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Original Article

DESIGN, DEVELOPMENT AND EVALUATION OF MUCOADHESIVE FILM FOR WATER INSOLUBLE DRUG USING DIFFERENT PLASTICIZERS

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ABSTRACT

Objective: The goal of this present research finding was to formulate mucoadhesive film for a water insoluble drug using different plasticizers and to study the effect of plasticizers in formulating buccal films. Buccal drug delivery is a safer and easier method of drug utilization.

Methods: Buccal films were prepared by using Hydroxy Propyl Methyl Cellulose (HPMC) as the polymer and Glycerine, Propylene glycol, Dibutyl phthalate, Triethanolamine as plasticizers. Methanol and acetone were used as solvents. Prepared buccal films were evaluated in terms of surface pH, swelling index, folding endurance, film weight, film thickness and other parameters. Drug-polymer interaction was investigated through FT-IR spectroscopy. Percentage drug content was also determined. *In-vitro* drug release studies was carried out using open ended cylinder method in phosphate buffer of pH6.8.

Results: Results showed that formulation F2 gave sustained drug release compare to other formulations. FT-IR studies did not showed any significant drug polymer interaction.

Conclusion: It was concluded that buccal films prepared by using Propylene glycol as the plasticizer in the solvent methanol, promotes sustained drug release over a period of 6 hours of study and hence proves to be a good plasticizer in formulating buccal films which showed satisfactory results.

Keywords: Mucoadhesive, Plasticizers, Sustained release.

INTRODUCTION

Mucoadhesion generally can be defined as the adhesion between two materials with each other where one of the material is a mucosal surface. The mucosal or mucoadhesive drug delivery system plays a key role as a innovative drug delivery system of the modern era. In simple words, mucoadhesion can be stated as the attachment of drug along with a suitable carrier that attaches to the mucous membrane. It also has a significance in case of binding of drugs to the mucous membrane in the buccal cavity. Bioadhesive formulations have a wide scope of application for both systemic and local effects of drug[1].

Drug delivery through oral mucosa also helps in overcoming hepatic metabolism, controlled rate of drug release[2]. Mechanism which supports mucoadhesion includes the intimate contact between a bioadhesive and a membrane (wetting or swelling phenomenon) where as the term bioadhesion signifies to any bond between biological surface or the bond between synthetic or biological surface and the penetration of the bioadhesive into the tissue or the surface of the mucous membrane[3,4]. Apart from inhalable, injectables, transdermal routes, buccal route of drug delivery is at the most[5].

Polymer related factors which influence the mucoadhesion are molecular weight, flexibility, hydrogen bonding, concentration, hydration etc[6]. Environmental factors such as saliva also plays a key role. Polymers that can be used are like hydrophilic polymers such as Polyvinyl Pyrrolidone (PVP), Methyl Cellulose[6] etc. Non specific bioadhesive polymers include Polyacrilic acid, Cyanocryllates. Anionic polymers such as CMC, cationic polymers such as Chitosan can be used. Non ionic polymers include PVP, HPMC and Hydrogels[7].

Certain range of plasticizers can be used for formulating buccal films/patch which includes alcohol, Glycerine, Propylene glycol, Triethanolamine etc. Mucoadhesive drug delivery system possess some advantages which comprises of prolong drug delivery, improved patient compliance and therapeutic efficacy. In addition, buccal drug delivery promotes flexibility and comfortness.

MATERIALS AND METHODS

Materials

Ibuprofen, HPMC, Propylene glycol, Trithanolamine were purchased from Scorp Biomedicines (P) LTD, Chennai. Methanol, Acetone, Glycerine, Dibutyl phthalate and all other chemicals were of analytical grade.

Methods

Preparation of mucoadhesive buccal films

Mucoadhesive buccal films were prepared using solvent casting method[9]. They were prepared by dispersing 600mg of the polymer (HPMC) in 5ml of methanol and acetone. Calculated amount of the drug Ibuprofen (200mg) was dissolved in another 5ml of methanol and acetone and this mixture was added to the polymer mixture. 0.5ml of different plasticizers were added to all formulations and were allowed to dry under room temperature.

After that all the films were studied for further evaluation. The composition of films are shown in table 1, figure 1.

FT-IR studies

In order to study the positive interactions between the pure drug and the polymer, FT-IR studies was performed using Kbr pellets.

