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Development and Evaluation of Buccal Film of Carvedilol

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Carvedilol has a bioavailability of about 25 – 35 % because of extensive first-pass metabolism; to overcome this major drawback of carvedilol buccal film was formulated and evaluated for its weight variation, thickness, drug content, and percentage moisture absorption and percentage moisture loss. An in-vitro release study was designed using semipermeable membrane. Four formulations were prepared using 4% HPMC (CV_1), 6% HPMC (CV_2), 4%EC+0.05% PVP (CV_3) and 6%EC + 0.5% PVP (CV_4). The in-vitro release profile for the formulation CV_4 which contain 6%EC and 0.5%PVP and 8% EC showed sustain release up to 24 hours in Phosphate buffer pH 6.4 having constant ionic strength (μ=0.5) and constant concentration 0.05 μg/ml and obeyed first order kinetics.

Keywords: Carvedilol Buccal Film, Ethyl cellulose, Polyvinylpyrolidone, Hydroxypropylmethylcellulose.

Buccal[1] cavity has wide varieties of functions and it acts as an excellent site for the absorption of drug. Absorption of therapeutic agents from the oral cavity provides a direct entry of such agent in to the systemic circulation[2]; metabolism and gastro-intestinal degradation. However the buccal route of drug delivery has received much more attention because of its unique advantages over other transmucosal routes. Various adhesive mucosal dosage[3] forms have been developed, which include adhesive tablets, gels, ointment, patches and more recently films.

Carvedilol is a nonselective β-adrenergic blocker with α- blocking activity. It is used in the treatment of severe heart failure, bradycardia and hypertension. Since the buccal route bypasses the hepatic first[6] pass effect, the dose of carvedilol could be reduced. The physicochemical properties of carvedilol its suitable half-life and low mol. wt. 406.5 makes it suitable candidate for administration by buccal route.

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EXPERIMENTAL

Materials

Carvedilol was obtained as a gift sample from Sun Pharma Ltd. The polymers Hydroxypropyl methylcellulose (HPMC 15 cps), ethyl cellulose (EC 20 cps) and polyvinyl pyrolydone (PVP K-30) were obtained from Ozone Pharmaceutical Ltd. H.P. Other chemicals were of analytical grade.

Methods

Preparation of calibration curve

Calibration curve was prepared in methanol and absorbance was determined UV Spectrophotometrically at λmax =285 nm. Linear regression equation having r 2=0.9997 was observed in concentration range 2-12 µg/ml.

Preparation of Reservoir Film

A number of buccal film containing 20 mg of carvedilol in an area of 1 cm sq. was prepared by solvent casting[8] technique. PEG-600, glycerol in a concentration of 30% w/w of polymer was in corporate as plasticizer[9] in HPMC and EC film respectively. A film of 1 cm sq, area was cut from the total film area.

Rate Controlling Membrane

A rate controlling membrane was cast on a glass plate using ethyl cellulose (8% w/w) by incorporating glycerol (30% w/w of polymers) as plasticizer. Membrane of 1 cm sq in area was cut and both sides of drug reservoir[10] was sealed using this membrane to control the release[11] of drug.

Drug Content Determination

Different polymers like HPMC, EC, prepared Carvedilol Buccal film of (1 cm sq.). The size of film was 1 cm sq. The film of HPMC was dissolved in small amount of methanol shaken vigorously for 5 minutes and then diluted with 10 ml of methanol. Buccal film of carvedilol with EC was dissolved in small amount of methanol shaken vigorously for 5 minutes and then diluted 10 ml with methanol. Both the solution was filtered through Whatmann[11] filter paper no.1.

***In-vitro* Release**

The *in-vitro* release study was carried out using semipermeable membrane. The membrane used was permeable to low molecular weight substance. The membrane was tied to one end of the open ended cylindrical tube[12], which acts as donor[13] compartment. A buccal film containing 20 mg of carvedilol was placed inside the compartment. This set up was placed over the beaker, which act as receptor compartment, containing 100 ml buffer pH 6.4 having constant ionic strength (μ=0.5) and constant concentration 0.05 μg/ml, the temperature was maintained 37± 1°C and continuous stirring was performed throughout the experiment.

5 ml of aliquots was withdrawn from receptor compartment at every one-hour time interval for 24 hours. The withdrawn quantity of aliquots was replaced with fresh phosphate buffer solution (6.4 pH) immediately. The samples were collected and analyzed spectrophotometrically.

