INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

# EFFECT OF MORINGA GUM IN ENHANCING BUCCAL DRUG DELIVERY OF PROPRANOLOL HYDROCHLORIDE

**B. Arun Prasanth*, R. Sankaranand, V. Venu gopal, M. Anoosha, P. Sunitha, T. Swetha, P. Laxmi and A. Lalitha**

Department of pharmaceutics, SLC'S College Of Pharmacy, Hyderabad, Andhra Pradesh, India.

*Corresponding Author: arunprasad3210@gmail.com

**ABSTRACT**

Purpose of this research was to study mucoadhesive buccal tablets of Propranolol hydro chloride using Moringa gum as bioadhesive natural polymer. The conventional oral dosage form of this drug has low bioavailability due to high first pass metabolism, so it is modified as buccal drug dosage form to improve bioavailability and for the localized drug release because of high vascularity and drugs diffusing across the membrane have easy access to the systemic circulation via internal jugular vein. The various formulations F0 (oral), F1 , F2 , F3 , F4, F5 with respect to concentrations of Moringa gum 0 , 15, 25, 35, 45, and 55mg was prepared by direct compression method. Swelling index and force of detachment are directly proportional to the Moringa gum concentration. F1 formulation releases the drug more rapidly (almost 99.26±0.67) compared to other formulations in the 4$^{th}$ hour with the swelling index (1.4735±0.02).

**Keywords:** Mucoadhesion, Buccal drug delivery system, Moringa gum, Microcrystalline cellulose.

## INTRODUCTION

Recent investigations stated that buccal drug delivery system was found to be advantageous for both localized and systemic delivery of drugs because of high vascularity and drugs diffusing across the membrane have easy access to the systemic circulation via internal jugular vein. Mucoadhesion is defined as attachment of synthetic or natural macromolecules to mucin layer of mucus tissue. Mucoadhesive drug delivery systems utilize the property of bioadhesion of certain water-soluble polymers which become adhesive on hydration and hence can be used for targeting the drug to a particular region of the body for extended period of time. Mucoadhesive polymers can be used to overcome the physiological barriers in long term drug delivery, presystemic metabolism and instability in acidic environment associated with oral administration. Presence of saliva ensures relatively large amount of water for drug dissolution and also for drug permeation across mucus membrane compared to non mucus membrane. It can be administered to unconscious patients and provide rapid therapeutic serum concentration.

Propranolol hydrochloride (PRO-HCL), a nonselective beta-adrenergic blocking agent, has been widely used in the treatment of hypertension, angina pectoris, and many other cardiovascular disorders. The buccal mucoadhesive dosage form of propranolol hydro chloride was prepared and characterized by measuring the force of detachment, swelling index to improve residence time of drug.

## MATERIALS AND METHODS

### Materials

Propranolol hydrochloride (Knoll Pharmaceuticals Ltd), Moringa gum (the Indian materia medica), Microcrystalline

cellulose, Magnesium stearate, Ethyl cellulose were gifts from international speciality products (ISP) and other chemicals were obtained from commercial sources.

**Methods**

Buccal tablets were prepared by direct compression method. It involves two steps namely mixing or blending and compression. Various formulations were prepared by varying the concentrations of Moringa gum and microcrystalline cellulose to identify most effective formulation.

**Preparation of bilayered buccal tablets: It involves two steps**

**Step-1: Preparation of mucoadhesive layer**

The mucoadhesive layer was prepared by using the drug and natural polymers. The composition of the different formulations was represented in Table-1.The various components of each formula were weighed, mixed and passed through mesh (250 micrometer) to ensure complete mixing. The average weight of about 150 mg were separately weighed and compressed using a 13 mm diameter of a die on a Rotary Tablet machine (CADMACH 16 station ) using a force of 8 tons for 60 seconds. The prepared adhesive tablets were 13.32 mm in diameter and 1mm thickness.

