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Formulation and Evaluation of Topical Microemulgel for the Treatment of Joint Pain

Abhishek Singh[1], Dr. Prabhakar Vishvakarma[2], Suraj Mandal[3]
[1]M. Pharma Scholar, IIMT College of Medical Science, IIMT University Ganga Nagar Meerut.

[2]Associate Professor, Professor/HOD IIMT College of Medical Science, IIMT University Ganga Nagar Meerut.

[3]Assistant Professor, IIMT College of Medical Science, IIMT University Ganga Nagar Meerut.

Abstract:

When used as a delivery mechanism, microemulgel has several advantages over straightforward conventional formulations, including simplicity of administration, increased residence duration at the application site, constant drug release with improved bioavailability, superior thermodynamic stability, and excellent transdermal permeability. Using Carbopol-940 and Liquid Paraffin as gelling agents, oleic acid as the oil, parabens as the preservative, and Tween-20 as the emulgent and penetration enhancer, the microemulgel of Trolamine Salicylate was created. The made-up microemulgel formulation underwent visual examination for Appearance, Spreadability, Viscosity, pH% Drug Release, and In vitro diffusion tests. The development of microemulgels containing trolamine salicylate will be more successful, according to the results obtained, but clinical trials are necessary to understand their clinical usefulness. In order to distribute drugs topically, trolamine salicylate microemulgel can be utilized as a painkiller for the treatment of joint and muscle pain.

Keywords: *Microemulgel, Trolamine Salicylate, Joint and Muscle Pain,* Transdermal *Drug Delivery System.*

Transdermal Drug Delivery Systems:

Currently, Transdermal drug delivery is one of the most promising methods for drug application. Increasing numbers of drugs are being added to the list of therapeutic agents that can be delivered to the systemic circulation *via* skin. Transdermal drug delivery systems (TDDS) can be defined as self contained discrete dosage forms which, when applied to the intact skin, delivers the drug(s) through the skin at a controlled rate to the systemic circulation [1].

The potential of using intact skin as the route of drug administration has been known for several years. The inspiration of using skin for delivery of drug isfrom ancient time. Ebers papyrus used the husk of castor oil plant bark imbibed with water placed on aching head. Historically, the medicated plaster can be viewed as the first development of transdermal drug delivery; this medicated plaster became very popular in Japan as over the counter pharmaceutical dosage form.

Transdermal delivery not only provides controlled, constant administration of the drug, but also allows continuous input of drugs with short biological half- life and eliminates pulsed entry into systemic circulation, which often undesirable side effect. TDDS facilitate the passage of therapeutic quantities of drug substances through the skin and into the general circulation for their systemic effects.

In developing a transdermal delivery system, two criteria are considered: one is achieving adequate flux across the skin and the other is minimizing the lag time in skin permeation. One strategy overcoming this constraint is the incorporation of various chemical skin enhancers into the vehicle. Another strategy is a choice of an appropriate vehicle that corresponds to the drug being used for the dermal route of administration. Concerning dermal application the microemulsions can interact with the stratum Corneum changing structural rearrangement of its lipid layers and consequently increasing transdermal drug permeation and so act as penetration enhancer [2-3].

Advantages of TDDS:

- Avoidance of first pass metabolism.
- Avoidance of gastro intestinal incompatibility.
- Predictable and extended duration of activity.
- Minimizing undesirable side effects.
- Provides utilization of drugs with short biological half life.
- Narrow therapeutic window.
- Improving physiological and pharmacological response.
- Avoidance the fluctuation in drug levels.
- Termination of therapy is easy at any point of time.
- Greater patient compliance due to elimination of multiple dosing profile.
- Ability to deliver drug more selectively to a specific site.
- Provide suitability for self administration.
- Enhance therapeutic efficacy [4].

Limitations of TDDS:

- Transdermal route administration is unsuitable for drugs that irritate orsensitize the skin.
- Transdermal route cannot deliver in a pulsatile fashion.
- Transdermal delivery is neither practical nor affordable when required to deliver large doses of drugs through skin.
- Transdermal delivery cannot administer drugs that require high bloodlevels.
- Drug of drug formulation may cause irritation or sensitization.
- Not practical, when the drug is extensively metabolized in the skin and when molecular size is great enough to prevent the molecules fromdiffusing through the skin.
- Not suitable for a drug, which doesn't possess a favourable, O/W partitioncoefficient.
- The barrier functions of the skin of changes from one site to another on thesame person, from person to person and with age [5-6].

Arthritis:

Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes inflammation of the joints and may cause inflammation of other tissues in the body. The immune system consists of the cells and proteins in our bodies that fight infections. An autoimmune disease occurs when our immune system doesn't recognize part of our body and attacks it as if it were an invader such as a bacteria or virus. In rheumatoid arthritis, the immune system targets synovial membrane and attacks it. The synovial membrane is secretes synovial fluid into the joint. Synovial fluid is the joint fluid that lubricates and nourishes the joint. Other tissues can also be targeted by the immune system in rheumatoid arthritis, but the synovium, or synovial membrane, is generally the primary target. When the synovial membrane is attacked, it becomes inflamed (synovitis) and can thicken and erode. As the synovial membrane is destroyed, the synovial fluid fluid is also destroyed because it is not being secreted. The surrounding structures can also become involved leading to the joint deformities that can be seen in rheumatoid arthritis [7-8].

By inhibiting fatty acid COX enzyme, trolamine salicylate inhibits the production of prostaglandins and thromboxanes in inflammatory cells involved in generating pain and inflammation [44].

