Research Article

Formulation, optimization and evaluation of buccal films of Diclofenac Sodium

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Abstract

Objective: Aim of present study was to prepared formulation, optimization and evaluation of buccal films of Diclofenac Sodium. **Material and methods:** Different formulations of diclofenac sodium were statistically optimized by Taguchi method and prepared individually. Four different formulations were prepared by using HPMC as polymer and PEG-200 as a plasticizer. Formulations were prepared and evaluated for different parameters like weight variation, surface pH, swelling index, folding endurance, drug content uniformity. **Results:** Various parameters like *In-vitro* permeation study and physical parameters of different formulations were evaluated. Data showed that formulation F₂ has less weight variation as compared to other formulations. The surface pH of all formulation films were found 6.5-7.0. Patches of F₂ formulation showed higher percentage radial swelling as compared to other formulations. The folding endurance of formulations F₁, F₂, F₃, F₄ are found 88, 72, 56 & 64, respectively. The calibration curve of diclofenac sodium was obtained in pH 6.8 phosphate buffer solution. $\lambda_{\max}$ was determined at 279.8 nm with a UV-VIS spectrophotometer. Drug content uniformity of different formulations e.g. F₁, F₂, F₃, F₄ were found out to be 26.85, 31.26, 33.25, 33.58, respectively. *In-vitro* permeation study of F₁, F₂, F₃, F₄ formulations have percentage permeation of 42.6%, 37.22%, 34.17%, and 33.92% respectively, after 75min. **Conclusion:** The buccal films prepared with PEG-200 and HPMC can be used for the quick release of drug and so fast action, whereas HPMC films can be used for the sustained release of the drug.

Keywords: Diclofenac sodium, taguchi method, patches, PEG-200, buccal films

Introduction

In modern days, a general research is being carried out on the plan and improvement of to develop innovative drug delivery systems for the safety, efficacy and patient fulfilment. Such as buccal film technology (BFT) has emerged as an advanced choice to the other conventional types of drug delivery systems. It is the confirmed technology for the systemic release of active pharmaceutical ingredients [API's]. The buccal mucosa is the most excellent suited site for local, as well as systemic delivery of drugs due to its physiological

characteristics. The buccal film is an elegant and efficient dosage form with superior bioavailability, when compared to other dosage formulation as it bypasses the hepatic first pass metabolism (Madhavi et al., 2013). It is the most suitable and palatable dosage formulation due to its economic, small size, small dose and thickness of the film. Moreover, it does not need swallowing of the drug, which is also most suitable for pediatric as well as old age patients. The present research provides insight into diverse issues like profit of buccal films, manufacturing methods, evaluation parameters and the market potentiality of dosage formulation and its future prospect on global market as an efficient pharmaceutical dosage form. In BFT, mucoadhesion property of formulation is the key element. The mucoadhesive natural polymers currently used for the development of various dosages form such as tablets, patches, tapes, films, semisolids and powders successfully

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(Garg et al., 2018; Shukla et al., 2018; Shukla et al., 2017).

The diclofenac sodium is a potent proto type non-steroidal anti-inflammatory drug (NSAID). It is used for the treatment of rheumatoid arthritis, anti-inflammatory and other rheumatic disorders. The continuing use of this drug causes gastrointestinal irritation and ulceration. The physical and chemical properties of diclofenac sodium having, short half-life, make it a appropriate candidate for management by buccal route. Under the Biopharmaceutics Classification System (BCS), diclofenac sodium comes BCS class II active pharmaceutical ingredients. It means less soluble in water and high permeability compound (Shukla et al., 2017). The buccal delivery of diclofenac sodium drug avoids direct contact to mucosa therefore the formulation of buccal patches reduces the chances of gastrointestinal ulceration. The objective of this research project was to formulate the buccal film of diclofenac sodium with mucoadhesive polymers like PEG and HPMC.

Material and Methods

Materials

The material & Chemicals were collected by procurement from different companies. HPMC was collected from Nice Chemical (Pvt) Ltd. PEG was procured from Qualigens Fine Chemicals, Diclofenac sodium drug from Marc Chemicals. Agar- Nice Chemical (pvt) Ltd., Disodium Hydrogen Phosphate from Nice Chemical (Pvt) Ltd. Potassium Dihydrogen orthophosphate from Nice Chemical (Pvt) Ltd. Different apparatus and chemicals used were of analytical grades.

