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FORMULATION AND EVALUATION OF DICLOFENAC SODIUM MICROEMULSION SUBCUTANEOUS DRUG DELIVERY SYSTEM

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Keywords:

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ABSTRACT: The objective of this current work is to develop the formulation and evaluation of a subcutaneous drug delivery system based on diclofenac sodium microemulsion. A different formulation has been formulated using a modifying amount of gelling agent and a penetration enhancer. Pseudo ternary phase diagrams were constructed for different microemulsion formulations composed of the formulations FEG1, FEG2, and FEG3 manufactured by Carbopol 934 and FEG4, FEG5, and FEG6 by Xanthan gum, and the formulations FEG7, FEG8, and FEG9 were prepared by HPMCK15M as a dispersion phase. The formulation was an evaluation for physicochemical properties of drug and polymers, rheological studies, In-vitro drug release studies, Zero-order, and first-order release kinetics studies. The in-vitro release of the microemulsion drug was greater than the commercialized formulation. The Hind paw method (Acute inflammatory model) test was performed in rate to evaluate the analgesic activity of fabricated emulgel. The overall findings of this study suggest that the developed emulgel formulation of diclofenac sodium can be used potential approach for the management of analgesic effect.

INTRODUCTION: In the current work, an attempt fabrication microemulsion-based sub-cutaneous drug delivery in a lipid-containing dosage form as in an oil-in-water microemulsion. The microemulsion concept was introduced in 1940 by Hoar I and Schulman, who generated a clear, single-phase solution by titrating a milky emulsion with hexanol [1]. Schulman and his colleagues coined the term "microemulsion," and since then, it has been defined and redefined several times [2].

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Danielsson and Lindman, in 1981, described the microemulsion as a "water, oil and amphiphilic system that is an optically isotropic and thermodynamically stable liquid solution" [3]. Microemulsions, as defined by Attwood, are water, oil, surfactant, and co-surfactant system, which is a unique, optically isotropic, and thermodynamically stable, clear liquid [4]. In other words, “microemulsions are liquid dispersions of water and oil that become homogeneous, transparent (or translucent) and thermodynamically stable by adding relatively large amounts of surfactant and cosurfactant and having a drop diameter in the range of 100 at 1000 A0 (1 at 100 nm)” [5].

Microemulsions are attractive drug delivery systems because of their advantage in increasing drug solubility and thermodynamical stability, in

addition to ease of preparation [6, 7]. This transparent and stable nano-sized system is spontaneously formed when a certain amount of oil, water, surfactant, and co-surfactant are mixed. Moreover, it has been found that transdermal permeability improves when microemulsions are used as topical delivery vehicles [8]. The advantages of the micro-emulsion include its ease of preparation due to spontaneous formation, thermodynamic stability, transparent and elegant appearance, increased drug load, and better penetration through biological membranes, greater bioavailability, and less inter and intraindividual variability in drug pharmaco-kinetics [9, 10]. These advantages make micro-emulsion drug delivery systems attractive [11, 12, 13].

MATERIALS AND METHODS:

Materials: Materials required in this study were active pharmaceutical ingredient Diclofenac Sodium (Alps Pharmaceuticals limited, New Delhi), Excipients/Chemicals are Carbopol 934, Tween 20, Span 80, Liquid paraffin, Propylene glycol, Methyl parabens, Mentha oil (Procured from CDH, India), Xanthan gum, HPMC K15M (Procured from Sigma Aldrich, India) all other chemicals are used were of analytical grade and the various types of equipment used in this study were Digital weighing balance (Citizen CY-220), UV–Visible Spectrophotometer (Shimadzu-1800, Kyoto, Japan), FT-IR Spectrophotometer (Shimadzu-8400S), USP dissolution apparatus type II (Electrolab-08L, Goregaon, Mumbai), Brookfield rheometer (DV-III ULTRA) and Deluxe pH meter (151-R, Labindia Instruments, India).

Methods:

Identification of Diclofenac Sodium: 50 mg of the drug diclofenac sodium was dissolved in enough methanols to produce 100 ml. To 1 ml of the above solution, 0.5 ml of 0.1M hydrochloric acid was added and diluted to 100 ml with methanol. The resulting solution was protected from bright light and the maximum absorbance of approximately 254 nm was measured; Absorbance at 254nm was found to be approximately 0.44 in correspondence with the Indian Pharmacopoeia [14].

Determination of Wavelength of Maximum Absorbance (λ_{max}): A stock solution (1 mg/ml) of diclofenac sodium in 0.1 M HCl was prepared. This solution was appropriately diluted with water to obtain a concentration of 10 µg/ml. The solution was stored in a 10mm silica tank. The UV spectrum was recorded in the range 200-400 nm on a double beam spectrophotometer at 1nm, slit width. The same procedure was carried out in distilled water.

Preparation of Calibration Curve for Diclofenac Sodium: 100 mg of the drug were accurately weighed and dissolved in 100 ml of 0.1M HCl (pH 1.2). 10 ml of the above solution was transferred to a 100 ml volumetric flask and diluted to the mark with 0.1 M HCl. Aliquots of 1 to 14 µg / ml were extracted from this mother solution. It was transferred to 10 ml volumetric flasks, and a volume of up to 10 ml was taken with 0.1N HCl (pH 1.2). The absorbances of these solutions were measured at 276 nm against a 0.1 M HCl blank [15].

IR Characterization of Diclofenac Sodium: The FTIR analysis of the Diclofenac sodium was carried out for qualitative compound identification. The KBr pellet of approximately 1 mm diameter of the Diclofenac sodium was prepared to grind 3-5 mg of a sample with 100-150 mg of KBr in the pressure compression machine. The sample pellet was mounted in the FTIR spectrophotometer and taken scan at wavelength 4000cm^{-1}-400cm^{-1}.