Inflammation:

Inflammation (Latin, inflammo, "I ignite, set alight") is part of the complex biological response of vascular tissues to harmful stimuli, such as pathogens, damaged cells, or irritants (Fig.15).Inflammation is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. Inflammation is not a synonym for infection, even in cases where inflammation is caused by infection. Although infection is caused by a microorganism, inflammation is one of the responses of the organism to the pathogen. However, inflammation is a stereotyped response, and therefore it is considered as a mechanism of innate immunity, as compared to adaptive immunity, which is specific for each pathogen 9-10.

Materials and Methods

Materials:

Table.1: List of Chemicals

S. No.	Chemicals	Brand
1	Trolamine Salicylate	Enomark Biotech India Vastral, Delhi
2	Triethanolamine	IIMT University Meerut
3	Benzyl Alcohol	IIMT University Meerut
4	Liquid Paraffin	IIMT University Meerut
5	Oleic Acid	IIMT University Meerut
6	Carbopol-940	IIMT University Meerut
7	Tween-20	Bio-Sols *Pvt. Ltd.*, Mumbai *India*
8	Na-Methyl Paraben	IIMT University Meerut
9	Propylene Glycol	IIMT University Meerut

Table.2: List of Equipments Used

S. No	Equipments	Manufacturer	Use
1	UV-Visible double beam spectrophotometer	Shimadzu UV 1700 (Pharmaspec)	To measure the absorbance of the sample
2	Electronic Balance	Sortorius Single Pan	For weighing purpose
3	Magnetic Stirrer	Remi equipment, Mumbai.	Microemulsions preparation
4	pH meter	Elico L 1120	Measure the pH of the sol.
5	Brookfield Viscometer	LVII model	To measure the viscosity
6	Cooling centrifuge	Remi	Phase separation study
7	FTIR	Perkin Elmer	Compatibility study
8	Particle size Analyser	Microtrac-Blue wave	To measure particlesize

Preformulation Study:

Preformulation may be described as a stage of development process during which the researches characterize the physical, chemical and mechanical properties of the drug substance to form effective, stable and safe dosage form. Hence, pre-formulation studies are essential to characterize the drug for proper designing of the drug delivery system. The pre-formulation studies which were performing in this project include,

Description:

Organoleptic characters of drug was observed and recorded by using descriptive terminology [11].

Melting Point:

Capillary tube, which is sealed at one end is charged with sufficient amount of dry powder to form a column in the bottom of the tube 2.5mm to 3.5mm, and packed down as closely as possible by moderate tapping on a solid surface. The apparatus is operated according to the standard operating procedure. The block is heated until the temperature is about 30^{o}C below the expected melting point. The capillary tube is inserted into the heating block, and the heating is continued at a rate of temperature increased of about 1^o C to 2^o C per minute until melting is completed.

The temperature at which the detector signal first leaves its initial value is defined as the beginning of melting, and the temperature at which the detector signal reaches its final value is defined as the end of melting, or the melting point.The two temperatures fall within the limits of the melting range [12-13].

Solubility Studies:

The spontaneous interaction of two or more substance to form a homogenous molecular dispersion is called as solubility.

10 mg of drug was a suspended separately in 10 ml of different solvents at room temperature in tightly closed tubes and shaken. The solubility profiles of two drugs in various solvents are shown in the table.4.3 [14-15].

Table.3: Solubility Profile I.P. 1996

Descriptive term	Parts of solvent required for 1part of solute.
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly Soluble	From 30 to 100
Slightly Soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10, 000
Practically insoluble of Insoluble	Greater than or equal to 10,000

Estimation of the Drug by UV Spectroscopy:

The absorption maxima were found for drug identification. Ultraviolet visible spectrophotometer has been used to obtain specific information on the chromophoric part of the molecules. Organic molecules in solutions when exposed to light in the visible/ultraviolet region of the spectrum absorb light of particular wavelength on the type of electronic transition associated with the absorption [16].

Preparation of Phosphate Buffer Solution [pH 7.4] I.P 1996:

- 27.218 g of potassium dihydrogen ortho phosphate was dissolved in 1000ml of distilled water to give a 0.2N solution**.**
- 8g of sodium hydroxide was dissolved in 1000ml of distilled water to give 0.2N solution**.**
- 1250ml of 0.2N potassium dihydrogen ortho phosphate and 977.5ml of 0.2N sodium hydroxide were mixed together and made up to 5000ml with distilled water**.**
- The drug solution (10, 20, 30, 40, 50, 60g/ml) in Phosphate buffer pH 7.4 was taken in standard cuvette, and scanned in the range of 200-300nm in a UV spectrophotometer.
- It exhibits maxima at 260nm. UV spectrum of drug taken in phosphate buffer pH 7.4 also exhibits maxima at 260nm.
- Therefore, further all measurements were taken at 260nm. The results are shown in fig.

Standard Curve:

Preparation of Standard Plot for Trolamine Salicylate in Phosphate Buffer pH 7.4:

Accurately weighed amount of Trolamine Salicylate (10mg) was dissolved in small quantity of 0.1N sodium hydroxide and then diluted to 100ml with phosphate buffer pH 7.4. Each ml of the stock solution contains 100mg of Trolamine Salicylate. From this stock solution different standard of working standard solutions i.e., 10, 20, 30, 40, 50, 60µg /ml were made up with phosphate buffer Ph 7.4 and the absorbance was measured at 260nm using phosphate buffer pH 7.4 as blank by UV spectrophotometrically method. A graph is plotted by using concentration at X-axis and absorbance at Y-axis. The values are given in the table & fig [17].

