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Formulation Development of Diclofenac Sodium Emulgel Using *Aloe vera* Gel for Transdermal Drug Delivery System

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ABSTRACT

Diclofenac sodium has many side effects like nausea, vomiting, GIT disorders. These side effects can be reduced by converting into emulgel formulations. The emulgel formulation of Diclofenac Sodium was prepared by incorporation method, using span 20 and tween 20 as non-ionic surfactants, clove oil and cinnamon oil as penetration enhancers, *Aloe vera* as a gel base and sesame oil as a solvent. The prepared emulgel formulations were evaluated for compatibility study, physical examination, viscosity, spreadability, *in vitro* diffusion studies, various release kinetic studies and stability studies. *In vitro* diffusion studies were carried out using cellophane membrane, results showed that emulgel formulations (F2-F7) showed higher cumulative percent drug release (49-65%) compared to normal gel (48%) and marketed gel (35%). Results of *in vitro* diffusion studies showed that formulation F3 and F6 exhibited 64% and 65% drug release respectively over a period of 6 hrs. In conclusion, a physiochemical stable diclofenac emulgel was formulated, which could deliver significant amount of drug across the skin in steady-state manner for the prolong period of time in the treatment of osteoarthritis.

KEYWORDS: Diclofenac Sodium; Emulgel; *Aloe vera*; Osteoarthritis.

Introduction

Novel drug delivery systems are new strategies of drug delivery, based on interdisciplinary approaches that combine polymer science, pharmaceutics, bio-conjugate chemistry, technology, and molecular biology. Some of the new drugs require new delivery systems because the traditional systems are inefficient and ineffective, due to this reason new technology and devices are now available in market. Over last decades of the treatment of illness has been accomplished by conventional routes namely oral, sublingual, rectal, parental etc. Topical drug administration is a localized drug delivery system anywhere in the body through ophthalmic, rectal, vaginal and skin as topical routes. The main advantage of topical delivery system is to bypass first pass metabolism. Avoidance of the risks and inconveniences of intravenous therapy and of the varied conditions of absorption like pH changes, presence of enzymes, gastric emptying time are other advantages of topical preparations. Gel formulations generally provide faster drug release compared with conventional ointments and creams. In spite of many advantages of gels a major limitation is in the difficulty in delivery of hydrophobic drugs. Therefore, to overcome this limitation emulgels are prepared and with their use, even a hydrophobic drug can enjoy the unique properties of gels. When gels and emulsions are used in combined form the dosage forms are referred as Emulgels (Mohammed et al., 2013).

Transdermal route delivers precise amount of drug through the skin for systemic action. Interest in transdermal delivery has increased on several fronts over the past several years. However, the small group of marketed products has represented drugs of many important classes; antianginal, antihypertensive, antiemetics, hormones, urinary antispasmodic, local anaesthetic and CNS drugs. The fundamental reason for such transdermal drugs is that impermeable human skin limits daily drug dosage, delivered from an acceptable sized patch to about 10mg. Although there are only limited numbers of marketed transdermal patches available, many others are in development or awaiting FDA approval (Mohammed et al., 2004; Cleary et al., 2003).

Emulgels are emulsions, either of the oil-in-water or water-in-oil type, which are gelled by mixing with a gelling agent. They have a high patient acceptability since they possess the previously mentioned advantages of both emulsions and gels. Therefore, they have been recently used as vehicles to deliver various drugs to the skin (Barry, 2001). Emulgels or gellified emulsions are the topical formulations comprising of emulsion and gel, hence, possessing properties contributed by both. The oil phase, gelling agent and emulsifying agents constitute major components of an emulgel system, their concentrations significantly affect the rate and extent of drug release from the formulation. Emulgels for dermatological use have several favourable properties

such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water soluble, more stable, bio-friendly, transparent and pleasant appearance. The advantages of emulgels include easy incorporation of hydrophobic drug into gel using oil-in-water emulsion system, which increase stability, better loading capacity and controlled release. Owing to the merits of emulgels over the conventional dermatological formulations, many drugs have been incorporated into them. Emulgels have been formulated for varied drug categories such as non-steroidal anti-inflammatory drugs, anti-fungal agents, anti-viral drugs, anti-bacterial drugs and local anaesthetics (Kumar et al., 2014).

In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel. Direct (oil-in-water) system is used to entrap lipophilic drugs whereas hydrophilic drugs are encapsulated in the reverse (water-in-oil) systems. Emulsions possess a certain degree of elegance and are easily washed off whenever desired. They also have a high ability to penetrate the skin (Mohammed et al., 2013).

Important constituents of emulgel preparation

Aqueous material: Water, alcohols

Oils: Light Liquid Paraffin, Isopropylmyristate, Isopropyl stearate, Isopropyl palmitate, Propylene glycol.

