Research Article

Preparation and Evaluation of Gel-Type Transdermal Drug Reservoir of Aceclofenac

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ABSTRACT

The aim of the present research is to design and development of gel-type transdermal drug reservoir of aceclofenac using natural polymer i.e. xanthan gum and examined the effects of polymeric concentration on drug release from the prepared transdermal gel system. All the prepared gel formulation showed satisfactory results of various physicochemical parameters such as visual observation, pH, clarity, spreadability, extrudability, drug content, etc. The viscosity and drug content of the prepared transdermal gels were found within the range of 4561 ± 102 cP to 9672 ± 115 cP and 93.14 ± 1.58 % to 99.13 ± 2.77 % respectively. In-vitro drug release studies revealed that xanthan gum concentration have a significant influence on drug release from the prepared transdermal gels. TEM study revealed that prepared aceclofenac loaded transdermal gel was uniform in appearance and no particles aggregations were observed. FTIR study revealed no interaction between drug and polymer where as DSC and XRD studies confirmed the presence of aceclofenac as an amorphous form in the prepared transdermal gel formulation. It was also observed that among all the formulations, AX4 (drug: xanthan gum 1:2) showed the best drug release profile as well as able to sustained the drug release for 12 hours and was selected as an optimized formulation. So it is concluded from the above research that aceclofenac loaded xanthan gum based transdermal gel was successfully prepared and will further investigated for its permeation studies and skin irritation studies.

Keywords: Aceclofenac, Xanthan gum, Transdermal gel reservoir, Drug release, viscosity, TEM.

INTRODUCTION

Aceclofenac is a non steroidal anti-inflammatory drug and chemically it is a phenyl acetic acid derivative used to manage inflammation and pain.[1] It is a selective COX-2 inhibitor, mainly used for the treatment of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis etc. Aceclofenac stimulates the synthesis of extra cellular matrix of human articular cartilages, inhibits the neutrophil adhesion, accumulates at the inflammatory site in the early phase and blocks the pro-inflammatory actions of neutrophils. [2] The biological half-life of aceclofenac is about 3-5 hours and it undergoes extensive first pass metabolism by the liver after oral administration. The oral administration of aceclofenac also shows different side effects such as ulcerative stomatitis gastritis, abdominal pain, anemia, etc. [3] Apart from this, the dissolution of aceclofenac in GI fluid is very low which may due to its insoluble nature in water which adversely affects the bioavailability. [4]

This need of an alternative non oral route to administer aceclofenac, which can bypass the first-pass metabolism and simultaneously reduce the stomach related side effects. Transdermal gel is an alternative way to deliver aceclofenac which helps to prolong the drug release, reduces the side effects, decrease the frequency of dosing as well as increase the patients compliance. High lipophilicity and other physiochemical properties make aceclofenac a suitable candidate to deliver through transdermal gel system. [5] Transdermal gel system has several advantages i.e. prevent GI irritation, nausea, vomiting tendency, avoids the first pass hepatic metabolism, reduce the dosing frequency, improve the patient compliance, deliver the drug in a steady rate over an extended period of time, prevent the enzymetical degradation of drugs as well as widely accepted non-oral route for non-responsive and unconscious patients. [6.7]

In recent years, polysaccharides are widely used as natural polymers to design and develop transdermal gel formulation. Formulation scientists are mainly focus with polysaccharides such as xanthan gum for dosage form designing due to its low cost, nontoxicity, biodegradable properties. [8] It is generally recognized as safe with respect to its applications in pharmaceutical dosage forms. [9]

So in this present research attempt has been made to design and develop gel-type transdermal drug reservoir of aceclofenac using natural polymer i.e. xanthan gum and examined the effects of polymeric concentration on drug release from the prepared transdermal gel system.

MATERIALS AND METHODS

Materials

Aceclofenac (AC) was obtained as a gift sample from Nicholas Piramal India Ltd., India. Xanthan gum was obtained as a gift sample from Signet Chemical Corporation, India. Ethanol was purchased from S.D. Fine-

Chem. Ltd., India. Glycerin was purchased from Merck, India. All other chemicals used were of analytical reagent grade.

Preparation of Gel-Type Transdermal Drug Reservoir of Aceclofenac

The gel-type drug reservoir of aceclofenac for transdermal delivery was prepared as per the method described by Dua et al. [10] (Table 1). Weighted quantity of xanthan gum was socked in sufficient amount of distilled water for 4 hours. Aceclofenac was dissolved in ethanol and the solution was added to xanthan gum dispersion with a continuous stirring at 500 rpm by magnetic stirrer (Remi Motors, India) for 2 hours. Then glycerin was incorporated as a humectant and stirred continuously until a translucent gel is obtained. The final weight of the gel was adjusted with distilled water. The gels were allowed to stand for 24 hours at room temperature for de-aeration and further swelling before they were used for the study. The final gel was examined visually so that there were no formation of crystals and no phase separations.