Fourier Transforms Infrared (FTIR) Spectral Analysis:

FTIR is used to identify the functional groups in the molecule. The drug is mixed with KBr disk was scanned at 4mm/s at a resolution of 2cm over a wave number region of 400 to 4000cm^{-1}. The characteristic peaks were recorded. The results are shown in fig & table [18].

Drug-Excipients Compatibility Studies by FT-IR Analysis:

Infrared spectrum of any compound or drug gives information about the groups present in that particular compound. The IR absorption spectra of the pure drug and physical admixtures of drug with various Excipients were taken in the range of 4000-400 cm^{-1} using KBr disc method (Schimadzu IR- Prestige-21) and observed for characteristic peaks of drug. Drug-Excipient compatibility was carried out by FT-IR analysis. Initially the IR spectrums of pure drug, Trolamine Salicylate, Liquid Paraffin, Oleic Acid, Carbopol-940, Benzyl Alcohol and Propylene Glycol were obtained. After that admixtures of drug with other Excipients were prepared and IR Spectra was obtained. The obtained spectra of physical admixtures was observed for major peaks and recorded. The results of this observation were concluded that there is no interaction between the drug (Trolamine Salicylate) & other Excipients [19-20].

Preparation of Trolamine Salicylate Microemulgel Formulation:

The preparation of microemulgel was carried out containing Trolamine Salicylate (API), oleic acid (oil), Tween-20 (surfactant), propylene glycol (co-surfactant), carbopol-940 & Triethanolamine as a (gelling agent), Na-Methyl Paraben (preservative), Benzyl alcohol (solvent).

The microemulgel formulations were prepared in two steps:

1) Formation of micro-emulsion.

2) Conversion of micro-emulsion to Emulgel.

Micro-emulsions were formulated by dissolving drug into oil phase subsequently addition of water takes place with drop wise addition of surfactant mixture on a continuous magnetic stirrer. The clear, isotropic-micro-emulsion obtained then mixed with pre-swelled gelling polymer and preservatives using a homogenizer to form micro-Emulgel. Quantities of ingredients taken are mentioned in Table.4.4.

Table.4 Composition of different Trolamine Salicylate Microemulgel Formulations (%W/V)

Ingredients mg/ml	Formulation batch							
	F1	F2	F3	F4	F5	F6	F7	F8
Trolamine Salicylate	10	10	10	10	10	10	10	10
Triethanolamine	0.2	0.2	0.4	0.4	0.2	0.2	0.4	0.4
Benzyl Alcohol	4	6	8	10	4	6	8	10
Liquid Paraffin	0.2	0.4	0.6	0.8	0.2	0.4	0.6	0.8
Oleic acid	2	2.5	2	2.5	2	2.5	2	2.5
Carbopol-940	1.5	2	1.5	2	1.5	2	1.5	2
Tween-20	1	1.5	2	2.5	3	3.5	4	4.5
Na-methyl Paraben	0.2	0.4	0.2	0.4	0.2	0.4	0.2	0.4
Propylene Glycol	4	6	4	6	4	6	4	6
Purified water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Evaluation of Formulation:

Physical Examination:

Each formulation was visually examined for clarity, colour.

Size Distribution:

Size distribution measurement of microemulgel were carried out by dynamic light scattering using (Zetasizer 3000, Malvern Instruments, Malvern UK) particle size analyzer. Samples were placed in square glass cuvettes & droplet size analysis was carried out at temperature 25℃. The droplet size was found of micro-Emulgel range that is 92.50nm and influenced by the conc. of the formulation. The effect of Smix (mixture of surfactant & co-surfactant) conc. on droplet size distribution of microemulgel was investigated [21-15].

pH Measurement:

A one-gram aliquot of the Microemulgel in one formulation was dissolved in distilled water and left to settle for about 2 h before measuring the pH using a digital pH meter (Panday et al., 2015). This was repeated for all the formulations. The acceptable pH range was 5-7 and this was necessary to avoid any skin irritation since pH of the human skin is usually within this range.

Viscosity Measurement:

A viscometer was used to determine the viscosity of all the formulations at room temperature. The torque readings were obtained between 15%–95% of the base scale. The L4 spindle type set at 10 rotations/min was used [26].

Zeta Potential:

Zeta potential is the measurement of attraction or repulsion in between particles. Its measurement brings details about the dispersion mechanism which is used to measure electrostatic dispersion. The zeta potential calculation is important limitation across a various range of industries incorporates pharmaceuticals, brewing, medicine, ceramics, and water treatment. For colloidal stability, the repulsive forces between two particles should be ascendant. Zeta potential is a useful index of magnitude for interaction between colloidal particles. In general, the colloidal systems stability is determined using measurements based on zeta potential [27-28].

Spreadability Studies:

Spreadability was determined by placing 1g of each microemulgel within an already pre-marked circle of 1cm diameter on a glass slab. Another pre-weighed glass slab was positioned on top and a weight that totaled to about 1kg was put on the upper glass slab for 5 min. The resulting spread of the microemulgel caused an increase in diameter which was measured using an electronic digital caliper (Shinde et al., 2019; Singh and Bedi, 2016; Bachhav and Patravale, 2010).

