

Development and evaluation of mucoadhesive buccal tablet containing metronidazole for the treatment of periodontitis and gingivitis

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Abstract: The current study was designed to evaluate mucoadhesive buccal tablet containing metronidazole (MTZ) for local action aided by Hydroxypropylmethylcellulose K4M (HPMC) and Carbopol 940® (CP) as mucoadhesive polymers with other ingredients like sodium starch glycolate (SSG), polyvinyl pyrrolidone K30 (PVP) as disintegrant and binders respectively. Formulations (F1-F8) were prepared by direct compression method and characterized for different physicochemical parameters. Results showed that the average weight and friability were within USP limits. Maximum mucoadhesive time was observed for F2 (14 hr) containing moderate amount of HPMC and CP used in the study. Up most mucoadhesive strength value was observed with F3 containing highest amount of HPMC used. Results indicated that high amount of HPMC was linked with the moderate to higher mucoadhesive strength and time. Maximum swelling index was observed in F7 (191.3%). Only F1-F3 showed complete in vitro MTZ release within 3 hr. Formulations containing PVP released MTZ incompletely over time while SSG released earlier. Formulation F1 was considered best in terms of MTZ release (100.5%) with diffusion based Korsmeyer-Peppas release kinetics. Therefore, MTZ exhibiting best physicochemical characters in mucoadhesive buccal tablet was found in F1 containing HPMC and CP in amounts of 37.5 mg and 25 mg, respectively, for local action.

Keywords: Carbopol tablet, HPMC k4M, metronidazole buccal tablet, mucoadhesive buccal tablet, Korsmeyer-Peppas release.

INTRODUCTION

Periodontal diseases are combination of Gingivitis and Periodontitis according to American Association of Periodontics (Socransky and Haffajee, 2002). The disease classification is based on area of gums involved. Gingivitis is an inflammatory response of gingival tissues due to aggregation of plaque on gingival margin (Campbell, 2011). It is just an inflammation as no alveolar bone loss occurs unless progressed to periodontitis (Barrington and Nevins, 1990; Polson and Caton, 1985). It is reversible condition. While periodontitis is caused by gingival ulceration consequently distracting tooth supporting structure. Biofilm (deposition of plaque) affect gingival lining and provide ideal environment for the growth of anaerobic bacteria. The progression of such destructive process leads to tooth loss. Certain bacteria causes illness by developing sub gingival plaque and destroy supporting structure. Most causative agents are gram negative anaerobic bacteria (Loesche, 1996).

The therapeutic goal is to suppress disease condition with the aid of some chemical agents like chlorhexidine, essential oils, triclosan mouth washes, antibacterial gels, oxygenating agents, sanguinarine or use of fluorides. But such treatments alter the taste buds, teeth staining,

formation of calculus, lesions, ulceration and sometimes allergic reactions (Ciancio, 1992). The variable dose of these chemical results in therapeutic failure that urge to develop other alternatives. Non-surgical anti-infective therapy is a cornerstone of periodontal infections. Supportive therapy such as maintenance of oral hygiene along with anti-infective therapy reduces the severity of illness (Plessas, 2014).

Mouthwashes, gels, chips, filaments these dosage forms have become fail to satisfy or control the formation of biofilm because it doesn't reach sufficiently to the target site for sustained period of time. The disadvantage of systemic therapy is adverse effects that restrict its use to some extent (Soskolne, 1997). Another attractive dosage form is mucoadhesive buccal drug delivery system that releases drug into buccal region for absorption. It has certain advantages like high blood flow and ease of administration or removal of tablet from the mucosa. The table is attached to the buccal mucosa of the patient at any time of the day while working. In dosage form is attached with the buccal mucosa so that the drug is released from polymeric matrix over time locally (Salamat-Miller *et al.*, 2005). The extent of release from dosage is controlled using different mucoadhesive polymers. The tablet may be inserted under the cheeks or lips and fixed onto buccal mucosa (Perioli *et al.*, 2007). Local administration is preferable over systemic administration for such