Emulsifiers: Polyethylene glycol 40 stearate, Span 80, Tween 80, Stearic acid, Sodium stearate.

Gelling agent: Carbopol-934, Carbopol-940, HPMC-2910, HPMC, Sodium CMC.

Permeation Enhancers: Oleic acid, Lecithin, Urea, Isopropyl myristate, Linoleic acid, Clove oil, Menthol, Cinnamon.

Method of Preparation

Step 1: Formulation of Emulsion either O/W or W/O

Step 2: Formulation of gel base

Step 3: Incorporation of emulsion into gel base with continuous stirring

Osteoarthritis (OA) is a progressive and painful chronic disease affecting mainly the hand, knee and/or hip joints. OA represents a final and common pathway for all major traumatic insults to synovial joints (Hiligsmann et al., 2014). Osteoarthritis (OA) also known as degenerative arthritis, degenerative joint disease, or osteoarthritis, is a type of joint disease that results from breakdown of joint cartilage and underlying bone. The most common symptoms are joint pain and stiffness. Other symptoms may include joint swelling, decreased range of motion, and when the back is affected weakness or numbness of the arms and legs (Mobasheri et al., 2014). The most commonly involved joints are those nearthe ends of the fingers, at the base of the thumb, neck, lower back, knees, and hips (Batlouni, 2010).

The non-steroidal anti-inflammatory drugs (NSAIDs) are among the most often prescribed drugs in the world. They are used mainly in the treatment of inflammation, pain and oedema, as well as of osteoarthritis, rheumatoid arthritis and musculoskeletal disorders. This heterogeneous class of drugs includes aspirin and several other selective or non-selective cyclooxygenase (COX) inhibitors. The non-selective NSAIDs are the oldest ones and are called traditional or conventional NSAIDs. The selective NSAIDs are called COX-2 inhibitors (Batlouni, 2010).

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) taken or applied to reduce inflammation and as an analgesic reducing pain in certain conditions. Chemically it is 2-(2,6-dichloranilino) phenylacetic acid (Ahuja, 2008).

The main objective of the study is to prepare and evaluate the emulgel using aloe vera as a gel base for the treatment of osteoarthritis through topical route and comparative evaluation.

Materials and Methods

Materials

Diclofenac Sodium (Yarrow Chem products, Mumbai, India.) ,Carbapol 934 (S.D. Fine Chem. Ltd, Mumbai, India.), Tween 20 (Yarrow Chem products, Mumbai, India.), Span 20 (Rolex Laboratory research, Mumbai.), Methyl Paraben (Karnataka Fine Chem., Bangalore.), Propyl Paraben (S.D. Fine Chem. Ltd, Mumbai, India.), Clove Oil (Leo Chem, S.Puram, Bangalore.), Cinnamon oil (S.D. Fine Chem. Ltd, Mumbai, India.), Triethanolamine (Ranbaxy Laboratory, Punjab.), Potassium dihydrogenortho phosphate (S.D. Fine Chem. Ltd, Mumbai, India.), Sodium Hydroxide (Thomas Baker chemicals, Mumbai, India).

Methods

Preparation of Diclofenac Sodium Emulgel formulation

Preparation of gel from aloe juice: The mucilage or pulp of Aloe vera leaf, which is free from any resinous content (the dark red resin has to be drain out by holding the leaf upside for several seconds until the resin drips out), has to be taken to prepare *Aloe vera* gel. Then the mucilage was washed repeatedly with pure water, since it is highly acidic finally washings with 0.1N sodium hydroxide (NaOH) solution increase the pH of Aloe pulp. By using a blender, the pulp is to be blended to obtain the juice. Then the juice is pre-filtered for many times by using a cotton bed to remove any adhered rind. Then repeated subjection of the juice to the vacuum filtration produces a clear fluid. The Carbopol 934 (1%) is mixed with aloe juice to prepare *Aloe vera* gel by dispersion technique, were lump free mixture will be formed, and it allows free entrapped air upon standing. During the dispersion of juice to Carbopol (jellifies under alkaline conditions), 0.5%w/w methyl paraben and 0.16%w/w propyl paraben was added. Then 0.5 N NaOH solutions was added drop wise until to form a gel (Khullar, 2012).

Preparation of emulgel: Different formulations were prepared using varying amount of gelling agent and penetration enhancers. The preparation of emulsion was oil in water method. The oil phase of the emulsion was prepared by dissolving span 20 in sesame oil while the aqueous phase was prepared by dissolving tween 20 in

purified water. Methyl, propyl paraben and Diclofenac Sodium were dissolved in water, and both solutions were mixed with the aqueous phase. Clove oil and cinnamon oil were mixed in oil phase. Both the oily and aqueous phases were separately heated to 70-80 °C, then the oily phase was added to the aqueous phase with continuous stirring until it got cooled to room temperature. The obtained emulsion was mixed with the gel in 1:1 ratio with gentle stirring to obtain the emulgel. Finally triethanol amine is added drop wise to maintain pH (Venkataharsha et al., 2015).

