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# FORMULATION AND EVALUATION OF BUCCAL PATCHES OF DICLOFENAC SODIUM

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## ABSTRACT

In the present study was an attempt to formulate and evaluate the Buccal patches of diclofenac sodium. Buccal patches were prepared by solvent casting technique using different concentration of polymer, hydroxy propyl methyl cellulose (HPMC) and sodium starch glycolate as superdisintegant, using plasticizers, permeation enhancers, saliva stimulating agent and sweetener were added. Patches were evaluated for weight variation, thickness, drug content, folding endurance and *vitro* drug release. All formulated patches were shown satisfactory results which complies with an official limits. The results shown the formulation exhibited acceptable drug content, film thickness, folding endurance, surface $p^H$ and swelling index.The results revealed that 4% sodium starch glycolate (F5) was found to be more promising *in vitro* drug release of prepared diclofenac sodium baccal patches. It can be concluded that diclofenac buccal patches offer more stable, predictable and faster drug release/absorption at higher concentration of sodium starch glycolate .

**KEYWORDS:** Buccal patch, diclofenac sodium, HPMC, sodium starch glycolate.

## INTRODUCTION

The rapidly dissolving dosage forms were introduced in 1970's as an alternative to the conventional tablet and capsule which require swallowing of the dosage form.[1]

Nearly 35-50% of the general population, especially the elderly and children suffer from dysphagia or difficulty in swallowing, which results in high incidence of non-compliance and ineffective therapy. Swallowing problems also are very common in young individuals

because of their poorly developed muscular and nervous systems. Other groups who may experience problems in swallowing conventional oral dosage forms are the patients with tremors of extremities, mentally ill, developmentally disabled, non-cooperative and patients with reduced liquid intake or patients suffering from nausea, as well as patients travelling or who do not have access to water.

A new drug delivery system was introduced as fast dissolving oral films (FDOFs). FDOFs are the most advanced dosage form due to more flexibility and comfort.[2]

Diclofenac belong to the family of non-steroidal anti-inflammatory drugs (NSAID) or cyclo-oxygenase (COX) inhibitors. It is an effective antiinflammatory, analgesic and antipyretic agent. It is commonly used in the treatment of acute and chronic pain, rheumatoid and osteoarthritis. It acts by inhibiting COX activity and consequently the formation of pro-inflammatory mediators such as prostaglandins (PGs) and thromboxanes. The mode of analgesic action of diclofenac sodium is through inhibition (COX-2) causing a reduction in the conversion of arachidonic acid into inflammatory prostaglandins. Chemically it is 2-(2,6-dichlorophenyl) amino benzeneacetic acid 4-(3H1,2,dithiol-3-thione-5-yl)phenyl ester and is a low-molecular-weight drug (MWt: 318.13). The long-term use causes gastro-intestinal irritation and ulceration. The physico-chemical properties of Diclofenac sodium and its short half-life (1.2 – 2 Hrs) make it a suitable candidate for administration by buccal route. The buccal delivery of Diclofenac Sodium avoids direct contact to mucosa hence the formulation reduces the possibility of gastrointestinal ulceration. The objective of this research project is to formulate the buccal film of Diclofenac sodium using mucoadhesive polymers like HPMC and sodium starch glycolate used as super disintegrant.[3]

- The objective of study is to formulate and evaluate fast dissolving buccal patches of Diclofenac Sodium with an aim to improve the solubility characteristic., reduce the disintegration time of the patches, and improve dissolution efficiency in view to provide quick on set of action their by improve patient compliance, etc.

## MATERIALS AND METHODS

### Materials

Diclofenac sodium was procured from Strides arcolabs Ltd .Bangaluru, hydroxyl propyl methyl cellulose, sodium starch glycolate, sodium lauryl sulphate, glycerine, vanilla and citric acid were purchased from S.D. Fine Chemicals. Bangaluru.

