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Permeation studies of Diclofenac sodium from buffalo ghee as an oleaginous base

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ABSTRACT

The present research is aimed to explore permeation capabilities of a model drug diclofenac sodium from buffalo ghee as an oleaginous base. The four prototype compositions (F_1 to F_4) were prepared by using different proportions of buffalo ghee. The diffusion and permeability studies of the prepared compositions were studied by using Franz diffusion cell. The optimized composition (F_4) was compared with marketed formulation. The study indicates that permeability and diffusion of the diclofenac sodium from the ghee base is dependent on the proportion of ghee. The diffusion and permeability of diclofenac sodium is highest at higher proportions as in F_4.

Keywords: Diclofenac sodium, Buffalo Ghee (Pure), Ointment, Diffusion, Permeability.

INTRODUCTION

Diclofenac sodium is a non-steroid-type of anti-inflammatory agent and is used widely and clinically because of its strong analgesic, antipyretic and anti-inflammatory effects. It is known that this drug inhibits biosynthesis of the prostaglandins in vivo and in vitro and the drug is considered to have only a slightly adverse effect on the stomach and intestines. It is extensively metabolized in the liver and because of its short biological half-life; the drug has to be given frequently. Therefore developing a therapeutic system to provide a transdermal delivery is beneficial. Transdermal delivery of drugs promises many advantages over oral or intravenous administration however, the success of a transdermal drug delivery system depends on the ability of the drug to penetrate the skin in sufficient quantities to maintain therapeutic level. The main barrier to most transdermal drug delivery is the stratum corneum, the outermost layer of the skin comprising keratin-rich cells embedded in multiple lipid bilayers. Many strategies have been suggested in order to overcome the low permeability of drugs through the skin [1][2][3][7]. A popular approach is the use of penetration enhancers (or accelerants) which enhance the permeability of the stratum corneum. These agents partition into, and interact with, the stratum corneum constituents to induce a temporary, reversible increase in skin permeability. [4][6]. As diclofenac sodium is not absorbed easily by transdermal application the unionized form of the

drug, diclofenac diethylamine, has been used in some preparations. [11][15] On the other hand it is possible to increase the skin absorption of diclofenac sodium by the use of penetration enhancers in the topical formulations. [12][14] Clinical evidence suggest that the topical applied diclofenac sodium are much safer than oral diclofenac sodium because it has good tissue penetrability and concentration in synovial fluid is maintained for 3 times longer period than in plasma, exerting extended therapeutic action in joints. Also it is having lower plasma half life ($t_{1/2}$ = 2 hrs.) because of which it has to be administered 2-3 times a day. [6][9] To overcome above problems associated with diclofenac sodium administration topical delivery by using buffalo ghee as a base is explored.

MATERIALS AND METHODS

Diclofenac sodium was obtained as a gift sample from Troikaa Pharmaceuticals Ltd. Thol (Gujarat).The buffalo ghee (Pure) (Saraswati®) was purchased from local market. The butylated hydroxyl anisole (BHA) of Merck Ltd. Mumbai was purchased from the market. Marketed formulation of diclofenac sodium was procured from a local pharmacy. All the chemicals used were of analytical grade.

Preparation of composition

Four different compositions (F_1 to F_4) of diclofenac sodium by using buffalo ghee as an oleaginous base were prepared as per formula mentioned in table no.1. Briefly the ghee was melted and diclofenac sodium and BHA was added. The content was stirred and then cooled down to produce stiff mass.

Ingredients (g)	Composition			
	F1	F2	F3	F4
Diclofenac sodium	0.1	0.1	0.1	0.1
Butylated hydroxyl anisole	0.0018	0.0018	0.0019	0.02
Buffalo ghee	6.0	7.0	8.0	9.0

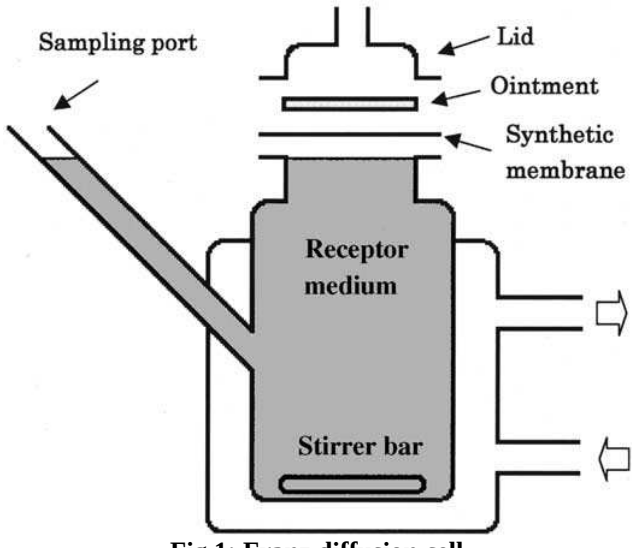

Fig.1: Franz diffusion cell

In vitro diffusion study[11-12]

