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Reseach Article

PREPARATION AND EVALUATION OF BUCCAL FILMS CONTAINING ANTI-HYPERTENSIVE DRUG

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Amiloride hydrochloride, solvent casting method, HPMC K4M, HPMC E 15.

A B S T R A C T

Background: To prepare and evaluate of buccal films containing anti-hypertensive drug.
Material and Methods: Buccal mucoadhesive films were prepared by solvent casting method.
Results: The maximum drug release was found to be 95.20 % in formulation A3. The tensile strength of the film as the concentration of plasticizer (Propylene Glycol and Glycerin) was increased, the tensile strength of formulation was found to be decreased. The decrease in tensile strength may be due to weakening of bond linkage between the polymer chains.
Conclusion: The formulation A3 containing HPMC K4M as a film forming polymer and Propylene glycol as a plasticizer was selected as an optimized formulation because it gave higher plasticity, good in-vitro drug release and less tensile strength etc. Hence, finally it was concluded that the prepared buccal film containing Amiloride Hydrochloride is considered as a potentially useful dosage form for treatment of hypertension.

INTRODUCTION

A drug can be administered in the body through many routes such as oral, parenteral, transdermal, sub mucosal etc [Muhammad Hanif *et al*, 2015]. Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery [B. Krishnaveni *et al*, 2014]. Buccal delivery is defined as drug administration through the mucosal membranes lining the cheeks and as an attractive route for systemic delivery of drug with relative permeable with a rich of blood supply. It has excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of retentive dosage forms. Drugs are absorbed into the systemic circulation through the deep lingual or facial vein, internal jugular vein, and braciocephalic vein which bypasses drugs. Avoids hepatic first pass metabolism leading to high bioavailability amongst various routes of drug delivery, an oral route is perhaps the most preferred to the patient and clinicians alike. The inherent problem associated with in some drug, can be solved by modifying the formulation. There are the need alternative routes for the systemic drug delivery system [Ashish Gorle *et al*, 2015].

The film can be defined as a dosage form that employs a water dissolving polymer, which allows the dosage form to quickly hydrate, adhere and dissolve when placed on the tongue, or in the oral cavity, which results in systemic drug delivery. The main property of the buccal film is that due to the large surface area of the film, it allows quick wetting of the film which accelerates absorption of the drug quickly when compared to tablets. Buccal films are the most recently developed dosage form for buccal administration due to the films are implied for attachment to the buccal mucosa, they can be formulated to exhibit local as well as systemic action. Buccal films have direct access to the systemic circulation through the internal jugular vein, which bypass the drug from the hepatic first pass metabolism leading to high bioavailability. Further, these dosage forms are self administrable, pharmacoeconomic and have superior patient compliance. So we are proposed to do the buccal films for low bioavailability anti hypertensive drugs by decreasing its hepatic first pass metabolism [Radha Madhavi B *et al*, 2013].

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MATERIAL AND METHODS

Amiloride Hydrochloride was received as gift samples from Panchsheel Organics Ltd. (Indore). Hydroxy Propyl Methyl Cellulose (HPMC) E 15, HPMC K4M, Glycerin, Propylene glycol, Aspartame and Citric acid were purchased from Loba Chemicals (Mumbai, India). All other reagents and buffer solutions were of analytical grades.

Preparation of buccal films

Buccal mucoadhesive films were prepared by solvent casting method. HPMC K-4M was weighed accurately and added in 3 ml of distilled water. The contents in the beaker were stirred

on magnetic stirrer for 15 min for swelling of polymer. Then Propylene glycol was added to the polymer solution. Amiloride Hydrochloride was weighed and dissolved in 2 ml of distilled water. The drug solution was added to the polymer dispersion and Aspartame and Citric acid was mixed thoroughly with the help of magnetic stirrer. Then the solution was subjected to sonication in a bath sonicator to remove the air bubbles. The mould containing polymeric solution of drug was kept for 24hours at room temperature for drying. After drying the films were removed by peeling from the moulds then cut into a square dimension of 2× 2 cm. Films were packed in aluminium foil and stored in air tight container to maintain their integrity and elasticity [MehrajUd Din Ganaie *et al*, 2014]. The compositions of the buccal films formulations are listed in following table:

