INTERNATIONAL JOURNAL OF
PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

CRUDE BANANA POWDER: A POTENTIAL EXCIPIENT FOR TABLET FORMULATION

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Accepted Date: 18/03/2014; Published Date: 27/04/2014

Abstract: Effectiveness of medication administered through oral route is determined by several factors that affect the overall bioavailability of the drug. The efficacy of oral drug is further reduced in patients suffering with gastrointestinal diseases. Thus, in current work, mucoadhesive tablet formulation is presented that might improve the erratic absorption problem in such patients. Aqueous wet granulation method is used to formulate tablets of 300 mg batch size using 0-40% of crude banana powder (CBP), where diclofenac potassium is used as an active pharmaceutical ingredient. A series of physiochemical parameters together with force of mucoadhesion and *in vitro* dissolution profile were studied. Among four different formulations, tablets without CBP was found to posses least mucoadhesive strength with immediate drug release effect while that treated with CBP showed increase in mucoadhesive strength with sustained drug release pattern. The highest force of mucoadhesion was found in formulation with 40% CBP while drug was almost completely released after 8 hr of dissolution study in formulation with 10% and 20% of CBP.

Keywords: Diclofenac potassium, Mucoadhesive strength, Crude banana powder, *In vitro* dissolution

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How to Cite This Article:

Nabin Poudel, IJPRBS, 2014; Volume 3(2): 172-179

PAPER-QR CODE

INTRODUCTION

Oral drug delivery is natural, thus it is the most convenient and preferred route for drug administration. However, the amount of drug that reaches to the site of action through oral route depends on several factors such as: gastric emptying rate, degradation of drug by gastric pH, first pass metabolism, degree of drug absorption etc. The amount of drug that gets absorbed through gastrointestinal tract (GIT) is a major concern in diseases like gastric ulcer, and ulcerative colitis where mucin turnover rate is high [1]. This phenomenon might lead to decrease in efficacy of medication as drug absorption is altered. In past, a number of approaches have been applied to formulate a drug to increase its efficacy; among which enteric-coated [2] and controlled drug delivery system are most popular [3]. These formulation techniques are successful to increase drug bioavailability by either preventing gastric breakdown or improving drug release profile in patient with normal GIT. However, in GIT altered patients, such a formulation is desired that can improve drug absorption despite alerted mucin turnover rate.

Thus, in this work, we present mucoadhesive tablet drug delivery system that can localize to gastric mucosa by bioadhesion and increase drug absorption. For this purpose, CBP is used as a mucoadhesive excipient to alter the drug release profile of diclofenac potassium.

2. MATERIALS AND METHODS

2.1 Materials

Unless stated otherwise, materials were obtained from the following manufacturers: Diclofenac potassium, Deurali Janta Pvt. Ltd, Kathmandu, Nepal; Sodium hydroxide, Okhla Industrial area, New Delhi; Potassium dihydrogen orthophosphate, Thermo Fischer Scientific, Mumbai, India; Sodium chloride, Ranbaxy fine chemical Ltd.; Sodium dihydrogen orthophosphate, Qualigens fine chemicals, India; Sodium bicarbonate, Ranbaxy fine chemical Ltd.; Glucose, Qualigens fine chemicals, India; Isopropyl alcohol, Qualigens fine chemicals, India Magnesium stearate, S Kant Healthcare Ltd.; Sodium metasulphite, Qualigens fine chemicals, India; Lactose, na life Pvt. Ltd, India; Sodium chloride, Ranbaxy fine chemical Ltd, India; Potassium chloride, Qualigens fine chemicals, India; Calcium chloride, Qualigens fine chemicals, India; Sodium dihydrogen phosphate, Qualigens fine chemicals; Glucose, Qualigens fine chemicals.

Ripe banana fruit and intestinal goat mucosa were purchased from local market in Banepa, Nepal.

2.2 Preparation of crude banana power

The ripe banana fruit were peeled off, sliced transversely (~2 mm thickness), incubated in 0.5% (w/v) sodium metasulphite solution for 5 minutes and dried in oven at 60°C for 18 hours [4]. The dried slices were grinded in mill and passed through sieve (mesh size 60) to obtain CBP.

2.3 Formulation of Mucoadhesive Tablets

Aqueous wet granulation was used to formulate the tablets of batch size 300 mg where amount of CBP was varied from 0-40% (Table 1). The formulation without CBP was considered as control over the treated tablets (formulation containing CBP). Diclofenac potassium was mixed geometrically with CBP (soaked in water for 6 hrs), followed by lactose and magnesium stearate. The sample was mixed homogenously for 15 minutes and compressed in a single-stroke using 10-station rotary machine (Remek minipress, India) using die-punch of 10 mm diameter.

2.4 Evaluation of Mucoadhesive Tablets

2.4.1 Weight Variation

Weight variation was determined based on protocol of Indian Pharmacopoeia (IP). Thereby, twenty tablets from each formulation were weighed to get average weight and standard deviation.