## Methods

**Preparation of Diclofenac sodium buccal patches:** The buccal orally dissolvable films (ODFs) films were prepared by using polymer along with the drug and a suitable solvent. Table. 1. Shows the composition of ODFs the six formulations prepared. The buccal films of diclofenac sodium were prepared using HPMC by casting technique. HPMC polymer required was weighed accurately and placed in 3 ml of ethanol; the contents in the beaker were stirred on magnetic stirrer for 15 minutes for swelling of polymer. The drug 100mg weighed and dissolved in suitable solvent (methanol, ethanol) and then the polymer solution was prepared by dissolving the required quantity of HPMC, Sodium Lauryl Sulphate (SLS), vanilla; citric acid and glycerin to this add 20 ml of distilled water. The drug solution was added to the polymer dispersion and mixed the solution homogeneously by keeping it in a sonicator for 5 mins. The prepared viscous formulation was poured on the Petri dish in room temperature for 2 hrs and followed to evaporate the solvent in hot air oven for 1hrs at 50°C for drying and sudden evaporation. After this period, an inverted funnel was placed over the mould overnight to remove the remaining solvent. The dried films were meticulously taken out of the petri dishes, inspected for any imperfections, and cut into 2 cm × 2 cm sizes with a scalpel. The films were packed in an aluminium foil and stored in an air tight glass container to maintain the integrity, elasticity and pending assessment of the films.[4]

**Table: 1. Composition of diclofenac sodium buccal patches.**

| Ingredients | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Diclofenac sodium (mg) | 100 | 100 | 100 | 100 | 100 |
| HPMC % | 2 | 2 | 2 | 2 | 2 |
| SSG % | - | 1 | 2 | 3 | 4 |
| SLS (gm) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Glycerin (ml) | 2 | 2 | 2 | 2 | 2 |
| Vanilla (gm) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Citric acid (gm) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Distilled water (ml) | 20 | 20 | 20 | 20 | 20 |

## Evaluation of buccal patches

### Appearance and Uniformity of Thickness

All prepared films were checked for their appearances, whether uniform or not, and for the presence or absence of air bubbles, and so forth. The thickness of five randomly selected 2 cm × 2 cm films from each ODF formulation was determined using a screw gauge at five different positions of the patch and the average was calculated.[5]

**Folding Endurance**

The folding endurance of the films was determined by repeatedly folding one film at the same place place until it break. The number of times the film could be folded at the same place without breaking was the folding endurance value.[5]

**Uniformity of weight of the patches**

Patches sizes of 2 × 2 cm2 were cutted, The weights of five patches were taken using Shimadzu balance and the weight variation was calculated. the average weight was determined.

**Content determination**

Drug content uniformity was determined by dissolving the 2cm X 2cn size film in 100 ml of phosphate buffer (pH 6.8) for 8 h by homogenization under occasional shaking. Then 5 ml solution was taken and diluted with phosphate buffer pH 6.8, and the resulting solution was filtered through a 0.45 μm Whatman filter paper. The drug content was then determined after proper dilution at spectrophotometer at λmax 276 nm.[5]

**Surface pH**

The patches was allowed to swell then in contact with 0.5 ml of distilled water (pH 6.5±0.5) for one hour at room temperature and pH was noted down by bringing electron in contact the surface the pH , allowing it equilibrate for 1 minute.[6]

**Film swelling**

Film swelling studies is conducted using simulated saliva solution. A patch of 10 mm size diameter from every batch was weight on a pre-weight cover slip. It was kept in petridish and 10 ml phosphate buffer, pH 6.8 was added. After one hour, the cover slip was removed and measures the weight. The difference in the weight gives the weight increase due to absorption of water and swelling of patch. The degree of swelling was calculated using formula;

The degree of swelling was calculated using the formula $= \frac{W_t - W_0}{W_0}$

Where $W_t$ is the weight of the film at time t

$W_0$ is the weight of film at time 0

**In-vitro disintegration time:** In vitro disintegration time is determined visually in USP disintegration test apparatus. The disintegration time is the time when the film starts to break

or disintegrates when brought in contact with water, is less than 1 minute for the fast dissolving film. So here F1 –F5 batches were found to be in the optimum range.[6]

***In - vitro* dissolution studies:** In vitro release of drug from all formulations was determined using USP apparatus type II (Paddle method). The following conditions were followed to study the *in-vitro* dissolution study of diclofenac sodium mouth dissolving film.

1. Dissolution apparatus: USP Type II (Paddle method)
2. Volume of dissolution medium: 900 ml
3. Temperature: 37±0.5$^0$C
4. Dissolution medium: phosphate buffer (pH 6.8)
5. Sampling interval: 2 min
6. Quantity of sample withdrawn: 5ml
7. Stirring: 100 rpm

Samples were assayed spectrophotometerically at 276 nm. Three trials were carried out for all the samples and the average value was taken. The percentage of the drug dissolved at various time intervals was calculated and plotted against time.[7]

## RESULTS AND DISCUSSION

Diclofenac obeys the Beer's law in concentrations range of 5-30 µg/ml in water with regression of coefficient of 0.999.

