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Research Article

Design and characterization of buccal drug delivery system of losartan potassium

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ABSTRACT

Buccal drug delivery has been considered as an alternative to oral dosing of drugs subjected to degradation in the gastrointestinal tract or to hepatic first pass metabolism. Buccal drug delivery offers a safer mode of drug utilization, since drug absorption can be promply terminated in cases of toxicity by removing the dosage form from the buccal cavity. Losartan potassium is an angiotensin-II receptor antagonist having lesser bioavailability (25-33%). The aim of the present study is to increase the bioavailability to avoid the hepatic metabolism, using buccal tablets of losartan potassium. Tablets of losartan potassium were prepared by direct compression method using bioadhesive polymers like chitosan, sodium carboxy methyl cellulose and poly vinyl pyrrolidine (PVP) either alone or in combinations with backing layer of ethyl cellulose. Precompression parameters like bulk density, tapped density, compressibility index, hausner's ratio were evaluated. Post compression parameters like hardness, friability, uniformity of weight, drug content, swelling index, *invitro* drug release study and kinetics were evaluated. Among all the formulations F5 containing NaCMC was found to be good with better drug release i.e., 93.62% in 9 hours. Kinetic studies were performed and it followed Higuchi release kinetics and was diffusion controlled. FT -IR results proclaimed that there are no interactions between drug and polymers used.

Keywords: Losartan potassium; chitosan; sodium carboxy methyl cellulose; poly vinyl pyrrolidine; *invitro* dissolution; evaluation.

INTRODUCTION

The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which susceptible tso acid hydrolysis in the stomach or which are extensively metabolized in the liver (first pass effect). The total area of the oral cavity is about 100 cm^2. Out of these about 1/3rd is the buccal surface which is lined with an epithelium of about 0.5mm thickness.

Delivery through buccal mucosa

Administration of a drug via the buccal mucosa (the lining of the cheek) to the systemic circulation is defined as buccal delivery. Despite, the buccal mucosa is significantly less permeable than the sublingual mucosa and usually not able to provide rapid drug absorption or good bioavailability (G Praveen 2012); it is relatively more permeable than the skin and also offers other advantage over alternative delivery routes.

Various strategies employed for buccal delivery

- Bioadhesive buccal tablets
- Bioadhesive buccal gels
- Bioadhesive buccal patches

Losartan (Tripathi KD 2013) is a selective, competitive angiotensin receptor type1 receptor antagonist, reducing the end organ responses to angiotensin II. Losartan administration results in a decrease in total peripheral resistance and cardiac venous return (Velmurgan, 2013).

MATERIALS AND METHODS

Losartan potassium was obtained as a gift sample, excipients like magnesium stearate, talc, ethyl cellulose, chitosan (Sreenivas 2006), sodium carboxy methyl cellulose (Manivannan Rangaswamy 2009), poly vinyl pyrrolidine (J.Varshosaz 1998), were used and all the ingredients used are of analytical grade. Losartan potassium was estimated by determination of ʎ max in phosphate buffer pH 6.8 solution. Drug-excipient compatibility studies were carried out using FT-IR spectroscopy.

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Table 1: Composition of buccal tablets of Losartan potassium

S.No.	Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Losartan potassium	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**	**25**
2	Chitosan	**10**	**15**	**20**	-	-	-	-	-	-
3	NaCMC	-	-	-	**10**	**15**	**20**	-	-	-
4	PVP	-	-	-	-	-	-	**10**	**15**	**20**
5	Talc	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
6	Magnesium stearate	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**	**3**
7	MCC	**Qs**	**Qs**	**Qs**	**Qs**	**Qs**	**Qs**	**Qs**	**Qs**	**Qs**
8	Ethyl cellulose	**50**	**50**	**50**	**50**	**50**	**50**	**50**	**50**	**50**