Table 1: Formulation of gel-type transdermal drug reservoir of aceclofenac.

Ingredients	AX1	AX2	AX3	AX4	AX5
Aceclofenac (g)	1	1	1	1	1
Xanthan Gum (g)	0.5	1	1.5	2	2.5
Ethanol (ml)	10	10	10	10	10
Glycerin (ml)	1	1	1	1	1
Distilled water qs. to (g)	30	30	30	30	30

AX: aceclofenac xanthan gum transdermal gel.

Characterization of Aceclofenac Transdermal Gel Systems

Visual Observation

The physical appearance such as transparency, homogeneity, texture and stability of the prepared gel formulations were studied by visual observations.

Clarity

The clarity of the prepared gels was determined by visual inspection under black and white background and it was graded as follows [11]; turbid: +, clear: ++, very clear (glassy): +++.

pH Determination

The pH of the prepared gels was measured using pH meter (Systronics, India). Prepared gels were first diluted with distilled water in the dilution factor of 100 (gel : distilled water 1 : 100). Then the pH of the diluted samples was tested by using pH meter.

Viscosity Measurement

The viscosity of the prepared gel formulations was measured using digital viscometer (Brookfield digital viscometer, DV II RVTDV-II USA). The gel formulations were placed in the sample holder of the viscometer and allowed to settle for 5 min. The viscosity was measured using the spindle (TF 96) at a rotating speed of 50 rpm at 25 °C. [12]

Spreadability

The spreadability of the gel formulations was determined as per the reported method Vannat et al. [13] 1 g gel mass was placed within a circle of 1 cm diameter pre marked on a horizontal glass slab over which a second horizontal glass slab was placed (20 × 20 cm). A weight of 125 g was allowed to rest on the upper glass slab for 1 min. The increase in the diameter due to spreading of the gel was noted and spreadability was calculated using the following formula,

$$S = {}^{(M \times L)}/_{T}$$

Where, S = spreadability, M = weight attached to upper glass slab, L = length of spread, T = time taken in seconds.

Extrudability

Proper consistency of a gel formulation is very much essential with respect to its application and patient acceptance point of view. High consistency of the gel formulation may not extrude from the tube whereas low viscous gels may flow quickly. 10 g formulation was filled in a collapsible aluminum tube. Then the tube was compressed and extrudability of the formulation was determined in terms of weight in grams required to extrude 0.5 cm ribbon of the gel in 10 seconds. [14]

Drug Content Analysis

The drug content of the prepared gel formulations was determined by the method of extraction of drug present in the formulations. 1g formulation was placed in 100 ml of phosphate buffer (pH 7.4) and was sonicated at 125 W for 30 min (Imeco Sonifier, Imeco Ultrasonics, India). Then the solution was filtered through Whatman filter paper (0.45 µm). The drug content of the filtrate was determined spectrophotometrically at 273 nm (UV-2450, Shimadzu, Japan). Each determination was made in triplicate and average values were reported.

Drug Release Studies from Transdermal Gel Formulations

In-vitro release of aceclofenac from the prepared gel-type transdermal drug reservoir was measured using dialysis

bag technique. [15, 16] Accurately weighed amount of gel (equivalent to 100 mg of pure aceclofenac) was placed in one end of the dialysis bag (Cellophane membrane, molecular cut off 10,000-12,000 Da, Hi-Media, India). Then the other side of the dialysis bag was hermetically sealed and immersed in 900 ml of phosphate buffer (pH 7.4) contained in the USP type II dissolution apparatus at 37 ± 1°C under 100 rpm speed. In this process, the dialysis bag acts as a donor compartment and the dissolution vessel acts as the receptor compartment. At each predetermined time intervals, 5 ml samples were withdrawn from the dissolution vessel and the same amount of pre warmed fresh dissolution medium was replaced into dissolution vessel to maintain the sink condition throughout the experiment. The samples were then filtered through Whatman filter paper and analyzed for drug content using UV-Visible spectrophotometer (UV-2450 Shimadzu, Japan) at 273 nm. The release studies were conducted in triplicate and the percentage of aceclofenac released at various time intervals was calculated.

Analysis of Release Profiles

To investigate the kinetics of drug release from the prepared transdermal gels, various kinetics models such as zero order, first order, Higuchi and Korsmeyer-Peppas model were used.

Zero-order equation,

$$Q_t = Q_0 + K_0 t$$

where Q_t is the amount of drug released at time t, Q_0 is the amount of drug in the solution at t = 0 (usually, Q_0 = 0), and k_0 is the zero-order release rate constant.