2.4.2 Friability

The friability test was performed based on standard operating procedure as mentioned in IP. Thereby, the weight of twenty tablets before and after tumbling at speed of 25 rpm for 4 minutes in friability test apparatus (Grover Enterprises, Delhi, India) was taken. The weight loss was determined as:

Loss (%) = (Weight before tumbling - weight after tumbling)/weight before tumbling x 100%

2.4.3 Thickness

The thickness of six randomly selected tablets from each formulation was determined using a Vernier calliper (Mitutoyo Corporation, Japan). Thereafter, average and standard deviation was calculated.

2.4.4 Hardness

The hardness of six randomly selected tablets from each formulation was determined using tablet hardness tester (Mitutoyo Corporation, Japan).

2.4.5 Assay for Diclofenac potassium

For assay, weight equivalent to 75 mg of diclofenac potassium from crushed tablets of each formulation were taken, dissolved in 100 ml of 0.1 M sodium hydroxide and stirred for 1 hour. 1 ml of resulting solution was further diluted to 50 ml with phosphate buffer of pH 6.8 and absorbance was measured at 275 nm using spectrophotometer (Simadzu Corporation, Japan). The assay was determined based on standard calibration curve obtained from 5-25 µg/ml of standard Diclofenac potassium prepared with same procedure as stated [5].

2.3.6 Evaluation of in vitro Mucoadhesion

Fresh intestinal goat mucosa (IGM) obtained immediately after slaughter was used for in vitro evaluation of mucoadhesiveness of tablets. The intestinal goat mucosa was transported to the laboratory while it was incubated at 40 ºC in tyrode solution (0.8% sodium chloride, 0.02% potassium chloride, 0.0134% calcium chloride, 0.005% sodium dihydrogen phosphate and 0.1% glucose). The tablet to be tested for mucoadhesive property was placed on a vial (10 ml) with a bilayered adhesive tape. The IGM was washed, cut into slices (~30* 30 mm2) and placed (mucosal surface facing outward) against a glass vial (10 ml) using a thread. The vial-mucosal surface setup was incubated at 37°C for 2 hours. The setup was fixed on a height adjustable pan (Descolab, India) with mucosal surface facing downwards (Figure 1). The height of the lower vial-tablet setup was adjusted so that the tablet could adhere to IGM of the upper vial. Two minutes after adhesion of tablet to IGM, weight on right side of the pan was slowly added with an increment of 0.5 g, until the two vials just separated from each other. The total weight required to detach two vials was taken as a measure of mucoadhesive strength. The force of bioadhesion was calculated as [6]:

Force of adhesion = (mucoadhesive strength x 9.81)/ 100

2.3.7 In vitro Dissolution

In vitro dissolution study was conducted based on protocol stated in the United States Pharmacopoeia (USP) that relied on rotating basket method. Thereby, 6 tablets from each formulation (each tablet to be placed on a separate basket) were rotated at a speed of 50 rpm (wire sinkers) as the tablet was exposed to dissolution medium containing 900 ml of phosphate buffer (0.05 M, pH 6.8, 37 ± 0.5°C). After that, 10 ml of sample was pipetted out after 15 min-8 hours, filtered, diluted suitably and absorbance for presence of Diclofenac potassium was recorded at 276 nm using Spectrophotometer (Simadzu Corporation, Japan). With each aliquot taken out, 10 ml of fresh phosphate buffer was added. Thereafter, the amount of drug release (%) was calculated by comparing absorbance of sample with standard Diclofenac potassium solution of 5-25 µg/ml prepared on same medium based on following formula:

Amount of drug release (%) = (As x Cc)/ (Au x Cs x 900 x 100 x Df)

Where, As and Au represent absorbance of standard Diclofenac potassium and sample solution respectively. Cc represents the tablet label claim/Assay for Diclofenac potassium, Cs is the concentration of standard solution in mg/ml and Df represents dilution factor [5].

Table 1: Composition of different ingredients in oral mucoadhesive tablet formulation

Amount of ingredients				
CBP (%)	Diclofenac Potassium (mg)	CBP (mg)	Magnesium Stearate (mg)	Lactose (mg)
0	75	-	5	220
10	75	30	5	190
20	75	60	5	160
40	75	120	5	100

Figure 1: Fabrication of assembly for mucoadhesion

3. RESULT

3.1 Weight Variation

The weight variation was found to be 0.30 ± 0.01g (Table 2). As relative standard deviation was found to be merely 7.5% the data presented is in accordance with IP.

3.2 Friability

The friability of tablets varied from 0.1 to 0.3% (Table 2) which is less than 1% in all formulations. Thus, the tablets comply with the friability test.

3.3 Thickness

The thickness of tablets was found in range of 2.8 ± 0.07 mm to 2.9 ± 0.04 mm (Table 2). Thus, all of the formulations comply with the thickness test.

3.4 Hardness

The hardness of tablets varied from 39.0 ± 8.04 N to 57.8 ± 5.35 N (Table 2).