### Post formulation parameters

**Table. 2: Evaluation parameters of buccal films of diclofenac sodium.**

| Parameters | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Transparency | Best | good | Good | Good | Good |
| Thickness (mm) | 0.178 | 0.185 | 0.189 | 0.195 | 0.199 |
| Avg. Weight (mg) | 125 | 129 | 132 | 147 | 152 |
| Folding endurance | 168 | 176 | 181 | 186 | 192 |
| Surface PH | 6.4 | 6.2 | 6.3 | 6.5 | 6.7 |
| Swelling Index | 0.190 | 0.198 | 0.208 | 0.216 | 0.228 |
| Drug content (%) | 92.05 | 94. 24 | 96.65 | 97.02 | 98.89 |
| Disintegration time(S) | 41 | 36 | 32 | 26 | 22 |

Each value is the mean, n = 3 determinations

***In-vitro* release studies**

**Table. 3: *In-vitro* Drug release profile of buccal films of diclofenac sodium.**

| Time (min) | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| 2 | 9.89±0.21 | 14.76± 0.13 | 16.32± 0.31 | 19.23± 0.43 | 22.43± 0.37 |
| 4 | 15.32±0.45 | 19.78± 0.56 | 22.89± 0.21 | 29.45± 0.11 | 31.55± 0.51 |
| 8 | 22.89± 0.67 | 27.98± 0.54 | 30.21± 0.11 | 39.44± 0.33 | 48.98± 0.44 |
| 12 | 30.32 ±0.43 | 38.98± 0.93 | 41.34± 0.34 | 47.07± 0.65 | 53.22 ±0.21 |
| 16 | 39.00± 0.21 | 49.09± 0.23 | 55.56± 0.56 | 68.32± 0.21 | 74.88± 0.13 |
| 20 | 58.45± 0.34 | 66.98± 0.67 | 71.89± 0.78 | 80.68± 0.34 | 88.12± 0.12 |
| 24 | 63.98 ±0.67 | 79.90± 0.45 | 88.33± 0.87 | 93.66± 0.78 | 98.12± 0.12 |

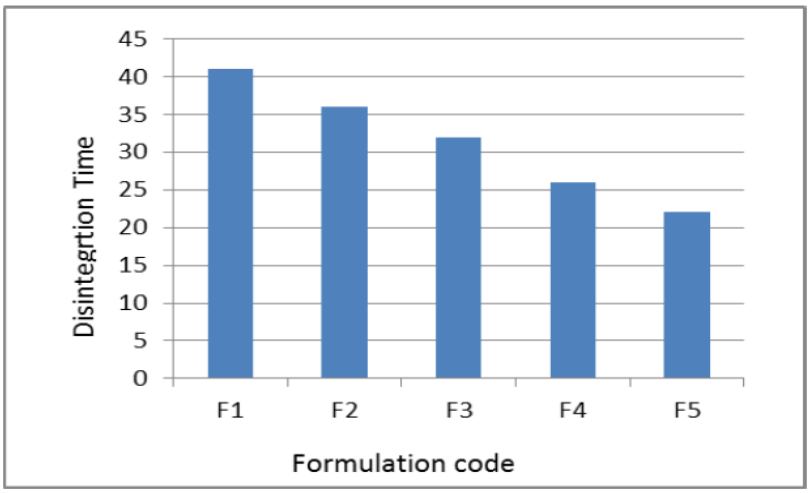


**Fig. 1: Graphical representation of disintegration time.**

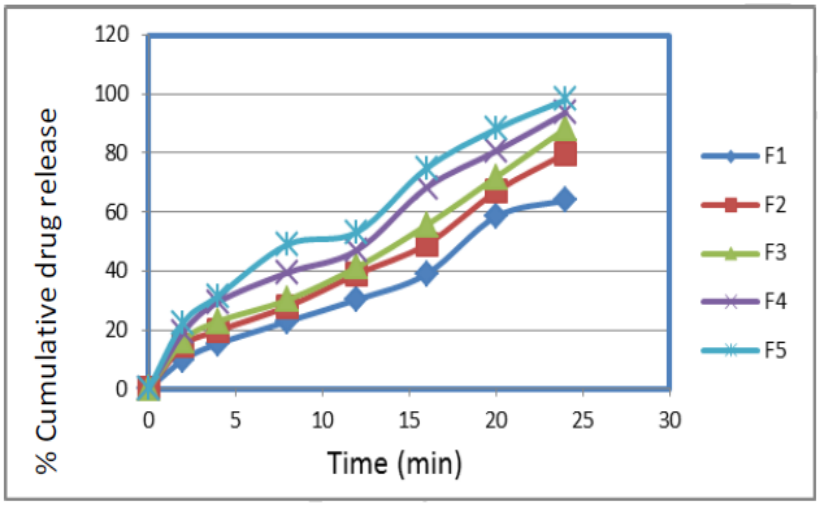


**Fig. 2: *In-vitro* drug release profile of formulations F1-F5.**

## DISCUSSION

Several methods were described in the methodology for the development and evaluation of film containing diclofenac sodium as a drug. These formulations were intended to produce

