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Original Article

Formulation and Evaluation of Mucoadhesive Herbal Buccal Patch of *Psidium Guava L.*

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Abstract

Mucoadhesive drug delivery system is a distinct advantage over the traditional dosage forms such as, tablet, gels and solution etc. In the Mucoadhesive buccal patch for systemic drug delivery of drug like flavonoid which is isolated from the leaves of Psidium guajava in which system avoid first pass effect of hepatic metabolism. The buccal patch shows desired physicochemical and mechanical properties. The various evaluation parameter are used to evaluate the Mucoadhesive buccal patch. In-vitro drug release study shows that buccal patch deliver the drug like Quercetin to oral mucosa for the period of 7:30 hrs and also exhibit the stability study under desired condition. HPMC K15 buccal adhesion patch shows satisfactory physico-chemical properties. The ratio of hydrophilic polymer carbopol 940 to HPMC K15 had significant Mucoadhesive characteristics like swelling index, ex-vivo mucoadhesion strength and in-vitro drug release is observed between drug release and permeation study in-vitro. So it can conclude that the HPMC K15 and Carbopol 940 could be good carrier in buccal delivery of Quercetin.

Keywords: Carbopol 940, mucoadhesive buccal patch, HPMC K15, Psidium Guajava, Quercetin.

1. Introduction

The oral cavity is viewed as a convenient and easily accessible site for the delivery of therapeutic agents. Sobero, the discoverer of nitroglycerine, noted absorption of drugs through oral cavity as early as 1847 and Walton and Lacey first reported systemic studies of oral cavity absorption in 1935. Since then, substantial efforts have been focused on drug absorption from a drug delivery system in the particular region of oral cavity. Since the early 1980s there has been renewed interest in the use of bioadhesive polymers to prolong contact time in the various mucosal routes of drug administration [1, 5]. The ability to maintain a delivery system at a particular location for an extended period of time has great appeal for both local as well as systemic drug bioavailability [3].

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Drug absorption through a mucosal surface is efficient because mucosal surfaces are usually rich in blood supply, providing rapid drug transport to the systemic circulation and avoiding degradation by gastrointestinal enzymes and first pass hepatic metabolism [2, 6].

Conventional Dosage Form

The conventional type of buccal dosage forms are buccal tablets, troches and lozenges, and mouth washers. These tablets should be designed not to disintegrate but to slowly dissolve, typically over a 15 to 30 minutes period to provide for effective absorption. Troches and lozenges are two other types of tablets used in oral cavity where they are intended to exert a local effect in the mouth or throat (3).The present study demonstrated that the Methanolic extract of the aerial part of *Psidium Guajava* Linn and to isolate the flavonoid Quercetin showed significant Antibacterial activity and formulation as Antiulcer activity, Formulation and Development of Anti-ulcer Herbal

Mucoadhesive Buccal patch. The mouth ulcer are small painful inside lining of mouth. The usually developed on the inside of the lips and cheeks and under the edge of tongue. Studies were carried out with a view to select suitable polymer composite using in combination with polymers. The *Psidium Guajaval* is a most common plant usually used as a various treatment which is mention in the literature review. Psidium guava has been found most important rich chemical constituent Quercetin as flavonoid which is responsible to cure a mouth ulcer. However no specific formulation for mouth ulcer has been reported as mucoadhesive herbal buccal patch. Therefore the aim of the research project is to develop a formulation easily palatable, absorbable oral formulation rendering significant oral antiseptic activity that can be effectively used in mouth ulcer [14, 15].

2. Materials and Methods

2.1. Materials

Quercetin was obtained by the isolation from the leaves of Psidium guajava L. in laboratory. HPMC K-15, Carbopol 940, Ethanol, water, glycerin and Tween 80 were procured from Loba chemicals, Mumbai.

2.2. Method of Preparation of Buccal Patch[7]

Methods used to prepare Mucoadhesive adhesive buccal patches using *Solvent casting.* Carbopol 940 was placed in ethanol and stir for 60 min and HPMC K15 was dissolve separately in ethanol. The two polymeric solution mixed with the drug Quercetin which dissolves in ethanol. The all solvent mixed and pour in petriplates. Dried the patch for 72 hrs. After solvent evaporation, a thin layer is as like a laminated on petri plates. As per required size. The sample was packed in aluminum foil in cardboard box at room temperature.