RESULTS AND DISCUSSION

In the present study, buccal film of carvedilol was prepared using the polymers like HPMC, EC and PVP. The polymeric membrane acts as the rate controlling membrane. Evaluation was done on the parameters like weight variation, thickness, moisture absorption; moisture loss and drug content (Table 2).

The thickness of film ranges from 0.17 ± 0.01 mm to 0.21 ± 0.01mm. The thinnest formulation was CV_1 and the thickest being CV_4. The uses of plasticizer in the formation of buccal films led to transparent, flexible films. Moreover the film was also checked for its cracks. This showed a uniform film formation. The weight of the film varied between 0.018 to 0.019mg (Table 2): Moisture absorption of the films were also studied and it was shown that CV_2 showed highest moisture absorption and CV_3 showed minimum absorption: the percentage moisture loss was highest in CV_1 and minimum in CV_3. Drug content in the formulation was more or less same

Table 1. Formulation of Buccal film of CV

S.No.	Batch Code	Composition
1	CV1	4% HPMC
2	CV2	6% HPMC
3	CV3	4% EC + 0.5% PVP
4	CV4	6% EC + 0.5% PVP

Table 2. Evaluation of buccal film of cv

S. No.	Batch Code	DRFC (%w/w)	PL (mg)	WV (±sd)mm	T (±sd)	%MA (±sd)	%ML (mg)	DC±SD
1	CV 1	4%HPMC	PEG-600 (30%)	0.017	0.017±0.01	0.51±0.64	0.54±0.01	18.14±0.25
2	CV 2	6%HPMC	PEG-600 (30%)	0.018	0.017±0.02	0.55±0.50	0.47±0.02	18.27±0.22
3	CV 3	4%EC+0.5%PVP	Glycerol (30%)	0.017	0.019±0.01	0.33±0.02	0.24±0.10	19.21±0.22
4	CV 4	6%EC+0.5%PVP	Glycerol (30%)	0.018	0.021±0.01	0.35±0.02	0.28±0.26	19.25±0.26

DRFC – Drug Reservoir Film Composition, PL – Plasticizer, % W/Wp: W/W of Polymer,
WV: Weight Variation, S.D: Standard deviation, T: Thickness, %MA: Moisture loss, DC: Drug content.

with a variation of 0.08%, which is the indication for the formulation to be considered as a formulation having the drug uniformly dispersed in the film. The increase in polymer concentration decreases the diffusion of the drug from the matrix. On comparison of the release results from the fourth formation CV_4 showed prolonged release of drug for a period of 24 hrs (Fig. 1). The formulation CV_4 showed first order release pattern (Fig. 1). CV_4 was considered as the best formulation from the study for providing an extended release of the drug.

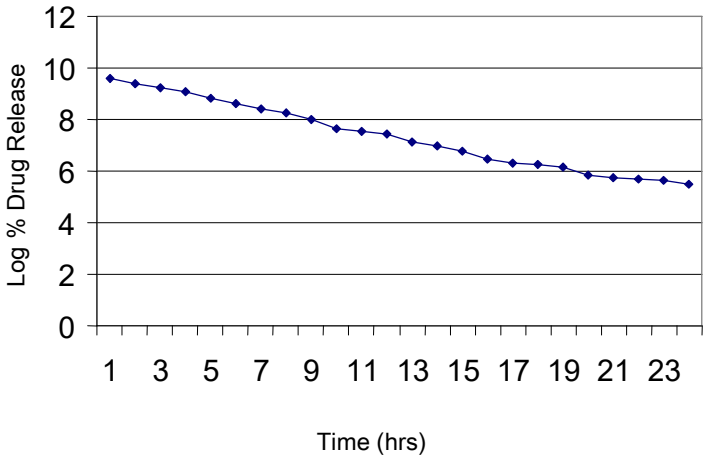

Fig. 1. Release pattern of Carvedilol

Carvedilol buccal film, CV_4 (drug reservoir with6% EC + 0.5% PVP and 8% EC as rate controlling membrane). Showing first order release.