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pathological condition in order to avoid the systemic adverse effects. Metronidazole, tetracycline, clindamycin and ciprofloxacin are used extensively in the management of gingival plaque. Due to broad spectrum activity against protozoa and anaerobic cocci as well as positive and negative bacilli (Stoltze and Stellfeld, 1992) metronidazole is highly recommended for the treatment of periodontal infection. Metronidazole is choice of drug for the treatment of anaerobes such as Porphyromonas gingivalis due to less MIC (Ramadan *et al.*, 2010). It exhibits rapid bactericidal activity against anaerobes. It is selectively toxic to anaerobic bacteria under anaerobic condition and show concentration dependent bactericidal activity. Post antibiotic effects are observed for more than 3hr for metronidazole (Lamp *et al.*, 1999). Per oral delivery of metronidazole produce significant adverse effect so local delivery is preferred to minimize such hazards. Buccal route has gained prime consideration to administer drug through it such as mucoadhesive buccal tablet. Buccal route is preferable for both local and systemic action. Local action of mucoadhesive use to target those disorders that can treat locally thereby reducing dose (Sudhakar *et al.*, 2006). The advantages of this route are improved efficacy, ease of administration and removal in case of emergency, dose reduction and variability of drug (Varum *et al.*, 2008). Mucoadhesive dosage form facilitates the contact of dosage form with the mucosal membrane that ultimately increases the surface area to enhance the release of drug at targeted site (Carvalho *et al.*, 2010).

So, the aim of present study was to develop mucoadhesive buccal tablets of metronidazole for the treatment of gingivitis with dose that remain in therapeutic concentration within local region. The objective of the study was to characterize tablet and to assess in vitro release of metronidazole buccal tablet.

MATERIALS AND METHODS

Materials

Metronidazole was obtained as a gift from Remington Pharmaceuticals. Other following excipients like hydroxypropylmethyl cellulose (HPMC K4M) as release retardant were gifted by Servier Research Pharmaceuticals (Pakistan). Carbopol (CP® 940) was used in concentration to produce gelling effect (Rowe *et al.*, 2009) sodium starch glycolate (SSG) as super-disintegrant and polyvinylpyrrolidone (PVPK30) as tablet binder. Magnesium stearate (Mg.St.) and sucrose were gifted by Harmann Pharmaceuticals Pvt. Ltd. (Pakistan).

Mixing and tableting

Each formulation was coded with pre mark "F" i.e. F1, F2, F3.....F8. Mucoadhesive formulations (F1-F8) were prepared by varying the composition of mucoadhesive polymers. All active and excipients, whether used in fixed

or varied quantities (mg), were weighed according to the composition listed in table 1. All ingredients were weighed in an electrical analytical grade balance. Ingredients were blended geometrically and shaken vigorously for 5 minutes in closed polythene bags before compression. Each bag was marked with formulation code. Mixed ingredients were then compressed by using single punch manual tablet machine at a pressure of 2 tons for 30 sec, having flat faced punch of 8mm diameter. Since powder did not resist compression, direct compression method was employed throughout the study and 50 tablets were prepared for each formulation batch.

Physicochemical evaluation of buccal tablet

All the physical tests for tablets including weight variation, thickness, diameter, friability, hardness, mucoadhesive strength, mucoadhesive time, swelling index and in vitro metronidazole release were performed on each formulation of the tablet.

Weight Variation

To calculate average weight, 20 tablets were taken from each batch separately and average weight of the individual formulation was calculated using the Equation 1. Results were expressed in terms of average weight (mg) $\pm$ S.D (Standard deviation).

$$\text{Average Weight} = \frac{\text{weight of tablets}}{\text{no. of tablets}} \quad \text{Eq. 1}$$

Thickness and diameter

Thickness and diameter were calculated with the help of Vernier Caliper and results were expressed in terms of standard deviation (Mizrahi and Domb, 2008).

Hardness

Hardness test was performed using semi-automated hardness tester MGT 2020 on tablet of each formulation. tablet was placed in the tester horizontally and applied force was noted to break up the tablet diametrically. Results were expressed as S.D of 10 tablets.