Evaluation of Diclofenac Sodium Emulgel

Physical examination: The prepared emulgel formulations were inspected visually for their colour, appearance and consistency and phase separation.

pH determination: The pH of the prepared emulgel was determined by using a digital pH meter. 1g of the emulgel was stirred in distilled water, until a uniform dispersion was formed. It was kept aside for 2 hours. The volume was then made up to 100 mL, i.e. 1% solution of prepared formulation and pH measured. The test was carried in triplicate using a digital pH meter and the mean was calculated.

Viscosity andrheological studies: Brookfield digital viscometer (Model DV2TRVTJ0) was used for the determination of viscosity and rheological properties of emulgel using spindle No7. 100 g of the gel was taken in a beaker and the spindle was dipped in it. The viscosity of gel was measured at different angular velocities at a temperature of 25°C. A typical run comprised changing of the angular velocity from 0.5 to 2.5 rpm. The averages of two readings were used to calculate the viscosity (Devi, 2014).

Spreadability: For the determination of spreadability, excess of sample was applied between the two glass slides and was compressed to uniform thickness by placing 1000 gm weight for 5 min. Weight (50 gm) was added to the pan. The time required separating the two slides, i.e. the time in which the upper glass slide moves over the lower plate was taken as measure of spreadability (S) (g.cm/s) (Devi, 2014).

$$(S) = M \times L/T$$

Where, M = weight tied to upper slide, L = length moved on the glass slide, T = time taken.

Drug content determination: The emulgel formulations were dissolved in ethanol and the volume was made up to 100 mL with ethanol. The resultant solution was suitably diluted with ethanol and the absorbance was measured at 276 nm, using the Shimadzu-1800 UV-Visible spectrophotometer. The drug content was determined from the calibration curve of diclofenac sodium. This test was performed in triplicate and the average drug content for each formulation was calculated.

In-vitro release studies: The release of diclofenac Sodium from emulgel was determined using membrane diffusion technique. The emulgel equivalent to 100 mg of diclofenac Sodium was taken in a glass tube having a diameter 2.5 cm with an effective length of 8 cm that was previously covered with soaked osmosis cellophane membrane, which acts as a donor compartment. The glass tube was placed in a beaker containing 350 mL of phosphate buffer of pH 7.4 which acts as receptor compartment. The whole assembly was fixed in such a way that the lower end of the tube containing gel was just touched the surface of diffusion medium. The temperature of receptor medium maintained at 37 ± 1^0C. The receptor medium was stirred by a Teflon-coated magnetic bead fitted to a magnetic stirrer at a speed of 500 rpm. At appropriate time intervals (1, 2, 3, 4, 5 and 6 hrs) aliquots of 1mL sample were withdrawn periodically and after each withdrawal same volume of medium was replaced. The collected samples were analysed at 276 nm in UV spectrophotometer using phosphate buffer of pH 7.4 as a blank (Ahuja N., 2008).

Stability studies: Stability of a drug has been defined as "the ability of a particular formulation in a specific condition, to remain within its physical, chemical, therapeutically and toxicological specifications". The reason of stability testing is to provide evidence on how the quality of drug formulation varies with time under the influence various environmental conditions such as temperature, humidity, light. From this study, we know about recommended storage conditions; re-test periods and self-life of the drug can be established.

The selected formulations were subjected for three-month stability study as per ICH guidelines**.** The selected formulations were placed in a wide mouth glass bottles, mouth of the bottle was tightly closed and packed in aluminium foils. In the present study, stability studies were carried out at 25ºC ± 2/60% ± 5 and 40ºC ± 2/75% ± 5 RH for a specific period of 3 month for the selected formulations (Ahuja N., 2008).

Results

Compatibility studies using FT-IR: The FTIR spectroscopy is a useful tool for identifying both organic and inorganic chemicals. It can be utilized to quantify some components of an unknown mixture and can be used to analyze liquids, solids and gases.

The FTIR spectrum of the diclofenac sodium pure drug was found to be similar to the standard spectrum of diclofenac sodium as in I.P. The individual FT-IR Figure of the pure drug diclofenac sodium, as well as the combination with excipient is shown in the Figure 1-4 and results showed that drug was compatible with physical mixtures.

Physical appearance: Emulgel formulations were yellowish white viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Results have been discussed in Table 1.