2.3. Evaluation of Mucoadhesive Buccal Patch

1. Patch Thickness and diameter of patch[8]

Thickness and diameter was measured patches of each formulation were taken and the patch thickness was measured using micrometer screw gauge at different places and mean value and diameter was calculated.

2. Surface pH[8]

Buccal patches were left to swell for 2 h on the surface of an agar plate, prepared by dissolving 2% (*m/V*) agar in warmed isotonic phosphate buffer of pH 6.75 under stirring and then pouring the solution into a Petri dish till gelling at room temperature. The surface pH was measured by means of a pH paper placed on the surface of the swollen patch. The mean of two readings was recorded.

3. Folding endurance[9]

Three patches of each formulation of size (2x2 cm) were cut by using sharp blade. Folding endurance was determined by repeatedly folding a small strip of patch at the same place up to maximum 300 times or till it broke. The number of times, the patch could be folded at the same place without breaking gave the value of folding endurance. The mean value was calculated.

4. Swelling Index[9]

After determination of the original patch weight and diameter, the samples were allowed to swell on the surface of agar plate kept in an incubator maintained at 37±0.2.

Increase in the weight of the patch (n=3) was determined at preset time intervals (1-3h).

The percent swelling of the patches was calculated using the formula,

$$S_d\ (\%) = [(d_t - d_0)/d_{0]} \times 100$$

Where dt is the weight of swollen patch after time t, d_0 is the initial patch weight at zero time.

5. Residence time[10,11]

The *in-vitro* residence time was determined employing a modified USP disintegration procedure. The disintegration medium was composed of 800 ml isotonic phosphate buffer of pH 7.4 (IPB) maintained at 37^0C. A piece of porcine buccal tissue was used for this study. The tissue was attached to a rectangular glass piece using cynoacrylate adhesive from non-mucosal surface. The patch was tuck to the mucosal surface by applying small pressure. The glass piece with tissue and patch placed in the basket of disintegration apparatus and set in motion. The time necessary for complete erosion or detachment of the patch from the mucosal surface was observed and recorded.

6. Drug Content Uniformity[10]

The 1 cm² area of the medicated patch was allowed to dissolve in 100 ml IPB, pH 6.8. The amount of Quercetin in the solution was measured spectrophotometrically at λ max of 256 nm. From the absorbance and the dilution factor, the drug content in the film was calculated.

7. Viscosity[8]

Aqueous solutions containing both polymer and plasticizer were prepared in the same concentration as that of the patches. A model LVDV-II Brookfield viscometer attached to a helipath spindle number 4 or 18 was used. The viscosity was measured at 20 rpm at room temperature. The recorded values were the mean of five determinations.

***8. In-vitro* Bio-adhesion Studies[12]**

Mucoadhesive strength of the buccal films was measured on the modified physical balance using the method described by Gupta et al. The test assembly was fabricated as shown in schematic presentation in Fig no 1. This method involves the use of porcine membrane as the model mucosal membrane. The fresh porcine membrane was purchased from slaughter house and used within 2hrs then it was washed in isotonic phosphate buffer (6.8). The two sides of the balance were balanced with a 5gm weight on the right hand side. A piece of fresh membrane was glued to a support (glass block) with cyanoacrylate adhesive. The block was then lowered into the glass container, which was then filled with isotonic phosphate buffer (pH 6.8) kept at 37^0C, such that the buffer just reaches the surface of mucosal membrane, and keeps it moist. This was then kept below the left hand setup of the balance. The test film was glued with the same adhesive to a rubber block hanging on the left hand side and the balance beam raised with the 5gm weight on the right pan was removed off the weight. This lowered the rubber block along with the film over the mucosa with a weight of 5gms.The balance was kept in this position for 3 minutes and then slowly water was added to the plastic container in the right pan by pipette. The detachment of two surfaces was obtained. Weight of water was measured. Then the Bioadhesive strength of the film was calculated. Three films were tested on each porcine membrane. After each measurement, the tissues were gently and thoroughly washed with phosphate buffer (pH 6.8) and left for 5 minutes before the next experiment. Fresh membrane was used for each batch of films.

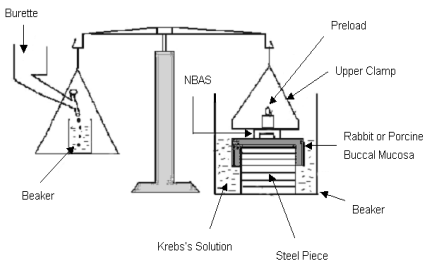

Fig 1. Measurement of Mucoadhesive strength.