**Step-2: Formation of backing layer to the mucoadhesive layer**

The backing layer was made up of ethyl cellulose. The solution was prepared by dissolving 6% w/v of ethyl cellulose in chloroform. The prepared solution was sprayed on to one surface of the mucoadhesive layer leaving the other side free and both sides of the tablets coated with the ethyl cellulose layer solutions. Then it was air dried at room temperature. The double layered structure design was expected to provide drug delivery in a unidirectional fashion to the mucosa. It avoids loss of drug due to wash out of saliva and the swelling profile of the buccal tablet can be changed dramatically by the amount of backing material and those changes could alter drug release profile. The resulting bilayered tablets were 13.32 mm in diameter and 1.4 mm in thickness.

**Evaluation of Tablets**

Ten tablets from each batch were evaluated for uniformity of weight and medicament content. Six tablets from each batch were examined for friability using a Roche-m type friabilator (DBK, India) and hardness using a Monsanto-type hardness tester (Edison, India).

**Swelling Study**

The moisture uptake studies give an indication about the relative moisture absorption capacities of polymers and an idea whether the formulations maintain their integrity after absorption of moisture. The swelling index of the tablets (Table–2) was evaluated by using six tablets of each formulation. These were weighted and placed separately in a pre-weighed basket made of stainless steel mesh. The total weight was recorded (W1). This basket was placed in a plastic vessel containing 4 ml of demineralized water, and placed in an incubator at 37°C±5°C. At various time intervals 45, 90, 135, 180 and 225 minutes, excess water was carefully removed, and the swollen tablets were weighed (W2).

The swelling index was determined from the formula:

$$\text{Swelling index} = (W2 - W1) / W1$$

**Surface pH of the tablet**

An acidic or alkaline pH may cause irritation to buccal mucosa. The surface pH of the tablet (Table- 4) was determined to investigate the effect of pH on the bioadhesion and possible side effect of the tablet in vivo. This was determined by allowing the tablet to swell in 1.0 ml. of demineralized water (pH 6.3 ± 0.06) for 135minutes. A combined glass pH electrode was brought into contact of the swollen tablet and pH was measured after 1 min equilibration. The surface pH of all the formulation was found to be within the pH range of 5-7 (salivary pH) and hence these formulations do not produce any irritation in the buccal cavity.

**Bioadhesion study**

Detachment force is measured by wilhelmy plate method is one of the traditional methods for the measurement of the force of adhesion of various bioadhesive dosage forms. The method involves the measurement of the dynamic contact angles and utilizes a microtensiometer and a microbalance. The

CAHN dynamic contact angle analyzer is used for this purpose. Wilhelmy plate method measures the bioadhesive force between the mucosal tissue and the polymer or dosage form attached to a metal wire and suspended into the microtensiometer. The mucosal tissue is used which is placed in the tissue chamber, this chamber is raised so as to make contact between the tissue and the test material. After a certain period, the stage is lowered and the force of adhesion is measured.

**In vitro drug release studies**

Release of Propranolol HCl from the buccal tablets (Table- 3) was studied in phosphate buffer (250ml) of pH 6.8 using an USP dissolution rate test apparatus, with a paddle rotating at a rate of 75 rpm and at 37°C±0.5°C. A specially designed glass cylinder closed at one end and opened at other end was placed inside the dissolution apparatus and it allows the tablets to dissolve from the fixed place without any movement (since the tablet should release the drug from a fixed area in the buccal region). Samples were withdrawn through a filter (0.45m) at different time interval and were assayed at 290 nm for propranolol hydrochloride using UV visible double beam spectrophotometer.

## RESULTS

**Hardness**

Microcrystalline cellulose used in the formulation produces sufficient hardness to the tablet which can withstand the abrasive forces, pressure during packing, storage etc.