% Drug Release:

An accurately measured amount of microemulgel formulation equivalent to 20mg was introduced in a cellophane bag and was kept in an eight stage dissolution test apparatus containing 1000ml of phosphate buffer pH 7.4. The temperature was set to 37 ± 0.5 °C and the RPM was set to 50. Aliquots of 5ml of the medium were withdrawn every 30 min and replaced with fresh phosphate buffer. The absorbance of the sample was measured by using UV-Visible Spectrophotometer at 260nm. Percentage transmittance was used as a response to optimise the amount of Smix and oil to get desired microemulgel. Obtained formulation was then incorporated into the gel [29-30].

In vitro Drug Diffusion Study:

The in vitro drug diffusion study was carried out using diffusion cell method. In this method, 1gm of Micro-Emulgel is placed indoor compartment which is allowed to penetrate diffusing membrane which separate receptor compartment containing phosphate buffer. The whole assembly is maintained at 37°C and stirred with the help of a magnetic stirrer. Samples from receptor compartment were withdrawn at different time intervals and replaced with fresh buffer7.4 to maintain sink condition. Sample withdrawn were analyzed at 260nm on UV [31].

Stability Study:

All the formulations are subjected to short term accelerated stability study as per ICH guidelines at in an airtight container with proper sealing and conditions maintained at 40±2°C, 75±5% RH. The formulation was withdrawn and evaluated for physico-chemical parameters after particular period of interval [32-33].

Results and Discussion

Preformulation Study:

Description:

Table.4: Physical appearance of all batches F1-F8

Formulation Code	Physical appearance
F1	Clear transparent dispersion
F2	Clear transparent dispersion
F3	Clear transparent dispersion
F4	Milky White
F5	Milky White
F6	Clear transparent dispersion
F7	Clear transparent dispersion
F8	Clear transparent dispersion

Melting Point:

Table.5: Melting Point Determination

Drug	Melting Point	Normal Range
Trolamine Salicylate	48°C	50°C

Solubility:

Table.6: Solubility Profile of Trolamine Salicylate

S. No	Solvents System	Solubility (mg/ml) at 37±2˚C
1	Distilled H2O	11.3
2	Ethanol	76
3	Chloroform	82
5	CCL4	90
6	Diethyl Ether	26

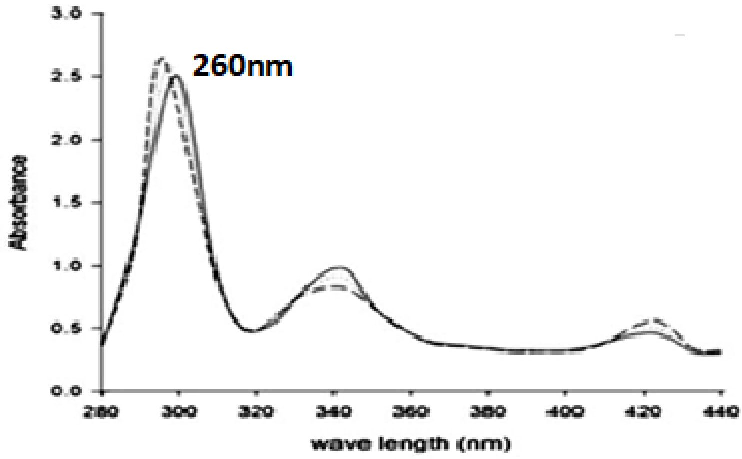

Fig.1: UV spectrum of Trolamine Salicylate in phosphate buffer pH 7.4

Table.7: Abs maxima of Trolamine Salicylate in phosphate buffer pH 7.4

Solvent	Conc. (µg)/ml	µmax (nm)	Abs.
Phosphate bufferpH 7.4	80	260	0.8604

Standard plot of Trolamine Salicylate in phosphate buffer pH 7.4:

Table.8: UV Abs of phosphate buffer pH 7.4

S. No	Conc. (µg/ml)	Abs. at 260nm
1	10	0.1432
2	20	0.2242
3	30	0.3614
4	40	0.4676
5	50	0.5830
6	60	0.6898
7	70	0.7865
8	80	0.8604

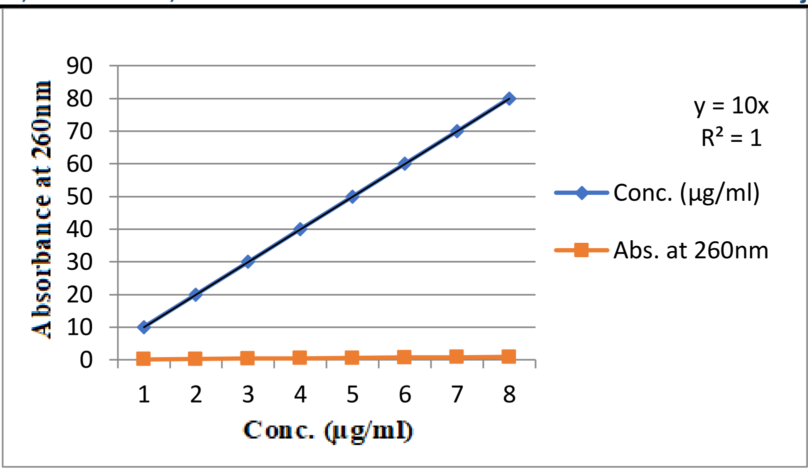

Fig.2: The standard plot exhibits linearity and has a strong regression coefficient

FTIR Study:

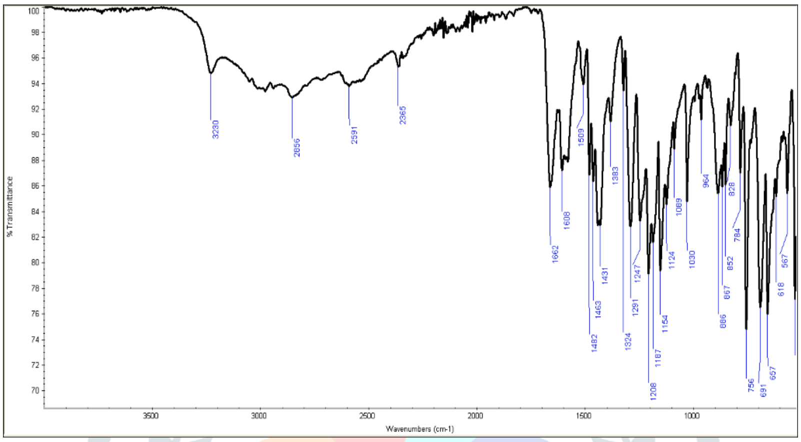

Fig.3: FT-IR of Trolamine Salicylate

Table.9: FT-IR Spectral assignment of Trolamine Salicylate

Wave number in (cm^{-1})	Functional groups
3000.65	O-H stretching
2860.43	N-H stretching
2620.82	C-H (Aromatic) stretching
1656.10	Carbonyl –C=O stretching
1478.54	NH (Amide) stretching
1310.13	S=O stretching
1289.47	C-S Stretching
1186.42	C-O Stretching
1064.76	C-N Stretching
929.62	C-H out plane bending

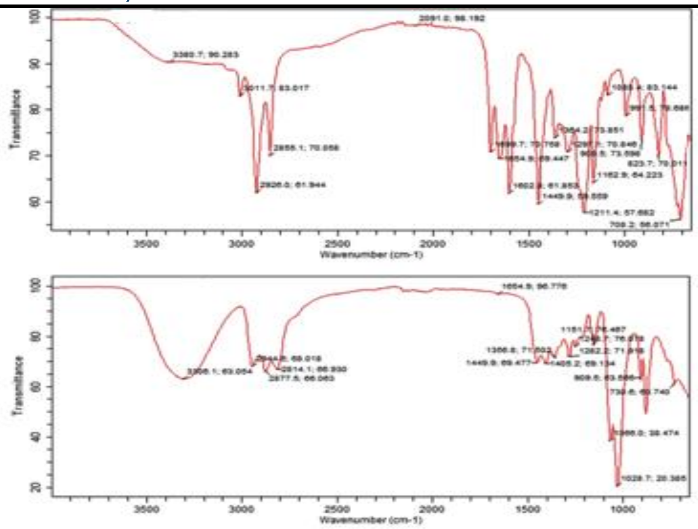

Fig.4: FT- IR of Trolamine Salicylate & Triethanolamine

Table.10: FT-IR spectral assignment of Trolamine Salicylate & Triethanolamine

Wave number in (cm^{-1})	Functional groups
2870.65	C-H Stretching
2240.43	C-O Stretching
2040.40	C-O Stretching
1688.26	C-H Out of plane bending
1264.72	NH (Amide) stretching
1162.54	S=O stretching
1089.32	C-S Stretching

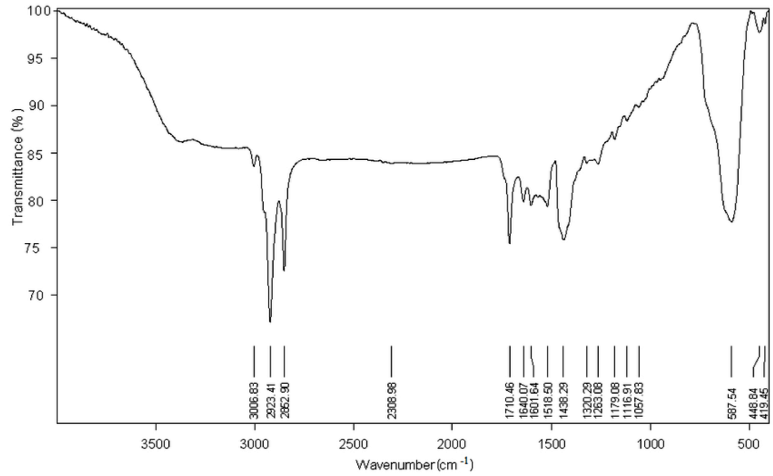

Fig. 5 : FT-IR of Oleic Acid

Table.11: FT-IR spectral assignment of Oleic acid

Wave number in (cm^{-1})	Functional groups
2613.14	C-H Stretching
1715.57	C-O Stretching
1395.96	C-O Stretching
874.65	C-H Out of plane bending