First order equation,

$$\ln(100 - Q) = \ln 100 - k_1 t$$

where k_1 is the first order release rate constant.

Higuchi's square root model [17] can be used to describe the drug release from different types of modified release pharmaceutical dosage forms.

$$Q = k_H t^{1/2}$$

Where, Q is the percentage of drug released at time t, k_H is the Higuchi rate constant.

Peppas equation, [18, 19]

$$Q_t / Q_\infty = k t^n$$

Where n = release exponent indicative of the mechanism of drug release, Q_t/Q_∞ is the fractional release of the drug, t is the release time, K is the kinetic rate constant. Thus Q_t/Q_∞ is the fraction of drug release at time t, a measure of the primary mechanism of the drug release and n characterizes the mechanism of drug release from the formulations.

The criteria for selecting the most appropriate model were based on the highest values of the coefficient of determination (r^2).

Statistical Analysis

Statistical analysis of the data was performed using the PRISM software (Graph pad, San Diego, CA). A confidence limit of P < 0.05 was fixed for interpretation of the results. *In-vitro* drug release from all the prepare gel formulations were subjected to one way analysis of variance (one way ANOVA) study to find any significant difference among the formulations or not.

Transmission Electron Microscope (TEM)

The morphology of the optimized drug-loaded transdermal gel was determined with the aid of Transmission Electron Microscopy (TEM) (Hitachi H7500, Japan) at an acceleration voltage of 80kV. Optimized formulation was diluted with water (1:100) so that it looks clear. From the clear suspension one drop was mounted on copper grid. Sample was negatively stained with 1% aqueous solution of phosphotungestic acid. It was then completely air dried and visualized under transmission electron microscope.

Fourier Transform Infrared (FTIR) Study

FTIR studies of aceclofenac (A), physical mixture (B) and optimized transdermal gel formulation (C) were performed using FTIR analyzer (Prestige-21, Shimadzu FT-IR, Japan). The samples were scanned over the wave number range of 4400 to 400 cm^{-1} at the ambient temperature.

Differential Scanning Calorimetric Analysis (DSC)

Differential Scanning Calorimetric (DSC) thermograms of aceclofenac (A), physical mixture (B) and optimized transdermal gel formulation (C) were obtained using a Differential Scanning Calorimeter (Diamond DSC, PYRIS, Perkin Elmer, USA). Indium standard was used to calibrate the DSC temperature and enthalpy scale. The samples were hermetically sealed in perforated aluminum pans and heated at constant rate of 20 °C/min over a temperature range of 20 °C to 400 °C. The system was purged with nitrogen gas at the rate of 100 mL/min to maintain inert atmosphere. This analysis was performed to evaluate the possible modifications in the internal structure of the drug after incorporation in the dosage form.

X-Ray Diffraction (XRD) Studies

X-Ray Diffraction (XRD) studies of aceclofenac (A), physical mixture (B) and optimized transdermal gel formulation (C) were performed by X-Ray Diffractometer (X'Pert Pro, Panalytical, Nertherlands) using monochromatized Cu K α-1 radiation (λ = 1.54 A) at a voltage of 45 kV and current of 40 mA. Measurements were carried out in the angular scan range from 5° to 40° (2ϑ) at a scan speed of 1°/min.

RESULTS AND DISCUSSION

Evaluation of Aceclofenac loaded Transdermal Gels

Visual Observation

The physical appearance, homogeneity, texture and stability of the prepared gel formulations were studied by visual observations (Table 2). This observation revealed that the appearance and texture of all the prepared gel formulations were translucent and smooth. It was also observed that prepared gels were highly homogeneous and stable in nature.

Table 2: Visual observation of prepared transdermal gels.

Parameters	AX1	AX2	AX3	AX4	AX5
Transparency	Translucent	Translucent	Translucent	Translucent	Translucent
Homogeneity	Highly homogeneous (no crystals observed)	Highly homogeneous (no crystals observed)	Highly homogeneous (no crystals observed)	Highly homogeneous (no crystals observed)	Highly homogeneous (no crystals observed)
Stability	No phase separation	No phase separation	No phase separation	No phase separation	No phase separation
Texture	Smooth	Smooth	Smooth	Smooth	Smooth

AX1 to AX5 = Different aceclofenac-xanthan gum transdermal gels.

pH Determination

In the development of transdermal gel formulation, pH of the formulation is very important. The more acidic or more basic pH of transdermal formulations may change the skin environment which may produce skin irritation upon application. The pH of all the prepared xanthan gum gels containing aceclofenac was found with in the range of 6.7 ± 0.2 to 7.1 ± 0.1 which is close to normal pH of the human skin (Table 3). So it was concluded that prepared gel formulations were compatible with the skin environment.