Drug Excipient Interaction: When designing any medication delivery system, it is imperative to consider the compatibility of the medication and the polymer used in the system. Therefore, it is necessary to confirm that the drug does not interact with the polymers in the experimental conditions and shelf life. For the present study, drug-polymer interaction studies were carried out comparing it with the pure drug and with the physical drug-polymer mixture through infrared analysis [16].

DSC Study of Diclofenac Sodium: Differential scanning calorimetry (DSC) is a thermoanalytical technique in which the difference in the amount of heat required to increase the temperature of a sample and the reference is measured as a function of temperature. The sample and the reference are kept at almost the same temperature throughout the experiment. It was used to determine the exact melting point of the drug and the other excipients used in this investigation. DSC analysis was performed at 50 to 500 °C at 5 °C / min [17, 18, 19].

Determination of Solubility of Diclofenac Sodium: The solubility of diclofenac sodium has been determined in various solvents, such as water, methanol, and non-polar hydrocarbons. Solubility is done to find the release of the drug from the formulation, hence the absorption of the drug into the bloodstream.

Fabrication of Emulgel of Diclofenac Sodium: Different formulations have been formulated using a modifying amount of gelling agent and penetration enhancer. The method differed only in the gel manufacturing process in various formulations. The emulsion formulation was the same in all formulations. Gel bases were prepared by dispersing Carbopol 934 and Xanthan gum in separate distilled water with constant stirring at a reasonable speed using a mechanical stirrer. FEG1, FEG2, and FEG3 formulations were formulated by Carbopol 934 and FEG4, FEG5, and FEG6 by xanthan gum as a gelling agent. In formulations FEG7, FEG8, and FEG9, the gel was prepared by dispersing HPMCK15M in heated distilled water (80 °C), and the dispersion was cooled and left overnight. The pH of all formulations was adjusted to 6.2-6.7 using triethanolamine. The oil phase of the emulsion was equipped by dissolving Span 20 in light liquid paraffin, while the aqueous phase was prepared by dissolving Tween 20 in purified water. The methyl and propyl parabens were dissolved in propylene glycol and mixed with the aqueous phase.

Diclofenac sodium, being hydrophobic, dissolved in the oil phase. Peppermint oil was also matched in the oil phase. The oily and aqueous phases were separately heated to 70 ° to 80 °C, and then the oily phase was added to the aqueous phase with continuous stirring until it cooled to room temperature. The formulated emulsion was mixed with the gel in a 1: 1 ratio with gentle stirring to obtain the emulsifier [20, 21, 22, 23]. The composition of different formulations has been discussed in **Table 1**.

TABLE 1: FORMULATION AND PROCESS DEVELOPMENT OF PREPARATION OF MICROEMULSIONS

Formulation Code	FEG1	FEG2	FEG3	FEG4	FEG5	FEG6	FEG7	FEG8	FEG9
Diclofenac sodium (mg)	100	100	100	100	100	100	100	100	100
Carbopol 934 (gm)	1	2	3	-----	-----	-----	----	----	----
Xanthan gum (gm)	----	-----	----	1	2	3	----	----	-----
HPMC K15M (gm)	----	-----	-----	-----	----	-----	1	2	3
Tween 20 (ml)	1	2	3	1	2	3	1	2	3
Spam 80 (ml)	2	4	6	2	4	6	2	4	6
Liquid paraffin (ml)	10	20	30	10	20	30	10	20	30
Propylene glycol (ml)	4	8	12	4	8	12	4	8	12
Methylparaben (gm)	0.1	0.2	0.3	0.1	0.2	0.3	0.1	0.2	0.3
Propylparaben (gm)	0.1	0.2	0.3	0.1	0.2	0.3	0.1	0.2	0.3
Mentha oil (ml)	4	8	12	4	8	12	4	8	12

Characterization Emulgel of Diclofenac Sodium Drug Content:

Determination of Drug Contains: Weigh accurately 1 g of emulgel and dissolve in 100 ml of phosphate buffer 7.4. The volumetric flask was held for 2 hr and stirred well on a shaker to mix well. The solution was passed through the filter paper and filtered. 1 ml of the solution was introduced into 10 ml of volumetric flask and the final volume was made with 7.4 phosphate buffer.

Absorbance was measured spectrophotometrically at 378 nm after appropriate dilution against 7.4 corresponding phosphate buffers as a blank [24, 25].

Physical Examination: The prepared emulgel formulations were visually inspected for color, consistency, consistency, granulation, and phase separation [16, 26, 27].

Measurement of pH: The pH of the emulgel formulations was determined using a digital pH meter. 1 g of the gel was dissolved in 100 ml of distilled water and placed for 2 h. The pH of each formulation was measured in triplicate, and the average values were calculated [28].

Determination of Viscosity: The viscosity of the formulated batches was determined using Ostwald's viscometer with a 07 screw. The formulation, the viscosity of which was to be determined, was added to the beaker and allowed to stand for 30 min at the test temperature before taking the measurement. The spindle was lowered

perpendicular to the center of the emulgel, taking care that the spindle did not touch the bottom of the bottle and that it rotated at a speed of 12 rpm for 10 min. The viscosity reading was observed [29, 30].

***In-vitro* Drug Release Study:** *In-vitro* drug release of diclofenac sodium from prepared formulations was studied through a cellophane membrane using a Franz diffusion cell. The cellophane membrane was pretreated with sodium hydroxide and soaked overnight in 0.1N HCl phosphate HCl at cooling temperature. The treated cellophane membrane is a sandwich between the donor and recipient compartments of the Franz diffusion cell. A formulation evaluation of 1 mg of diclofenac sodium was added to the cellophane membrane. A magnetic bar was continuously stirred in a diffusion medium to avoid the effect of the diffusion layer. The sample taken was analyzed by UV spectrophotometer [31].

Release Kinetics of Diclofenac Sodium Emulgel Formulations: To examine the kinetics and mechanism of drug release, the cumulative release data were fitted to models representing zero-order (cumulative% drug release *v/s* Time), first-order (% cumulative record of drug retained *v/s* Time), Higuchi model (cumulative % of drug retained *v/s* Square root of time) and Peppas model (log% cumulative drug release *v/s* log time) [32, 33].