Determination of pH: The pH of emulgels of diclofenac were determined by using a calibrated pH meter. The readings were taken for average of three samples. Skin compatibility is the primary requirement for a good topical formulation. The pH values exhibited by emulgels are tabulated in table no. 2 and found in range of 5.8 to 6.8 at 25 ºC

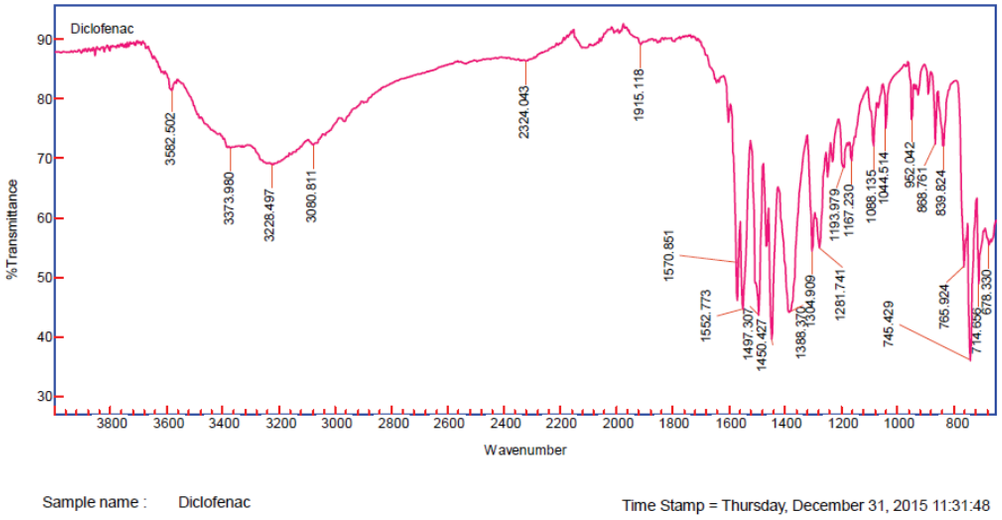

Fig. 1. FT-IR Spectra of Diclofenac Sodium drug.

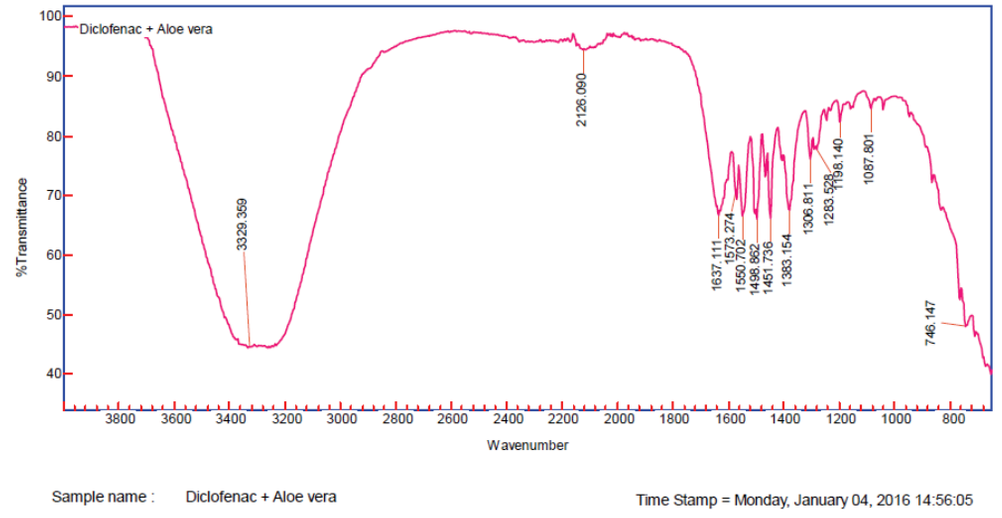

Fig. 2. FT-IR Spectra of Diclofenac Sodium + Aloe vera.