EVALUATION OF MUCOADHESIVE BUCCAL FILMS (Table 2a, 2b)

Film weight, film thickness and surface texture

All films were weighed on a digital weighing balance and their weights were noted. Film thickness was measured using Vernier Callipers from all sides at different position and the average value was noted. Surface texture of all the films were noted by touching the surface of the films.[9,10]

Folding endurance

Folding endurance of buccal films was determined by folding each films at the same place repeatedly until it breaks. Number of times the films can be folded until it breaks gives the value of folding endurance and the average value was noted.[11,14]

Surface pH

Buccal patches were allowed to swell in 2% agar in phosphate buffer solution of pH 6.8 in a clean, dry petridish for two hours consecutively. Surface pH of film was determined by placing a pH paper on the surface of films.[14,15]

Table 1: Composition of mucoadhesive buccal films

S. No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Ibuprofen	200mg	200mg	200mg	200mg	200mg	200mg	200mg	200mg
2	HPMC	600mg	600mg	600mg	600mg	600mg	600mg	600mg	600mg
3	Methanol	10ml	10ml	10ml	10ml	-	-	-	-
4	Acetone	-	-	-	-	10ml	10ml	10ml	10ml
5	Glycerine	0.5ml	-	-	-	0.5ml	-	-	-
6	Propylene glycol	-	0.5ml	-	-	-	0.5ml	-	-
7	Dibutyl phthalate	-	-	0.5ml	-	-	-	0.5ml	-
8	Triethanolamine	-	-	-	0.5ml	-	-	-	0.5ml

Fig. 1: Formulated mucoadhesive buccal film

Swelling Index

Each films of size (1cmx1cm) was cut and their initial weight was noted. Films were allowed to swell for 5min in 20ml of distilled water. Films were than taken out, dried and weighed. Percentage of swelling was noted using the following formula:

Swelling Index (SI) = Final weight-Initial weight/Initial weight x 100

Percentage Moisture Absorption (PMA)

All films of size 1cmx1cm was initially weighed. They were placed in dessicator containing Aluminium chloride and the internal humidity was maintained, After three days, all films were taken out and they were weighed again. Average value was noted using the following formula**:**

Percentage Moisture Absorption (PMA) = Final weight-Initial weight/Initial weight x 100

Percentage Moisture Loss (PML)

All films of size 1cmx1cm was initially weighed. They were placed in dessicator containing Calcium chloride and the internal humidity was maintained. After three days, all films were taken out and they were weighed again[12]. Average value was noted using the following formula**:**

Percentage Moisture Loss (PML) = Initial weight-Final weight/Initial weight x 100

Estimation of percentage drug content

Three films of 1cmx1cm was cut and dissolved in 5ml of methanol and was diluted to 100ml with phosphate buffer of pH 6.8. From this 10ml was taken out using a pipette and diluted to 100ml with phosphate buffer of pH 6.8 to get a primary solution. From this 10ml was again diluted to 100ml to get 10µg/ml solution and the drug content was measured using UV spectrophotometer at 274nm.[10,14] (Table 3).

Percentage drug content= Test absorbance /Standard absorbance x 100

***In-vitro* drug release studies**

The *in-vitro* drug release studies was carried out using open ended cylinder method with the use of a membrane that is semi-permeable. There are normally two compartments in the open ended cylinder that is donor and receptor compartments. The top portion of the donor compartment was opened which was exposed to the environment and cellophane paper was used as a semi- permeable membrane to separate the receptor compartment.

Phosphate buffer of pH 6.8 was used as the diffusion medium. Films were than placed in the donor compartment and they were kept seperated from the receptor compartment using the cellophane paper membrane which was initially soaked in the mixture of glycerine and water. Temperature was maintained at 37°C at 50 rpm. 10 ml of the sample was withdrawn after every half an hour for 6 consecutive hours and simultaneously the receptor compartment was replaced with the fresh buffer. The absorbance was determined using UV spectrophotometer at 274nm.[17] (figure 2).

RESULTS AND DISCUSSION

Evaluation parameters

1)Film weight, film thickness and surface texture

Overall film weights were found in the range of 0.59±0.01-1.19±0.03g and film thickness were found in the range of 0.11±0.01-0.13±0.03mm. Surface texture were found to be smooth exceptionally F4 and F8 were very smooth.

2)Folding endurance

Folding endurance of all the films were found to be flexible for F3 and F7 exceptionally F1, F2, F5, F6 were very flexible and F4 and F8 were highly flexible.

