.
23. Deshmukh V.N. Formulation and in vitro evaluation of theophylline anhydrous bioadhesive tablets. Asian journal of pharmaceutics 2009; 3(1): 54.
24. Yadav V.K., A. G. Mucoadhesive polymers: means of improving the mucoadhesive properties of drug delivery system. J chem pharm Res. 2010; 2(5):418-432.
25. Patel J. K., M. M. P. Stomach specific anti-helicobacter pylori therapy: preparation and evaluation of amoxicillin-loaded chitosan mucoadhesive microspheres. Current drug delivery 2007; 4(1):41-50.