Viscosity Measurement

Viscosity is an important parameter for characterizing the gel formulations because it affects the spreadibility, extrudability and drug release. Highly viscous gel retards the drug release by retaining the drug in the gel base and whereas low viscous gel, increases the spreadibility as well as drug release rate. The viscosity of the prepared gel formulations was found from 4561 ± 102 cPs to 9672 ± 115 cPs (Table 3) and the viscosity was increased by increasing the concentration of xanthan gum.

Clarity

The visual inspection under black and white background revealed that formulations AX1 to AX4 were clear whereas formulation AX5 was turbid (Table 3). This may be due to the fact that in this formulation (i.e. AX5), highest amount of polymer was present which increases its viscosity and become turbid.

Spreadability

Spreadability is one of the important parameter for transdermal gel preparation when patient compliance is concerned. If the gel preparation spread on the skin surface properly in minimum time then only it considered as a good formulation. All the formulations showed excellent spreadability (except formulation AX5) and was found within the range of 13.23 ± 2.14 g.cm/s to 30.78 ± 3.02 g.cm/s (Table 3). The spreadability of the formulations was decreased as the concentration of xanthan gum increased. This may be due to the fact that higher polymeric concentration increases the viscosity of the gel base which may restrict the spreadability of the formulation. The spreadability of formulation AX5 was very less which may difficult to spread properly on the skin surface.

Extrudability

Proper consistency of a gel formulation is very much essential with respect to its application and patient acceptance point of view. The high consistency of the gel formulations may not extrude from the tube whereas low viscous gels may flow quickly. The extrudability was found to be 11.25 ± 1.68 N to 21.35 ± 1.11 N for all the gel formulations (Table 3). It was also observed that formulation AX5 showed lowest extrudability among all the formulations.

Drug Content Analysis

Drug content analysis revealed good uniformity of drug content for all the gel formulations and drug content values were found to be 93.14 ± 1.58 % to 99.13 ± 2.77 % (Table 3). The drug content of the prepared formulations was within desired range of 90 % to 110 %. [20]

In-Vitro Drug Release Characteristics

In-vitro drug release from the prepared aceclofenac loaded transdermal gels was evaluated using dialysis bag technique in phosphate buffer (pH 7.4). The cumulative percentage drug release from these formulations was found to be sustained over a period of 12 hours (Figure 1).

Table 3: Physicochemical properties of prepared transdermal gels.

Parameters	AX1	AX2	AX3	AX4	AX5
pH	6.7 ± 0.2	6.9 ± 0.1	6.8 ± 0.3	7.0 ± 0.1	7.1 ± 0.1
Viscosity (cPs)	4561 ± 102	5268 ± 96	6734 ± 42	7839 ± 87	9672 ± 115
Clarity	++	++	++	++	+
Spreadability (g.cm/s)	30.78 ± 3.02	28.11± 1.79	25.90 ± 2.11	22.91 ± 1.04	13.23 ± 2.14
Extrudability (N)	21.35 ± 1.11	18.77 ± 1.09	16.47 ± 2.41	15.96 ± 1.78	11.25 ± 1.68
Drug content (%)	98.73 ± 2.67	96.05 ± 1.46	97.98 ± 2.09	99.13 ± 2.77	93.14 ± 1.58

Mean ± SD., n = 3.

The *in-vitro* drug release from formulation AX1 and AX2 showed an initial burst release of drugs, which might be attributed due to the presence of less polymeric concentration in the formulation. Formulation AX1, AX2, AX3 and AX4 (drug : polymer ratio 1:0.5, 1:1, 1:1.5 and 1:2 respectively) were able to sustain the drug release up to 6, 7, 10 and 12 hours respectively. Formulation AX1 shows 92.13 ± 1.46 % drug release at 6 hours; formulation AX2 shows 91.55 ± 2.51% drug release at 7 hours; formulation AX3 shows 92.84 ± 1.22 % drug release at 10 hours and formulation AX4 shows 91.55 ± 1.78 % drug release at 12 hours respectively. Further increasing the xanthan gum concentration in formulation AX5 (drug : polymer ratio; 1:2.5), failed to release the drug completely at the end of 12 hours and only 79.77 ± 2.17 % drug was released at the end of 12 hours. This may be due to the presence of maximum amount of polymer in this formulation which entrapped the drug in its gel structure and not allowed the drug to diffuse out from the formulation. It may also due to the fact that higher polymeric concentration increases the viscosity of the gel system. Higher concentrations of xanthan gum in aqueous media yield viscid solutions that are jelly like in nature. This higher concentration of xanthan gum resists the diffusion of drug from the jelly mass due to excessive hydrogen bonding in the helix structure. [21]