**Swelling studies (Moisture Uptake Studies)**

The results of moisture absorption studies are presented in Table- 2. Results show that there are differences in moisture absorption with difference in concentration of Moringa gum polymer. The percentage moisture for all formulations F0, F1, F2, F3, F4 and F5 were observed at every 45 minutes by placing the drug without backing membrane in demineralised water, then complete swelling followed by erosion was observed indicating that the drug release mechanism involves swelling of the polymer initially followed by drug release from the matrix by diffusion. The swelling at 45 minutes was slower in F1 (i.e 3.6337±0.03) than compared to other formulations.

**Surface pH**

The table-4 states that increase in Moringa gum concentration does not have much effect on pH but pH range between 5-7 (salivary pH) is necessary for all the formulations to avoid irritation in the buccal cavity.

**Bioadhesion**

Fracture strength is the distance required to move the stage before complete separation occurs. It clearly states that from the figure-1, bioadhesive bond strength increases with increase in Moringa gum concentration so more fracture strength is required to break adhesive bond at the end of drug release for detachment of dosage form from buccal mucosa.

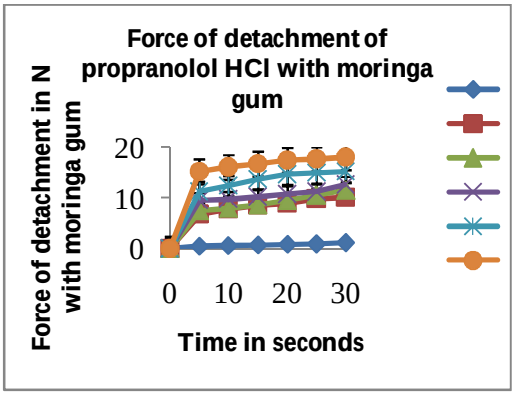


**Fig. 1**

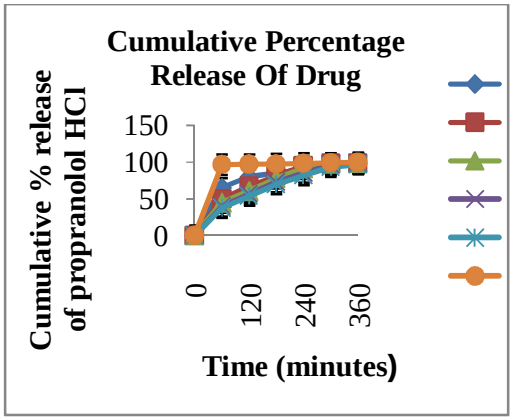


**Fig. 2: Cumulative mean (± standard deviation) percentage release of Propranolol HCl from directly compressed buccal tablets containing 15,25,35,45 and 55 mg of Moringa gum in Phosphate Buffer pH 6.8**

The formulation F0,F1,F2,F3,F4,F5 was selected to evaluate the bioadhesive properties of the propranolol HCl and F1 formulation was found to be better dosage form for buccal drug delivery because peak detachment force was found to be minimal (i.e. 6.82±0.52) than other formulations which is essential. Buccal dosages developed with the polymer Moringa gum possess reasonable bioadhesion in terms of peak detachment force and elongation at break values.

**Invitro Drug Release Profile**

The drug release profiles of drug (Table- 3) from buccal Dosage form clearly indicates from the plots that formulation containing Moringa gum, the drug release was governed by polymer content. No lag time was observed as the drug is directly exposed to the dissolution medium. An increase in the polymer content was associated with decrease in the drug release rates. There appeared no significant difference in the final percentage of drug release, which might be due to the fact that in all the formulations the drug dissolved completely in the dissolution medium. In case of F1 formulation 98.26% of the drug was released when compared with other formulations. In case of other formulation, increased amount of the polymer produced the water-swollen gel like state that could substantially reduce the penetration of the dissolution medium into the patches and so the drug release was retarded.

## DISCUSSION

**Evaluation of tablets**

The microcrystalline cellulose is added in the formulation as a direct compression adjuvant since the Moringa gum alone does not produce sufficient hardness. Thus all the parameters of the compressed tablets were practically within control.

