The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

ISSN 2277-7695

Vol. 1 No. 7 2012
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION

Design and In Vitro Evaluation of Buccal Film of Terfenadine

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The buccal films of Terfenadine were formulated using mucoadhesive polymers like Sodium alginate, Sodium carboxy methyl cellulose, Hydroxy propyl methyl cellulose. The films were evaluated for their folding endurance, drug content uniformity, moisture content, weight variation, surface pH, an in vitro drug release study was designed, and it was carried out using commercial semipermeable membrane. The films were found to have good tensile strength and elasticity. The drug content was found to be uniform. The buccal films prepared with Sodium alginate are having good drug release. All of these buccal patches slowly released the drug incorporated and sustained over a period of 180 minutes. The drug release from buccal films varied with respect to the polymer composition. Among all formulations, the maximum in vitro drug release was observed in the case of formulation F1(85%).

Keyword: Buccal Film, Terfenadine, Mucoadhesive Polymers, Sodium Alginate.

INTRODUCTION: Mucoadhesive delivery system is a new type of drug delivery system having excellent advantages over the conventional dosage forms. Peptide and protein drugs are unsuitable for oral administration and require parentral administration. This problem can be over come by delivering the drug through buccal mucosa. The permeation of peptides and protein drugs have been found to be higher through buccal mucosa than the transdermal route.Mucoadhesive delivery system is one of the most exiting novel application of control release technology using bioadhesive polymers.

The buccal route,as an alternative to other traditional methods of systemic drug administration,is a subject of growing interest because of its numerous advantages .It is well known that the absorption of therapeutic compounds from the oral mucosa provides a direct entry of the drug into the systemic circulation, therefore, avoiding the first pass

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hepatic metabolism and gastro intestinal drug degradation ,which is associated with oral administration.The oral cavity is easily accessible for self medication and ,hence is well accepted by patients, and is safe ,since device can be easily administered and even removed from the site of application, stopping the input of drug when ever desired.

Buccal mucosa has rich blood supply and it isrelatively permeable. Buccal drug delivery has become an important route ofadministration.Various mucoadhesive dosage forms have been developed including adhesive tablets,gels, ointments, patches and films . Buccalfilm is preferred over adhesive tablets. Theycan circumvent the relatively short residencetime of oral gels. The buccal film also protectsthe wound surface thus reduces pain and alsocan treat oral diseases more effectively. Terfenadine is an antihistamine that does not generally cause sedation or antimuscarnic action.Terfenadine undergoes extensive first pass metabolism to two primary metabolites that is active acid metabolite and inactive dealkylated metabolite.There fore,systemic availability of Terfenadine is low under normal conditions.In order to avoid first pass effect and to increase absorption the buccal delivery Terfenadine is more suitable than conventional dosage form.The objective of this research project is to formulate the buccal film of Terfenadine using mucoadhesive polymers like sodium alginate,sodium caboxy methyl cellulose and hydroxyl propyl methyl cellulose.

MATERIALS AND METHOD

Materials

Terfenadine was a gift sample from shilpa pharmaceuticals Raichur, Sodium alginate, Hydroxypropyl methyl,cellulose (HPMC);sodium carboxy methyl cellulose(SCMC) procured by colorcon asia pvt.ltd ,Mumbai.

PREPARATION OF BUCCAL FILM:

A series of buccal patches composed of different proportions of SA,SCMC, HPMC containing Terfenadine(25 mg) were prepared using a 25-cm^2 petri dish by solvent casting technique. Glycerin was incorporated as a plasticizer at a concentration of 15% *w*/*w* of dry weight of polymers. Backing membrane was casted by pouring 4% *w*/*v* aqueous solution of PVA on aluminum foil in petri dishes at 42°C and left for 10 h. Phosphate buffer saline, pH 6.6, was used as solvent in the casting method.25mg of Terfenadine was incorporated in mixtures containing different ratios of polymers and plasticizer. The matrices were prepared by pouring 8ml of the homogeneous solutions on the PVA-aluminum foil backing membrane. Then, these buccal patches were dried at 42°C in an incubator.After 24 h, the dried patches were removed from the petri dishes and kept in desiccators until use.Formulation table was given in table 1

table 1

Formulation of Terfenadine Buccal Patches

Formulation	**F1**	**F2**	**F3**
SA	2%	-	-
SCMC	-	2%	-
HPMC	-	-	2%
Alcohol	q.s	q.s	q.s
Glycerine(%)	15	15	15
Distilled water(ml)	8	8	8

SA- Sodium alginate, *SCMC*-Sodium carboxymethyl cellulose, *HPMC*- Hydroxypropyl methylcellulose.

EVALUATION OF BUCCAL FILM:

Folding endurance

Three films of each formulation of size 2x2 cm were cut. Folding endurance was determined by repeatedly folding one film at the same place. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.

Measurement of film thickness

The thickness of the film was measured using a Screw gauge micrometer at 10 different spots from each batch. The mean and standard deviation were calculated.

Drug content uniformity

Drug content uniformity was determined by dissolving 4.9sq.cm of buccal film in 25ml of methonal.The solution was then suitabily diluted with **pH** 6.6 phosphate buffer and assayed for Terfenadine content by UV-spectrophotometer.

Surface pH

For the determination of surface pH three films of each formulation were allowed to swell for two hours on the surface of an agar plate .The surface pH was measured by using a pH paper placed on the surface of the swollen film.A mean of three readings was recorded .