Analgesic Activity: Analgesic activity was carried out by healthy albino Wistar rats divided into five experimental groups such as Group I control group, Group II, Group III, and Group IV are selected FEG, and Group V is a standard group treated by the marketed formulation of diclofenac sodium. The analgesic effect was performed by the Hind paw method (Acute inflammatory model). After 30 minutes of the topically apply of the drug, 0.1 ml of 1% Carrageenan will be administrated to the rats into the plantar surface of the right-hand limb to induce paw edema. The value will be measured immediately and after 3 h using a plethysmometer. The change in the paw value was compared with the control group. The percentage of edema compeer to the control by the test drug was calculated using formula.

$$\% \text{ Oedema inhibition} = \frac{Vc - Vt}{Vc} \times 100$$

Where: *Vc*- means increase paw value in rats treated with a control group and *Vt*- means increase paw value in rats treated with test and a standard group of animals [34].

RESULTS AND DISCUSSION:

Identification of Diclofenac Sodium:

Determination of Wavelength of Maximum Absorbance (λ_{max}): The UV spectrum was recorded in the range of 276 nm on a double beam spectrophotometer at 1nm, slit width.

Preparation of Calibration Curve for Diclofenac sodium: Statistical parameter related to the standard curve of Diclofenac sodium was found to be regression coefficient 0.997, intercept on Y-axis 0.028, and the equation of line Y=0.068x-0.028 result shown in **Fig. 1**.

TABLE 2: CALIBRATION CURVE DATA OF DICLOFENAC SODIUM

S. no.	Concentration (µg/ml)	Absorbance 0.1M HCl
0	0	0
1	2	0.021
2	4	0.048
3	6	0.078
4	8	0.105
5	10	0.130

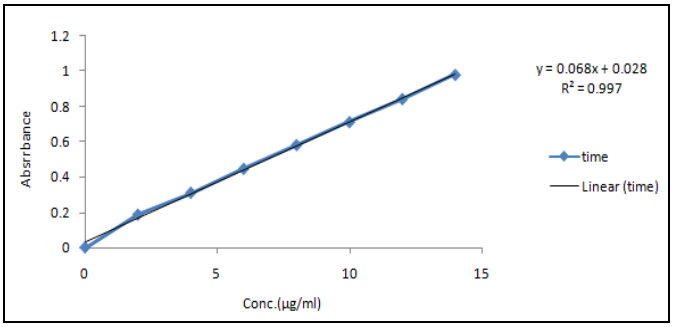

FIG. 1: CALIBRATION CURVE OF DICLOFENAC SODIUM AT 232 nm

IR Characterization Diclofenac sodium:

IR Characterization Standard Diclofenac Sodium: The IF spectrum of pure diclofenac sodium **Fig. 2** shows a characteristic peak at 3317.34 cm^{-1} due to the N-H stretching frequency of the secondary amine. The absorption bands at 1305.72 and 1153.35 cm^{-1} resulted from the C-N stretch and the peaks at 1552.59 and 1574 cm^{-1} due to the C=C stretch and the C=O stretch of the carboxylic group, respectively. The characteristic C-Cl stretch peak was observed at 7710.47 cm^{-1}.

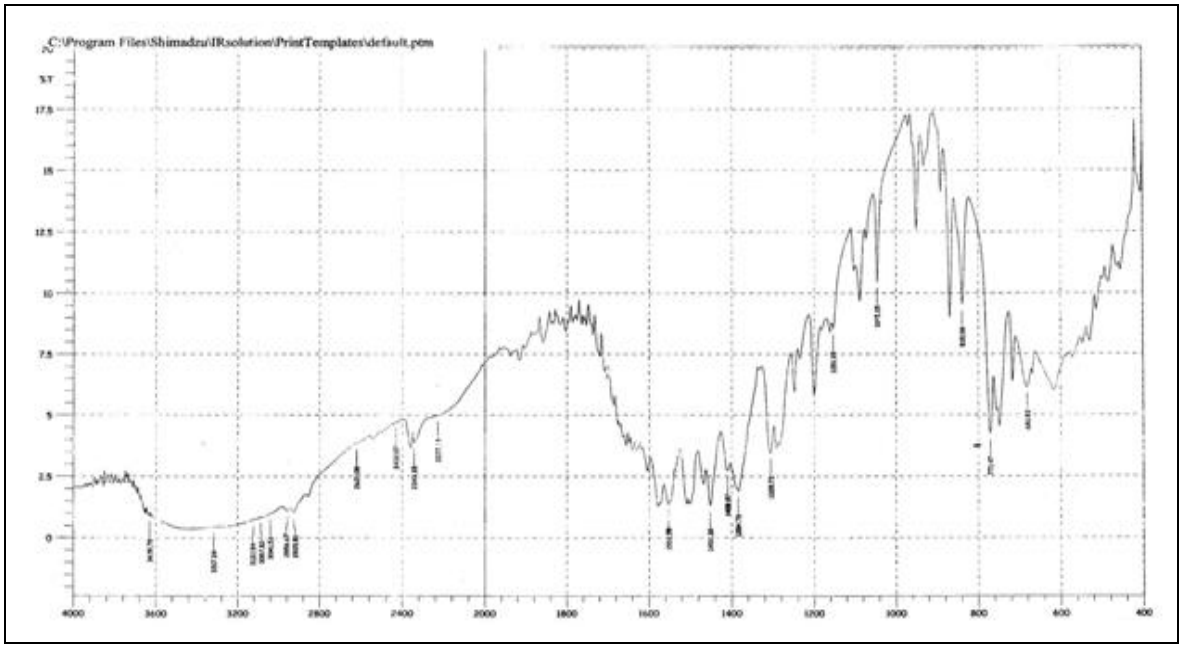

FIG. 2: IR CHARACTERIZATION STANDARD DICLOFENAC SODIUM

IR Characterization of Xanthan gum + Span 80 + Tween 20: The infrared spectra of the Fourier transform of diclofenac sodium showed the main absorption peaks at 3317.34 cm^{-1} due to stretch N-H of secondary amines, 1552.01 cm^{-1} due to stretching - C = O carboxyl ions, and 771.47 cm^{-1} due to the stretch of C-Cl in the spectrum. The pure xanthan gum showed a characteristic alcoholic peak at 2925.51 cm^{-1}, a stretch C = O at 1735.81 cm^{-1}, a stretch C = CH2 at 1736.81 cm^{-1}, a stretch C-O-C. The XGD4 formulation showed characteristic drug peaks at 3387.28 cm^{-1}, 1552.01 cm^{-1}, and 856.26 $cm^{-1,}$ with minor changes shown in **Fig. 3**.