**Swelling study**

The Moringa gum formulations take up water over the first 45 minutes, the rate depending on the concentration of the polymer present (lower concentrations swell more rapidly). Higher Moringa gum polymer concentrations showed slower initial water uptake, but take longer to become fully hydrated. After one hour formulation F1 containing 15mg Moringa gum polymer displays loss of weight due to tablet disintegration. The formulation F2, F3,F4 and F5 containing 25 mg, 35 mg ,45 mg and 55mg Moringa gum continue to swell over the 4 hour test with the degree of swelling being dependent on the Moringa gum concentration, higher concentration display a greater hydration capacity.

**Surface pH**

The surface pH of all the formulations was found to be within 1.5 units of the neutral pH and hence these formulations would not produce cause any irritation in the buccal cavity.

**Bioadhesion study**

The mean values of the force of detachment increased with time and reached a plateau at later time points. They were significantly greater at each time point for tablet containing 15, 25, 35 and 45 mg of Moringa gum. In the present study, the amount of Moringa gum incorporated into the buccal tablets was observed to be a critical factor in defining the resulting bioadhesive strength. The bioadhesive bond strength increases with increase in Moringa gum concentration.

**Drug release characteristics**

Propranolol HCl was more rapidly released from F1 when compared with F2, F3, F4 and F5. However increasing concentration of Moringa gum decreased the release of propranolol HCl.

## CONCLUSION

In recent years, there has been increasing interest in the use of bioadhesive polymers to control the delivery of biologically active agents systematically or locally. These bioadhesive systems are useful for the administration of drugs, which are susceptible to extensive gastrointestinal degradation and first pass metabolism. This route provides on alternative for the administration of various hormones, narcotic analgesics, steroids, enzymes, cardiovascular agents etc. It allows for the local modification of tissue permeability, inhibition of protease activity or reduction in immunogenic response.

Thus selective use of therapeutic agents like peptides, proteins and ionized species can be achieved.

Buccal drug delivery of propranolol HCl gains easy access to the systemic circulation via internal jugular vein results in improvement of bioavailability. Percentage of drug released decreases with increasing in the

concentrations of Moringa gum. So among various formulations, formulation containing 15 mg of Moringa gum is the best suitable buccal dosage form of propranolol hydrochloride**.** Further in vivo studies are in progress for the successful discovery of buccal dosage form of propranolol HCl.

**ACKNOWLEDGEMENTS**

Authors are thankful to the SLC'S college of pharmacy, Hyderabad, INDIA for providing all the facilities required for the study and also ISP (International speciality products) Hyderabad, INDIA for providing the number of excipients as gift samples.

**Table 1: Composition of Mucoadhesive layer of buccal tablets of Propranolol HCl with Moringa gum**

| Formulation | Propranolol hydrochloride (mg) | Moringa Gum (mg) | Microcrystalline cellulose (mg) | Magnesium Stearate (mg) |
|---|---|---|---|---|
| F0 | 10 | 0 | 139 | 1 |
| F1 | 10 | 15 | 124 | 1 |
| F2 | 10 | 25 | 114 | 1 |
| F3 | 10 | 35 | 104 | 1 |
| F4 | 10 | 45 | 94 | 1 |
| F5 | 10 | 55 | 84 | 1 |