Drug-Polymer Compatibility

Drug-polymer interaction was observed by IR spectrophotometry. The FTIR study of pure diclofenac sodium and physical mixture of diclofenac sodium and polymers were performed by KBr dispersion method.

Preparation of calibration curve of Diclofenac sodium

Calibration curve of Diclofenac sodium was prepared by using 6.8 Phosphate buffer: In a 100 ml standard calibrated flask, stock solution was prepared by dissolving 100 mg of diclofenac sodium drug in 6.8 phosphate buffer and make up to the volume with 6.8 Phosphate buffer. From this stock solution (1%w/v),

serial were diluted and prepared by withdrawing 1ml, 2ml, 3 ml, 4 ml and 5 ml and transferred separately into 10 ml standard flask and the volume was make up to the mark by using 6.8 Phosphate buffer. The absorbance of resulting solutions was taken using shimadzu UV-1601 visual-spectrophotometer at 282 nm and the values are $r = 0.998$, $y = 0.037x$.

Formulation preparation

Formulations were prepared and optimized by Taguchi method. Formulations of polymers HPMC with PVP were designed by Taguchi method. Two factors with two levels (2^2), "L4" were taken for study. Concentrations of HPMC and PVP were taken for study as factors and their two levels for each factor. Taguchi Method of Orthogonal Arrays: - Parameters: Concentrations of HPMC, Concentrations of PVP=2 Levels: 2=2.

Initially chemicals were collected and weighed and apparatus and glass wares were cleaned and dried and HPMC 15(2gm) was added to 15ml warm distilled water. Then after dispersed the HPMC with continuously stirring in water for few minutes and polymer PEG (15gm) is added to the mixture and stir continuously. Diclofenac sodium drug accurately weight and added to the polymeric mixture and make up the volume up to 50ml and mix with continuous stirring. The formulations are prepared and cool and stay overnight. Consequently that, formulation obtained free from bubbles. Pour the content over Petri plates already covered with aluminium foil. After homogenous spreading over Petri plate dried the Petri plate in oven at 40°C for 4-5 days. Dried films are collected cut into equal size round films (Mishra et al., 2012). Stored in aluminium foil separately and put into desiccator. The composition of the formulation is shown in table 1.

Evaluations of buccal Films formulation

Weight variation

For evaluation of film, weight, three films of every formulation are taken and weight individually on a digital balance. And the total weight of the films on digital balance. The average weights are calculated.

Table 1. Formulation composition for F₁, F₂, F₃, F₄

Ingredients	F ₁	F ₂	F ₃	F ₄
HPMC	2gm	3gm	2gm	3gm
PEG	15gm	10gm	10gm	15gm
DRUG	5gm	5gm	5gm	5gm
WATER	q.s.	q.s.	q.s.	q.s.

F₁:- All films weight-6.77gm

Average Weight of 10 films=1.84/10=0.184gm

F₂:- All films weight-6.94gm

Average Weight of 10 films=1.35/10=0.135gm

F₃:- All films weight-8.22gm

Average Weight of the 10 films=1.46/10=0.146gm

F₄:- All films weight-11.44gm

Average weight of the 10 films=1.82/10=0.182gm

Surface pH of film

For determination of surface pH, three films of each formulation are allowed to swell for 2 hrs, on the surface of an agar plate. The surface pH is measured by using the pH paper placed on the surface of the swollen film.

Swelling index

After determination of the film diameter, the films are allowed to swell on the surface of agar plate. The previous and final diameters of films were recorded.

$$\% S = \frac{D_{\text{final}} - D_{\text{initial}}}{D_{\text{initial}}} \times 100$$

Folding endurance

Three films were taken for each formulation. Folding endurance was 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.

Drug content uniformity

One film of each formulation has to be taken in separate 100 mL volumetric flasks, 100 mL of solvent has to be added & continuously stirred for 2 h. The solutions have to be filtered, diluted suitably (with buffer solution pH 6.8) & analyzed at specified nm in UV spectrophotometer. The average of drug contents of three films has to be taken as final reading.