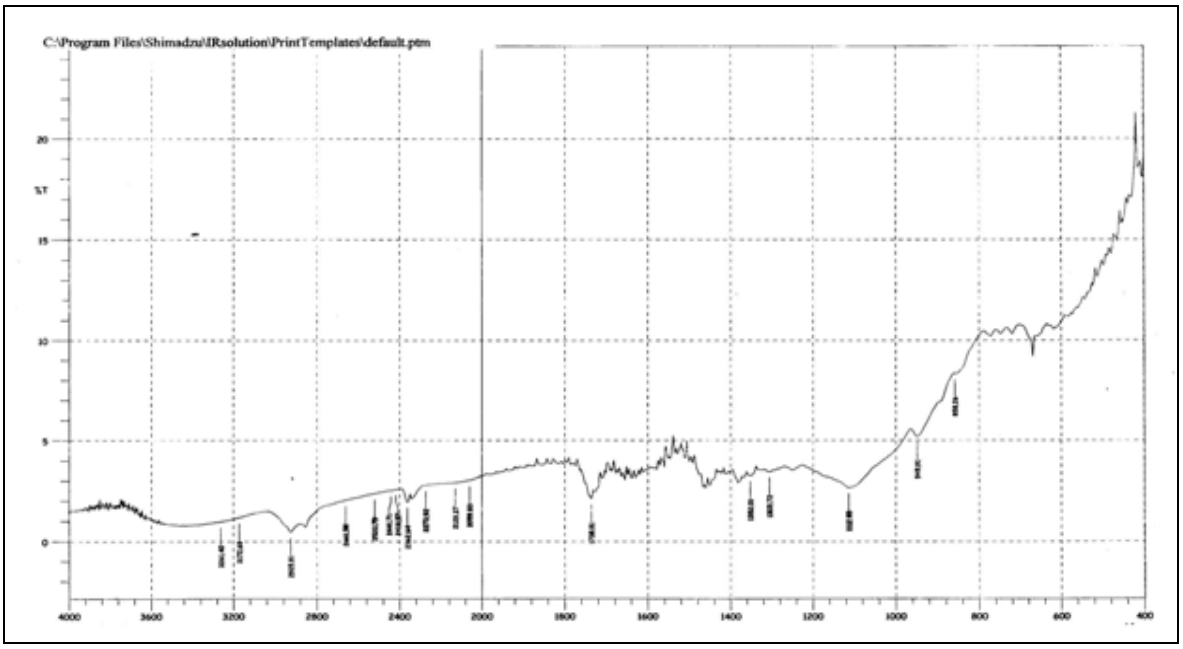

FIG. 3: IR CHARACTERIZATION OF XANTHAN GUM + SPAN 80 + TWEEN20

IR Characterization of HPMCK15M + Span 80 + Tween 20: Span 80 has shown characteristic peaks at 1491.86 cm^{-1} (aromatic ring), 2923.86 cm^{-1} (–OH group), 1463.49 cm^{-1} ($–CH_3$), 1355.86 cm^{-1} ($–CH_3$ symmetrical deformable) and small peaks in the range of 1091.63 cm^{-1} (aliphatic) Tween 20 also depicted characteristic bands at 3452.14 cm^{-1} (–OH, strong), 2852.52 cm^{-1} (–OH str very broad), 1677.66 cm^{-1} (5-membered ring) result show in **Fig. 4**.