It was observed from the dissolution study that concentration of polymer was the main influential factor for drug release and had a significant effect on Q_{12}, K_H and $t_{50\%}$ (Table 4). The K_H value of the prepared gel formulations i.e. AX1, AX2, AX3, AX4 and AX5 was found to be 38.64 ± 2.73, 36.88 ± 3.22, 31.54 ± 1.57, 29.44 ± 2.21 and 26.64 ± 1.02 respectively whereas $t_{50\%}$ value of the prepared formulations i.e. AX1, AX2, AX3, AX4 and AX5 was found to be 1.76 ± 0.16 hours, 2.31 ± 0.11 hours, 3.11 ± 0.37 hours, 4.19 ± 0.28 hours and 5.46 ± 0.44 hours respectively (Table 4).

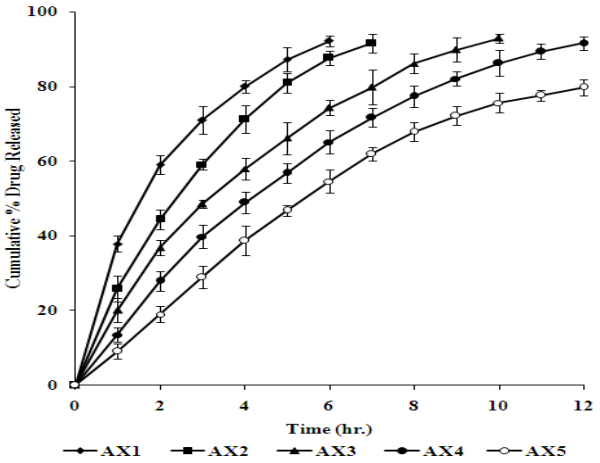

Figure 1: *In-vitro* dissolution profile of prepared transdermal gels of aceclofenac.

Higuchi rate constant (K_H) was found to decrease with increase in concentration of xanthan gum whereas $t_{50\%}$ was found to increase with increase in concentration of xanthan gum.

Table 4: Effects of polymer concentration on dependent parameters (Q_{12}, K_H and $t_{50\%}$).

Formulation	Drug : Polymer	Q_{12}	K_H	$t_{50\%}$ (hour)
AX1	1:0.5	-	38.64 ± 2.73	1.76 ± 0.16
AX2	1:1	-	36.88 ± 3.22	2.31 ± 0.11
AX3	1:1.5	-	31.54 ± 1.57	3.11 ± 0.37
AX4	1:2	91.55 ± 2.13	29.44 ± 2.21	4.19 ± 0.28
AX5	1:2.5	79.77 ± 1.98	26.64 ± 1.02	5.46 ± 0.44

AX1 to AX5 = Different aceclofenac-xanthan gum transdermal gels.

Analysis of Release Profiles

The coefficient of determination (r^2) values of drug release data of all xanthan gum transdermal gels are reported in Table 5. Formulation AX1 suggested a higher coefficient of determination with first order kinetics (r^2 = 0.997) followed by fickian diffusion mechanism (n = 0.41). Kinetic data of formulations AX2 to AX5 suggested higher coefficient of determination (r^2 = 0.990 to 0.994) with the Higuchi model followed by non-fickian diffusion mechanism (n = 0.58 to 0.80). This finding revealed that aceclofenac gets released from the prepared transdermal gels by diffusion mechanism.

Table 5: Model fitting drug release from aceclofenac loaded transdermal gels*.

Models Formulation	Zero order R^2	First order R^2	Higuchi R^2	Korsmeyer-Peppas R^2	 n
AX1	0.878	0.997	0.983	0.992	0.41
AX2	0.938	0.983	0.990	0.986	0.59
AX3	0.965	0.989	0.994	0.984	0.58
AX4	0.991	0.982	0.993	0.987	0.66
AX5	0.988	0.975	0.990	0.978	0.80

* Analyzed by the regression coefficient method.

Statistical Analysis

In-vitro drug release from all the prepare gel formulations were subjected to one way analysis of variance (ANOVA) study. Statistical analysis suggested a significant difference ($P<0.05$) in drug release among all the formulations. Among all the xanthan gum based transdermal gels, AX4 shows the best drug release profile (more than 90% drug was released in 12 hours). So, formulation AX4 was selected as optimized formulation for further studies.

Transmission Electron Microscope (TEM)

The optimized gel formulation (AX4) was subjected to TEM analysis to evaluate the gel morphology as well as examine the distribution of particles in the prepared gel (Figure 2). This study revealed that the prepared gel was uniform in appearance (Figure 2A). At higher magnification (Figure 2B) it was observed that the particles were thoroughly distributed through out the gel system and no aggregations were observed.