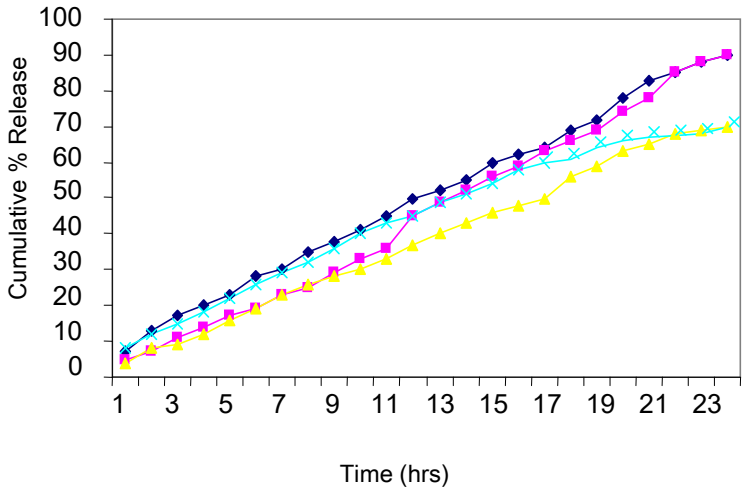

Fig. 2. Comparative *in vitro* release profile of Carvedilol Formulations

(-♦-) Formulation CV_1 4% HPMC (- ■-) Formulation CV_2 6% HPMC (-▲-) Formulation CV_3 4% EC+0.5% PVP (-x-) Formulation CV_4 6% EC + 0.5% PVP. In all Formulations from CV_1 to CV_4 8% EC was Used as the rate controlling membrane.

CONCLUSION

The buccal film of carvedilol was successfully developed with using 4% HPMC (CV_1), 6% HPMC (CV_2), 4%EC+0.05% PVP (CV_3) and 6%EC + 0.5% PVP (CV_4). By using PCP –disso software, version 3.0 and applying statistical approaches CV_4 was considered as the best formulation showing an extended release pattern of the carvedilol. The in-vitro release profile for the formulation CV_4 showed 81.3% release up to 24 hrs in phosphate buffer pH 6.4 having constant ionic strength (μ=0.5) and constant concentration 0.05 mg/ml confirms and obeyed first order kinetics

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REFERENCES

1. Raghuraman S., Velrajan G., Ravi R., Jeuabai B., Bentino Johnson D., Sankar V. Design and evaluation of propranolol hydrochloride buccal films. *Ind. J. Pharm.Sci*., 2002; **64**(1): 32-36.
2. Bhaskara J., Xiaoliing L., Gary C. Recent advances in mucoadhesive systems, *Pharma. Tech.*, 2003.
3. Notari R.E. ,Biopharmaceutics and clinical pharmacokinetics, 4th ed. marcel dekker Inc. New York 1987; 160.
4. Kashappa Goud H. Desai, Pramod Kumar T.M., Preparation and evaluation of a novel buccal adhesive system. *AAPS Pharm.sci.tech*, 2004; **5**(3): 1-9.
5. Tripathi K.D, Essentials of Medical Pharmacology,5th ed Jay-pee brothers Medical Publishers Pvt. Ltd., New Delhi, 1994; 128.
6. Scirra J.J, Gidwani R.N, Evaluation of selective physical constants of polymeric films and proposed drug release *J. Pharm. Sci*., 1972; **61:** 754.
7. S.Budavari, The Merck Index,12th ed ,Merk and co.,inc. NJ,USA, 1996; 5178.
8. Rathbone M.J., Hadgraft J. Robert M.S., *Modified release drug delivery technology,* **126**: Marcel dekker Inc. New York, 2003; 372-374.
9. Bhaskaran S., Sanmathi, B.S., Poly(lactic acid) microsphere of ketorolac tromethamine for perantral controlled drug delivery system. *Indian J. Pharm. Sci.,* 2001; **63:** 538-540.
10. Pignatello, R., Bucolo C., Ferrara P., Maltese A., Puleo A., Puglisi G., Eudragid RS-100 nanosuspension for the ophthalmic controlled delivery of ibuprofen. *Eur. J. Pharm. Sci*., 2002; **16:** 53-61.
11. Sweetman, S.C., Martindale: The complete drug reference 33rd ed the royal society of Great Britain, Japan 2002, 48.
12. Mashru.R.C, Sutariya.V.B, Sankalia.M.G and Parikh, Devalopment and evaluation of fast dissolving film of salbutamol sulphate. *Drug Dev.Ind. Pharm.,* 2005; **1:** 25-34.