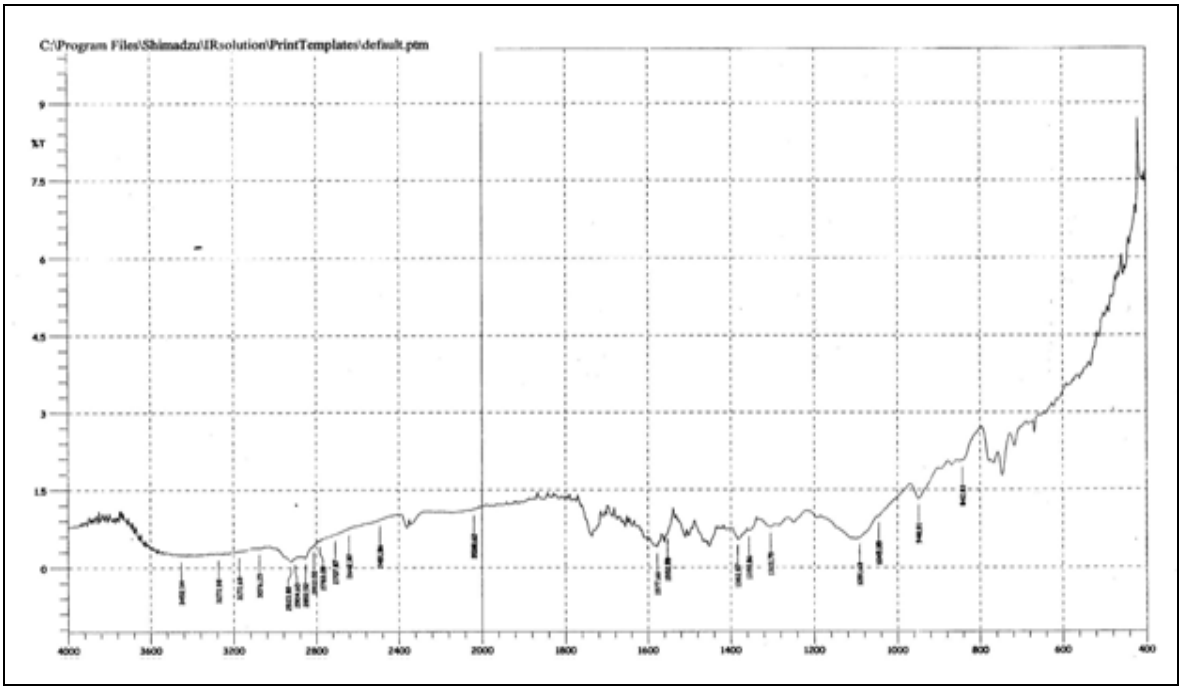

FIG. 4: IR CHARACTERIZATION OF HPMCK15M+SPAN80+TWEEN20

IR Characterization of Xanthan gum + Span 80 + Tween 20 + Diclofenac Sodium: Drug-polymer compatibility in the optimized microsponges was evaluated by FTIR and analysis. The main IR peaks of pure diclofenac sodium appeared at wavelengths of 12849.89 cm^{-1} and 1382.67 cm^{-1} and were the result of the C-N stretch. The peaks at 1575.90 cm^{-1} resulted from the C = C stretch, and 1685.67 cm^{-1} resulted from the C = C and C = O stretch of the carboxylate functional group result shown in **Fig. 5**.

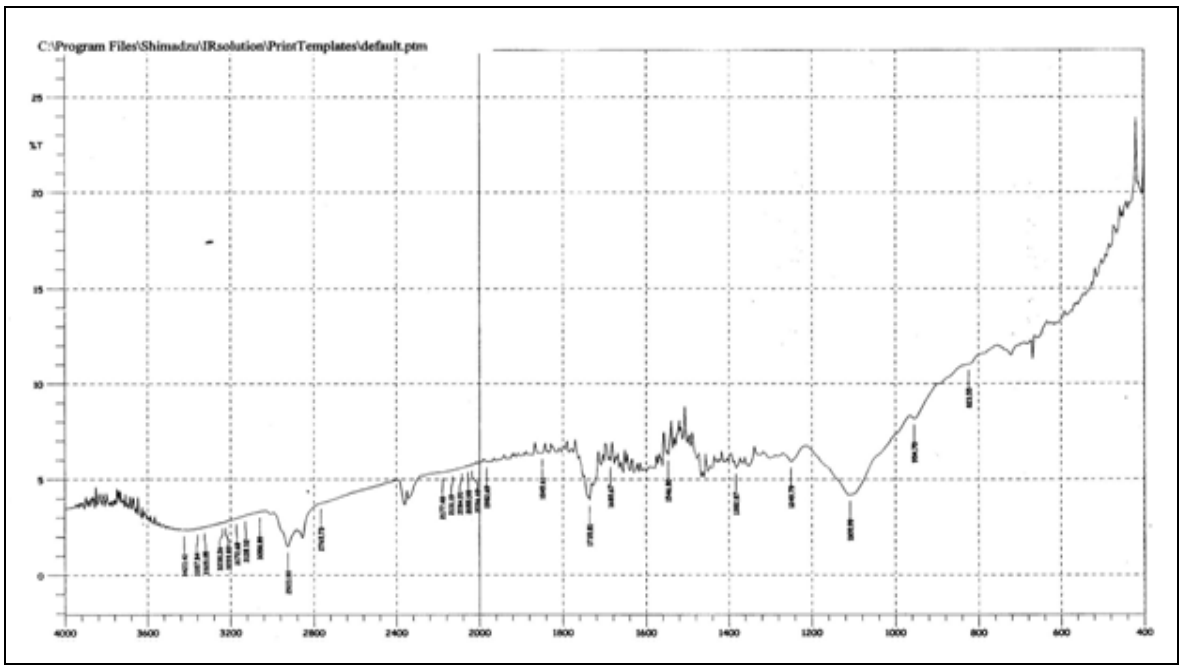

FIG. 5: IR CHARACTERIZATION OF XANTHAN GUM + SPAN 80 + TWEEN 20 + DICLOFENAC SODIUM

IR Characterization of HPMCK15M + Span 80 + Tween 20 + Diclofenac Sodium: The main IR peaks appeared at wavenumbers of 12,248.88 cm^{-1} and 1,352.66 cm^{-1} and were the result of a C-N stretch. The peaks at 1565.90 cm^{-1} resulted from the C = C stretch, and 1675.65 cm^{-1} resulted from the C = C and C = O stretch of the carboxylate functional group result shown in **Fig. 6**.