10. *Invitro* release study (Modified USP Apparatus)

Adequate sink conditions were provided by placing 50ml of McIlvanic buffer (phosphate buffer pH 6.6). The United States Pharmacopeia (USP) XXIII rotating paddle method used to study the drug release from the bilayered and multilayered tablets. The dissolution medium consisted of phosphate buffer pH 6.8. The release was performed at 37-C ± 0.5-C, with a rotation speed of 50 rpm. The backing layer of buccal tablet attached to glass disk with instant adhesive (cyanoacrylate adhesive). The disk was allocated to the bottom of the dissolution vessel. Samples (5 mL) were withdrawn at predetermined time intervals and replaced with fresh medium. The samples filtered through Whatman filter paper and analyzed after appropriate dilution by UV spectrophotometry at suitable nm.

11. Drug polymer Interaction

By use of various available spectrophotometric methods the incompatibility of drug with excipients or within different excipients can be detected. Drug-polymer interaction is observed by IR spectrophotometry. An FTIR study of pure Drug and physical mixture of polymers were performed by KBr dispersion method.

12. Short-term stability studies [8, 13]

According to I.C.H. guideline the shelf-life of formulation can be established, secondly any incompatibility within formulation, if present can be detected changes in the appearance, residence time, release behavior and drug content of the stored bioadhesive patches were

investigated after 1, 2, 3, 4, 5, and 6 months. The data presented were the mean of three determinations. Fresh and aged medicated patches, after 6 months storage, were investigated.

Results and Discussion

Formulation and characteristic of mucoadhesive herbal buccal patch containing drug used as isolated Quercetin from Plant Psidium Guajava L. which shown in Table 2.

1. Thickness and diameter

All patches have a different thickness and uniformity diameter which are mention in the Table 2.

2. Weight Uniformity

The average weight found to mucoadhesive herbal buccal patch can be +– 0.00892, +- 0.01365gm which shown in table 1, because of using different concentration of polymer used in formulation of 2X2 cm weight of different patches.

3. Folding Endurance

The folding endurance recorded of the patch does not crack after folding of 300 times, so it can be taken as an end point of folding endurance, because of polymer concentration ratio (H.P.M.C K-15 and Carbopol 940) so it can be good mechanical and elasticity properties.

4. Surface pH

In the mucoadhesive herbal buccal patch formulation was observed pH in within the range of neutral pH in between +- 0.5hence it has no buccal irritation inside of oral cavity and achieve patient compliance. As the formulation in range of salivary pH which is 6.5 to 6.8 within the range except patch no IV pH +-7 where, patch no I+- 6.4, II+-6.8 and III +-6.7 having similar to salivary pH. This had shown in table 2.

5. Drug content uniformity

This indicates that, the drug can be dispersed uniformly in the mucoadhesive Herbal buccal patch. The absorbance λmax is uniformly seen in formulation.

6. Swelling index

It is most important property because it compliance with the patient. The swelling is depending on the polymer concentration used in the patch. The concentration in the patch carbopol 940 and HPMC K-15should be inversely proportional. The swelling study was observed in the agar plate method. The higher swelling of patch in the oral cavity and which shows the dislodgment in the various formulation in buccal patch. The buccal patch I and IV has lower swelling index while patch II and III has good swelling index which shown in table 1.

7. Viscosity

Viscosity can be checked by using the LVDII Brookfield viscometer by using spindle no18.at 20 rpm at room temperature which gives uniform viscosity except patch no. III and IV. Optimize Viscosity observed in patch no I and II which shown in table 1.

8. *In-vitro* Bioadhesion Studies

In bio adhesion study in which the mucoadhesion can be checked. The mucoadesion can affect the various factor like swelling rate, molecular weight of polymer, contact time of buccal mucosa and the biological membrane, can be study in bio adhesion study. Mucoadesion is formed in between the 8 to 21 gm of average range in which result indicate patch II and III has good mucoadesion property. The concentration range used in patch II and III of HPMC K-15 and Carbopol 940 effective than the concentration of patch I and IV.

