

Formulation and Evaluation of Transdermal Patch of Diclofenac Sodium



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Abstract

Transdermal drug delivery has made an important contribution to medical practice. It is a medicated patch that delivers a specific amount of medication through the skin into the blood stream. An advantage of a transdermal drug delivery route over other types of medication delivery is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The present investigation was aimed to formulate transdermal films of non steroidal anti-inflammatory drug, Diclofenac sodium using mercury substrate method and evaluated for physicochemical parameters like thickness, weight variation, moisture uptake, moisture content, folding endurance, and drug content values. Three transdermal patches were prepared using different concentrations of ethyl cellulose. It was concluded that as the concentration of polymer increases the thickness of patch, weight uniformity and folding endurance increases. Percentage moisture content and percentage moisture uptake decreases with increase in polymer concentration.

Keywords : Transdermal; Inflammation; Skin; NSAID; Polyethylene glycol

Introduction

Transdermal patch generally refers to topical application delivers agents to healthy intact skin either for localized treatment of tissues underlying the skin or for systemic therapy. Transdermal Patch offers many advantages over the conventional dosage forms or controlled release oral systems. Transdermal patch provides constant blood levels, avoids first pass metabolism, increased patient compliance, and avoids dose dumping [1,2]. The application of transdermal delivery to a wider range of drugs is limited due to the significant barrier to penetration across the skin which is allied primarily with the outermost stratum corneum layer of the epidermis. Formulation on skin can be classified into two categories according to the target site of the action. One has systemic action after drug uptake from the cutaneous micro vascular network and other exhibits local effects in the skin. Transdermal drug delivery can closely mimics the slow intravenous infusion without its potential hazards and also offer another most important advantage in allowing the patient to terminate the drug therapy by simply removing the patch at desired time if toxicity develops [3].

NSAID (Non-steroidal anti-inflammatory drugs) are mostly used for the preparation of transdermal patches for the

treatment of inflammation or pain. The NSAID patches are safer and convenient than its oral form. Patient with rheumatism received different NSAID tablets. The side effects like stomach bleeding, increased acidity, ulcers are avoided by using transdermal patches of NSAID. The analgesic patch of NSAID may be used on the site of bruise, sprain or strain. These patch when applied topically in the form of transdermal patch, without reaching higher plasma drug concentrations the drug penetrate the skin, subcutaneous fatty tissue, and muscle in amounts sufficient to exert local therapeutic effects. Hence NSAIDs offer the advantage of local, enhanced drug delivery to affected tissues with a reduced incidence of systemic adverse events. In Rheumatoid Arthritis patients are advised to take the NSAIDs for prolong period but the side effects related to systemic toxicity and GIT irritation are the main drawbacks of NSAIDs drugs [4,5].

Diclofenac sodium is non steroidal anti-inflammatory agent, widely used in musculoskeletal disorders, arthritis, toothache, etc., for symptomatic relief of pain and inflammation. Diclofenac sodium is reportedly used for topical applications. The drug undergoes substantial hepatic first-pass metabolism and only about 50% of administered dose reaches systemic circulation. In Rheumatoid Arthritis patients are advised to take the NSAIDs

for prolong period but the side effects such as systemic toxicity, GIT irritation, nausea, vomiting, gastric erosion, headache are the main drawbacks of Diclofenac sodium. Because of its short biological half-life and frequent administration, it is considered as a suitable candidate to formulate it into a sustained release matrix type transdermal patch system. Main objective of study is to develop transdermal patch of Diclofenac sodium to achieve more patient compliance, to reduce the dosing frequency, to enhance the release rate of drug for quick onset of action, to avoid the oral administration of drug to omit the GIT related bioavailability problems and to improve local availability of drug to site of action in arthritis [6].

Materials and Methods

Materials

All the chemicals used in this research were of standard pharmaceutical grade. Diclofenac sodium was procured as a gift sample from Cipla Pharmaceuticals, Mohali. Ethyl Cellulose (Titan biotech Ltd., Bhiwadi, Rajasthan), PEG-400 (SD Fine chemicals, Mumbai), Dibutylphthalate (Nice Chemicals, Cochin), Methanol (Nice Chemicals, Cochin) and chloroform (SD Fine chemicals, Mumbai) were of analytical reagent grade.

Methods

Ethyl Cellulose was used for the formulation of Transdermal Patch. Polyethylene glycol (PEG 400) was used as a plasticizer. Dibutylphthalate is used as penetration enhancer. The polymer was dissolved in chloroform: methanol (1:1) solvent. The drug was dispersed uniformly in the viscous solution with continuous stirring. The resulting mass was poured into leveled mercury surface in a Petri dish covered with inverted funnel. The Petri dish was left undisturbed at room temperature for one day. The patch was obtained intact by slowly lifting from the Petri dish and transdermal patches were cut into radius of 2cm² [7-9] (Table 1).