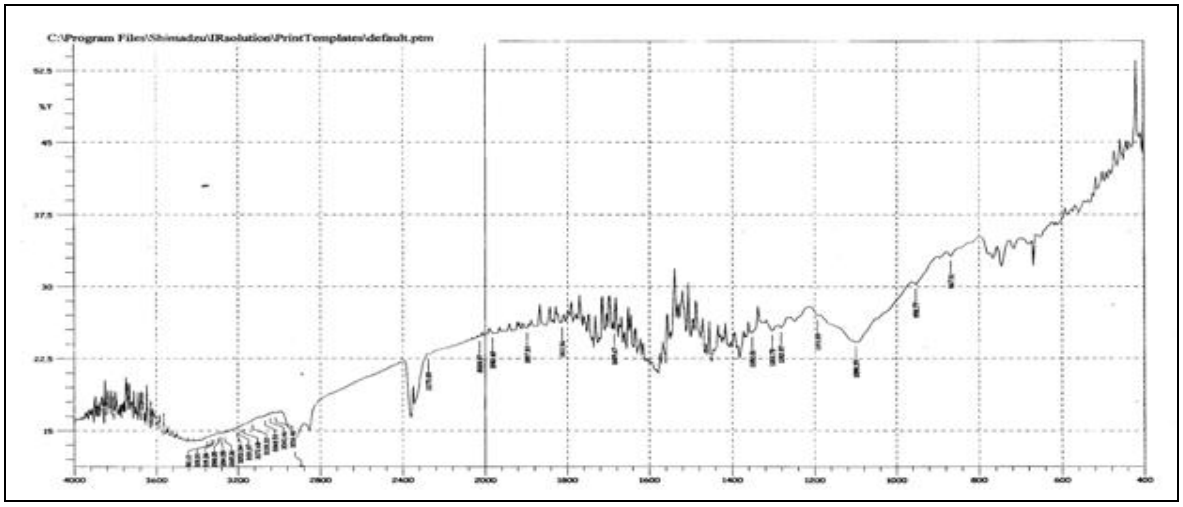

FIG. 6: IR CHARACTERIZATION OF HPMC15M + SPAN80 + TWEEN 20 + DICLOFENAC SODIUM

DSC Characterization: Differential scanning calorimetry (DSC) was used to determine the exact melting point of diclofenac sodium used in this investigation. DSC analysis was performed at 40-350 °C at 5 °C/min, using 5 mg samples in pressed aluminum pans. Indium samples were used to calibrate the DSC instruments.

DSC Study of Diclofenac Sodium: The DSC thermogram of diclofenac sodium has an endothermic peak at 289.88 °C, corresponding to its melting transition point in **Fig. 7**.

DSC Characterization of Xanthan Gum + Tween 20 + Span 80: The DSC thermogram of Xanthan + Tween 20 + Span 80 gum has an endothermic peak at 46.68 °C, which corresponds to its melting point and H delta transition at 34.954 j / g in **Fig. 8**.

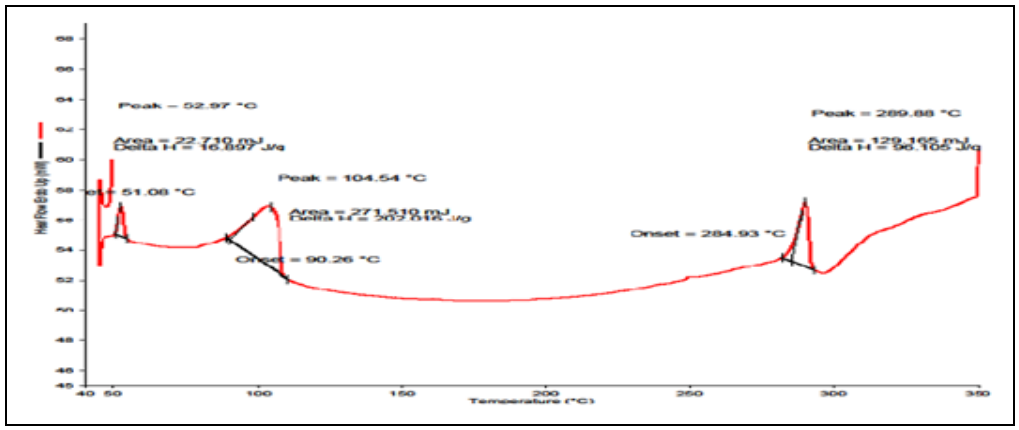

FIG. 7: DSC STUDY OF DICLOFENAC SODIUM

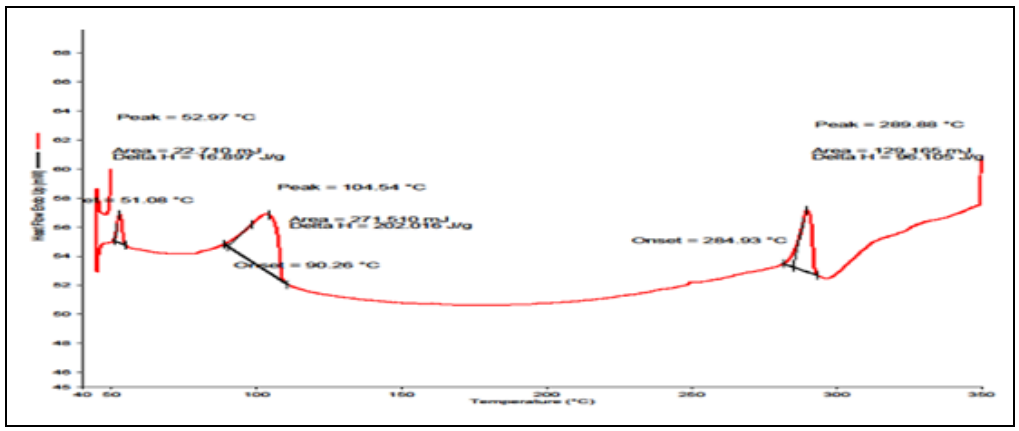

FIG. 8: DSC CHARACTERIZATION OF XANTHAN GUM+TWEEN20+SPAN80

IR Characterization of HPMCK15M + Span 80 + Tween 20: The HPMCK15M + Tween20 + Span 80 DSC thermogram exhibits an endothermic peak at 47.61oC, 132.25 ºC at 63.469 mj and 304.0030C corresponding to its melting point and delta H transition at 34.954 j / g in **Fig. 9**.

