Aceclofenac Penetration Studies from Transdermal Patch Prepared with *Ficus benghalensis* Fruit Mucilage as Matrix Forming polymer

Sruthi Marthadu, Jyoshna Medindla, Bathalapalli Sreelekha, Beduduri Nishkala
Balaji College of Pharmacy, Sanapa Road, Rudrampeta, Anantapur-515001, AP, India
E-mail address: pharmaanantapur@gmail.com

ABSTRACT: Preparation of Aceclofenac (ACF) transdermal films with *Ficus benghalensis* fruit mucilage (FBFM) and Eudragit L100 (ELC) was the prime motto behind this work. Physicochemical parameters, ACF permeation and skin irritation studies were performed for the patches. The films haunted acceptable all evaluator's parameters. Hence, it was summarized that ACF can be developed as a transdermal delivery system with natural (FBFM) and synthetic (ELC) matrix forming polymers with minimal opposing effects and good patient compliance.

Keywords: Aceclofenac, *Ficus benghalensis*, Eudragit, transdermal

INTRODUCTION

Aceclofenac (ACF), is prescribed for pain and inflammation that requires controlled discharge owing to its t ½ of 4h, was used as the core in these transdermal matrix patches. Various research outcomes revealed that ACF as a good candidate for controlled discharge formulations [1].

Ficus benghalensis is an edible fruit in some areas around Anantapur [2] and its safety profile made to think in the area of matrix forming polymer and minimal work has done for exploring its matrix constraints. In this study, Eudragit L 100 and *Ficus benghalensis* fruit mucilage (FBFM) was as a matrix forming polymer for controlled discharge of Aceclofenac.

MATERIALS AND METHODS

Materials

Aceclofenac was obtained as a gift sample from Waksman Selman Pharmaceuticals Ltd, Anantapur, AP, India. *Ficus benghalensis* fruits were obtained from plant growing around Anantapur. Eudragit L 100, Propylene glycol and Span-60 were procured from S.D. Fine chemicals Mumbai. Double distilled water was utilized whenever desirable.

Methods

Extraction of mucilage

The procedure adopted as described by Ahad et al., 2009 [3]. The *Ficus benghalensis* fruits were washed with water, sliced, seeds detached, crushed and sodden in water for 5h, boiled for 30 min and kept aside for 1 h, extracted with a muslin cloth. Acetone (3 times the volume) leads to precipitation of the mucilage. Later FBFM was parted, dried at 40°C, collected, pulverized, passed through a # 80 sieve and kept in desiccator (30°C and 45% RH) till use.

Designing transdermal films

Various amounts of FBFM was taken in a beaker. Propylene glycol, Span-60 and ACF (200 mg) were added together with nonstop stirring in mechanical stirrer for 0.5h at 750 rpm. These mixture was transferred inside the glass bangles (6.1 cm diameter) located in a Petri dish later funnel was inverted on it (for uniform evaporation). After 24 h the dried films were removed and preserved in a desiccator [4, 5]. The amounts in the formulae were given in table 1.

Table 1: Ingredients used in various films

Ingredients	F-1	F-2	F-3	F-4	F-5	F-6
Aceclofenac (mg)	200	200	200	200	200	200
Eudragit L 100	1	2	3	3	2	1
Ficus benghalensis fruit mucilage (mg)	2	4	6	2	4	6
Propylene Glycol (ml)	0.12	0.12	0.12	0.12	0.12	0.12
Span- 60 (ml)	0.06	0.06	0.06	0.06	0.06	0.06
Water (ml)	10	10	10	10	10	10

Evaluation of Films

The films were assessed for the given physicochemical constraints [7, 8, 9]:

Thickness: Digital caliper (BAKER-EC 10) was used for this and the average thickness was judged after taking readings on 5 different points of the film.

Moisture content: The pre weighed films were placed in a dessicator (having an activated silica) and stored at 30°C for 12 h. The patches were individually weighed till to get an unchanged weight. The % of moisture was assessed.

Flatness and elongation brake: The films were longitudinally cut and the thickness was assessed at different points with vernier calipers. The % elongation brake was assessed by eq.1

$$\text{Elongation } (\%) \frac{L2 - L1}{L1} X100 \text{ ----- (1)}$$

Moisture uptake: The pre weighed films were placed in a dessicator at 40°C and 75 % RH (saturated $CaCl_2$) and RH 93% (saturated solution of NH_4HPO_4) for 24h. Then weighed the films to get constant readings. The % upsurge in the weights of the films gives the moisture uptake values.

Tensile strength: A 1x1cm film's tensile strength was assessed with automatic Precisa bottom-loading balance with little alterations.