**Table 2: Swelling Index of Propranolol HCl Buccal Tablets using Moringa gum**

| Formulation code | 45 minutes | 90 minutes | 135 minutes | 180 minutes | 225 minutes |
|---|---|---|---|---|---|
| F0 | 0.4976±0.04 | 0.5610±0.04 | 0.5273±0.03 | 0.4834±0.02 | 0.3890±0.02 |
| F1 | 3.6337±0.03 | 2.6847±0.01 | 2.2993±0.01 | 1.6370±0.02 | 1.4735±0.02 |
| F2 | 3.9754±0.05 | 2.9241±0.04 | 2.7810±0.02 | 2.7097±0.03 | 1.8109±0.04 |
| F3 | 4.6329±0.02 | 4.0639±0.02 | 3.4533±0.01 | 3.4418±0.04 | 2.9501±0.01 |
| F4 | 6.0772±0.04 | 4.5845±0.01 | 4.5435±0.04 | 4.0085±0.04 | 3.9735±0.02 |
| F5 | 7.9607±0.02 | 6.3480±0.04 | 5.0873±0.01 | 4.0683±0.01 | 3.8273±0.04 |

**Table 3: Cumulative mean (±standard Deviation) percentage release of Propranolol HCl from directly compressed Buccal Tablets Containing 15,25,35,45 and 55 mg of Moringa gum in phosphate buffer pH 6.8**

| Time in min | Cumulative percentage release of Propranolol HCl from Buccal Tablets | | | | | Oral Tablets |
|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F0 |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 60 | 65.53±1.31 | 50.06±1.37 | 44.83±0.67 | 40.07±0.74 | 37.78±0.72 | 96.66±0.62 |
| 90 | 72.56±0.35 | 54.02±0.75 | 56.82±0.68 | 53.42±0.52 | 43.52±0.68 | 96.78±0.001 |
| 120 | 80.32±1.18 | 66.93±1.63 | 60.26±0.22 | 56.95±0.45 | 54.07±0.74 | 97.05±0.001 |
| 180 | 85.05±1.05 | 81.26±0.77 | 77.74±0.50 | 73.26±0.83 | 69.82±0.71 | 97.68±0.001 |
| 240 | 90.26±0.67 | 94.74±0.59 | 91.15±0.36 | 85.49±1.00 | 81.63±0.93 | 98.23±0.001 |
| 300 | 95.78±0.67 | 98.44±0.46 | 97.69±0.70 | 96.40±0.40 | 93.14±0.37 | 98.86±0.001 |
| 360 | 98.26±0.67 | 98.44±0.46 | 98.53±0.34 | 98.42±0.82 | 96.48±0.38 | 99.56±0.001 |

**Table 4: Surface pH of the Propranolol HCl Buccal Tablets Containing Moringa gum**

| Drug+ Polymer | Formulation | Surface pH |
|---|---|---|
| Propranolol HCl + Moringa gum | F0 | 6.9 |
| | F1 | 6.5 |
| | F2 | 6.3 |
| | F3 | 6.2 |
| | F4 | 5.8 |
| | F5 | 5.9 |

**REFERENCES**


1. Ganga S, Mucosal drug delivery – a review, Vol. 5 issue 6, 2007. http//www.pharmainfo.net. Accessed on 08/07/2010.
2. Laverty TP and Jones DS. Mucoadhesive polymeric platforms for controlled Drug delivery. Eur J Pharm Biopharm. 2009;71:505–518.
3. Chowdary KPR and Srinivas L. Mucoadhesive drug delivery systems.
4. Gandhi RB and Robinson JR. Bioadhesion in drug delivery. Ind J Pharm Sci. 1988;50(3):145-152.
5. Peppas NA and Buri PA. Surface, interfacial and molecular aspects of polymer Bioadhesion on soft tissue. J Controlled Release. 1985;2:257-275.
6. Mikos AG and Peppas NA. Measurement of the surface tension of mucin solutions. Int J Pharm. 1989;53:1-5.
7. Lenaerts V and Gurny R. Bioadhesive Drug Delivery Systems, CRC Press: BocaRaton, FL; 1990.
8. Chen WG and Chi Hwang GC. Adhesive and in vitro release characteristics of Propranolol Bioadhesive Disc system. Int J Pharm.1992;82:61-66.
9. Wong CF, Yuen KH and Peh KK. An in vitro method for buccal adhesion studies Importance of instrument variables. Int J Pharm. 1999;180:47-57.