Friability

Roche Friabilator® was used to calculate the friability of the tablets. Initially, pre-weighted 26 tablets of individual formulations were placed in the Friabilator to mark the weight near to 6.5g with a speed of 25rpm for 4 min. After operation, tablets were dusted and weighed again. The percentage loss or Friability was calculated according to Equation 2 (Shidhaye *et al.*, 2010)

$$\text{Friability (\%)} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100 \quad \text{Eq. 2}$$

Surface pH

Tablet from individual batch was placed in a petri dish containing 10ml distilled water adjusted to pH 6.8 with 0.1N HCl. The pH was measured after 2 hr by touching the electrode of digital pH meter to the surface of tablet (Shidhaye *et al.*, 2010).

Swelling index

To calculate the swelling index, weighted dry tablet was placed in separate petri dishes containing 10 ml of distilled water adjusted to pH 6.8 with 0.1N HCl. The weight gain by tablet due to sorption of water was measured by reweighing the tablet after defined interval i.e. 0.5hr, 1hr, 2hr...8hr on an electrical balance. This weight gain was considered as swelling index of respective formulation. The swelling index was calculated according to Equation 3 (Hussain *et al.*, 2016).

$$\text{Swelling index} = \frac{\text{final swelling} - \text{initial swelling}}{\text{initial swelling}} \times 100 \quad \text{Eq. 2}$$

In vitro mucoadhesive time

To calculate *in vitro* mucoadhesion time, an apparatus similar to Hussain *et al.* was constructed. For this, freshly cut piece of rabbit buccal mucosa was fixed on to glass slide. One face of the tablet, wetted with 50μL distilled water adjusted (pH 6.8), was pressed gently for 20 sec against buccal mucosal surface. The glass slide was then placed at an angle of about 45° in a beaker containing 800 ml distilled water adjusted to pH 6.8. The solution was rotated at a speed of 100 rpm with the help of magnetic stirrer. The whole system was maintained at 37°C throughout the experiment. The time in which tablet detached from the slide or disappeared due to disintegration was considered as the mucoadhesion time for that respective formulation (Hussain *et al.*, 2016).

In vitro mucoadhesive strength

In vitro mucoadhesive strength was calculated by physical balance (Bhanja *et al.*, 2010) through a modified arm to calculate the force of detachment. Both faces of the tablet were wetted with a drop of distil water and was pressed gently between two glass slides, each already attached with rabbit buccal mucosa on its surface. One glass slide was fixed with the base while other was attached with moveable strung limb of the pan. By adding weight to the other pan, the minimum weight that is required to detach the tablet from mucosa was considered as the mucoadhesive strength. The same procedure was repeated on tablet of each formulation.

In vitro release

The USP type II dissolution paddle apparatus Erweka (DT-700) was used to study *in vitro* release of MTZ. Dissolution media of 900ml distilled water adjusted to 6.8 was filled in the dissolution apparatus by maintaining whole system at 37±1°C throughout the experiment. The paddles speed was set at 50rpm. Sample were collected at an interval of 0.5hr, 1hr, 2hr....3hr or till complete release to calculate % amount of drug released over time. Samples were analyzed using UV spectrophotometer.

In vitro release kinetics

To determine the mode of release of MTZ, DD solver® was applied on the *in vitro* release results of those

formulations which almost released completely over time. Different kinetic models i.e. zero order, first order, Higuchi, Korsmeyer-Peppas and Hixson Crowell were applied to evaluate the mode of release of MTZ. These models can be quantified as, The zero order release is depicted in Equation 4 which is:

$$Q_t = Q_0 + K_0 t \quad \text{Eq. 4}$$

Where “ Q_t ” corresponds to the quantity of drug dissolved in time “ t ”, Q_0 is the quantity of drug in the solution and K_0 is the zero order release constant. For first order release, the equation was:

$$\log Q = \log Q_0 - Kt / 2.303 \quad \text{Eq. 5}$$

In it, “ Q_0 ” reflects the initial drug concentration and “ Q ” is the concentration at time “ t ”. The value “ K ” is the rate constant for 1st order kinetics. For Higuchi model, the assumptions are expressed in Equation 6:

$$Q = K_H = \frac{1}{2} \quad \text{Eq. 6}$$

The value “ K_H ” represents the Higuchi dissolution constant. Hixson Crowell model is as follows:

$$W_0^{1/3} - W_t^{1/3} = \kappa_s t \quad \text{Eq. 7}$$

Where “ W_0 ” and “ W_t ” are the drug concentrations initially and at time “ t ” respectively. The constant “ κ_s ” is dependent on surface-volume ratio. The Korsmeyer-Peppas model is expressed as shown in Eq. 8.