Folding endurance: The films were pleated on same axis till it breaks.

Film Drug content: 6 films of 1x1cm size, cut at different parts. Each taken in a distinct stoppered conical flask (100 ml of 0.1 N HCl: CH_3OH) and mixed energetically for 6 h with a magnetic stirrer. Later filtered, diluted and analysed with UV-Visible spectrophotometer (Systronics 117) at 203nm.

Skin irritation study: The hairs at the rabbits back were removed and patch was attached for 6 rabbits and left in place for 48h. Parallel to it control patch was also applied. The films were protected on the back for a week, then the patches were aloof and inspected for any indications of erythema or oedema on rabbits.

***In vitro* skin permeation:** The patches were placed on back of cadaver skin (cleaned from hair, tissue and blood vessels). The skin was fixed on receptor compartment for overnight (to eliminate any UV absorption disturbing material). Keshary-Chien diffusion cell with receptor cell volume of 17.5 ml (PBS of pH 7.4), at 35±2°C, stirred by magnetic bead. Sample media was introverted at regular time (sink conditions maintained) and analysed at 203 nm [10].

RESULTS AND DISCUSSION

The physical constraints of the films were within the limits (table 2). The weights, moisture content, ACF amount in the films were acceptable (table 3). The absence of Erythema/edema (table 4) illustrates the safety of patches with the skin. The *in vitro* infusion results when treated mathematically which proved the zero order release from the films.

Table 2: Mechanical properties of Aceclofenac transdermal patches

Formulation	Thickness (µm)	Moisture content	Elongation (%)	Moisture uptake		Tensile strength (N/mm^2)	Folding endurance	Drug content
				RH (75%)	RH (93%)			
F-1	525±5.35	3.5±0.22	32±0.25	2.5±0.08	3.2±0.08	0.428±0.02	52±2.1	96.82±3.62
F-2	526±8.51	3.9±0.13	36±0.36	2.9±0.05	3.6±0.07	0.475±0.03	61±1.3	98.65±2.25
F-3	532±6.25	2.5±0.27	45±0.95	1.8±0.03	2.5±0.04	0.598±0.02	82±3.5	98.84±4.65
F-4	519±7.84	2.8±0.16	34±0.84	2.5±0.06	3.8±0.02	0.447±0.01	64±4.5	97.56±6.52
F-5	542±1.95	3.0±0.24	33±0.51	2.3±0.08	3.3±0.09	0.485±0.02	70±2.3	94.52±2.38
F-6	529±3.25	3.4±0.22	40±0.75	2.4±0.08	3.1±0.05	0.507±0.01	76±3.5	96.50±4.51

Values in mean± SD; trial made 3

Table 3: Skin irritation studies for the patches

Formulation	Visual observation	
	Erythema	Edema
USP adhesive tape	1.05±0.02	1.03±0.02
F-3 patch	1.27±0.01	1.31±0.03
Blank	1.11±0.08	1.19±0.05
1% v/v of Formalin	4.51±0.06	5.22±0.01