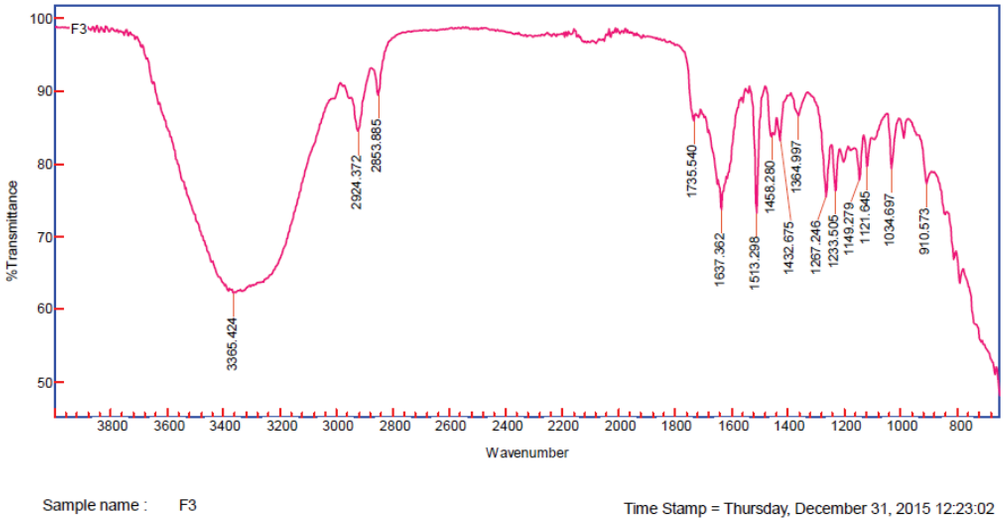

Fig. 3. FT-IR Spectra of Formulation 3.

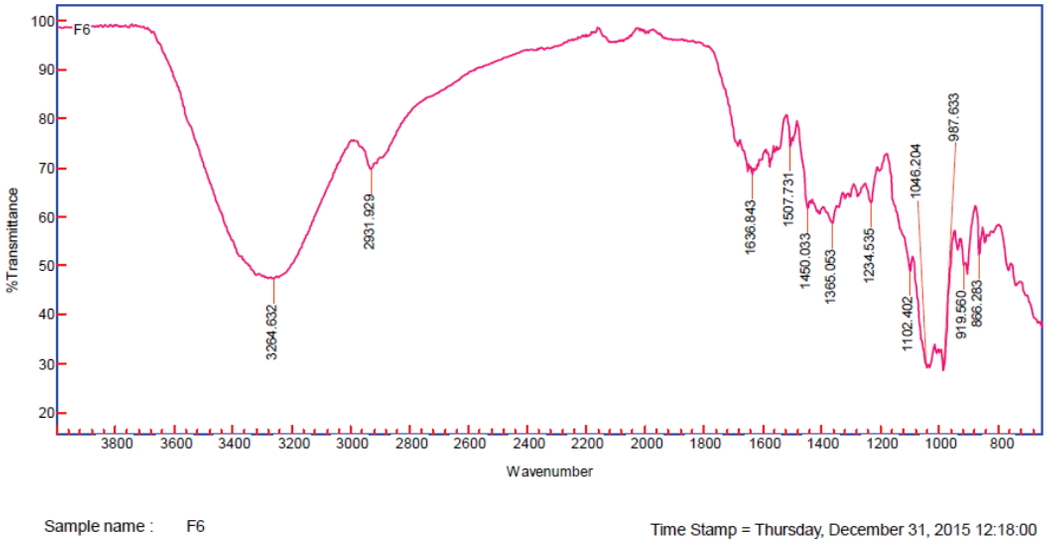

Fig. 4. FT-IR Spectra of Formulation 6.

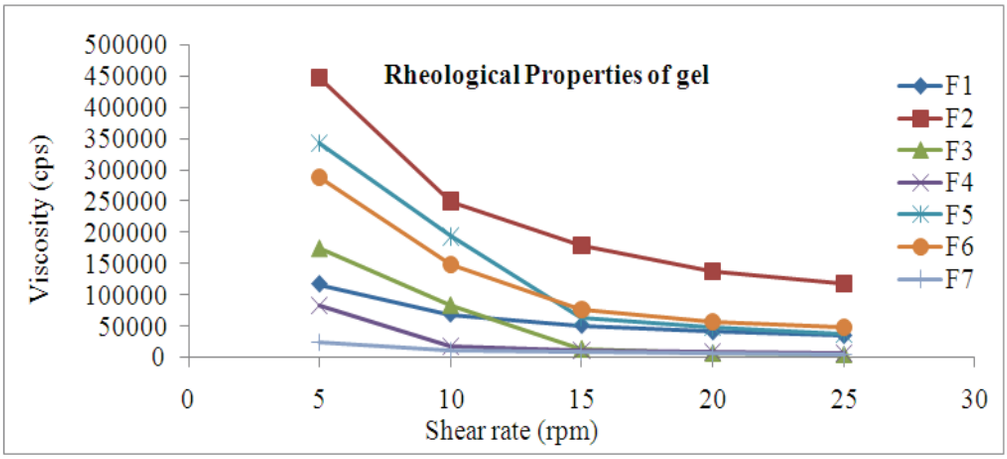

Fig. 5. Rheological profile of Diclofenac Sodium emulgel formulations.