The diffusion study of prepared compositions was performed using onion membrane as a semi permeable membrane and phosphate buffer (pH 7.4) at 32 ^{0}C ± 0.5 ^{0}C. The Franz diffusion cell of 20 ml capacity was used. The composition equivalent to 10 mg of diclofenac sodium was

applied on the membrane and diffusion study was performed over a period of 4 h. The samples (3 ml) were withdrawn at 5, 15, 30, 60, 120 and 240 min and fresh medium were added to maintain sink condition. The collected samples were filtered through 0.22 µ filter and analyzed at 276 nm by using UV/VIS Spectrophotometer (Chemito 2600).

In-vitro permeation study [5, 9-10]

The *in-vitro* permeation study of diclofenac sodium from prepared compositions by using buffalo ghee base was carried out by using excised abdominal skin of albino rat and Franz diffusion cell. The rat skin was mounted between the compartments of the diffusion cell with stratum corneum facing the donor compartment. Teflon bead was placed in the receptor compartment filled with 20 ml of phosphate buffer pH 7.4 and stirred with a magnetic stirrer and a temperature of 37 ± 0.5 ^{0}C. Samples were withdrawn at 5, 15, 30, 60, 120 and 240 min, simultaneously replacing equal volume by phosphate buffer pH 7.4 after each withdrawal and the removed samples were analyzed on UV/Vis spectrophotometer at 276nm.

RESULTS AND DISCUSSION

In-vitro diffusion data for diclofenac sodium through Onion membrane

Sr. No.	Time (Min.)	% Drug Diffusion				
		F1	F2	F3	F4	Marketed Formulation
1	00	00.00	00.00	00.00	00.00	00.00
2	05	02.42	02.46	03.20	03.48	23.06
3	15	10.20	11.12	13.56	14.56	32.30
4	30	19.21	20.10	21.25	25.44	33.41
5	60	27.15	28.10	29.25	38.20	38.04
6	120	32.44	35.58	36.89	41.06	39.44
7	240	40.12	40.69	40.98	43.32	41.07

In-vitro permeation data for diclofenac sodium through excised abdominal skin of albino rat

Sr. No.	Time (Min.)	% Drug Permeation	
		F4	Marketed formulation
1	00	00.00	00.00
2	05	00.25	00.02
3	15	00.59	00.5
4	30	01.10	00.95
5	60	01.75	01.15
6	120	02.48	01.86
7	240	02.95	02.54

Flux value & Permeability coefficient for F4 composition & Marketed formulation

Composition	Flux (µg./ cm^2 / Hr.)	Permeability coefficient
F4	0.283	5.6×10^{-5}
Marketed formulation	0.226	4.5×10^{-5}