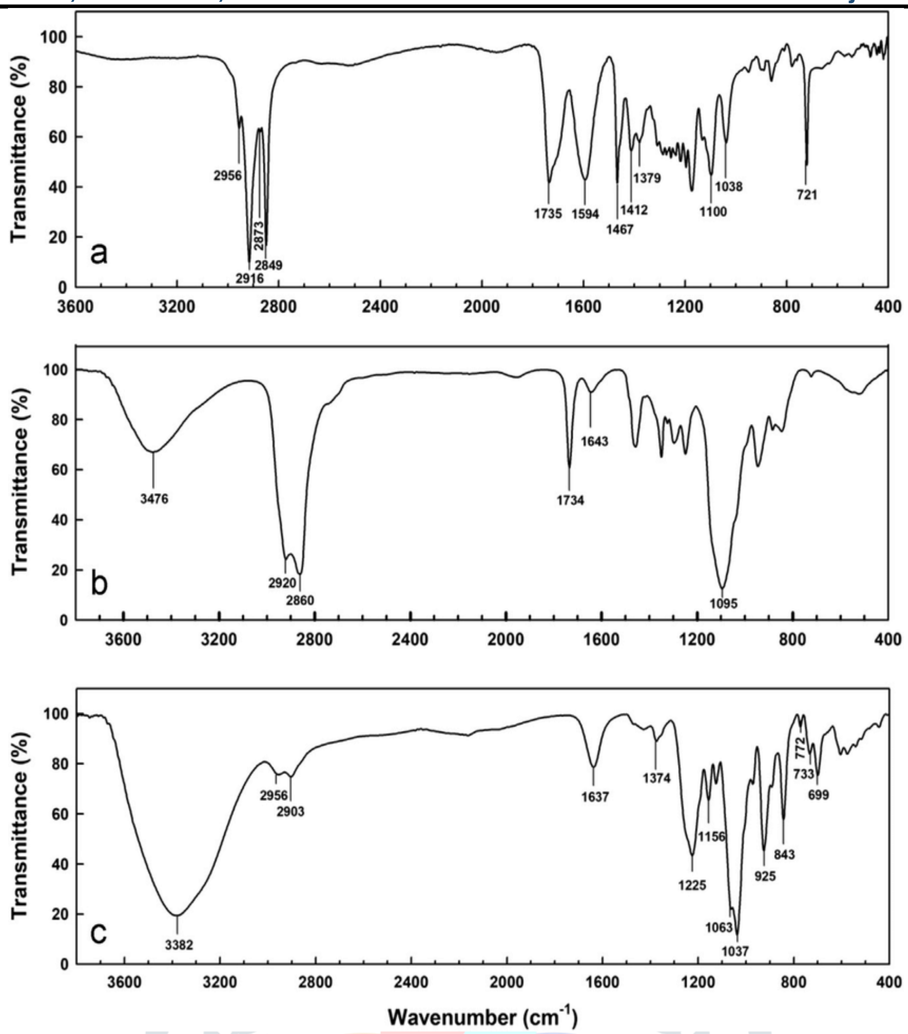

Fig. 5 . 6 : FT-IR of Trolamine Salicylate +Tween-20+Propylene Glycol

Table.12: FT-IR spectral assignment of Trolamine Salicylate +Tween-20+Propylene Glycol

Wave number in (cm^{-1})	Functional groups
1708.20	O=C= stretching
1410.80	C_4H_4O stretching
1296.64	C-H bend Alkane
1250.56	C-O-C stretching
1107.39	C-F Bending
1100	C-O Stretching
1038	C-H Out of plane bending
721	C-H Out of plane bending

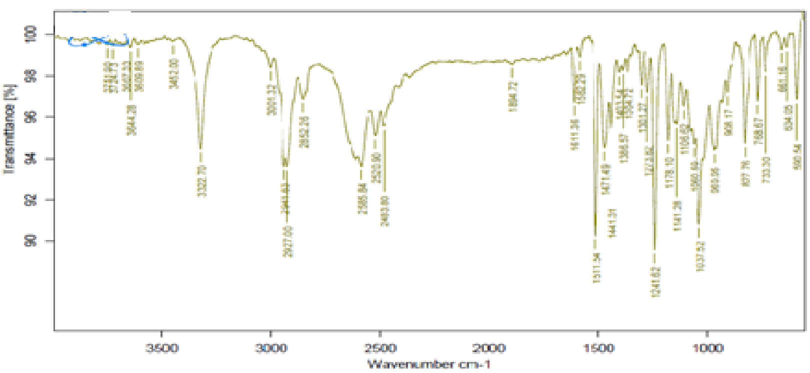

Fig. 7 : FT-IR of Carbopol-940

Table.13: FT-IR spectral assignment of Carbopol-940

Wave number in (cm^{-1})	Functional groups
3389.55	N-H Stretching in Primary amine
2932.48	C-H Stretching
2645.34	O=C= stretching
2400.54	C_4H_4O stretching
2010.21	C-H bend Alkane
1678.76	C-O-C stretching
1310.97	C-O Stretching
1100.32	
837.76	C-O Stretching
664.32	C-H Out of plane bending

In the spectra of the mixture of the drug and excipients, there are no additional peaks visible in addition to the typical peak, indicating that there is no interaction between the drug and excipient and that they are compatible. When the IR spectra of the drug and polymer combination were contrasted with those of the pure drug and individual excipients, no appreciable peak shifting was discovered, confirming the stability of the drug throughout the production of the microemulgel formulation.

Evaluation of Formulation:

Table.14: Physical Examination

Formulation Code	Physical appearance	pH	% Drug Content
F1	Clear transparent dispersion	7.1	88.90
F2	Clear transparent dispersion	6.8	90.42
F3	Clear transparent dispersion	6.6	92.76
F4	Milky white	5.8	89.26
F5	Milky white	7.5	94.56
F6	Milky white	6.9	96.36
F7	Clear transparent dispersion	7.2	98.76
F8	Clear transparent dispersion	5.9	97.92