$$M_t / M_\infty = at^n \quad \text{Eq. 8}$$

Where “ M_t / M_∞ ” is the ratio of drug released from the tablet in time “ t ”. The value of “ n ” is used to illustrate the release mechanism based on fickian, non-fickian, super-case etc. release of the drug (Costa and Lobo, 2001).

RESULTS

Eight different formulations containing different proportions of HPMC, CP, SSG and polyvinylpyrrolidone (PVP) were evaluated for different physicochemical tests i.e. weight variation, friability, hardness, mucoadhesive strength, mucoadhesive time, surface pH, swelling index and *in vitro* MTZ release. F1-F5 were without disintegrating agent i.e. SSG while formulations F6-F8 were containing SSG. In F1-F3, increasing and decreasing concentrations of mucoadhesive polymers i.e. HPMC and CP were added, respectively. It is because Carbopol possesses gelling as well as mucoadhesive properties which were desirable in the case of mucoadhesive tablet (Singla *et al.*, 2000). Similarly, HPMC also possesses such properties and has been used extensively for buccal mucoadhesive drug delivery (Salamat-Miller *et al.*, 2005). Formulations F4 and F5 contained PVP additionally as binder in different concentrations. The purpose of adding binder and disintegrating agent was to study the effect of such on the release of the drug. The release of the drug was to release the drug over short period of time for local action (Hussain *et al.*, 2016).

Table 1: Composition by weight (mg) of different mucoadhesive buccal formulations (F1-F8) containing metronidazole

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
MTZ	20	20	20	20	20	20	20	20
CP	25	10	5	4.5	6.5	5	5	2.5
HPMC	37.5	62.5	112.5	10	15	20	7.5	7.5
Sucrose	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
Mannitol	117.5	107.5	62.5	160.5	153.5	147.5	157.5	157.5
Mg.St.	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
SSG	-	-	-	-	-	7.5	10	12.5
PVP	-	-	-	5	5	-	-	-
Total	250	250	250	250	250	250	250	250

Table 2: Physical characterization of mucoadhesive buccal formulations F1-F8 (Mean $\pm$ S.D)

Code	Weight variation (mg)	Friability (%)	Hardness (Kg/cm ²)
F1	242 $\pm$ 2.45	0.81	6.06 $\pm$ 0.04
F2	245 $\pm$ 4.21	0.64	6.66 $\pm$ 0.40
F3	242 $\pm$ 2.58	0.81	6.27 $\pm$ 0.41
F4	244 $\pm$ 2.58	0.65	6.68 $\pm$ 0.13
F5	244 $\pm$ 3.99	0.65	6.11 $\pm$ 0.36
F6	241 $\pm$ 3.16	0.81	5.97 $\pm$ 0.08
F7	249 $\pm$ 2.10	0.81	6.51 $\pm$ 0.88
F8	242 $\pm$ 2.58	0.61	6.56 $\pm$ 0.48

Value of n is 10 for hardness, 20 for weight variation and 26 for friability.

Table 3: Mucoadhesive time, mucoadhesive strength and surface pH of mucoadhesive buccal Formulations F1-F8

Code	Mucoadhesive time (hr)	Mucoadhesive strength (g)	Surface pH
F1	12	17.59	5.92
F2	14	20.37	5.9
F3	12	20.73	7.39
F4	12	9.45	5.64
F5	12	12.77	5.93
F6	0.5	9.33	5.95
F7	1	5.67	5.8
F8	1.5	6.47	5.91