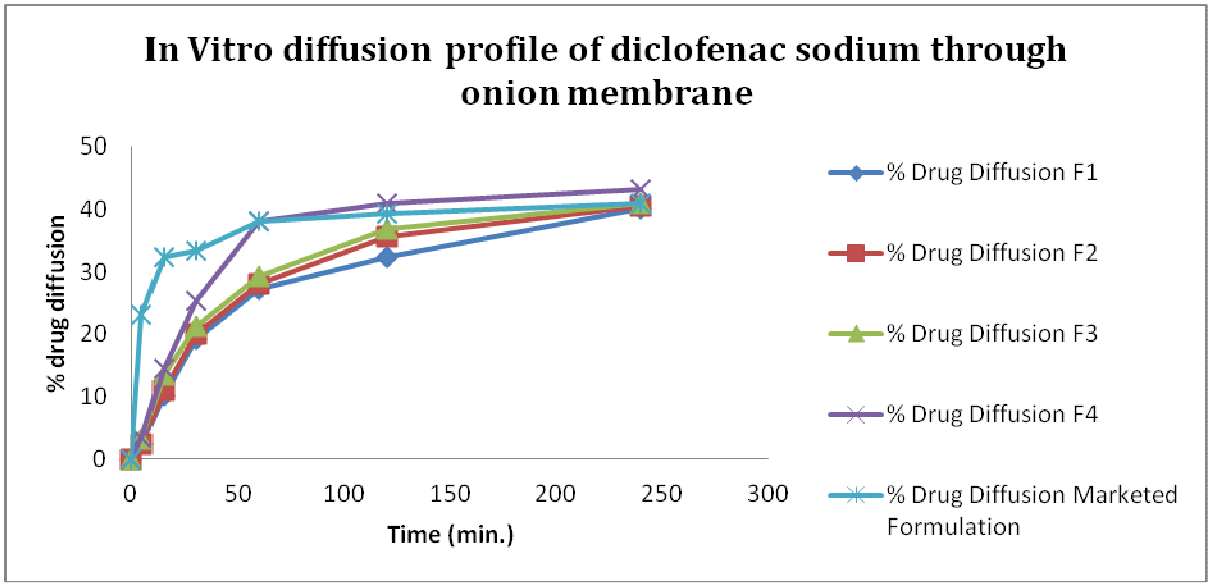

Fig 2: In-vitro diffusion study of the ghee based formulation and the marketed formulation in phosphate buffer pH 7.4.

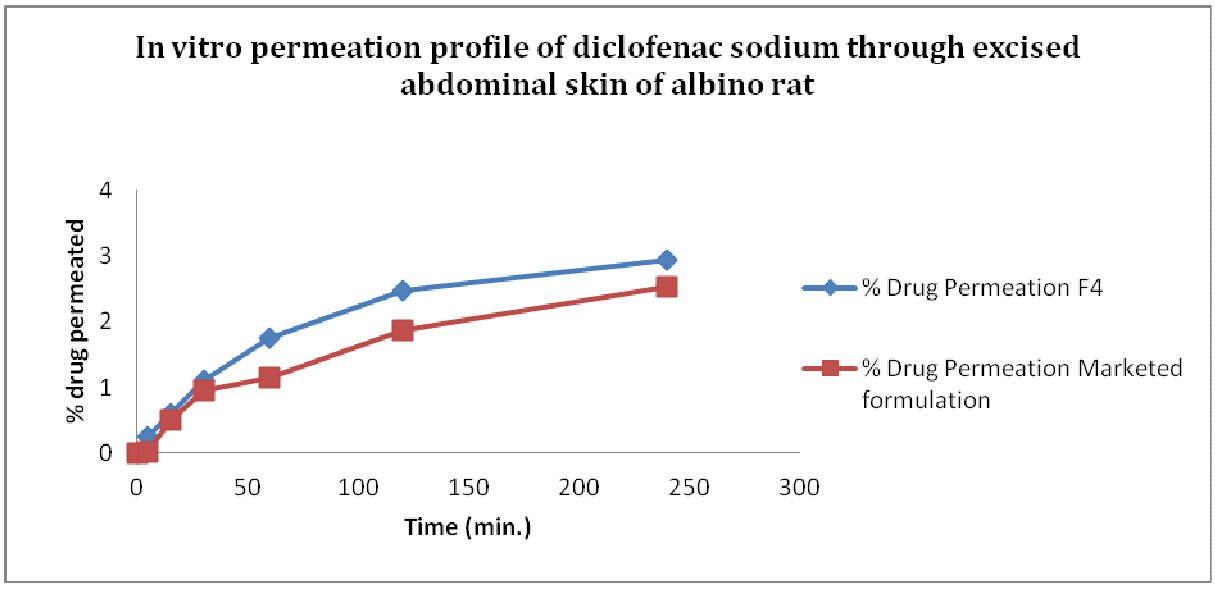

Fig 3: In-vitro permeability study of the optimized formulation (F4) in comparison with the marketed formulation.

The diffusion value for diclofenac sodium from in-vitro diffusion profile showed that the composition F_4 has higher diffusion as compared to other compositions and marketed formulation. Also the flux value of F_4 (0.283µg/cm^2/hr.) was more as compared to marketed formulation (0.226µg/cm^2/hr.). The permeability coefficient value for F_4 (5.6×10^{-5}) was more than marketed formulation (4.5×10^{-5}). So it was concluded that the prepared composition was more beneficial for improving permeation and diffusivity of diclofenac sodium if used in the selected base as compared to permeation from marketed formulation.

Future prospect

The stability and in-vivo bioequivalence study need to be done on the prepared optimized composition to obtain the correct human data. Also skin irritation and toxicity study need to be evaluated to justify the safety and efficacy of the prepared compositions.

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