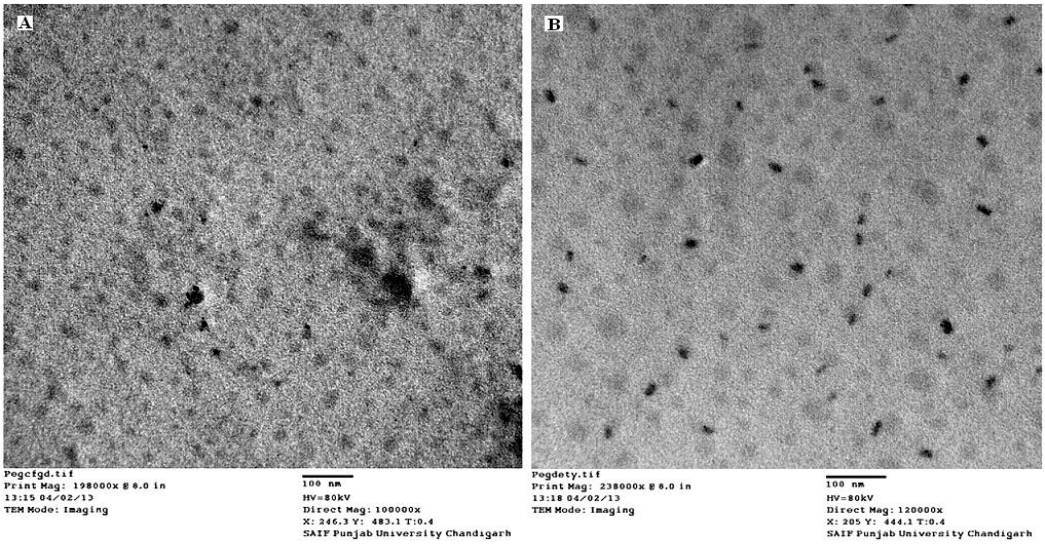

Figure 2: Transmission electron photomicrographs of optimized transdermal gel formulation (AX4) (A=100000X and B=120000X).

Drug-Excipient Compatibility Studies

Fourier Transform Infrared Analysis

The FTIR spectra of pure aceclofenac (A), physical mixture (B) and optimized gel formulation (AX4) (C) are shown in Figure 3. Pure aceclofenac showed different characteristic peaks at 3318.45, 2936.30, 1920.65, 1771.72, 1716.44, 1589.14, 1508.06, 1344.24, 1256.38, 1149.46, 1055.76, 926.72, 850.88, 747.82, 609.31, and 510.79 cm^{-1} (Figure 3A). Among the different characteristic peaks, some major peaks are 3318.45 representing the secondary NH rocking vibrations, 3028.44 for aromatic CH stretching vibrations, 2936.30 representing aliphatic CH stretching vibration of CH_2 groups (symmetric), 1771.72 due to CO stretching of carboxylic acid, 1716.44 for stretching vibration of C=O attached with methylene group and ether, 1589.14 and 1508.06 for C=C ring stretching, 1344.24 for C-H bending vibration of CH_2 groups (symmetric) respectively, 1256.38 for C-N stretching vibration of secondary aromatic amine, 1149.46 for C-O-C, 850.88 and 747.82 representing substituted phenyl rings (Khandai et al., 2014). All the characteristic peaks appeared in the FTIR spectra of aceclofenac were also appeared clearly in the optimized aceclofenac-loaded transdermal gel (AX4) (Figure 3C). Thus, it can be said that aceclofenac was successfully entrapped into the gel formulation and no significant changes occurred in drug properties. So the results concluded that there was no interaction between the drug and polymer in the optimized gel formulation.