Table 1 Formula for different batches of buccal films of Amiloride Hydrochloride Containing HPMC K4M and HPMC E15

Formulation	Drug	HPMC K4M	HPMC E15	Propylene glycol (ml)	Glycerin (ml)	Citric acid	Aspartame	Water (ml)
A1	5	150	-	0.3	-	15	25	5
A2	5	150	-	0.4	-	15	25	5
A3	**5**	**150**	-	**0.5**	-	**15**	**25**	**5**
A4	5	150	-	-	0.3	15	25	5
A5	5	150	-	-	0.4	15	25	5
A6	5	150	-	-	0.5	15	25	5
A7	5	-	150	0.3	-	15	25	5
A8	5	-	150	0.4	-	15	25	5
A9	5	-	150	0.5	-	15	25	5
A10	5	-	150	-	0.3	15	25	5
A11	5	-	150	-	0.4	15	25	5
A12	5	-	150	-	0.5	15	25	5

(Note: All solid ingredients are measured in milligram. Dose of drug per film is 5mg and Area of film is 2×2cm)

Characterization of buccal films

Weight variation

For weight variation three films of every formulation were randomly selected and weighed individually on digital balance then average weight was calculated [Y. Indira Muzib *et al*, 2011].

Thickness

The thickness of each film was measured using digital vernier calliper at different positions of the film and the average thickness was calculated. This is essential to ascertaining uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip [MehrajUd Din Ganaie *et al*, 2014].

Surface pH measurement

For determination of surface pH, three films of each formulation are allowed to swell for 2 h on the surface of an agar plate. The surface pH is to be measured by using a pH paper placed on the surface of this swollen patch. A mean of three readings is to be recorded [Mitra Jelvehgari *et al*, 2015].

Folding endurance

Three films of each formulation of required size are cut by using sharp blade. Folding endurance is to be determined by repeatedly folding the film at the same place, till it is broken. The number of times, the film could be folded at the same place without breaking gives the value of folding endurance [Shinde Pramod *et al*, 2012].

Swelling index

After determination of the original film weight and diameter, the samples are allowed to swell on the surface of agar plate kept in an incubator maintained at 37 ± 0.2ºC. Weight of the films (n=3) is determined at different time intervals (1-5 h). The percent swelling, % S is to be calculated using the following equation [N.G. Raghavendra Rao *et al*, 2013]

Percent swelling [% S]= [Xt–Xo/Xo]×100, eqn. (1)

Where,

Xt=The weight of the swollen film after time t,

Xo=The initial film weight at zero time

Tensile strength

The Tensile strength value of the films directly characterizes the flexibility of films. Tensile Strength of films was performed using tensile tester (Instron 1121, Japan). One end of film strip of dimension 2x2cm was fixed between the two iron screens to give support to the film and another end was connected to the paper holder in which hook was inserted. A thread was tied to this hook, passed over the pulley and a small pan attached to the other end to hold the weight. A small pointer was attached to the thread, which travels over the scale affixed on the base plate. To determine tensile strength, the patch was pulled by means of a pulley system. Weights were gradually added to the pan to increase the pulling force till the patch was broken. The weights required to break the patch was considered as a tensile strength and it was calculated as kg/cm2 using following formula [Sri K.V *et al*, 2013].

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Film width} \times \text{film thickness}} \quad \text{eqn. (2)}$$

Drug content

Three film units of each formulation has to be taken in separate 100 ml volumetric flasks, 100 ml of solvent has to be added and continuously stirred for 24 h. The solutions have to be filtered, diluted suitably and analyzed at specified nm in UV spectrophotometer. The average of drug contents of three films has to be taken as final reading [Elsheikh Tajelsir *et al*, 2016].