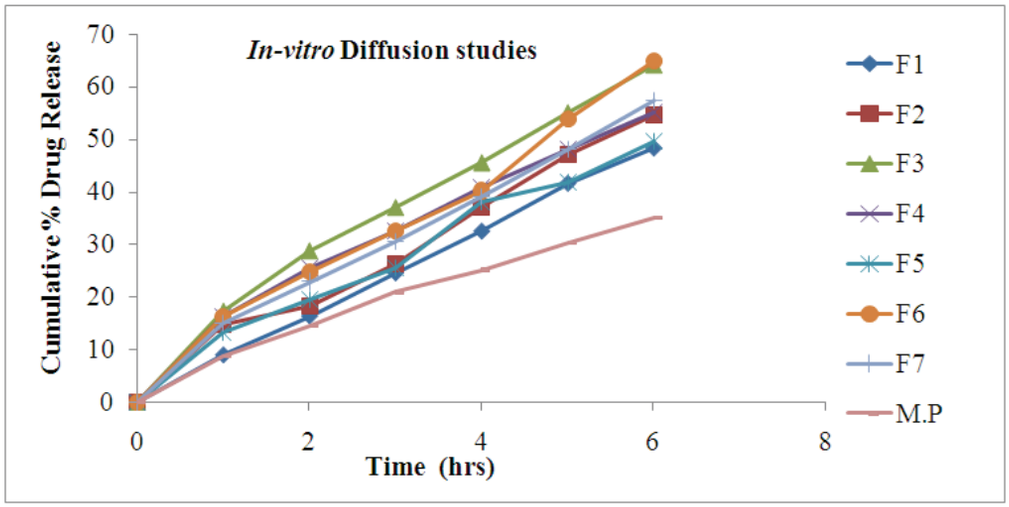

Fig. 6. Drug release profile of the Diclofenac Sodium emulgel formulation.

TABLE 1

Composition design of Emulgel formulation of Diclofenac Sodium.

S. No.	Ingredients	Formulation Code						
		F1	F2	F3	F4	F5	F6	F7
1.	Diclofenac Sodium (%)	1	1	1	1	1	1	1
2.	Aloe vera (%)	-	1	2	3	1	2	3
3.	Sesame oil (mL)	7.5	7.5	7.5	7.5	7.5	7.5	7.5
4.	Tween-20 (mL)	0.5	0.5	0.5	0.5	0.5	0.5	0.5
5.	Span-20 (mL)	1.0	1.0	1.0	1.0	1.0	1.0	1.0
6.	Clove oil (mL)	-	6	8	10	-	-	-
7.	Cinnamon oil	-	-	-	-	6	8	10
8.	Water	qs	qs	qs	qs	qs	Qs	Qs

TABLE 2

Physical parameters of different formulation batches.

Formulation code	Colour	Homogeneity	Consistency	Phase separation
F1	White	Good	Good	No
F2	Cream	Good	Good	No
F3	Pale yellow	Excellent	Excellent	No
F4	Pale yellow	Better	Better	No
F5	Cream	Good	Good	No
F6	Pale yellow	Excellent	Excellent	No
F7	Pale yellow	Better	Better	No

Viscosity and rheological studies: Brookfield digital viscometer was used for the determination of viscosity and rheological properties of Diclofenac Sodium emulgel using spindle no 7. In all the formulations Aloe vera was used as gel base. The viscosities of the gels were found to be same, as concentration of Aloe vera used in all the formulations is same (1%) except formulation 1. The results of viscosities are tabulated in Table 3. The rheological studies of the formulations were studied by plotting a graph of shear rate vs viscosity Figure 4.

Spreadability studies: Spreadability of the different gel formulations were determined and tabulated in Table 4. Hence the spreadability of the gels were seen significantly same, as Aloe vera used in all the formulations is in same concentration i.e. 1%.

TABLE 3

pH values of Diclofenac Sodium emulgel formulation.

Formulation code	pH
F1	5.82
F2	6.2
F3	6.5
F4	6.5
F5	6.2
F6	6.5
F7	6.8

TABLE 4

Viscosity of Diclofenac Sodium emulgels.

Shear Rate (RPM)	Viscosity of the formulations (cps)						
	F1	F2	F3	F4	F5	F6	F7
5	117600	448000	176000	84000	342400	288000	25500
10	69600	250800	85200	19600	193600	149200	12400
15	51470	179200	15200	12333	65070	75470	9800
20	41200	138400	8600	10600	49200	56400	8100
25	35040	119200	6080	8320	38080	48160	6100

Drug content estimation: Percentage drug content estimation of various emulgel formulations was done by UV spectrophotometer. The absorbance was measured and percentage drug content was calculated. Percentage drug content of various emulgel formulations was found be in the range of 92.12 % to 98.55 %, which is within the pharmacopoeia limits (Table 5).