In-vitro permeation study

In-vitro permeation study was performed by keshari chein type apparatus. Freshly prepared buffer solution of pH 6.8. The hollow tubes consist of two sides and the bottom side is

Figure 1. FTIR observation of Drug and polymer mixture

Table 2. Observation of weight variation, surface pH of film, swelling index, folding endurance and drug content uniformity of different formulation

S. No.	Formulations	Average weight (10 films)	Surface pH	Percentage of swelling (%S)	Folding Endurances	Drug content (mg)
1	F ₁	0.184±0.04	6.5-7.0	54.85±2.61	88±3.25	26.85±2.01
2	F ₂	0.135±0.084	6.5-7.0	88.57±4.02	72±3.81	31.26±3.27
3	F ₃	0.146±0.061	6.5-7.0	55.76±3.05	56±2.94	33.25±2.63
4	F ₄	0.182±0.072	6.5-7.0	36.67±2.16	64±3.27	33.58±2.45

attached to the cellophane membrane and upper side are put in the buccal film. The buccal film move from upper side to bottom side. Upper side is covered with closer. 900ml buffer solution taken in a beaker. Start the stirring in continuous motion and set temperature at $37 \pm 0.5^\circ\text{C}$. After 15, 30, 45, 60, 75 minute the 5ml sample are collect in volumetric flask and make up the volume upto 100ml with buffer solution .than 5ml buffer add to the 900ml beaker. A sample of drug film is used in each test. An aliquot of the sample is periodically withdrawn at suitable time interval and the volume is replaced with fresh dissolution medium (Mishra et al., 2011; Mishra et al., 2007). The sample is analyzed spectro-photometrically at specified wavelength.

Statistical analysis

All experiments were performed in triplicate and data were reported as a mean $\pm$ SD. Student's *t*-test was performed on the data sets using SPSS 16.0 for Windows®. Differences were considered significant for *P* values <0.05 .

Results and Discussion

Different formulations were prepared and evaluated for different parameters like weight variation, surface pH, swelling index, folding endurance, drug content uniformity, *In-vitro* permeation study. Table 2 shown physical parameters of different formulations. Data showed that formulation F₂ had less weight as compared to other formulations. The surface pH of all formulation patches were seen between 6.5-7.0. Patches of F₂ formulation showed higher percentage radial swelling value as compared to other formulations. The folding endurance of formulations F₁, F₂, F₃, F₄ are found 88, 72, 56 & 64 respectively. HPMC polymer is a hydrophilic polymer and has good swelling property when it comes in contact with water. PEG-200 is also water loving, hence reinforces swelling. HPMC swells forming a gel layer on the exposed patch surface (Akbari et al., 2004).

The calibration curve of diclofenac sodium in 6.8 pH phosphate buffer solutions were obtained at λ_{max} 279.8nm with a UV-VIS

spectrometer (Figure 1). From the present study carried out on diclofenac sodium of buccal film were prepared from drug content uniformity of different formulations F₁, F₂, F₃, F₄ are found 26.85, 31.26, 33.25, 33.58 were obtained.

In vitro permeation study showed the permeation of F₁, F₂, F₃, F₄ formulation have percentage permeation of 42.6%, 37.22%, 34.17%, 33.92% respectively after 75min (Figure 2).

Conclusion

The present study concludes that the buccal film is the most accurate and acceptable dosage form, which bypasses the hepatic first pass effect and shows good bioavailability. This is the most promising and innovative technology, which is useful to all the age groups, specifically paediatric, geriatric patients. Also to the patients with swallowing may occur difficulties. Buccal films can replace the conventional dosage forms, including fast disintegrating tablets due to its advantages over the conventional dosage forms, and they can be manufactured with low cost. This technology provides a good tool for maintenance of drug therapeutic value, as well as pharmacoeconomic value.

Figure 2. Calibration curve of diclofenac sodium in phosphate buffer pH 6.8

Table 3. Observation of percentage drug permeation of formulation F₁, F₂, F₃, F₄

Formulations	Percentage drug permeation in different time interval					
	0 hrs	15min	30min	45min	60min	75min
F1	0	8.541	17.035	25.51	34.12	42.6
F2	0	7.785	15.19	22.59	29.92	37.22
F3	0	7.08	13.75	20.55	27.39	34.17
F4	0	6.82	13.613	20.41	27.16	33.915

Figure 3. Percentage drug permeation for formulation (a) F₁ (b) F₂ (c) F₃ (d) F₄

Conflicts of interest: Not declared.

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