Table 4: Swellability indices of mucoadhesive buccal formulations F1-F8

Code	0.5hr	1hr	2hr	3hr	4hr	6hr	8hr
F1	16.67	25	25	25	37.5	41.67	79.17
F2	13.63	13.63	18.18	18.18	40.91	72.72	100
F3	10	5	5	5	25	25	140
F4	26.08	30.43	30.43	30.43	52.17	52.17	69.56
F5	22.72	36.36	36.36	40.91	50	50	59.09
F6	33.33	37.5	37.5	70.83	70.83	70.83	79.17
F7	73.91	78.26	104.35	143.47	173.91	173.91	191.30
F8	65.21	78.26	65.22	130.43	130.43	134.78	160.86

Physicochemical characterization

Result of physical parameters has been summarized in table 2. The hardness of the all formulations (F1-F8) was within range of 5.9 to 6.8kg/cm² (Aditya *et al.*, 2010). Maximum deviation was observed for F7 which was 0.88. The average weight of all the formulations was found in

between 241 mg and 249 mg. Maximum and least deviation was observed for F2 and F7, which were 4.21% and 2.10% respectively. It is complying with the allowed deviation according to USP i.e. 5% (Piau, 2007). The friability of all formulations was also within the stated USP limits i.e. less than 1%. Least friability value was

observed with F8 (0.61%) whereas maximum tablet contents loss was evident in F1, F3, F6 and F7. The physical tests results revealed that no significant impact was observed in formulations containing SSG and PVP as presented in table 2.

Table 5: *In vitro* release of mucoadhesive buccal formulations F1-F8

Code	0.5	1hr	1.5hr	2hr	3hr
F1	48.6	54.6	76.8	92.4	100.5
F2	51.9	57	66	70.2	97.9
F3	49.8	52.8	63	64.8	98.7
F4	35.7	44.1	57.6	68.1	83.1
F5	54.3	69.6	79.5	90.9	92.2
F6	41.4	71.1	93.9		
F7	45.3	64.2	97.9		
F8	65.7	100			

Table 6: Release kinetics of metronidazole in mucoadhesive buccal formulations F1 showing coefficient of correlation values for different kinetic models

Kinetic Models	r^2 value	n
Zero order1	0.1191	-
First order	0.8942	-
Higuchi	0.9326	-
Korsmeyer-Peppas	0.9393	0.45
Hixson Crowell	0.8898	-

Mucoadhesive strength and time

Maximum mucoadhesive time was observed F2 which was 14 hr. It might be due to cross linkage and hydrogen bonding with CP as it also contained greater amount of HPMC with no SSG. While PVP containing formulations i.e.F4 and F5 showed effects similar to F1 and F3. Since amounts of HPMC and CP were added in PVP containing formulations (F4 and F5) in least concentrations. It revealed that the mucoadhesive effect of PVP alone is comparable to the combined mucoadhesive effect of CP and HPMC. So, the mucoadhesion produced by PVP is satisfactory (Tan *et al.*, 2000). Poor mucoadhesive time values were observed with formulations containing SSG compared with others. The purpose of additions of binder and disintegrant in the formulations were to study the impact of such ingredients on mucoadhesive and *in vitro* MTZ release.

For mucoadhesive strength, higher force was observed in F2 and F3 which was above 20 g. It might be due to bioadhesive property of HPMC by forming crosslinking with polyacrylic polymers like CP. Highest value was observed with F2 which was 20.73g. As predicted earlier, formulations containing SSG possessed least mucoadhesive strength. Similarly, moderate values were observed with PVP containing formulations i.e. F4 and F5. Similarly, the maximum value of mucoadhesive

strength in PVP containing formulation was for F5 (12.77g). Results indicate that high amount of HPMC was linked with the higher mucoadhesive strength and time. To ascertain the possibility of buccal irritation surface pH test was performed on each tablet formulation. Surface pH should be in desired physiological range i.e. 5.5-7.0 (Patel *et al.*, 2011) in order to avoid any disturbances in physiology of buccal mucosa. Surface pH of all the formulations was within the desired physiological range as depicted in table 3, except F3 which was very slightly alkaline i.e. 7.39.