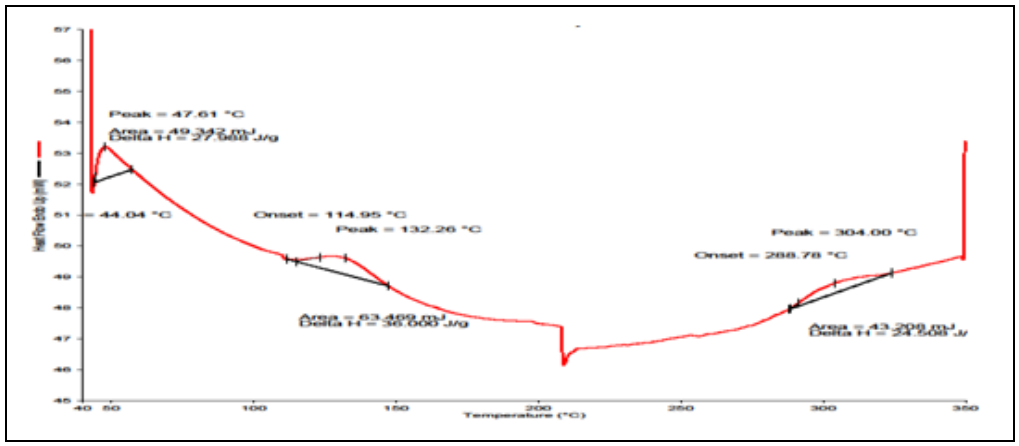

FIG. 9: IR CHARACTERIZATION OF HPMCK15M+SPAN80+TWEEN20

DSC Characterization of Xanthan Gum + Tween 20 + Span 80 + Diclofenac Sodium: The DSC thermogram of Xanthan gum + Tween20 + Span80 Diclofenac sodium exhibits an endothermic peak at 46.64 °C, corresponding to its melting transition point and delta H at 22.513 j/g in **Fig. 10**.

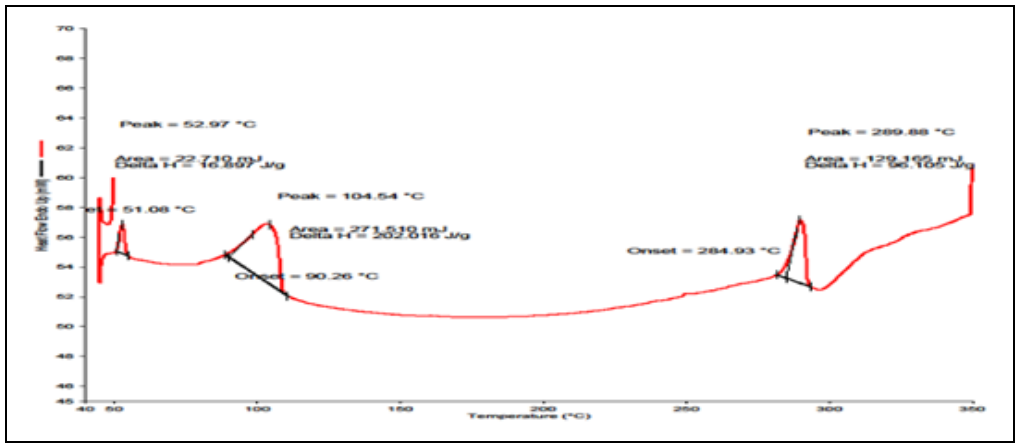

FIG. 10: DSC CHARACTERIZATION OF XANTHAN GUM + TWEEN 20 + SPAN 80 + DICLOFENAC SODIUM

DSC Characterization of HPMCK15M + Tween 20 + Span80 + Diclofenac Sodium: The DSC thermogram of diclofenac sodium HPMCK15M + Tween20 + Speen80 has an endothermic peak at 47.43 °C, which corresponds to its melting point and H transition at 85,920 j/g in **Fig. 11**.

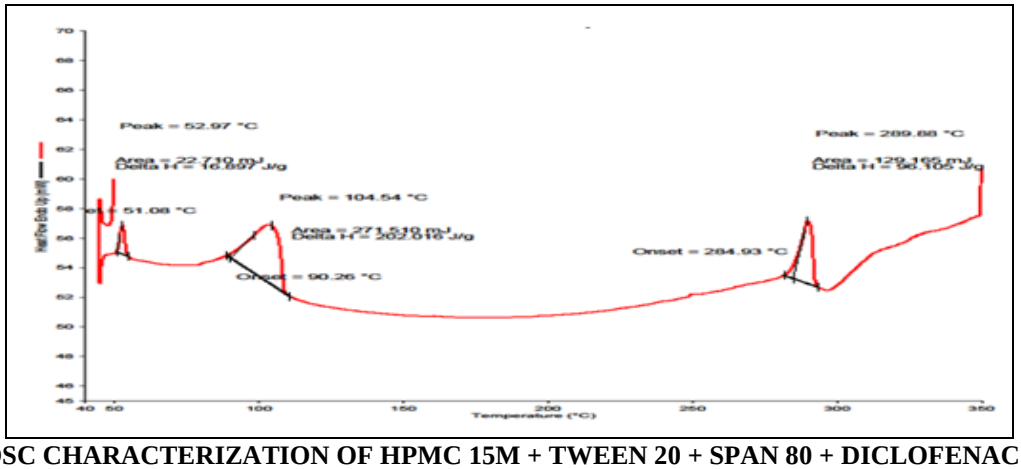

FIG. 11: DSC CHARACTERIZATION OF HPMC 15M + TWEEN 20 + SPAN 80 + DICLOFENAC SODIUM

Characterization Emulgel of Diclofenac Sodium Drug Content:

Physical Examination: The fabricated Diclofenac sodium emulgel illustrates yellowish-white watery transparent gel having non-Newtonian pseudo-plastic in nature with thixotropic character and was found to be an effective carrier system for the delivery of Diclofenac sodium topically.

Determination of Viscosity: The viscosity of the formulated batch FEG1-FEG9 ranged from 4155 – 15468 CPs, respectively result in the shoe in **Fig. 12**.

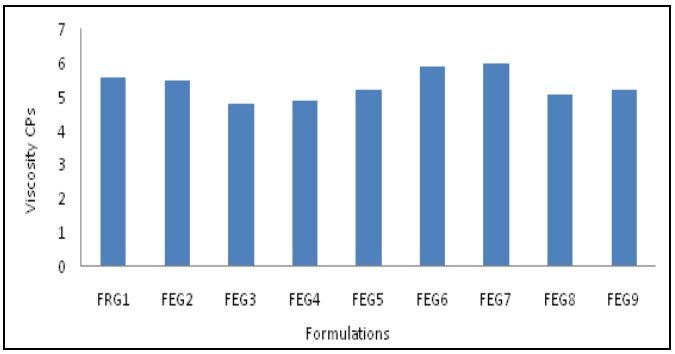

FIG. 12: VISCOSITY OF THE FORMULATION

Determination of pH values: The pH of the microemulsion formulations was in the range of 4.8 ± 0.4 to 5.8 ± 0.5, which is within the normal skin pH range and would not cause skin irritation. There were no significant changes in pH values over time for all formulations, as shown in **Fig. 13**.