In -vitro drug release studies

In-vitro dissolution of Amiloride Hydrochloride buccal film was carried out in USP paddle dissolution test apparatus using 500ml phosphate buffer pH 6.8 as the dissolution medium. The temperature was maintained at 37°C throughout the experiment. 5ml sample was withdrawn and the same quantity was replaced with phosphate buffer of pH 6.8. The cumulative percentage of drug released was determined using UV visible spectrophotometer at 361 nm. Sink conditions were maintained throughout the experiment [Murthy P. N *et al*, 2013].

Fourier transform infrared spectroscopy (FTIR)

Optimized formulation was subjected to FTIR analysis using FTIR Bruker. Samples were prepared in Potassium Bromide disks (2mg sample in 200mg potassium bromide) with a scan range of 450-4000 cm^{-1} & the resolution of 4 cm^{-1} [M. Aruna *et al*, 2011].

Differential scanning calorimetry (DSC)

The DSC was performed for optimized formulation was recorded using Model-Mettler-Toledo DSC 1. Samples were heated between 50 & 450°C in an inert nitrogen gas atmosphere [Pankaj Kumar *et al*, 2012].

RESULT

Evaluation of buccal films of Amiloride Hydrochloride

Table 2 Evaluation of buccal films

Formulation Code	Wt. of films(mg)	Thickness of films (mm)	pH value	Folding endurance	Swelling index %	Tensile strength (kg/cm^2)	Drug content %
A1	22.0±0.16	0.07±0.01	6.7±0.01	105 ± 0.72	24.8±0.01	2.83±0.04	90
A2	24.5±0.26	0.09±0.03	6.6±0.05	110 ± 0.85	25.9±0.03	2.81±0.01	92
A3	25.3±0.13	0.11±0.04	6.8±0.04	119 ± 0.45	28.5±0.02	2.79±0.00	95
A4	23.6±0.34	0.06±0.01	6.7±0.03	100 ± 0.81	23.6±0.02	2.82±0.03	89
A5	26.2±0.12	0.08±0.02	6.6±0.06	108 ± 0.67	24.4±0.04	2.80±0.01	88
A6	28.4±0.25	0.10±0.01	6.5±0.01	117 ± 0.88	26.6±0.01	2.79±0.05	86
A7	21.4±0.21	0.06±0.01	6.6±0.02	106 ± 0.64	22.8±0.01	2.81±0.03	89
A8	23.2±0.14	0.08±0.04	6.5±0.00	109 ± 0.51	23.9±0.04	2.79±0.04	90
A9	26.6±0.36	0.10±0.03	6.7±0.05	116 ± 0.47	26.5±0.02	2.76±0.02	93
A10	24.5±0.12	0.05±0.03	6.5±0.01	100 ± 0.94	21.6±0.01	2.80±0.01	87
A11	25.7±0.43	`0.07±0.01	6.4±0.02	107 ± 0.75	23.4±0.03	2.78±0.03	88
A12	27.2±0.27	0.06±0.04	6.6±0.00	113 ± 0.91	25.6±0.02	2.75±0.02	85

*Values are expressed as mean ± S.D (n=3)

In-vitro drug release studies

Table 3 Cumulative % drug release profile of formulation A1 to A12

Time (min)	% Cumulative drug release											
	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	A11	A12
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	15.25	13.4	23.42	19	18.5	21.25	12.6	10.25	20.42	15	14.5	19.31
2	28.59	25.1	39.25	34.86	21.5	38.45	24.43	20.64	35.25	30.84	19.42	25.24
3	36.23	35	50.69	46.79	39.75	45	34.25	30.54	46.41	43.15	36.53	33.91
4	43.64	40.64	60.35	53.94	42.14	48.35	40.12	38.85	57.94	50.64	40.72	42.14
5	51.47	46.16	67.12	58.90	53.12	51.37	51.64	45.61	65.31	55.90	50.12	48
6	56.35	52.65	73.75	65.95	67.64	55.34	58.21	50.33	70.24	62.34	64.31	53.64
7	63.75	66.71	80.63	70.19	72.75	64.75	65.31	64.21	77.63	68.42	69.61	62.72
8	72.68	75.16	87.26	83.07	80.4	76.37	70.45	73.45	82.61	75	73.56	70.25
9	82.41	84.65	90.41	87.54	85.41	83.94	76.94	78.51	86.72	80.91	83.24	80.43
10	90.02	92.85	95.20	89.29	87.35	88.5	87.10	88	90	84.23	86.41	85.61