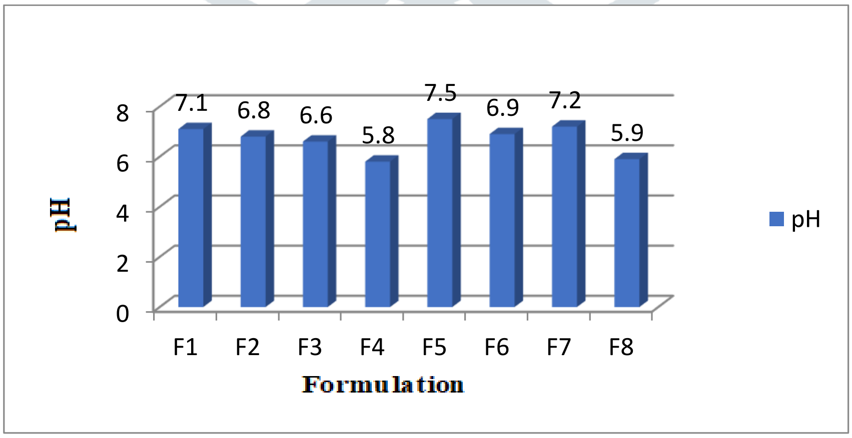

Fig.8: Representative graph of pH

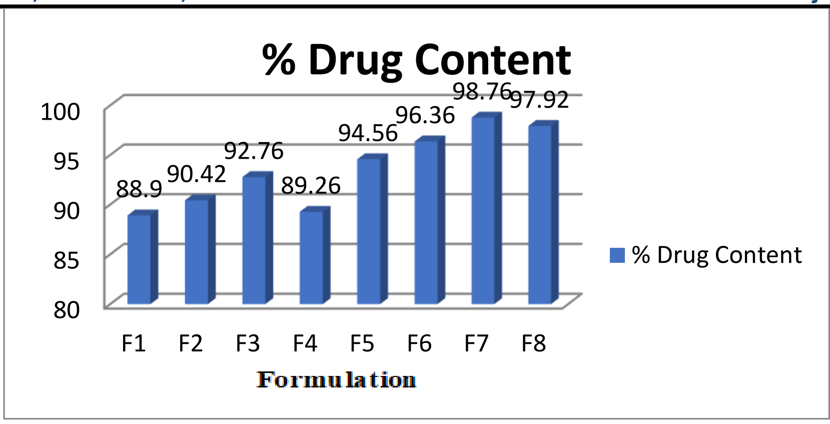

Fig.9: Representative graph of % drug Content

Table.15: Comparative Viscosity values and Spreadibility

Formulation Code	Viscosity (cps)*	Spreadibility
F1	56.8±0.8	16.42
F2	80.4±0.4	26.88
F3	100.5±0.2	28.90
F4	106.1±0.4	31.42
F5	128.9±0.1	32.54
F6	132.1±0.3	35.67
F7	138.6±0.5	36.98
F8	148.2±0.2	32.97

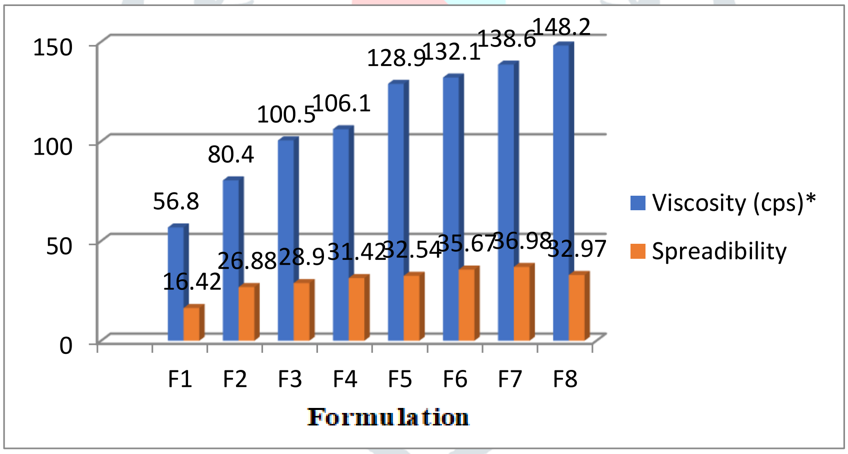

Fig.10: Comparative Viscosity values and Spreadibility

Table.16: Zeta Potential

Formulation Code	Zeta Potential (mv)
F1	-6.88
F2	3.07
F3	2.49
F4	-12.5
F5	-1.41
F6	2.16
F7	15.22