Table 1: Formulation Design.

Ingredients	F1	F2	F3
Diclofenac sodium (mg)	10	10	10
Ethyl Cellulose (mg)	200	300	400
PEG-400 (ml)	1.2	1.2	1.2
Dibutyl phthalate (ml)	1.2	1.2	1.2
Chloroform: Methanol	1:4	1:4	1:4

Evaluation and Characterization

Thickness of patch

The thickness of each patch was measured by using screw gauge at five different positions of the patch and the average was calculated [10].

Weight uniformity

Patches sizes of 2cm radius (4cm diameter) was cut. The weights of five patches were taken and the weight variation was calculated [11].

Folding endurance

A patch of 2cm radius (4cm diameter) was cut evenly and repeatedly folded at the same place till it brakes. The numbers of times the film was folded at the same place without breaking give the value of the folding endurance [12,13].

Percentage moisture content

The prepared films were weighed individually and kept in a desiccators containing fuse calcium chloride at room temperature for 24h. After 24h, the films were reweighed and determined the percentage moisture content from the mentioned formula [14,15].

Percentage moisture uptake

The weighed films were kept in desiccators at room temperature for 24h containing saturated solution of potassium chloride in order to maintain 84% RH. After 24h, the films were reweighed and determined the percentage moisture uptake from the below mentioned formula [16,17].

Drug content

A specified area of patch was dissolved in a phosphate buffer solution. The content was stirred to dissolve the film. The content was transferred to a volumetric flask. The absorbance of the solution was measured at wavelength 284nm and determines the drug content [18].

Results and Discussion

The spectrum of UV was analyzed by UV/Vis spectroscopy and λ_{max} found to be 267nm at pH 5.8 with R² value of 0.9856. (Table 2-4) (Figure 1). It can be concluded that as the concentration of polymer increases the thickness of patch, weight uniformity, folding endurance increases. Percentage moisture content and percentage moisture uptake and drug release decreases with increase in polymer concentration.

Table 2 : Preparation of Standard Curve of Diclofenac sodium at pH 5.8.

Concentration mcg/ml	Absorbance
2	0.001
4	0.039
6	0.099
8	0.178
10	0.247

Table 3 : Evaluation of Diclofenac sodium Transdermal Patch.

Formulation Code	Thickness (mm)	Weight Uniformity (gm)	Folding Endurance
F1	0.512±0.03	0.298 ± 0.02	120.0 ± 2.6
F2	0.514±0.06	0.352 ± 0.04	112.0 ± 2.7
F3	0.518±0.06	0.402 ± 0.02	99.0 ± 2.6

Table 4 : Evaluation of Diclofenac sodium Transdermal Patch.

Formulation Code	%Moisture Content	%Moisture Uptake	Drug Content (mg)
F1	6.16±0.12	5.85 ±0.22	80.64±0.25
F2	5.25±0.23	4.83 ±0.26	74.18±0.32
F3	4.22±0.66	4.65 ±0.45	68.43±0.50

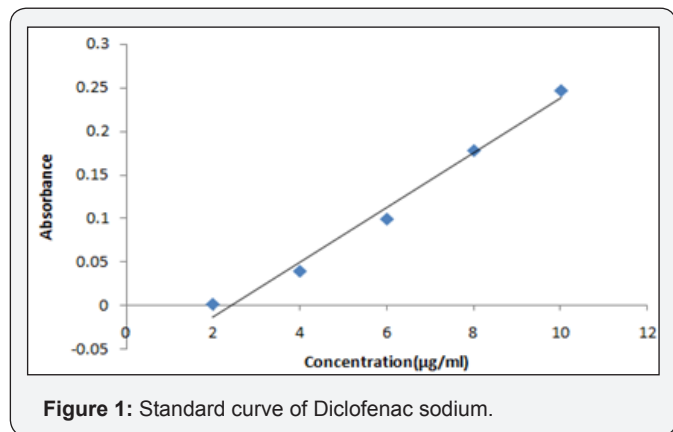


Figure 1: Standard curve of Diclofenac sodium.

Conclusion

The transdermal patch of Diclofenac sodium was prepared successfully by using different concentrations of ethyl cellulose by solvent casting method. The present work can further be proceeding with *in-vivo* study on healthy animals to evaluate the pharmacokinetic profile.

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