9. *In vivo* Residential time

Residential time was determining using U.S.P. disintegrating apparatus with using sheep buccal mucosal membrane for this study. The study record the time for the detachment of mucoadhesive patch from the buccal mucosa. The time required for detachment of patch +- 7 hrs has observed in patch II, while patch I+-4.8 hrs ,patch III +- 6.75 and patch IV 4.75.so the good concentration observed in Patch II containing HPMC K-15 and Carbopl 940 has excellent polymer concentration.

10. *Invitro* release study

Invitro study of mucoadhesive Herbal Buccal Patch can be study by using the U.S.P. diffusion apparatus on the basis maintain time and concentration on residential time. After 7 hrs. drug release and was found a graph was plotted between time (min) and % drug release which shown in figure 1. The patch II has greater concentration than the patch I, patch III and Patch IV. Higher concentration also affect the

binding the drug, so drug decrease was release observed in Patch III. While in patch I and patch IV having less polymer concentration which affected drug release pattern. Increase the concentration of HPMC K-15 and carbopol showed extended and drug barrier diffusion and in minimum concentration of patch I and Patch IV showed minimum drug release. Result are observed figure 2.While good concentration of HPMC K-15 and Carbopol 940was observed in patch II showed proper drug release pattern was observed i.e. 92.09% in 07:30 hrs in shown in figure 3.

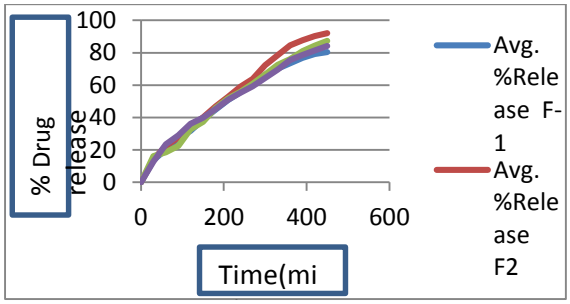

Fig. 2. Drug release in percentage of Formulation (F1, F2, and F3&F4) By U.S.P Dissolution study.

11. Drug polymer interaction

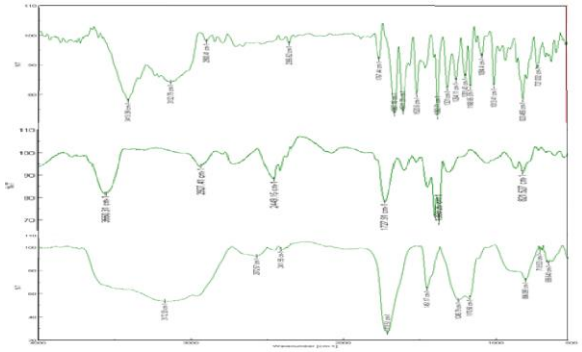

Fig. 3. Drug-polymer interaction studies I.R of isolated Quercetin, I.R. of HPMC K15, and I.R. of Carbopol 940

The IR spectra of Quercetin alone and its combination with polymer shown in graph, they cannot affected and prominently observed in IR spectra of Quercetin along with polymer which shown in figure 2 graph indicates no interaction between polymers and drug.

12. Stability study

On the basis of I.C.H. guideline short term stability study can be done for after 3mounths. The physical parameter can be observed, the appearance and texture does not change after the period of 3 months. The mucoadhesive herbal buccal patch concentration of drug Quercetin and polymer HPMC K15 and Carbopol 940 observed satisfactory result.

Conclusion

It may be conclude that Patch II containing polymer HPMC K-15 and Carbopol 940 was observed in preparation of mucoadhesive herbal buccal patch of psidium guava (quercetin). So the patch II has good polymer concentration to carry the mucoadhesive drug delivery of herbal constituent Quercetin, in which is isolated from *Psidium Guajava L*.

Research need

Drugs in clinical use today cause to attention of pharmaceutical companies because of their use in traditional medicines. Transmucosal Drug Delivery system using mucoadhesive polymers has been recently interested due to rapid onset of action, high blood level, avoidance of first pass effect and exposure of drug to gastrointestinal tract.

References

1. David Haris, Joseph R Robinson. Buccal drug delivery via the mucous membranes of the oral cavity. Journal of Pharmaceutical Sciences, 81, 1 (1992) 1-9.
2. Katarina Edsman, Helene Hagerstrom. Pharmaceutical applications of mucoadhesion for the non-oral routes. Journal of Pharmacy & Pharmacology, 57 (2005) 3-19.
3. Jin Whan Lee, Jae Han Park, Joseph R. Robinson. Bioadhesive-based dosage forms. Journal of Pharmaceutical Science, 85, 7 (2000) 850-17.
4. Controlled and Novel Drug Delivery by N.K. Jain, I st Edition, CBS Publishers and Distributors, New Delhi, (1997) 52-81.
5. Michael J. Rathbone, Drug and Pharmaceutical science. Oral mucosal Drug delivery, 74, 285.
6. Transdermal and Topical Drug Delivery by Tapash k. Ghosh, William R. Pfister, Interpharma, 259, 629, 650.

