COMPARATIVE EVALUATION OF TARA GUM AS A MUCOADHESIVE AND CONTROLLED RELEASE AGENT IN BUCCAL TABLETS

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Abstract- The present research work aimed at evaluation of a natural polymer, Tara gum, as a controlled release and mucoadhesive agent in buccal tablets. Tara Gum was characterized for various physiochemical parameters as well as for its mucoadhesive properties. Tablets containing Tara Gum were prepared with direct compression technique using Chlorpheniramine maleate as a model drug. Formulations containing Tara Gum as a mucoadhesive polymer were prepared and evaluated with the one containing synthetic mucoadhesive polymers, namely Carbopol 974P and Methocel K4M. The results of the study indicated that Tara Gum had good physicochemical and morphological characteristics. FTIR spectroscopy studies suggested absence of chemical interaction between the drug and Tara Gum and the tablets confirmed to the Pharmacopoeial specifications. The drug release kinetics showed that tablets containing Tara Gum showed a prolonged drug release of 83.71 to 93.17 % at 8 h with linear kinetics, comparable to Carbopol 974P and Methocel K4M. Mucoadhesive strength of Tara Gum tablets, 43.72 ± 1.78 gm, was satisfactory and comparable to that of synthetic polymers. Also, all the formulations showed satisfactory drug permeability flux. Acute toxicity studies revealed that Tara Gum did not cause any mortality up to 2000 mg/kg body weight and was considered to be safe. The present study proved the potential utility of Tara gum as a substitute for costly synthetic mucoadhesive polymers to achieve desired mucoadhesive effect of formulation along with controlled release. These prepared tablets might be advantageous with improved patient compliance.

Key words- Tara gum, Natural polymer, Mucoadhesive strength, Controlled release

I. INTRODUCTION

Buccoadhesive formulations, while controlling the drug release, overcome certain problems associated with conventional dosage forms such as initial burst of activity resulting in rapid decrease in drug concentration and limited in situ stability. It offers some distinct advantages such as rich vascularization of the mucosal lining of the oral cavity making it more accessible for the administration and removal of a dosage form, high patient acceptability compared to other non-oral routes of drug administration, avoidance of acid hydrolysis in the GIT and by passing the first-pass effect[1]. Tara gum (TG) is obtained from the endosperm of seed of Caesalpinia spinosa, commonly known as Tara. It is a small tree of the family Leguminosae or Fabaceae. An attempt is made to analyze the controlled release and mucoadhesive characteristics of this natural polymer in buccoadhesive tablets[2]. Chlorpheniramine maleate (CPM) [3], an antihistaminic drug, was employed as a model drug.

II. MATERIALS AND METHODS

CPM was obtained as a gift sample from Alembic Ltd. Vadodara, Gujarat and TG was procured from the market. Methocel K4M, Carbopol 974P were procured form Loba Chem, Mumbai, India and were used as received. All other reagents used were of analytical grade.

TG was characterized for identification and various physiochemical parameters[4]. CPM, TG and mixtures with different ratios of CPM/TG were subjected to FTIR analysis using a model BRUKER ALPHA T FTIR spectrophotometer (Bruker Optik GmbH, Germany) for checking the compatibility. The solution of Carbopol 974P, Methocel K4M and TG (3% w/v) was prepared separately and shear stress was calculated by self fabricated apparatus[5] to compare the mucoadhesive strength of natural polymers over synthetic polymers. Acute toxicity study was performed as per OECD-425 guidelines[6].

Formulation and evaluation of buccal tablets

Tablets were prepared by direct compression method using flat faced 6 mm punch (Rimek Mini Press-I machine) and 8 mg of CPM was used in all the batches. Different batches of tablets were prepared using Carbopol 974P, Methocel K4 and TG separately with three different concentrations of each, resulting in 9 different formulations (CF1, CF2, CF3 for Carbopol 974P; HF1, HF2, HF3 for Methocel K4M; TGF1, TGF2, TGF3 for TG). The tablet weight was adjusted to 150 mg and the tablets were evaluated for average thickness, hardness, friability test, weight variation test and mucoadhesive strength measurement[7,8]. Dissolution studies were performed using a USP dissolution apparatus 2 (paddle method) at 50 rpm. The release kinetics of each tablet can be assessed by inserting the experimental data in the semi-empirical equation $Mt/M\infty = Ktn$ where $Mt/M\infty$ is the fractional amount of the drug at the time t, K is a kinetic constant of the system which indicates rate of the release and n is the release exponent, indicative of the mechanism of release.

Mucoadhesion studies (force of detachment) of tablets was measured using self fabricated apparatus (modified physical balance)[9].