TABLE 5

Spreadability of Diclofenac Sodium emulgels.

Formulation code	Spreadability (gm.cm/sec)
F1	6.83
F2	7.41
F3	7.00
F4	7.22
F5	6.72
F6	7.16
F7	6.76

In-vitro drug release studies of the emulgel: The main aim of conducting *in-vitro* release studies was to predict how a delivery system might work in an ideal situation, which also reveals its *in-vivo* performance. Since drug release decides the amount of drug available for absorption. In this present study *in-vitro* release profile of Diclofenac Sodium emulgel was compared with control gel of Diclofenac Sodium (normal gel F1) and with marketed product (M.P). The *in-vitro* diffusion release profile of Diclofenac Sodium from emulgel of different clove oil or cinnamon oil concentration. In the release studies, constant and continuous release of drug was observed from almost all formulations (Table 6). However, at the end of 6 hrs, the formulations showed 34.98% to 64.76 % drug release. In case of control gel and marketed product release rate was found relatively low i.e. 48.33 % and 34.98% respectively after 6 hrs. Higher release rate of emulgel compared to control gel and Marketed product might be due to penetration enhancement effect of clove oil and cinnamon oil. The amount of drug released from different batches of emulgel formulations was in the order of F6 > F3 > F7 > F4 > F2 > F5 > F1 > marketed product.

TABLE 6

Drug content of Diclofenac Sodium emulgel.

Formulation code	Absorbance (nm)	Conc. in 1gm gel (µg)	% Drug content
F1	0.1210	5370	92.12 %
F2	0.1085	4822	96.44 %
F3	0.1092	4853	97.26 %
F4	0.1094	4862	97.04 %
F5	0.1089	4840	96.80 %
F6	0.1120	4977	98.55 %
F7	0.1098	4880	97.60 %

Stability studies: Stability studies were carried out at 25ºC ± 2/60% ± 5 and 40 ºC ± 2/75% ± 5 RH for a period of 3 month. The optimized emulgel formulations F3 and F6 were selected for stability studies in order to study the effect temperature and humidity on emulgel formulations. The emulgel formulation F3and F6 were analysed for visual appearance, pH, viscosity, drug content and *in-vitro* release studies. First month of

stability studies revealed that there was no change in the physiochemical characteristics of both emulgel formulations. In between 2 to 3 month both the formulation has shown slight changes in pH and viscosity which was in acceptable limits (±0.5). Storing the emulgel at 25ºC/60% RH and 40ºC/75% RH has no signifiant change in the drug content, *in-vitro* drug release, viscosity and pH that justify no drug degradation. No significant changes were observed in emulgel formulation during study period, thus it can be concluded that the formulations were stable.

TABLE 7

In-vitro release studies of Diclofenac Sodium emulgel.

Time (in hrs)	Cumulative % Drug Release							
	F1	F2	F3	F4	F5	F6	F7	M.P
0	0	0	0	0	0	0	0	0
1	9.01	14.86	17.28	16.21	13.36	16.32	15.01	8.76
2	16.4	18.23	28.74	25.53	19.50	24.69	22.94	14.42
3	24.58	26.26	36.97	32.59	25.48	32.50	30.65	20.89
4	32.54	37.05	45.47	40.98	38.14	40.12	39.04	25.09
5	41.64	47.08	54.96	48.25	41.75	53.81	48.19	30.22
6	48.33	54.66	64.01	55.18	49.61	64.76	57.42	34.98

TABLE 8

Stability studies of optimized Emulgel formulation F3 at 25ºC ± 2/60% ±5 RH.

Storing period	Visual appearance	pH	Viscosity (cps)	Drug Content (%)	Diffusion profile (%)
Initial	Pale yellow Emulgel	6.50	176000	97.26 ± 0.33	64.01 ± 0.74
After 1 month	No change in appearance	6.50	176000	96.77 ± 0.42	63.90 ± 0.66
After 2 months	No change in appearance	6.47	175950	96.72 ± 0.67	63.22 ± 0.51
After 3 months	No change in appearance	6.45	175870	96.42 ± 0.53	62.71 ± 0.45

TABLE 9

Stability studies of optimized Emulgel formulation F3 at 40ºC ± 2/75% ± RH.

Storing period	Visual appearance	pH	Viscosity (cps)	Drug Content (%)	Diffusion profile (%)
Initial	Pale yellow Emulgel	6.50	176000	97.26 ± 0.33	64.01 ± 0.74
After 1 month	No change in appearance	6.49	175970	96.76 ± 0.71	63.65 ± 0.24
After 2 months	No change in appearance	6.45	175930	96.29 ± 0.42	62.72 ± 0.32
After 3 months	No change in appearance	6.43	175905	95.89 ± 0.13	62.11 ± 0.55

TABLE 10

Stability studies of optimized Emulgel formulation F6 at 25ºC ± 2/60% ± 5 RH.