Values in Mean ±SEM, n=5

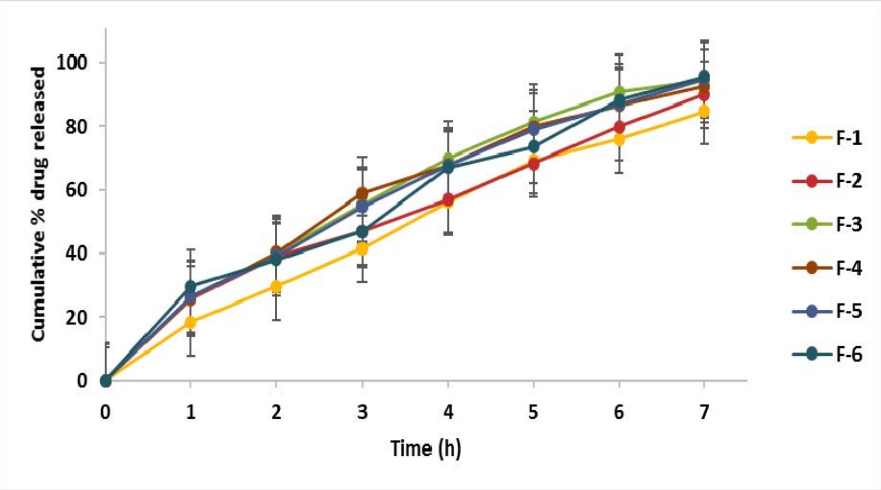

Fig.1: Zero order release kinetics from the films

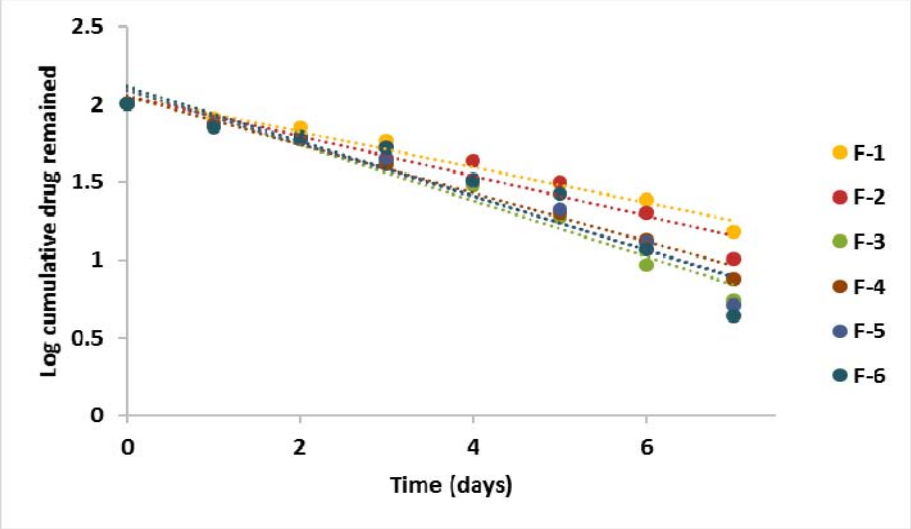

Fig.2: First order release kinetics from the films

CONCLUSIONS

This analysis discovered that *Ficus benghalensis* fruit mucilage (FBFM) has an additive matrix constraint with Eudragit L 100 for making transdermal patches. The patches showed appreciable physical constraints, *in vitro* permeation including skin friendly nature. The study concludes that dried FBFM is a good, naturally obtained, economical, matrix former in making transdermal patches.

ACKNOWLEDGMENT:

We gratefully thank to our lecturers for their support and encouragement.

CONFLICT OF INTEREST:

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

References

[1] Dooley M, Spencer CM, Dunn CJ. Aceclofenac. Drugs. 2001; 61(9):1351-78.
[2] Sirisha N, Sreenivasulu M, Sangeeta K, Chetty CM. Antioxidant properties of Ficus species–a review. Int. J Pharm Tech Res. 2010, 2(4): 2174-82.
[3] Ahad HA, Sreeramulu J, Bindu VH, Ramyasree P, Padmaja BS, Sravanthi M. Isolation and physicochemical characterization of Ficus reticulata fruit mucilage. Int. J Green Pharmacy, 2011; 5(2): 131-134.
[4] Abdul AH, Yesupadam P, Ramyasree P, Suma Padmaja B, Sravanthi M, Guru Prakash P. Isolation and physicochemical characterization of Hibiscus rosa-sinensis leaves mucilage. Int. J Cur Res. 2011; 3(4): 210-212.
[5] Ahad HA, Kumar CS, Ravindra BV, Sasidhar CG, Ramakrishna G, Venkatnath L, Gangadhar P, Navya K. Characterization and permeation studies of Diltiazem hydrochloride-ficus reticuleta fruit mucilage Transdermal patches. Int. J Pharm Sci. Review and Research. 2010; 1:32-7.
[6] Swetha T, Ahad HA, Reddy KK, Sekhar AC, Sivaji S, Kumar BA. Formulation and in-vitro permeation studies of Ketoprofen-Ficus reticulata fruit mucilage transdermal patches. Der Pharmacia Lettre. 2010; 2(6): 190-9.
[7] Ahad HA, Kumar BP, Haranath C, Reddy KS. Fabrication and evaluation of glimepiride Ficus benghalensis fruit mucilage matrix transdermal patches. Int. J Chemical Sci. 2009; 7(4): 2294-8.
[8] Anuradha CM, Ahad HA, Sreekanth K, Abhilash A, Prabhuraj KJ, Swapna K. Pharma Research Library, Int. J Med and Pharm Res, 2013; 1 (1): 127-134.
[9] Hindustan AA, Kumar CS, Anuradha CM, Reddy KK, Chandra SA. A Novel Mucilage from Ficus glomerata Fruits for Transdermal Patches: Taking Indomethacin as a Model Drug. Iranian J Pharm Sci. Winter 2011; 7 (1): 25-36.
[10] Abhilash A, Ahad HA, Anuradha CM, Prabhuraj KJ, Swapna K. Pharma Research Library, Int. J Med and Pharma Research, 2013; 1(1): 164-169.