PREPARATION AND CHARACTERIZATION OF MUCOADHESIVE TABLETS OF AMOXICILLIN USING NATURAL AND SYNTHETIC POLYMERS

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Purpose of this research was to study mucoadhesive tablets of Amoxicillin trihydrate using Neem gum as mucoadhesive natural polymer. The conventional oral dosage form of this drug has low half life and high dosing frequency. Plant gums and mucilages are being used due to their abundance in nature, safety and economy. So in The present investigation was an effort to study the suitability of gum obtained from *Azadirachta indica* as mucoadhesive polymer. The present study aims to reduce the dosing frequency by using single and combinations of synthetic and natural polymers for preparation of mucoadhesive tablets. Various approaches to combine synthetic (HPMC K4M, carbopol 934P and sodium alginate) and natural (neem gum) polymers have been made to prepare total ten formulations. Further, different evaluation studies like friability, content uniformity, surface *pH*, wash-off and dissolution tests was done for all formulations. Results for *in vitro* drug release and wash-off studies suggest that the formulation (F1) containing neem gum has shown better mucoadhesive property. Other studies have shown satisfactory results in all ten formulations. Thus, the present investigation suggests that neem gum is suitable for preparation of mucoadhesive tablets.

Keywords: Neem gum, mucoadhesive, amoxicillin, *H. pylori* infection

INTRODUCTION

An ideal controlled drug delivery system is the one, which can deliver the drug at a predetermined rate, locally or systematically, for a specified period of time. Thus unlike the conventional immediate release systems, the rate of appearance of drug in the body with such a system is not controlled by absorption process[1]. Mucoadhesion, an interfacial phenomenon, is based on two materials, one of which is mucus layer of mucosal tissue to which the drug is held together by means of interfacial forces for prolonged period of time. Control release system ensures localization of drug in a particular site to improve and increase the bioavailability. The contact time is also enhanced due to interaction between polymers and mucus lining of tissue for sustained action[2].

Amoxicillin trihydrate, a β-lactam antibiotic used for management of *H. pylori* infection having short biological half life of 1-2 hrs. Amoxicillin is rapidly and completely absorbed from GI track and stable in acid. The dosage regimen recommended for amoxicillin is 250-750 mg TDS for 7 days [3-4] above all favours sustained release dosage form. Advance polymer systems in controlled delivery systems maintain the release rate as well as the concentration in the biological system by increasing its localization and avoiding first pass metabolism [5]. Mucoadhesion as a means of influencing the duration of contact of medicinal formulations with mucous membranes immediately became a subject of interest to technologists [6].

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MATERIAL AND METHODS

Amoxicillin trihydrate (Ind-Swift Ltd., Parwanoo), HPMC-K4M, carbopol 934P, magnesium stearate and talc (Central drug house, New Delhi), neem gum (Omji herbs, Barnala, Punjab) and sodium alginate (Qualikems fine Chemicals Pvt. Ltd., New Delhi) were employed in the present study. All other chemicals were of analytical grade and were freshly prepared.

Preparation of mucoadhesive tablet

Mucoadhesive tablets each containing 250 mg of Amoxicillin trihydrate were prepared by conventional wet granulation method employing HPMC K4M, sodium alginate, Carbopol 934P and neem gum as

mucoadhesive materials. A batch of 100 tablets was prepared in each case a blend of 25 gm of Amoxicillin trihygrate with required amount of polymers which were then granulated along with a solvent blend of water and ethyl alcohol (1:1). At first the required quantity of drug and polymer taken in a motor and pestle for trituration. Then the solvent is added drop wise with continuous stirring until the wet mass is formed. Then the wet masses were passed through 12 mesh sieve and wet granules were dried at 60º C for 4 hrs. The dried granules (20 mesh) after blending with talc (0.25 gm) and magnesium stearate (0.25 gm) in a laboratory cube blender for 5 mins were compressed into 500 mg tablets of hardness 7-8 kg/sq.cm on a tablet compression machine. The tablets were then considered for further study [7].

Table I: Formulation codes of different Amoxicillin trihydrate mucoadhesive Tablets

Ingredients (mg/tab)	Formulation code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Amoxicillin trihydrate	250	250	250	250	250	250	250	250	250	250
Neem gum	250	-	-	-	125	125	125	-	-	-
Carbopol 934P	-	250	-	-	125	-	-	125	125	-
HPMC K4M	-	-	250	-	-	125	-	125	-	125
Sodium alginate	-	-	-	250	-	-	125	-	125	125
Talc	25	25	25	25	25	25	25	25	25	25
Magnesium stearate	25	25	25	25	25	25	25	25	25	25

Table II. Different evaluation parameters of Amoxicillin trihydrate mucoadhesive tablets

Formulation code	% Loss in weight	%Drug content	Hardness (kg/cm^2)	Surface pH	Average detachment time
F1	0.058	98.56	7.68	7.1	540
F2	0.049	97.60	7.89	7.0	513
F3	0.052	96.72	8.01	6.9	508
F4	0.063	96.96	8.18	7.1	475
F5	0.048	97.44	7.96	6.9	450
F6	0.057	97.28	7.76	6.8	470
F7	0.048	97.36	7.96	7.1	470
F8	0.052	97.72	8.13	7.2	473
F9	0.053	97.44	7.94	7.1	430
F10	0.058	96.64	8.15	7.1	461

Evaluation of mucoadhesive formulation

The physical evaluation tests for the mucoadhesive tablets of all the formulations were performed and mean values were calculated. Weight variation analysis was done by weighing 20 tablets individually, the average weight was calculated and % variation of each tablet from the average weight of tablets was calculated. Hardness and friability of the mucoadhesive tablet formulations were evaluated using Monsanto hardness tester and Roche friabilator respectively [8].