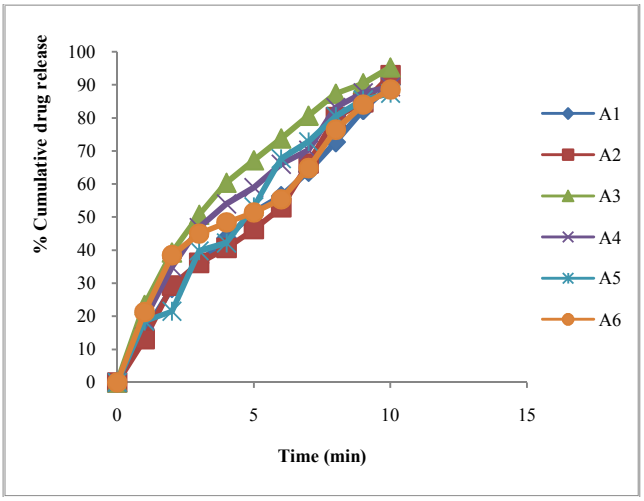

Fig 1 % Cumulative drug release profile of formulation A1 to A6

The IR spectrum of optimized formulation exhibited distinctive peak at 3271.60 (cm^{-1}) due to NH_2 stretching. The peak at 1637.74 (cm^{-1}) due to N-C=O stretching. The peak at 1218.82 (cm^{-1}) due to C-O stretching. All these peak are attributed to main functional groups of Amiloride Hydrochloride, HPMC K4M, which confirms that all components of formulation does not affected and Amiloride hydrochloride was available in its inherent form to elicit the action.

Differential scanning calorimetry (DSC)

Differential scanning calorimetry studies were carried out to examine the optimized formulation A3.

The thermogram of optimized formulation A3 shown endothermic peak starting at 104.01°C with melting peak at 113.76°C