Table 2: Micromeritic properties of powder blend

Formulation code	Bulk density	Tapped density	Compressibility index	Hausner's ratio
F1	0.49 ± 0.07	0.57 ±0.01	16.21 ± 0.06	0.86 ±0.06
F2	0.56 ± 0.06	0.62 ± 0.05	16.87 ± 0.05	0.98 ±0.05
F3	0.52 ±0.03	0.68 ±0.07	17.11 ±0.01	0.64 ±0.03
F4	0.54 ±0.04	0.64 ± 0.08	17.67 ±0.09	1.12 ±0.04
F5	0.53 ± 0.06	0.67 ± 0.03	16.92 ±0.04	1.20 ±0.09
F6	0.56 ± 0.05	0.66 ± 0.06	17.65 ±0.07	1.06 ±0.01
F7	0.58 ± 0.56	0.69 ±0.04	16.43 ± 0.05	0.76 ±0.08
F8	0.48 ±0.05	0.57 ±0.02	17.97 ±0.02	1.15 ±0.09
F9	0.54 ±0.08	0.62 ± 0.03	17.54 ±0.09	1.17 ±0.05

Table 3: Evaluation of losartan potassium mucoadhesive tablets

Formulation	Hardness (kg/cm)	Thickness (mm)	Weight variation (mg)	Friability (%)	Drug content (%)
F1	4.7±0.02	2.80 ± 0.01	279.6± 0.99	0.79± 0.01	100.09± 0.56
F2	4.3 ± 0.05	2.83 ± 0.06	278.8 ± 0.99	0.67± 0.01	102.73± 0.46
F3	4.3 ± 0.04	2.87 ± 0.06	279.8 ± 0.38	0.57± 0.00	98.75± 0.88
F4	5.7 ± 0.06	2.86 ± 0.05	280.7 ±0.99	0.55±0.01	99.70± 0.34
F5	5.4 ± 0.04	2.87 ± 0.04	279.8± 0.38	0.51±0.01	97.95± 0.38
F6	5.0 ± 0.05	2.90± 0.03	280.1 ± 0.99	0.87±0.03	98.64± 0.88
F7	5.6 ± 0.07	2.97 ± 0.06	279.6± 0.17	0.46± 0.01	103.36± 0.83
F8	5.3 ± 0.05	3.01 ± 0.01	281.0± 0.40	0.72± 0.01	101.09± 0.44
F9	5.1 ± 0.02	2.95 ± 0.02	280.0± 0.20	0.56± 0.02	99.75± 0.38

Table 4: Regression analysis of the *invitro* release data according to various release kinetic models

Formulation code	Zero order	First order	higuchi	Korsmeyer-peppas
	r^2	r^2	r^2	r^2
F5	0.960	0.935	0.993	0.925

Method of preparation of mucoadhesive tablets (Junginger 1990)

All the ingredients including drug, polymer and excipients were weighed accurately according to the batch formulations. All the ingredients except lubricants were mixed in the order of ascending weights and blended for 10min in an inflated pol yethylene pouch. After uniform mixing of ingredients, lubricant was added and again mixed for 2 min. The prepared blend (230mg) of each formulation was precompressed, on multi stationed tablet punching machine at a pressure of 0.5 ton for 30s to form single layered flat faced tablets of 9mm diameter. Then, 50mg of ethyl cellulose powder was added and final compression was done.

The assayed drug content in various formulations varied between 98.64% and 103.36%. the average weight of the tablet was found to be between 278.8mg and 281.0mg, % friability range between 0.46 and 0.87 and thickness of the tablets for all the formulations was found to be between 2.80mm and 3.00mm with an average of 2.90mm. The *invitro* drug release studies revealed that the release of losartan potassium from different formulations varies with characteristics and composition of matrix forming polymers. The release rate of losartan potassium decreased with increasing concentrations of polymers. Among all the formulations F5 containing NaCMC was found to be good with better drug release i.e; 93.62% in 9 hrs. Several kinetic

models describing drug release from intermediate and modified release dosage forms. The model that best fits the release data was evaluated by correlation coefficient(r). From the above results it is concluded that the drug release from the formulated mucoadhesive tablets of losartan potassium followed higuchi release kinetics and was diffusion controlled.

CONCLUSION

From the foregoing studies it is concluded that the release rate of the drug from the buccal tablets can be governed by the polymer and concentration of the polymer employed in the preparation of tablets. Regulated drug release in first order manner attained in the current study indicates that the hydrophil ic matrix tablets of losartan potassium were prepared using different polymers and excipients can successfully be employed as mucoadhesive controlled release drug delivery system. The precompression and post compression parameters for all the formulations were subjected to various evaluation parameters and the results were found to be within the limits. Slow, controlled and complete release of losartan potassium over a period of 9 hours was obtained from matrix tablets formulated employing NaCMC, F5 formula tion with 93.62% drug release.

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