immediate release of drugs in the buccal region. Fast-dissolving films of diclofenac sodium were evaluated for various parameters. In the present study, five formulations were prepared by varying the SSG concentration and by using HPMC as polymer.

***Melting point determination***

The melting point of the obtained drug sample was found to be in the range between 280-285 °C, which complied with IP standards thus indicating the purity of drug.

***Solubility analysis***

Solubility analysis of Diclofenac sodium was done in different solvent system. It is observed that Diclofenac sodium was sparingly soluble in water. The drug was freely soluble in ethanol. It is sparingly soluble in PBS (pH 6.8).

***Determination of $\lambda_{max}$***

The $\lambda_{max}$ of the Diclofenac sodium in phosphate buffer pH 6.8 was found to be 276nm.

**Standard calibration curve of Diclofenac sodium**

The absorbance of Diclofenac sodium standard solutions containing 5-30 µg/ml of drug in pH 6.8 phosphate buffer was obtained. Calibration curve with regression value of 0.999 and slope 0.022. The curve was found to be linear in the range of 5-30 µg/ml at $\lambda_{max}$ 276 nm.

**Preparation of Diclofenac sodium containing Buccal patches**

The Diclofenac sodium containing Buccal patches was prepared by HPMC polymer with increasing the concentration of SSG as super disintegrate using solvent casting technique.

**Evaluation of formulated buccal films**

**Physical appearance**

Physical appearance and Surface texture of developed patches along using HPMC and different concentration of SSG showed that films were found to be smooth, flexible, transparent, non-sticky, and homogeneous.

**Thickness uniformity:** The thicknesses of drug-loaded film were measured by using screw gauze the values are shown in the table: 2. It was observed that there was no significant difference in the thickness among the films, which indicated that the films were uniform and ranged between 0.178 to 0.199.

**Weight uniformity**

Drug loaded film was tested for uniformity of weight and the results are given in the table :2. The weight of all the prepared batches was found to quite uniform. Weight of all the film ranged between 125 and 152 mg. The change in the concentration of SSG could significantly show the difference in the weight of film.

**Folding endurance:** All the films, showed good folding endurance (near to 200), indicated that the films have good flexibility.

**Content uniformity:** The drug content was analyzed at 276 nm by using suitable blank. The results indicated that the drug was uniformly dispersed. Recovery was possible to the tune of 92.05 – 98.89 %.

**Surface pH:** The surface pH was found to be in the range of 6.2 - 6.7, which is close to the neutral pH, which indicated that films may have less potential to irritate the sublingual mucosa, and hence, more acceptable by the patients.

**Film swelling:** The swelling index study was carried out in pH 6.8 phosphate buffer solution. Among these five formulations F5 showed high swelling index and F1 showed low swelling index as shown in table: 2. Formulations containing HPMC & max concentration of superdisintegrants showed high swelling index due to the more water absorption as compared to the other formulations.

**Disintegration time:** A marked decreased in the disintegration time was exhibited by fast-dissolving film containing highest concentration of superdisintegrants with constant weight of HPMC when compared with other films, shown in table: 2.

**In-vitro dissolution study:** In-vitro drug dissolution study of various formulations was carried out in phosphate buffer pH 6.8; the release data of formulations are shown in table: 3. Dissolution time was found to be decreased by increasing the concentration of SSG. As the concentration of HPMC is same along with max concentration of SSG release was greater as compared to other formulations. Drug released was found to be highest for F5 with minimum time and release rate was decreased as the concentration of HPMC is same without any superdisintegrants. It was found to be 98.12 $\pm$ 0.12.

## CONCLUSION

In this study, Diclofenac sodium fast dissolving films were prepared using polymer HPMC and superdisintegrant SSG by solvent casting method. F5 formulation is considered as the best according to the obtained results. Percent drug release and disintegration time was taken as responses for study which were found within the accepted ranges.

Finally it is concluded that the drug release from the mouth dissolving film was increased by using the increased concentration of superdisintegrant thus assisting in faster disintegration in the buccal cavity.

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