Moisture content

The buccal films were weighed accurately and kept in desiccators containing anhydrous calcium chloride. After 3 days, the patches were taken out and weighed. The moisture content (%) was determined by using the formula:

$$\text{Moisture content}\,(\%) = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight variation

The films were weighed individually and the average weights were calculated.

In Vitro Release Study

The commercially available dialysis membrane was employed for the study, and the *in vitro* drug release study was carried out using a Franz diffusion cell. The effective diffusion area was 1.8 cm^2. The receptor compartment (40 ml) was filled with phosphate buffer saline (PBS), pH 6.6. The films were applied under occlusion on the dialysis membrane fitted between the donor and receptor compartments of the diffusion cell. The drug release was performed at 37 ± 0.5°C, at a stirring speed of 50 rpm using a magnetic stirrer. Five milliliters of the sample from receptor medium was withdrawn at regular intervals and replaced immediately with an equal volume of phosphate buffer saline, pH 6.6. The amount of Terfenadine released into the receptor medium was quantified by using UV–visible spectrophotometer at 220.8nm against a blank.
Drug release were given in table 3.

RESULTS

RESULTS AND DISCUSSION

The main goal of the present investigation efforts was to develop and evaluate new buccal films comprising a drug-containing mucoadhesive polymeric layer using polymers like sodium alginate, NaCMC, HPMC. The physicomechanical evaluation (Table 2) indicates that the weight variation of these formulated buccal films were found to be 1.99 ± 0.122 for F1,2.148 ± 0.45 for F2 and 1.94 ± 0.67 for F3. The thickness of these films were 0.40 ± 0.14mm for F1,0.44 ± 0.10mm for F2 and 0.34 ± 0.10mm for F3. Folding endurance was measured manually.Folding endurance of these films were found to be 81.07 ± 0.66 for F1,83.18 ± 0.80 for F2 and 88.22 ± 0.88 for F3. The range of folding endurance study ensured flexibility of these formulated buccal films. The drug content in buccal film was found to be uniform with a range of 99.47 ± 0.52 % for F1,98.25 ± 0.91% for F2 and 98.94 ± 0.67 % for F3.This indicates that the drug dispersed uniformly throughout the polymeric film.
The moisture content (%) study was done for 3 days. Moisture content of the buccal film was found to be 1.53 ± 0.36% for F1,1.71 ± 0.17 %for F2 and 1.52 ± 0.37% for F3.The low moisture content in the formulation is highly appreciable to protect from microbial contaminations and bulkiness of the patches also a low moisture content in formulations helps them to remain stable.

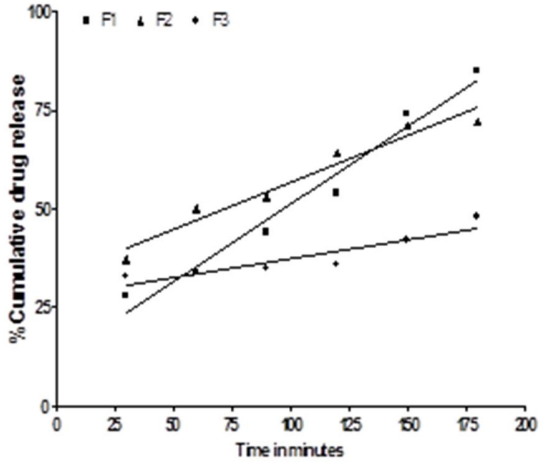
Table 2: Characteristics of buccal film

Characteristics	F1 Sodium alginate film	F2 SCMC film	F3 HPMC film
Weight variation	1.995 ± 0.1223	2.148 ± 0.458	1.943 ± 0.6700
Thickness	0.4042 ± 0.1418	0.4425 ± ± 0.1022	0.3492 ± 0.1044
Folding Endurance	81.07 ± 0.6683	83.18 ± 0.8010	88.22 ± 0.8841
Drug content Uniformity	99.47 ± 0.5280	98.25 ± 0.9167	98.94 ± 0.6705
Moisture content	1.538 ± 0.3650	1.712 ± 0.1733	1.520 ± 0.3521
Surface ph	6.267 ± 0.7607	5.733 ± 0.5167	6.083 ± 0.4956

Table 3: *In vitro* drug release profile of Terfenadine buccal patches

Time in minutes	%cumulative drug release		
	F1	F2	F3
30	28	37	33
60	34	50	21
90	44	53	35
120	54	64	36
150	74	71	42
180	85	72	48

The in vitro drug release pattern of Terfenadine from formulated buccal films is shown in graph 1. All of these buccal patches slowly released the drug incorporated and sustained over a period of 180 minutes. The drug release from buccal films varied with respect to the polymer composition. Among all formulations, the maximum in vitro drug release was observed in the case of formulation F1(85%), while the minimum in vitro drug release was found in the case of formulation F 3(48%). The in vitro drug release was more sustained for the Terfenadine buccal patches which were composed with sodium alginate.



Graph-1 *In vitro* drug release profile terfenadine buccal patch

CONCLUSION

Buccal patches of Terfenadine using polymers like sodium alginate, SCMC and HPMC in various proportions showed satisfactory mucoadhesive characteristics. The proportional amounts of various hydrophilic polymers in various formulations have influence on drug release from these formulated Terfenadine buccal films. From the present investigation, it can be concluded that such buccal films of Terfenadine may provide sustained delivery through buccal route, which can be a good way to bypass the extensive hepatic first-pass metabolism.

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