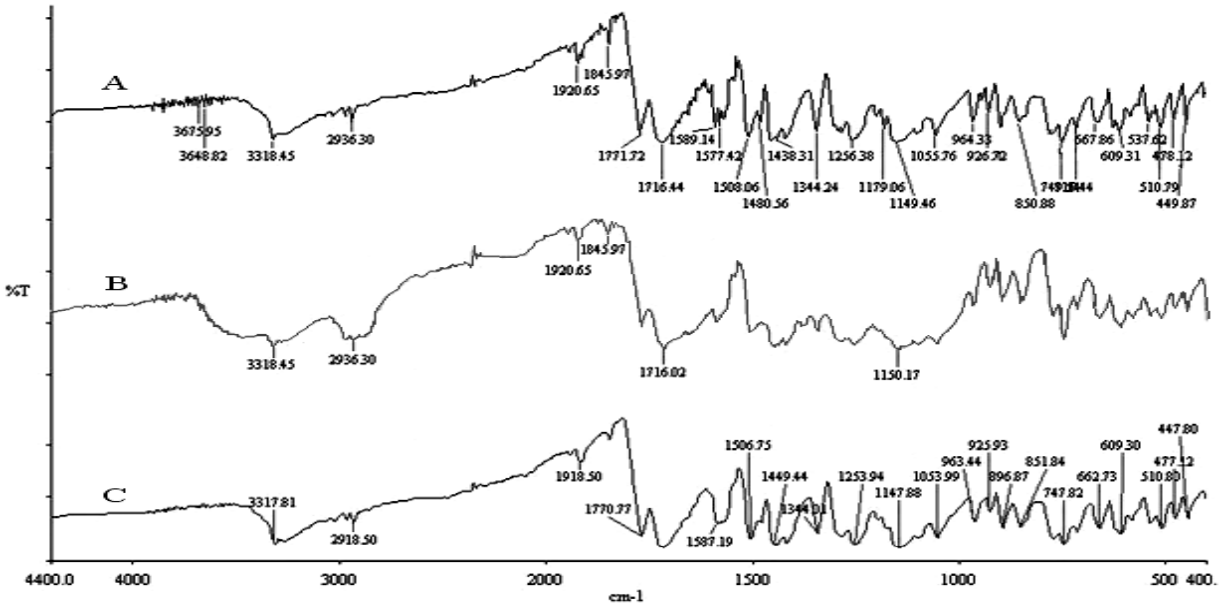

Figure 3: FTIR spectra of aceclofenac (A), physical mixture (B) and optimized transdermal gel (AX4) (C).

Differential Scanning Calorimetric Analysis (DSC)

DSC thermograms of pure aceclofenac (A), physical mixture (B) and optimized transdermal gel formulation (AX4) (C) are presented in Figure 4. The thermal graph of pure aceclofenac showed sharp endothermic peaks at 156.76°C (Figure 4A), indicating the melting point of aceclofenac. In case of aceclofenac-loaded optimized transdermal gel formulation (AX4), the intensity and sharpness of the endothermic peak corresponding to the melting point of aceclofenac was reduced and appeared at 124.87°C (Figure 4C). So DSC study revealed the amorphous state of aceclofenac in the optimized formulation. This observation was further confirmed by XRD.

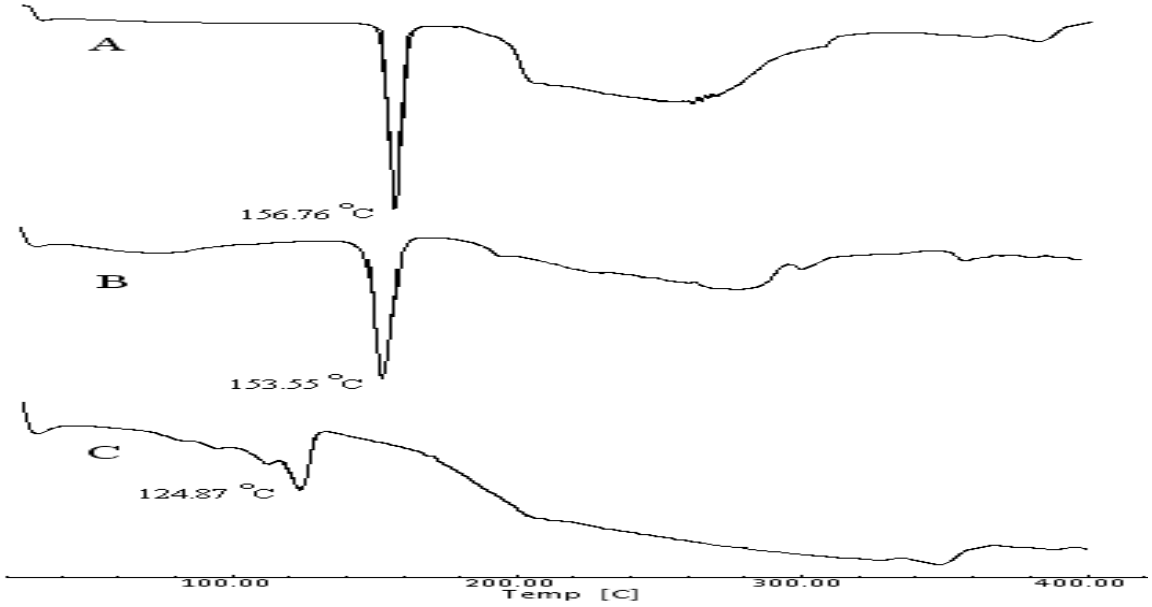

Figure 4: DSC Thermogram of aceclofenac (A), physical mixture (B) and optimized transdermal gel (AX4) (C).