3.5 Assay for Diclofenac potassium

The assay for Diclofenac potassium was in range of 97.7% to 104.4%, which is within the limit of IP. i.e. ± 5%.

3.6 Mucoadhesion

The force of mucoadhesion increased with amount of crude banana flour. It was found to be least in the formulation where crude banana flour was not added (0.2 N) and highest of 1.4 N in the formulation containing 40% of CBP.

3.7 In-Vitro Dissolution

The drug release profile of formulation without CBP was found to be approximately 96% at 0.5 hrs while diclofenac potassium was almost completely released after 1 hr. For all other formulations that contained CBP as a polymer, drug release profile followed the same trend. Thereby, diclofenac potassium was released in range of 17%-35% at 0.5 hrs and continuously increased until 8 hours. The active ingredient in the formulations with 10% and 20% crude banana flour was completely released by 8 hrs with values of 102% and 92% respectively. Interestingly, only 77% of the drug was found to be released at the time in formulation with 40% of CBP.

4. DISCUSSION

As stated in the results, physiological parameters of all four formulations meet the requirement of pharmacopoeia. This shows the correctness of aqueous wet granulation method used for tablet formulation. The force of mucoadhesion was found to be increased with CBP concentration, which proves the mucoadhesive property of CBP. The mucoadhesiveness is associated with the ability of sugars such as pectin and starch (that constitutes of hydroxyl groups) present in CBP to form hydrogen bond with the mucosal lining of IGM. The higher the hydrogen bonding greater is the strength of mucoadhesion. In addition, lectin is known to possess lower mucin turnover rates that supplements to the hydrogen bonding [7]. The dissolution profile in the treated samples showed a sustained drug release pattern over 8 hr

time. In absence of the polymer (control tablets), an immediate drug release was observed thus signifying the importance of polymer in development of sustained release tablet dosage form. Interestingly, with increase in force of bioadhesion a delay in drug release profile was seen as merely 77% of drug was found to be released after 8 hours in formulation containing 40% of the polymer. This observation is linked with entrapment of active ingredient within the matrix of polymer that gelatinized during aqueous granulation. Additionally, while drying the granules, starch, a major ingredient in banana hardens to form a solid bridge that shields diclofenac release into dissolution medium [8]. Thus, CBP can be regarded as an effective excipient in pharmaceutical dosage form which can serve as both mucoadhesive polymer as well as binding agent. The presented mucoadhesive sustained release drug formulation can be effective in patients with altered mucin turnover rate because of following reasons (i) it localizes the drug in the region of GIT thereby facilitating continuous drug release and absorption (ii) sustained release drug profile permits once or twice a day dosing [9].

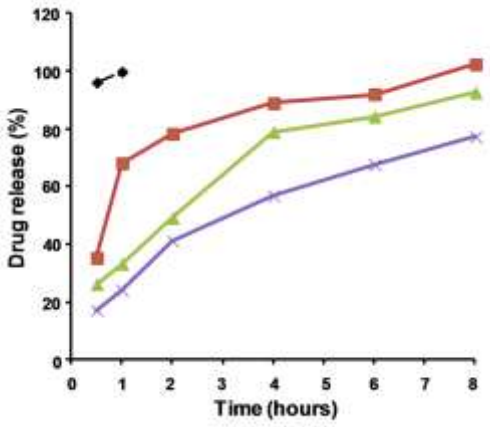

Figure 2: *In vitro* dissolution, drug-release profile of Diclofenac potassium. The line represents following formulations- black, 0% CBP; red, 10% CBP; green, 20% CBP and blue, 40% CBP

Table 2: Physiochemical parameters of oral mucoadhesive tablets

Amount of CBP (%)	Physiochemical parameters					Force of Mucoadhesion (N)
	Weight Variation (g)	Friability (%)	Thickness (mm)	Hardness (N)	Assay (%)	
0	0.30 ± 0.01	0.3%	2.9 ± 0.04	39.0 ± 8.04	104.4	0.2
10	0.30 ± 0.01	0.3%	2.8 ± 0.08	57.8 ± 5.35	101.3	0.7
20	0.30 ± 0.01	0.1%	2.8 ± 0.12	55.6 ± 4.56	97.7	1.1
40	0.30 ± 0.01	0.2%	2.8 ± 0.07	54.0 ± 7.31	97.7	1.4

5. CONCLUSION

In present work the applicability of crude banana powder as mucoadhesive polymer is found to be successful. Even in crude form, banana powder is found to be effective therefore, it cannot be excluded that mucoadhesive property and hence drug release profile can be enhanced if lectin is used in pure form. In addition to mucoadhesive property, lectin also permits site specific absorption of small peptides by altering permeability of GIT that even Carbapol (most popular mucoadhesive polymer) doesn't possess.

6. ACKNOWLEDGEMENT

We are thankful to Prof. Dr. Panna Thapa, Head of Department of Pharmacy for providing laboratory facilities. We are grateful to Deurali Janata Pvt. Ltd. for providing Diclofenac potassium.

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