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Formulation And Evaluation Of Transdermal Patches Of Diclofenac Sodium

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Abstract- Transdermal drug delivery system as a therapeutic system designed to transfer drugs through intact skin for systemic treatment. It offers controlled drug release pattern by simple application to the skin's surface, eliminating the various influencing the gastrointestinal absorption associated with oral administration and providing for more efficient drug utilization. The purpose of this report was to develop a film-type of Diclofenac with different ratios of hydrophilic (HPMC) and hydrophobic (EC) polymeric systems by the solvent evaporation technique and by using Glycerol as plasticizer. Tween-80 is used as a permeation enhancer. Formulated transdermal films were physically evaluated with regard to thickness, weight variation, drug content, flatness, tensile strength, folding endurance, percentage of moisture content and water vapour transmission rate. All prepared formulations indicated good physical stability.

Key Words- Transdermal, Treatment, Gastrointestinal, Diclofenac, HPMC, EC, Plasticizer, Endurance and Transmission.

Introduction- Transdermal drug delivery systems (TDDS), also known as patches, are dosage forms designed to deliver a therapeutically effective amount of drug across a patient's skin. In order to deliver therapeutic agents through the human skin for systemic effects, the comprehensive morphological, biophysical and physicochemical properties of the skin are to be considered. Transdermal delivery provides a leading edge over injectables and oral routes by increasing patient compliance and avoiding first pass metabolism respectively. Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation, which often causes undesirable side effects. Thus various forms of Novel drug delivery system such as Transdermal drug delivery systems, Controlled release systems, Transmucosal delivery systems etc. emerged. Several important advantages of transdermal drug delivery are limitation of hepatic first pass metabolism, enhancement of therapeutic efficiency and maintenance of steady plasma level of the drug.

Drug- Name of the Drug

Diclofenac sodium

Molar Weight: 318.13

Chemical name: sodium 2- [(2, 6- dichlorophenyl) amino] phenyl acetate

S.NO	CONSTITUENTS	SUPPLIED BY-

Description-Diclofenac sodium is an odourless, yellowish-white, crystalline powder sparingly soluble in water.

Pharmacology-

- Diclofenac sodium, a nonsteroidal compound, exhibits pronounced antirheumatic, antiinflammatory, analgesic and antipyretic properties.
- Inhibition of prostaglandin biosynthesis, which has been demonstrated experimentally, is regarded as having an important bearing on its mechanism of action. Prostaglandins play amajor role in the causation of inflammation, pain and fever.
- In rheumatic diseases, the anti-inflammatory and analgesic properties of DICLOFENAC-GA elicit a clinical response characterised by relief from signs and symptoms such as pain at rest, pain on movement, morning stiffness, and swelling of the joints, as well as by an improvement in function.
- In addition, clinical studies have revealed that in primary dysmenorrhoea diclofenac preparations are capable of relieving the pain and reducing the extent of bleeding.
- Low concentrations of diclofenac sodium inhibit the aggregation of platelets induced *in vitro* by collagen and by adenosine diphosphate.
- Diclofenac sodium *in vitro* does not suppressproteoglycan biosynthesis in canine cartilage at concentrations equivalent to theconcentrations reached in humans. It is unknown whether or not diclofenac sodium affects the integrity of human osteoarthritic cartilage.

Pharmacokinetics-Diclofenac is completely absorbed from the enteric-coated tablets after their passage through the stomach. Following ingestion of one tablet with or after a meal, its passage through the stomach is slower than when it is taken before a meal, but the amount of active substance absorbed remains the same. Following oral administration, about half the active substance is metabolised during its first passage through the liver (first-pass effect).Diclofenac becomes bound to serum proteins to the extent of 99.7%, chiefly to albumin(99.4%).The total systemic clearance of diclofenac in plasma is 263 ± 56ml/minute (mean value ±SD). The terminal half-life in plasma is I to 2 hours.