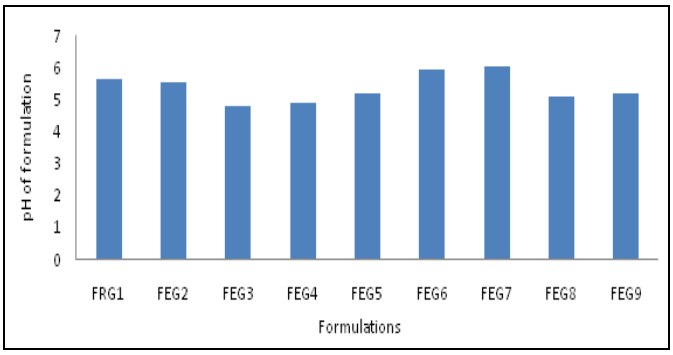

FIG. 13: THE pH OF THE FORMULATIONS IS RECORDED BY A DIGITAL pH METER

***In-vitro* Drug Release Study:** The release of diclofenac sodium from the microemulsion was different depending on the viscosity of various polymers. The drug release profile of your micro-emulsified gel formulation can result in the descending order: FEG8> FEG7> FEG2> FEG9> FEG6> FEG3> FEG5> FEG4> FEG1, where the amount of drug released after 7 h were 83.18%, 83.18%, 82.43%, 80.63%, 79.31%, 77.26%, 77.11%, 75.31%, 73.59% respectively. The gradual increase in the amount of drug gradually decreases the viscosity of the emulsifying result indicated in **Table 3**.

TABLE 3: % DRUGS RELEASE DICLOFENAC SODIUM EMULGEL DIFFERENT TIME INTERVAL

Formulation Code	Time (hr)							
	0	1	2	3	4	5	6	7
FEG1	0	9.37	15.37	29.26	38.21	47.41	61.31	73.59
FEG2	0	10.11	15.35	25.67	34.11	47.13	72.21	82.43
FEG3	0	8.18	13.72	24.32	32.31	44.16	68.31	77.26
FEG4	0	7.92	11.32	22.38	31.78	41.12	66.57	75.31
FEG5	0	11	15.38	28.84	36.26	48.51	69.21	77.11
FEG6	0	13.39	16.26	27.75	38.14	46.27	68.25	79.31
FEG7	0	10.12	15.67	26.24	35.37	47.51	72.12	83.18
FEG8	0	15.18	15.67	26.24	35.37	47.51	72.12	83.18
FEG9	0	11.31	14.21	23.51	34.28	43.16	69.43	80.67

Release Kinetics of Diclofenac Sodium Microemulsion Formulation: To examine the drug release kinetics models representing the zero-order, the first order, the Higuchi model, and the Peppas model were recorded in **Table 4**.

TABLE 4: RELEASE KINETICS OF DICLOFENAC SODIUM MICROEMULSION FORMULATION

Formulation Code	Drug Release Kinetics				
	Zero Order	First Order	Higuchi	Korsmeyer Peppas (n value)	N Value
FEG1	0.952	0.958	0.973	0.979	0.636
FEG2	0.958	0.978	0.992	0.982	0.677
FEG3	0.936	0.949	0.991	0.984	0.553
FEG4	0.941	0.989	0.943	0.928	0.583
FEG5	0.915	0.985	0.979	0.989	0.699
FEG6	0.916	0.982	0.956	0.986	0.740

FEG7	0.961	0.954	0.983	0.989	0.642
FEG8	0.967	0.964	0.896	0.978	0.570
FEG9	0.962	0.961	0.931	0.986	0.644

Analgesic Activity: The anti-inflammatory action of the manufactured formulation FEG1, FEG7, and FEG9 was calculated and compared with a commercialized preparation (standard formulation). The average paw volume in the rat after carrageenan induction is indicated in **Table 5**. This figure showed that the formulations were as effective as the commercialized formulation.

TABLE 5: THE PAW VOLUME IN RATS ON INITIAL AND 1 HR AFTER CARRAGEENAN ADMINISTRATION

Group of animals	Initial reading	Reading 1 hr after Carrageenan	The difference in paw volume
Group I: Control group	1.56±0.04	2.54±0.06	0.98±0.02
Group II: FEG 1	2.10±0.03	2.70±0.06	0.60±0.03
Group III: FEG 7	1.88 ±0.04	2.10±0.05	0.22±0.01
Group IV: FEG 9	1.70 ±0.05	2.32±0.05	0.62±0.05
Group V: Standard formulation	2.06 ±0.04	2.48±0.03	0.42±0.01

CONCLUSION: In the current work, an attempt fabrication of Emulgel based subcutaneous drug delivery in a lipid-containing dosage form as in an oil-in-water microemulsion. Gel bases were prepared by separately dispersing Carbopol 934 and Xanthan gum in distilled water, and the oil phase of the emulsion was equipped by dissolving Span 20 in light liquid paraffin while preparing the aqueous phase by dissolving Tween 20 in purified water. The methyl and propyl parabens were dissolved in propylene glycol and mixed with the aqueous phase. Diclofenac sodium, being hydrophobic, dissolved in the oil phase.

The formulation of emulgel was prepared successfully and evaluated physicochemical characteristics, cumulative drug release, the kinetics of drug release and analgesic activity of emulgel was higher as marketed formulation. The overall findings of the study suggest that the developed emulgel formulation of diclofenac sodium can be used potential approach for the management of analgesic effect.

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