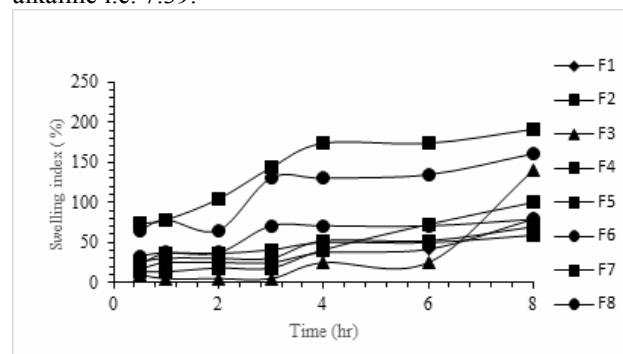


Fig. 1: Graphical depiction of swelling indices of mucoadhesive buccal formulations F1-F8.

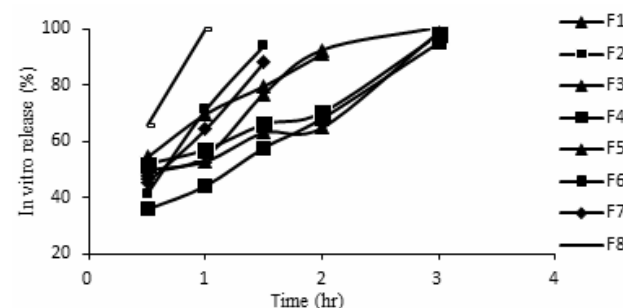


Fig. 2: Graphical depiction of in vitro metronidazole release of mucoadhesive buccal formulations F1-F8

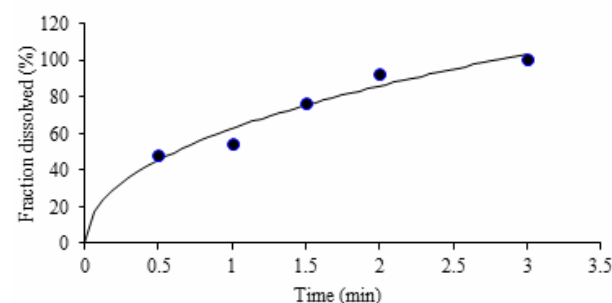


Fig. 3: *In vitro* release kinetics of mucoadhesive formulations (F1) containing MTZ for local action.

Swelling index

The swelling index was performed in distilled water pH 6.8 adjusted with 0.1N HCl and results were tabulated in as percent increase in weight during given time span (table 4). As depicted in fig. 1, different swelling behaviors were observed in different mucoadhesive formulations. Highest swelling indices were observed with formulations containing superdisintegrant.

Maximum swelling ability till the final hour was observed with F7 containing SSG, as has been reported for SSG to swell as much as 300 (Rowe *et al.*, 2009). The swelling index of F7 at any hour was most compared with others. Slowest initial swelling index was observed with F3 containing highest amount of HPMC used in the study. However, after 6 hr, steepest response was observed, unlike with other responses. Since HPMC is release retardant at higher concentrations in mucoadhesive formulations (Chopra *et al.*, 2007) through gel formation, it is suspected to cease inward and outward movement of water in matrix systems (Reza and Sara, 2010). It inhibited the sorption of mucoadhesive tablet, another reason for the less swellability of F3 is least concentration of carbopol because ionized polymer take up water and become hydrated.

In vitro release

In vitro dissolution test was performed using type II paddle apparatus containing 900ml of distilled water adjusted to pH 6.8 with 0.1 N HCL in dissolution. The whole solution maintained at $\pm 37^{\circ}\text{C}$. Samples were drawn at defined interval and was analyzed on UV spectrophotometer at wavelength of 277 nm. A calibration curve was also drawn for MTZ in dissolution medium which showed an r^2 value of 0.999. Results presented in table 5, showed that mucoadhesive formulations released drug within 3hrs. Different release behaviors were observed in all formulations whether or not, containing SSG or PVP. All formulations released MTZ faster where 50 % of the drug was released within 1 hr, except F4. Slower release was observed with F4 and did not released MTZ completely over time.