The in vitro buccal drug permeation studies[10,11,12] of CPM through the goat buccal mucosa were carried out using modified Franz diffusion cell at 37° C ± 0.5° C (Diameter of 1.5 cm with a diffusional area of 1.76 cm^2). A test on the reference solution was carried out by placing 2 ml of the solution in the donor compartment.

III. RESULTS AND DISCUSSION

In the present investigation, a natural polymer TG was evaluated for its controlled release and mucoadhesive properties. The results of characterization of gum as shown in Table 1 indicates that it was water soluble with pH of 6.5, indicating non-irritant nature of the gum[13, 14-17]. FTIR studies showed absence of a chemical interaction between CPM and TG. During sheer stress measurement, TG was found to possess remarkable adhesiveness which was comparable to that of Methocel K4M and Carbopol 974P within 30 minutes (Table 2). Acute toxicity studies indicated that the solution of TG did not cause any mortality up to 2000 mg/kg and was considered as safe.

Evaluation of buccal tablets

The thickness of all the nine formulations was in the range of 2.18 ± 0.02 to 2.41 ± 0.06 mm, the hardness was in the range of 4.0 ± 0.8164 to 5.33 ± 0.4714 kg / cm^2 and the percentage friability was found to be less than 0.1 %. The average weight for all formulations was in the range of 149.33 ± 2.6246 to 152.33 ± 1.2472 mg. The percentage of drug content for all formulations was in the range of 98.9 ± 1.3 to 99.7± 0.53 %.

From the results we can conclude that all the formulations passed test for weight variation, hardness, content uniformity and showed acceptable results in terms of % assay and friability.

Dissolution testing

At the first hour, Carbopol 947P, Methocel K4M and TG showed a drug release of 33.41, 35.53 and 35.2 % respectively. For tablets containing Carbopol 947P, n was between 0.6757 ± 0.055 and 0.7095 ± 0.015, for Methocel K4M between 0.6749 ± 0.0368 and 0.7207 ± 0.042 and for TG between 0.6736 ± 0.032 and 0.7089 ± 0.012 which indicated that the release from the tablets was determined by diffusion and swelling. The K values were found to decrease with the increase in the mucoadhesive polymer amount (from 25 mg to 50 mg to 75 mg) in all tablets, showing that the concentration of mucoadhesive polymer had an appreciable influence on the released drug amount. In view of the drug release retarding characteristics, it was observed that the tablets containing TG showed drug release between 83.71 and 93.17 % at 8 h followed by Carbopol 974P, 83.26 - 96.31 % and Methocel K4M, 86.18 and 99.7 %. Figure 1 depicts the comparative drug release profile of tablets at higher amount of polymers i.e. 75 mg (CF3, HF3and TGF3).

Mucoadhesion studies

From the results for mucoadhesion studies shown in Table 3, it is evident that the mucoadhesive strength of TG is comparable to that of Methocel K4M and Carbopol 974P. Due to the higher concentration of TG in TGF3, it showed more mucoadhesive strength than TGF1 and TGF2 which may be due to possibility of proper hydration and erosion of natural gum adhered to mucosal surface with strong bond in case of TGF3.

In vitro drug permeation

The permeation profile of the CPM solution in water is shown in Figure 2, while Figures 3 shows permeation profiles of tablets. From these studies, a permeability coefficient (Kp) value of 2.300 $x10^{-2}$ analogous to a flux of 7.39 $x10^{-4}$ $\mu g \times cm^{-2} \times h^{-1}$ was obtained.

The results revealed that drug permeation was increased with the increase in the concentration of the mucoadhesive polymer, probably because an increase in the mucoadhesive component allowed a closer contact between the tablet and the mucosa.

CONCLUSION

The studies conducted with the objective of exploring the controlled release and mucoadhesive property of TG gave satisfactory results. FTIR studies witnessed the compatibility between the drug and TG. The drug release kinetics confirmed the controlled release characteristics of TG that was comparable with the results of synthetic polymers. Also the tablets of TG showed satisfactory mucoadhesive strength. Hence, the gum under study proved to show potential utility as a suitable alternative to synthetic mucoadhesive polymers.