3)Surface pH

Surface films of all the films were found almost neutral i.e 7-8.

4)Swelling index

Overall swelling index of all the films were found in the range of 100-300% and appreciably it was high in F2, F3, F7.

5)Percentage Moisture Absorption (PMA)

Percentage Moisture Absorption was negligible in F2 and F6 whereas it was 200% in F1, F4 and F8. It was 100% in F3, F5 and F7.

6)Percentage Moisture Loss (PML)

Percentage Moisture Loss were negligible for all the films.

Table 2(a): Evaluation of prepared mucoadhesive films

S.no	Formulae	Folding endurance	Swelling index	Surface texture	Film weight (gm)
1	F1	++	100%	Smooth	0.98±0.01
2	F2	++	300%	Smooth	0.59±0.01
3	F3	*	300%	Smooth	0.71±0.02
4	F4	+++	200%	Very smooth	1.19±0.03
5	F5	++	200%	Smooth	1.04±0.01
6	F6	++	200%	Smooth	0.62±0.01
7	F7	*	300%	Smooth	0.72±0.02
8	F8	+++	200%	Very smooth	1.17±0.01

***flexible ++ very flexible +++ highly flexible**

Table 2(b)

S.no	Formulae	Film thickness (mm)	Surface pH	Percentage moisture absorption	Percentage moisture loss
1	F1	0.12±0.01	7	200	Negligible
2	F2	0.13±0.03	7	Negligible	Negligible
3	F3	0.12±0.01	7	100	Negligible
4	F4	0.12±0.01	8	200	Negligible
5	F5	0.11±0.01	7	100	Negligible
6	F6	0.12±0.01	8	Negligible	Negligible
7	F7	0.13±0.02	7	100	Negligible
8	F8	0.12±0.01	8	200	Negligible

FT-IR studies: No significant drug polymer interaction was found.

Estimation of percentage drug content: Percentage of drug content in all the films were in the range of 94.11% - 97.64%.

Table 3: Percentage drug content

S.no	Formulae	Test absorbance	Percentage drug content
1	F1	0.0080	94.11
2	F2	0.0082	96.47
3	F3	0.0081	95.29
4	F4	0.0080	94.11
5	F5	0.0082	96.47
6	F6	0.0083	97.64
7	F7	0.0080	94.11
8	F8	0.0081	95.29

In-vitro drug release profile

The drug release profile of all the formulations are shown in figure 2. Results indicated that the formulation F2 showed better sustaining effect amongst all formulations. This may be due to the addition of Propylene glycol as the plasticizer and methanol as the solvent. From the release profile of F2 it was found that the drug release was about 59.71% at the end of six hours of study. Comparing the drug release profile of formulation F6, it showed drug release about 64.87% at the end of six hours due to the addition of Propylene glycol as the plasticizer and acetone as the solvent.

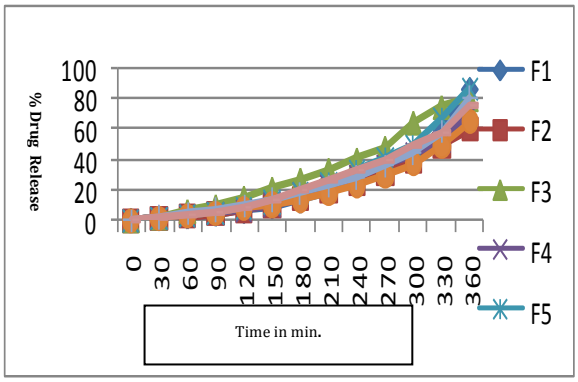

Fig. 2: *In-vitro* drug release profile of buccal films

Two solvents such as Acetone and Methanol were used because Ibuprofen is found to be soluble in both the solvents. Among all the plasticizer used like Glycerine, Propylene glycol, Dibutyl pthalate, and Triethanolamine and from the drug release profile, it was confirmed that, Propylene glycol serves as the good plasticizer in buccal film formulation and also sustaining the drug release.

CONCLUSION

Mucoadhesive buccal films were succesfully formulated using HPMC polymer and four different plasticizers and two solvents. This present study suggested that Propylene glycol serves as a good plasticizer in formulating buccal patches/films in combination with methanol as a solvent. Thus, it can be concluded that the mucoadhesive buccal films are good alternative to conventional drug by virtue of its ability to enhance bioavailability, reduction in dose frequency, overcoming first-pass metabolism and better patients acceptance.

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