The Kinetic analysis

DD solver® was employed on single formulation which showed complete release and significant mucoadhesive results. For this F1 was selected. Zero order, first order, Higuchi, Korsmeyer-Peppas and Hixson-Crowell models (Eq. 4 - Eq.8) were applied on the release profile of such formulations (Zhang *et al.*, 2010). The maximum value of R^2 in any model was considered as the best fit release for that formulation (Zuo *et al.*, 2014). Results showed that highest R^2 value was observed for Korsmeyer-Peppas model as shown in table 6. The value of “n” for this model was 0.45 which depicts that the mode of MTZ release from HPMC matrix was diffusion (Costa and Lobo, 2001) only (fig. 3).

DISCUSSION

As mucoadhesive strength and time depends upon mucoadhesive capability and nature of the polymer (Velmurugan *et al.*, 2010), values of mucoadhesive strength and time varied significantly as depicted in table 3. It appeared that the physical forces in terms of hydrogen bonding affected the intensity of adhesion. Unlike physical test results, formulations containing SSG

possessed least strength and time values. It might be due to the fact that SSG is a super-disintegrant and lessened the mucoadhesion property of polymers due to evident disintegration (Zhang and Christensen, 1996). For such formulations, a decrease in mucoadhesive response was observed. Because strength and time parameters were performed in moisture which boosted disintegration compared with others. For higher mucoadhesive force like with F2 and F3, CP has strong bio adhesion due to presence of carboxyl group, it is responsible for hydrogen bonding, ultimately leading to strong mucoadhesion.

For swelling indices values, rapid initial water uptake was also observed with SSG containing formulations i.e. F6-F8, where maximum initial swelling trend was observed with formulation F7. SSG facilitated the swelling as it contains carboxymethyl group that breaks the hydrogen bonding within and allows further hydration (Bala *et al.*, 2012). However, as both mucoadhesive polymers are hydrophilic polymers, significant water uptake was seen in formulations containing low concentrations of both mucoadhesive polymers i.e. F6-F8. Due to hydration polymeric network expanded and uncoil the binding sites. It was also observed that particles broke off from tablet during over time which predicts that super-disintegrant imparted its role (Kshirsagar *et al.*, 2011). It can also be observed that PVP containing formulations had minimal extent of swelling over time. Although it is highly soluble in water but does not able to swell enough (Marsano and Bianchi, 2002). It is because PVP as binder and thickener in tablet formulations reduces the extent of swelling (Kamal Hossen *et al.*, 2008). A slow increase in swell ability was observed with formulations not containing SSG and PVP (Bhanja *et al.*, 2010) as shown in table 4.

Generally, slower *in vitro* release was observed with PVP containing formulations. Logically it is suspected that the presence of binder retarded the release of MTZ. In F6-F8, complete drug release within 1.5 hr which depicts the function of super disintegrant. Super disintegrant helped to break the polymeric chains to release drug earlier. Except F4, all the formulations not containing SSG and PVP almost released drug completely within 3 hr. All the formulations containing HPMC and CP released MTZ almost completely but 100% release was depicted only by F1. The Korsmeyer-Peppas release model of drug suggests that interlocking of HPMC matrix was major hindrance for the water-soluble release of drug from mucoadhesive formulation.

CONCLUSION

Various tests on mucoadhesive buccal tablet to release metronidazole locally for the treatment of orodental infections was formulated with the polymeric blend of HPMC K4M, CP, SSG and PVP. The findings of various physicochemical tests on different formulations revealed that increase or decrease in the concentration of HPMC,

CP, SSG or PVP had significant change in the physical test results. With an exception, the pH values of the solution were also within the physiological limits. The increased swell ability index was associated with the addition of SSG as well as with lower amounts of both HPMC and CP. The low swell ability values with high HPMC correlates the release retardant effects of HPMC and CP. The higher mucoadhesive time and mucoadhesive strength values were directly associated with increased amount of HPMC (Singh., 2012). However, the formulations containing no PVP and SSG were associated with completely release overtime. Such formulations containing PVP and SSG released MTZ slowly and earlier than the stated time period. All the formulations containing HPMC and CP only showed satisfactory release in concentrations used in the study. Therefore, it was concluded that formulation F1 containing CP and HPMC in the concentration of 10% and 15% depicted the optimized mucoadhesion and exhibited complete in vitro release results up to 3 hr.

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