Methods and Materials-

Chemical Materials (Table-1)

1.	POLYMER (HPMC/EC)	S.D. fine chem. Ltd.
2.	SOLVENT (ETHANOL)	S.D. fine chem. Ltd.
3.	PLASTICIZER (GLYCERINE)	Meck Specialities Pvt. Ltd
4.	PENETRATION ENHANCER (TWEEN-80)	Otto Biochemical
5.	DRUG (DICLOFENAC)	S.D. Fine Chem. Ltd

Equipments (Table-2)

S.NO	EQUIPMENTS	SUPPLIED BY
1.	MICROMETER SCREW GAUGE	SHIMADZU, JAPAN
2.	DIGITAL BALANCE	SHIMADZU, JAPAN
3.	DESSICATOR	LR
4.	VERNIER CALLIPER	SHIMADZU, JAPAN
5.	TENSILE STRENGTH TESTER	SHIMADZU, JAPAN
6.	UV-VISIBLE SPECTROPHOTOMETER	RAYLEIGH MODEL NO.1800
7.	MUCOADHESION TESTER	SHIMADZU, JAPAN
8.	FRENDZ DIFFUSION CELL/ DIFFUSION CELL	SHIMADZU, JAPAN

Methods-The method for preparation of transdermal film is as follows:

By Solvent Casting Method-The casting solutions were prepared by dissolving weighed quantites of polymers, plasticizer and drug in to solvent compositions. The casting solution (10 ml) was poured into glass petridishes and dried at room temperature for 24 hours for solvent evaporation. The patches were removed by peeling and cut into square dimension of 5cm*5cm (25 cm^2) .These patches were kept in dessicator for 2 days for further drying and wrapped in aluminium foil, packed in self-sealing covers.

Preparation of Phosphate Buffer- Add 3.1 gm of $NaH_2PO4.H20$ and 10.9 gm of Na_2HPO4 (anhydrous) to distilled H_2O to make a volume of 1litre. The pH of the final solution will be 7.4.This buffer can be stored for upto 1 month at 4 degree celcius.

Results and Discussion-

Formulation Study (Table-3)

S.NO	INGREDIENTS	FORMULATION CODE			
		F_1	F_2	F_3	F_4
1.	DRUG(mg)	25	25	25	25
2.	HPMC(mg)	300	350	_	_
3.	EC(mg)	_	_	300	350
4.	ETHANOL(ml)	5	5	5	5
5.	GLYCERINE(mg)	60	60	60	60
6.	TWEEN-80(mg)	60	60	60	60

Physical Appearance Study (Table-4)

FORMULATION	SMOOTHNESS	CLARITY	BRITTLENESS	OVERALL APPEARANCE
F_1	+	+	*	SATISFIED
F_2	++	*	++	SATISFIED
F_3	++	+	*	SATISFIED
F_4	+	*	+	SATISFIED

(+) SATISFACTION

(*) DISSATISFACTION

(++) EXCELLENT

Phycochemical Properties/Evaluation Parameters (Table-5)

PARAMETERS	F_1	F_2	F_3	F_4
THICKNESS(mm)	0.17	0.19	0.20	0.23
Wt.UNIFORMITY(mg)	29.55	29	28.55	27.9
DRUG CONTENT (%)	97	95	96	97
FOLDING ENDURANCE	8	10	13	10
MOISTURE ABSORPTION (%)	4.2	3.6	4.0	3.9
MOISTURE LOSS (%)	3.0	2.1	2.8	1.9
% DRUG DIFFUSE (24 HRS)	77.104	74.70	60.75	47.75

Conclusions- The transdermal diclofenac patch seems to be a promising analgesic modality for the management of mild to moderate pain following dental extractions, given the evidence of its established analgesic potency with a lower incidence of systemic adverse effects. Transdermal diclofenac therapy may have a role to play in post-traumatic pain, perhaps with an increased strength of the analgesic drug in the transdermal patch. However, longer clinical trials with a larger sample need to be conducted before the real scope of the transdermal diclofenac patch can be clearly defined.

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