7. Harshad G. Parmar, Janak J. Jain, Tarun K. Patel, and Vishnu M. Patel Buccal Patch: A Technical Review, *International Journal of Pharmaceutical Sciences Review and Research*, 4, 3 (2010) 29.
8. Fatma Ahmed Ismail, Noha Adel Nafee, Nabila Ahmed Boraie, Lobna Mohamed Mortada. Design and characterization of mucoadhesive buccal patches containing cetyl pyridinium chloride. *Egypt Acta Pharm*., *53* (2003) 199–212.
9. Arpita Choudhary, Gulab Tiwari, Manisha Pandey, Koshy M. Kymonil, Shubhini A. Saraf. Formulation and characterization of carvedilol buccal mucoadhesive patches. Int. J. Res. Pharm. Sci., 1, 4 (2010) 396-401.
10. Rajesh Singh Patel* and S.S. Poddar, Development and Characterization of Mucoadhesive Buccal Patches of Salbutamol Sulphate *India Current Drug Delivery,* 2009, *6,* 140-144.
11. Dominique Duenene, Gilles Ponchel. Bioadhesion of solid oral dosage forms, why and how. European Journal of Pharmaceutics & Biopharmaceutics 44 (1997) 8-15.
12. K.R.Patel, Mukesh R. Patel, Tarak J. Mehta, Alpesh D. Patel, Natvarlal M. Patel. Formulation, Development and Evaluation of Mucoadhesive Buccal Patch of Carvedilol. International Journal of Drug Formulation & Research, 2, 2 (2011) 351-371.
13. Frank M. Painter, Quercetin: A Review of Clinical Application. www.chiro.org/nutrition/ABSTRACTS/ Quercetin_A_Review. html.
14. K.M. Nadkarni. Indian Materia Medica, I st Edition, Popular Prakashan Private Ltd., Bombay, India. (1999).
15. J.V Kamath, Nair Rahul, CK Ashok Kumar, S Mohana Lakshmi. *Review-Psidium guajava* L. International Journal of Green Pharmacy, 2, 1 (2008) 9-12.

Table 1. Formulation of Mucoadhesive Herbal Buccal Patch.

Sr. No	Ingredient	Formulation			
		F1	F2	F3	F4
1	Quercetin	0.5mg	0.5 mg	0.5 mg	0.5 mg
2	HPMC K15	100 mg	150 mg	200 mg	75 mg
3	Carbopol 940	25 mg	50 mg	75 mg	15 mg
4	Tween 80	0.0315 mg	0.0315 mg	0.0315 mg	0.0315 mg
5	Ethanol	4ml	7 ml	7 ml	4 ml
6	Water	3 ml	0.5 ml	1.5 ml	3 ml
7	Glycerin	0.0294 mg	0.0294 mg	0.0294 mg	0.0294 mg

Table 1. Characteristic of mucoadhesive herbal buccal patch of psidium guava (Quercetin).

Patch	Tk (mm) + mean	Di Cm +mean	Wu (gm) + mean	Fe	Surface. pH + mean	Du.	Si. % + mean	Vc. poise + mean	B.st (gm) + mean	*In vitro* res. time Hrs. + mean
I	±0.0475	±20.475	±0.01482	>303	± +6.4	0.02277	±42.75	10.5	±9.47	± +4.45
II	±0.0575	±20.225	±0.01215	>337	± +6.8	0.02380	±62.67	10.5	±18.80	± +7.00
III	±0.0620	±20.325	±0.01365	>324	± +6.7	0.02347	±67.15	14.6	±21.7	± +6.55
IV	±0.0825	±20.023	±0.0089	>313	± +7.0	0.02334	±39.46	9.7	±8.42	± +4.00

Tk-Thickness;Di-Diameter; Wu-Weight uniformity;Fe-Folding endurance;Du-Drug content uniformity;Si-Swelling index;Vc-viscosity;D.st-Bioadesion study.

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