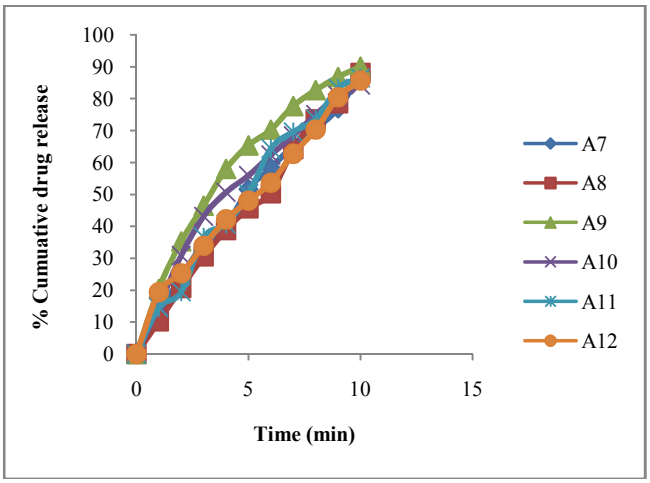

Fig 2 % Cumulative drug release profile of formulation A7 to A12

Fourier Transform infrared spectroscopy

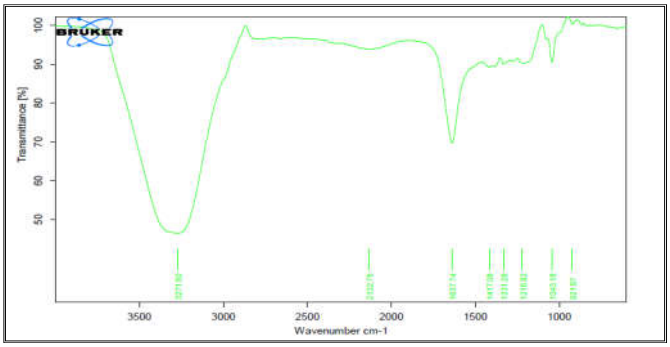

Fig 3 IR spectra of optimized formulation A3

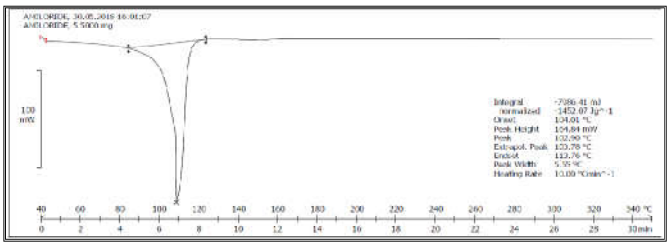

Fig 4 DSC thermogram of optimized formulation A3

DISCUSSION

Twelve formulation of mucoadhesive film of were prepared using HPMC K4M and HPMC E 15 as mucoadhesive polymers and evaluated for its mucoadhesive properties, release characteristics. In folding endurance test no films developed any visible cracks or breaks, thus showing good folding endurance (Table 2). The surface pH of the films was determined in order to investigate the possibility of any side effects, in the oral cavity, showed that all the formulation have a similar pH with the buccal cavity which reflects absence of side effects like irritation, buccal damage. The tensile strength of the film as the concentration of plasticizer (Propylene Glycol and Glycerin) was increased, the tensile strength of formulation was found to be decreased. The decrease in tensile strength may be due to weakening of bond linkage between the polymer chains (Table 2). The maximum drug release was found to be 95.20 % in formulation A3.

CONCLUSION

The data obtained from the study of "Preparation and Evaluation of Buccal Films Containing Anti-Hypertensive Drug". Reveals following conclusion:

In the present study, a satisfactory attempt has been made to formulate buccal films of an antihypertensive drug Amiloride Hydrochloride. The buccal films of Amiloride Hydrochloride were prepared using different film forming materials with same concentration i.e. HPMC K4M, and HPMC E-15, by solvent casting method. The results of folding endurance and tensile strength revealed that, as concentration of glycerin & Propylene glycol was increased, folding endurance was increased and tensile strength was decreased.

The formulation A3 containing HPMC K4M as a film forming polymer and Propylene glycol as a plasticizer was selected as an optimized formulation because it gave higher plasticity, good in-vitro drug release and less tensile strength etc.

Hence, finally it was concluded that the prepared buccal film containing Amiloride Hydrochloride is considered as a potentially useful dosage form for treatment of hypertension.

References

Apoorva Mahajan, Neha Chhabra, Geeta Aggarwal, "Formulation and Characterization of Fast Dissolving Buccal Films: *A Review", Scholars Research Library,* 2011; 3(1): 152-165.

Ashish Gorle, Prafulla Patil, Rajveer Bhaskar, Monika Ola, "Development and evaluation of buccal film containing antihypertensive agent'', The *Pharma Innovation Journal*, 2015; 4(1): 53-60.

Dr. Anna Balaji, B. Krishnaveni, Vishnuvardhan Goud, "Formulation & Evaluation of Mucoadhesive Buccal Films of Atorvastatin Using Natural Protein", *International Journal of Pharmacy & Pharmaceutical Sciences*, 2014; 6(2): 332-337.

Elsheikh Tajelsir, Aisha Khanum, "Formulation & Evaluation of Sustained Release Mucoadhesive Buccal Patch of Pantoprazole", *International Research Journal of Pharmaceutical Sciences*, (2016); 7: 001-009.

M. Aruna, Y.S.Manjunath, G. Ganesh Kumar, "Formulation and Evaluation of Perindopril Erbumine Buccal Films", *Indo American Journal of Pharmaceutical Research*, 2011;1(5):446-451.