Table 1: Physicochemical parameters of TG

Sr. No.	Parameter	Observation
1.	color	Yellowish white
2.	Solubility in water	Soluble
3.	pH (1% w/v)	6.5
4.	Loss on drying	7.2 %
5.	Swelling index (ml)	9 ± 0.5
6.	Viscosity (3.0 % solution in water)	1310 cp
7.	Thin layer chromatography	Spot corresponding to mannose

Table 2: Shear stress measurement

		Contact Time (minutes)			
		5	10	15	30
Weight Required[a] (gm)	A	29.5 ± 1.57	46.0 ± 1.30	63.0 ± 1.20	77.5 ± 1.09
	B	25.5 ± 1.30	52.0 ± 1.20	73.0 ± 1.30	81.5 ± 1.40
	C	24.0 ± 1.20	47.5 ± 1.21	63.5 ± 1.0	71.5 ± 1.50

A = TG, B = Carbopol 974P, C = Methocel K4M

[a]Each value represents the mean±S.D of 3 determinations

Table 3: Mucoadhesive strength determination

Formulation	Mucoadhesive strength (gm)
TGF1	28.64 ± 1.56
TGF2	39.39 ± 1.94
TGF3	43.72 ± 1.78
CF1	30.31 ± 1.14
CF2	42.80 ± 1.88
CF3	45.40 ± 1.62
HF1	26.30 ± 1.07
HF2	36.41 ± 1.89
HF3	39.56 ± 1.08

[a] Mean ± SD; n=3

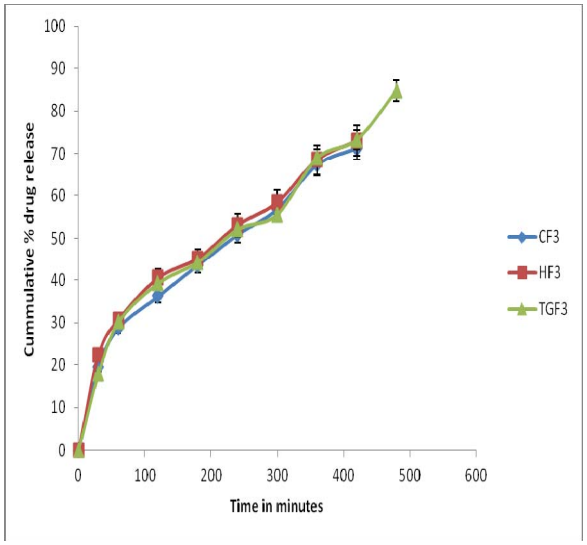


Figure 1: Comparison between the percentage release of drug from tablets containing Carbopol 974P, Methocel K4M, and TG at higher quantity.

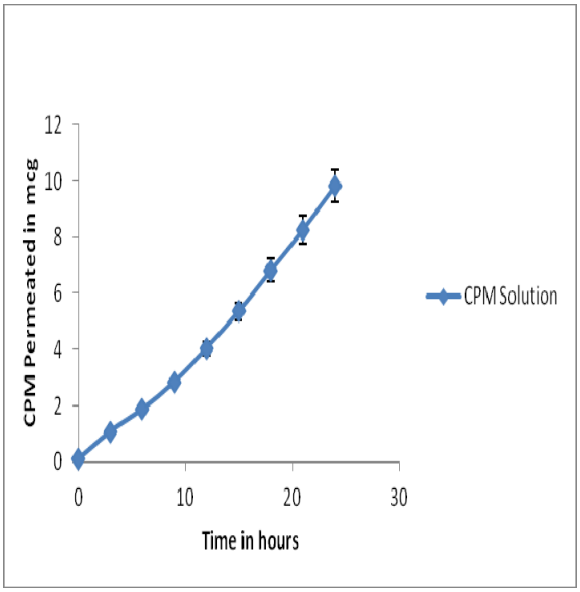


Figure 2: Cumulative amount of permeated CPM from a saturated solution in purified water

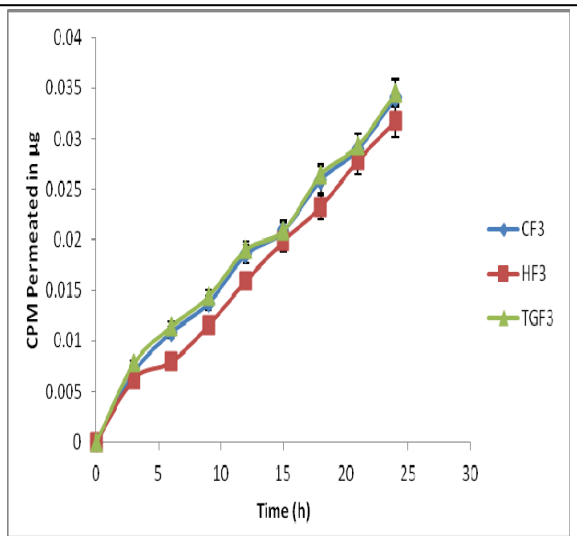


Figure 3: Cumulative amount of permeated CPM from the tablets (CF3, HF3 and TGF3) containing Carbopol 974P, Methocel K4M and TG.

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