Drug Content uniformity

The tablets were kept in 100 ml volumetric flask containing 0.1(N) HCl pH 1.2 for 24 hrs. When tablets

were completely dissolved the solution was centrifuged. After centrifuged the supernatant was collected. Absorbance was measured spetrophotometrically at 228 nm. Dilution was made using 0.1(N) HCl (pH 1.2) as per requirement [9].

Surface pH

The surface *pH* was determined to investigate the possible *in vivo* side effects of the formulation. An acidic or alkaline formulation causes irritation of the mucosal membrane and hence, this is an important parameter in developing a mucoadhesive dosage form. A combined glass electrode was used for determination of surface pH. The tablets were kept in contact with 5 ml distilled water pH 6.5±0.5 for 2 hrs in 10 ml beakers. The tablets swell up and pH was noted by bringing the electrode near the surface of the formulation after equilibrating for 1 min[10].

Wash-off test

The mucoadhesive properties of the tablets were evaluated by *in vitro* wash-off method. Pieces of intestinal mucosa of goat were mounted on the glass slides provided with suitable support. After fixing of 2 tablets to this glass slide, it was tied to the arm of USP tablet disintegration test apparatus and was run at 37°C the media was used 0.1(N) HCl (pH 1.2). A time of detachment of both tablets was noted down and the average was calculated [11].

***In vitro* drug release study**

The *in vitro* drug release study was performed using USP dissolution rate test apparatus (paddle type; 50 rpm, 37°C). Dissolution study was carried out for 12 hrs. 0.1(N) HCl (pH 1.2; 900 ml) was used as dissolution media. Samples of each 5 ml were withdrawn after every 1 hr for a period of 12 hrs. Volume in dissolution vessel was kept constant by equal replacement with fresh media maintaining the sink condition. The samples were collected in test tubes after filtration through Watt Mann filter paper. The amount of the drug in the aliquots was quantified by taking the absorbance of the sample at 228 nm spectrophotometrically, using 0.1(N) HCl pH 1.2 (dissolution media) as the blank.

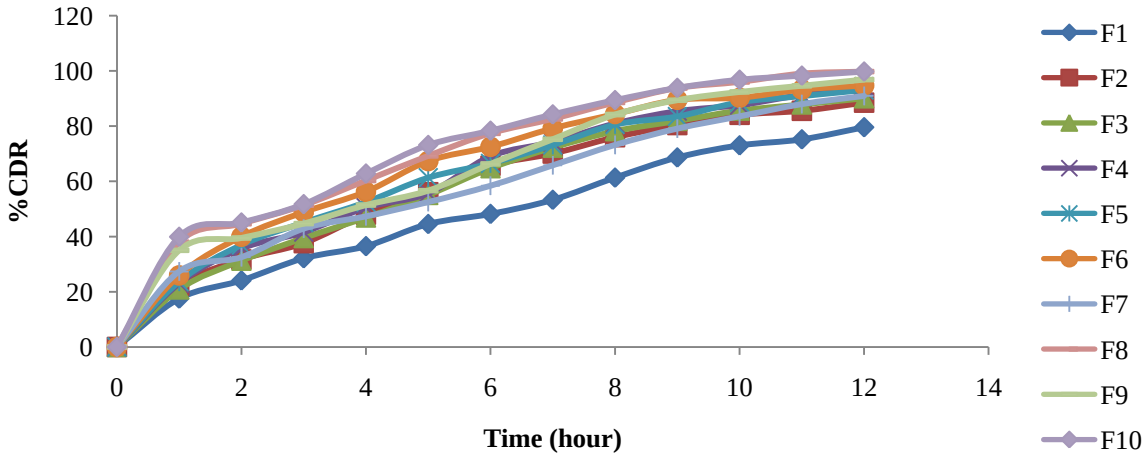

Figure I: Comparative dissolution profiles of all prepared formulations

RESULT AND DISCUSSION

The prepared mucoadhesive tablets were evaluated for various physical parameters such as weight variation, hardness, friability and drug content. All the batches were produced under conditions to avoiding processing variables. Hardness of tablets ranged from 7.68-8.18 kg/cm^2 and the percentage friability was between 0.048-0.063% as shown in table 2, is within limit as per IP. The values of hardness test and percentage friability indicates good handling property of prepared mucoadhesive tablets. The drug content uniformity in the mucoadhesive tablets was within the range from

96.64-98.56% as shown in table 2. The surface *pH* study in the mucoadhesive tablets was within the range from 6.8-7.2 as shown in table 3. The wash off test shows that the detachment time of tablet ranges from 430-540 mins, and the formulation F1 containing neem gum shows better mucoadhesive properties as shown in table 3. The release of Amoxicillin trihydrate from the prepared formulations was analyzed by plotting cumulative percentage drug release *vs* time as shown in fig 1. From all formulations, over 20% of the Amoxicillin trihydrate was release within the first hour of dissolution study. In the present study the formulation F1 (neem gum) has shown cumulative percent drug release of about 79.604% in 12 hrs as shown in Fig I.

CONCLUSION

The present study concludes that formulation containing Amoxicillin trihydrate with neem gum (F1) has given better drug release property than the other nine formulations and the wash-off test has shown that F1 has better mucoadhesive property as shown in Table II.

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