MehrajUd Din Ganaie, Govind Mohan, Shailesh Sharma, Shahista MohiUd DIN, Tarkeshwar Prasad Shukla, Irfan Hassan, "Formulation Development and Evaluation of Mucoadhesive Buccal Film of Methyldopa", *Journal of Global Trends in Pharmaceutical Sciences*,(2014);5(3):1893-1904.

Mitra Jelvehgari, Seyed Hassan Montazam, Saieede Soltani, Rahil Mohammadi, Karim Azar, Seyed Ataollah Montazam, "Fast Dissolving Oral Thin Film Drug Delivery Systems Consist of Ergotamine Tartrate and Caffeine Anhydrous", *Pharmaceutical Sciences,* (2015); 21: 102-110.

Muhammad Hanif, Muhammad Zaman and Vesh Chaurasiya, "Polymers used in buccal film: a review", Designed Monomers and Polymers, 2015; 18(2): 105-111.

Murthy. P N., "Formulation and Evaluation of Fast Dissolving Tablet of Lisinopril". *International Journal of Research and Reviews in Pharmacy and Applied Science,* (2013); 2(1): 65-81.

N. G. Raghavendra Rao, B. Shravani, Mettu Srikanth Reddy, "Overview on Buccal Drug Delivery Systems", *Journal of Pharmaceutical Sciences and Research*, (2013); 5(4): 80-88.

Nagwani C.P., Bharad S.S, Charhate K.B., Biyani K.R, "Formulation and Evaluation of Mucoadhesive Buccal Film Containing Drug", *Scholars Academic Journal of Pharmacy,* 2016; 5(5): 128-137.

P.P.Mane, S.S.Bushetti, G.G.Keshavshetti, "Development and In vitro Evaluation of Mucoadhesive Buccal Films of Nebivolol", *Indian Journal of Pharmaceutical Sciences*, 2014;76(2):163-166.

Pankaj Kumar, Gulshan Chhabra and Kamla Pathak, "Development and Statistical Optimization of Buccoadhesive Films of Amiloride Hydrochloride: In-vitro and Ex-vivo Evaluation", *Indian Journal of*

Pharmaceutical Education and Research, (2012); 46(2): 145-154.

Pokhariyal Tarun, Singh Vikas Kumar, Tiwari Ajay Kumar, "Formulation And Evaluation of Buccal Patch of Selective α –Receptor Blocker Prazosin Hcl", *Indo American Journal of Pharmaceutical Research*, 2013; 3(2): 4293-4303.

Radha Madhavi B, Varanasi S N Murthy, Prameela Rani A and Dileep Kumar Gattu, "Buccal Film Drug Delivery System-An Innovative and Emerging Technology", *Molecular Pharmaceutics and Organic Process Research*, 2013; 1(3): 1-6.

Shinde Pramod, Salunkhe Vijay and Magdum Chandrkant, "Buccal Film: An Innovative Dosage Form Designed to Improve Patient Compliance", *International Journal of Pharmaceutical and Chemical Sciences*,(2012); 1(4): 1262-1278.

Sravanthi R.R, Rajalakshmi. R, Krishna Moorthy S.B, Rupangada. V, Ramya Sudha.E, "Mucoadhesive Buccal Films: An Innovative Drug Delivery System", *International Journal of Pharm Tech Research*, 2014; 6(5): 1665-1678.

Sri K V., "Formulation and in vitro evaluation of sumatriptan succinate oral thin films", Indo *American Journal of Pharm Research*, (2013); 3(4): 3016-3025.

Umesh. D. Shivare, Parag. D. Bodkhe, Kishor. P. Bhusari, Vijay. B. Mathur, "Formulation and Evaluation of Buccoadhesive Films of Losartan Potassium", *Scholars Research Library*, 2010;2(5):251-260.

Y. Indira Muzib, K. Srujana Kumari, "Mucoadhesive buccal films of glibenclamide: Development & Evaluation", *International Journal Pharma Investigation*, (2011); 1(1): 42-47.

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