Storing period	Visual appearance	pH	Viscosity (cps)	Drug Content (%)	Diffusion profile (%)
Initial	Pale yellow Emulgel	6.50	288000	98.55 ± 0.61	64.76 ± 0.61
After 1 month	No change in appearance	6.50	288000	98.43 ± 0.44	64.72 ± 0.44
After 2 months	No change in appearance	6.47	287985	98.09 ± 0.52	64.09 ± 0.52
After 3 months	No change in appearance	6.42	287955	97.86 ± 0.31	63.86 ± 0.31

TABLE 11

Stability studies of optimized gel formulation F6 at 40ºC±2/75%±5 RH.

Storing period	Visual appearance	pH	Viscosity (cps)	Drug Content (%)	Diffusion profile (%)
Initial	Pale yellow Emulgel	6.50	288000	97.55 ± 0.61	63.76 ± 0.61
After 1 months	No change in appearance	6.47	287950	97.33 ± 0.44	63.52 ± 0.44
After 2 months	No change in appearance	6.43	287920	96.89 ± 0.52	62.92 ± 0.52
After 3 month	No change in appearance	6.41	287870	96.46 ± 0.31	62.36 ± 0.31

Stability studies: Stability studies were carried out at 25ºC ± 2/60% ± 5 and 40 ºC ± 2/75% ± 5 RH for a period of 3 month. The optimized emulgel formulations F3 and F6 were selected for stability studies in order to study the effect temperature and humidity on emulgel formulations. The emulgel formulation F3and F6 were analysed for visual appearance, pH, viscosity, drug content and *in-vitro* release studies. First month of stability studies revealed that there was no change in the physiochemical characteristics of both emulgel formulations. In between 2 to 3 month both the formulation has shown slight changes in pH and viscosity which was in acceptable limits (±0.5). Storing the emulgel at 25ºC/60% RH and 40ºC/75% RH has no signifiant change in the drug content, *in-vitro* drug release, viscosity and pH that justify no drug degradation. No significant changes were observed in emulgel formulation during study period, thus it can be concluded that the formulations were stable.

Discussion

The transdermal route is an alternative route of drug delivery for systemic effect and emulgel formulations is considered ideal for transdermal delivery. In the present work an attempt has been made to develop emulgel of Diclofenac Sodium using different concentrations of Aloe vera as gelling agent and penetration enhancers (clove oil and cinmom oil), for transdermal delivery. Since the formulation procedure is simple, inexpensive and less time consuming and from the results obtained it can be concluded that;

Emulgel formulations can be conveniently prepared by incorporation method using *Aloe vera* as gel base, clove and cinnamon oils as penetration enhancers at different concentrations.

Results obtained from FTIR studies confirmed that there are no possible interactions between Diclofenac Sodium and excipient.

All prepared emulgel formulations were evaluated for different parameters such as visual appearance, pH, viscosity and spreadability. The values obtained were found to be satisfactory and complies with standard range.

Results of rheological study showed all the formulation followed the Non-Newtonian flow (shear thinning) as the shear rate increase viscosity of all

formulation decreases, which are required characters for any transdermal emulgel.

Drug content of all emulgel formulations was in the range of 92.12% to 98.55%.

Six hours of *in-vitro* diffusion studies revealed that the drug release from emulgel is dependent on concentration of *Aloe vera*. In emulgel formulations containing clove oil F3 and cinnamon oil F6, *in-vitro* drug release increases with increase in concentrations of *Aloe vera*.

All six formulations have shown sustain release for the period of 6 hrs, which is due to optimum concentration of *Aloe vera*. Therefore, Aloe vera sustains the release profile of the drug.

The drug release follows Zero order (F1, F2 and F6) as well as first order (F3, F4, F5, F7) model and mechanism was found to be Super case II, for all formulations.

Two optimized formulations were subjected to 3 months stability studies at specific temperature and relative humidity. There was no significant change in physical appearance, pH, viscosity, drug content and *in-vitro* release profile. Thus, we can conclude that there is no significant drug degradation during study period and prepared formulations were stable.

Conclusions

From the above experimental data it can be concluded that the transdermal delivery of Diclofenac Sodium emulgel formulations has been prepared by incorporation method. Thus, emulgel formulation of Diclofenac Sodium with *Aloe vera* shows best drug release profile compare to marketed product, because anti-inflammatory effect of *Aloe vera*, Diclofenac Sodium with *Aloe vera* based emulgel shows synergistic effect. Thus, it can be used in the future for treatment of Osteoarthritis with improved bioavailability.

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