X-Ray Diffraction (XRD) Studies

XRD patterns of aceclofenac (A), physical mixture (B) and optimized transdermal gel formulation (AX4) (C) are presented in Figure 5. XRD of pure aceclofenac showed diffraction peaks at about 8.98°, 17.04°, 17.75°, 18.71°, 22.46°, 24.71°, 26.18°, 32.37° (2θ) with different signal intensities, indicating important crystallographic characteristics of aceclofenac (Figure 5A). In the XRD spectra of physical mixture, all the diffraction peaks of aceclofenac were almost unchanged along with intensities (Figure 5B). This revealed that in the physical mixture also aceclofenac present in crystalline form. But there were no crystalline peaks of aceclofenac observed in the optimized transdermal gel formulation (AX4) (Figure 5C). So it was concluded from the XRD study that the drug molecules were dispersed at the molecular level and aceclofenac was present as an amorphous form in the optimized formulation.

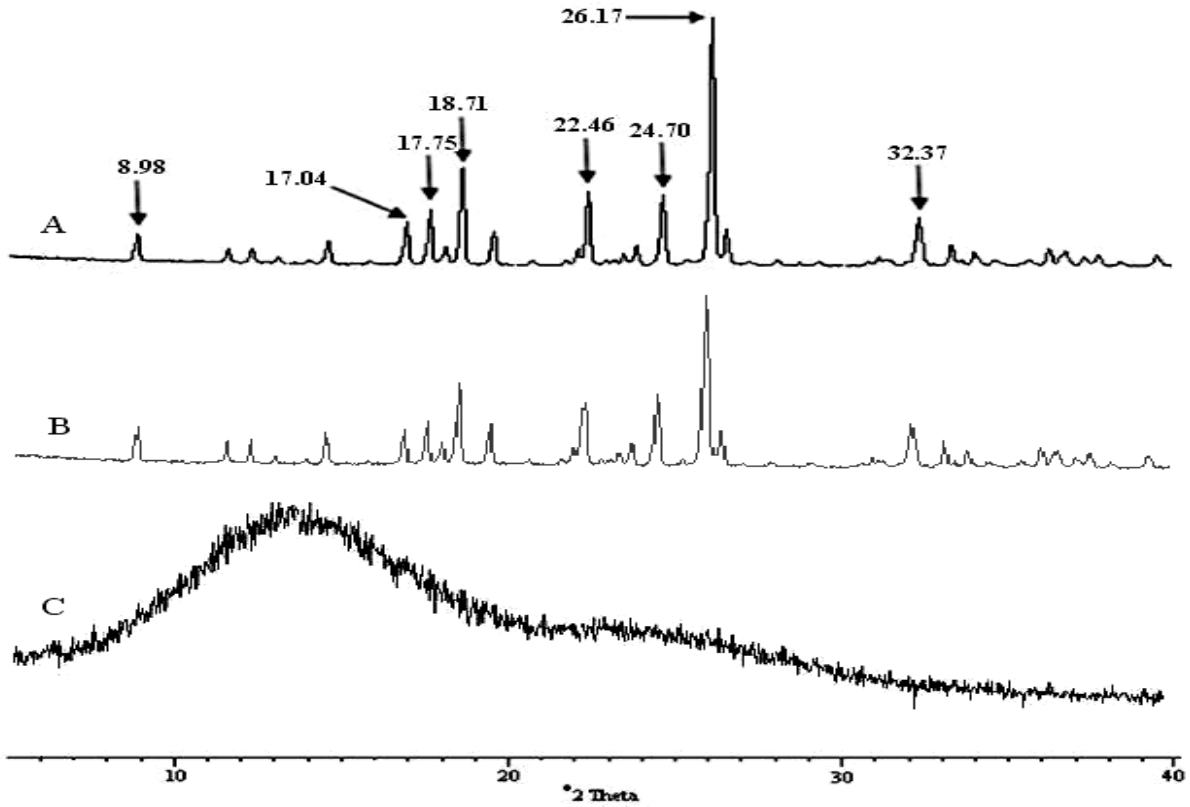

Figure 5: X-Ray diffraction pattern of aceclofenac (A), physical mixture (B) and optimized transdermal gel (AX4) (C).

CONCLUSION

It was concluded from the above research that xanthan gum based gel-type transdermal drug reservoir of aceclofenac was successfully prepared. It was also concluded that concentration of xanthan gum was the main influential factor for drug release and had a significant effect on percentage drug release at 12 hours (Q_{12}), Higuchi rate constant (K_H) and time taken for 50% drug release ($t_{50\%}$). So the optimized gel formulation of the present research could be used for further development of transdermal delivery of aceclofenac and skin permeation studies.

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