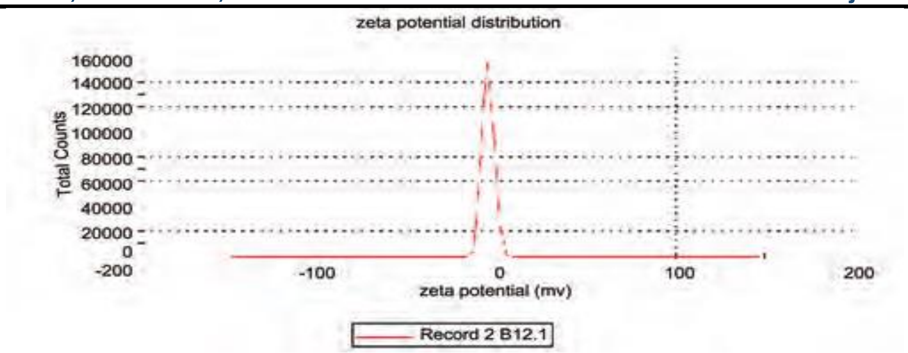

Fig.11: Zeta Potential Distribution

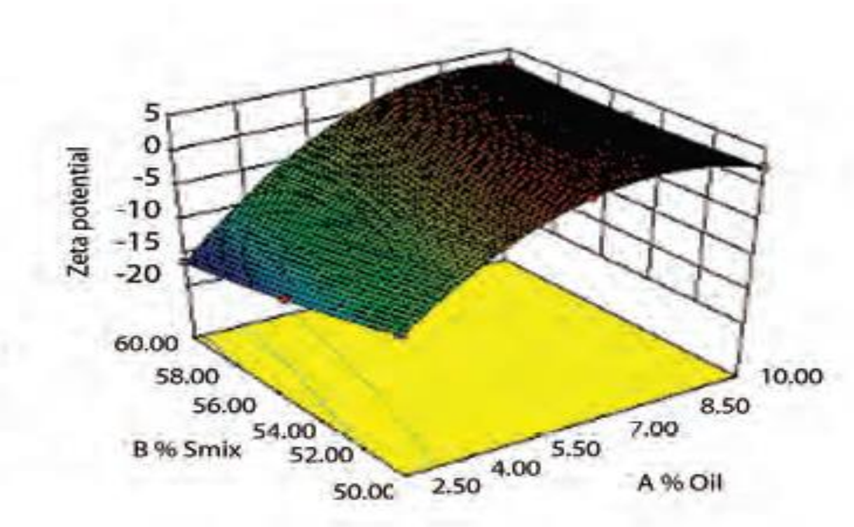

Fig.12: Zeta Potential

Table.17: Size Distribution

Formulation Code	Globule Size (nm)
F1	58.54
F2	132.10
F3	200.4
F4	37.70
F5	20.98
F6	184.4
F7	86.90

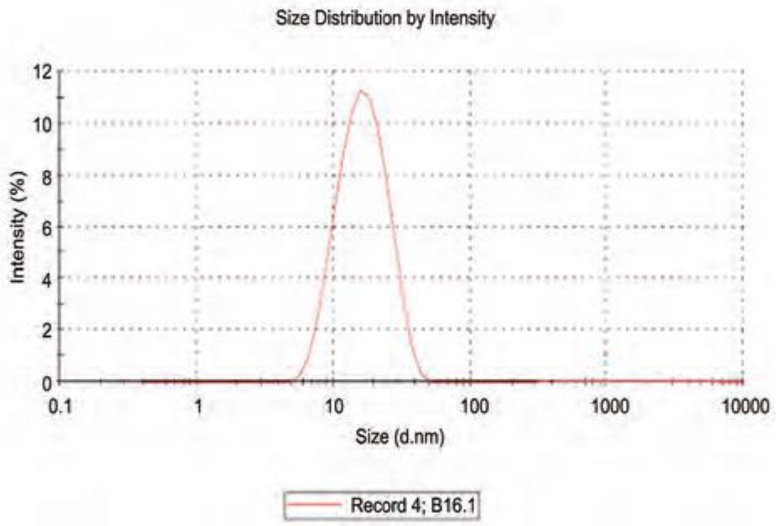

Fig.13: Size Distribution

In vitro drug diffusion study of Microemulgel:

Table.18: In-vitro drug diffusion study of Microemulgel

Time (hr)	% Drug Diffused							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	10.23	9.12	10.54	8.90	9.05	6.98	10.34	11.86
2	15.98	16.78	14.87	15.86	16.90	17.98	15.45	15.66
3	19.95	20.34	21.85	22.36	21.66	22.42	20.56	21.89
4	26.54	27.88	28.94	26.90	28.64	29.34	30.62	27.54
5	31.23	32.65	30.56	34.88	33.78	32.76	35.56	36.90
6	37.12	38.21	36.14	37.18	39.74	40.56	38.98	40.66
7	45.34	48.78	46.26	47.78	49.00	50.01	46.90	48.94
8	54.62	56.90	58.34	59.03	58.92	56.87	57.94	58.90
9	68.05	66.82	67.70	66.78	69.52	68.44	69.07	66.97
10	76.54	74.88	76.84	77.89	74.64	77.64	76.03	77.08
12	82.70	80.45	82.36	83.90	81.72	80.36	82.74	81.26
14	88.52	87.65	89.85	86.89	89.62	85.91	87.15	88.94
16	95.86	94.48	95.34	94.78	94.86	92.95	94.24	95.04
20	96.76	96.56	96.46	96.78	95.89	94.64	98.90	96.85

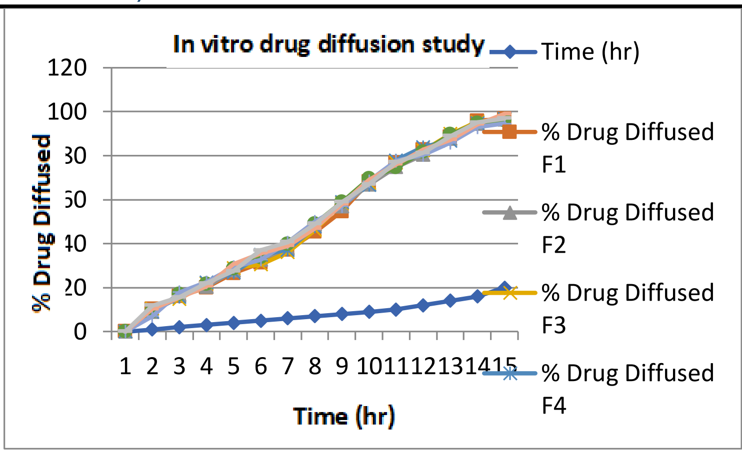

Fig.14: In-vitro drug diffusion study of Microemulgel F1-F8

Stability Study:

Table.16: Stability Study best formulation F7

Evaluation Parameters	Initial day	Stability after 1 month	Stability after 2 month	Stability after 3 month
Physical Appearance	Clear transparent dispersion	No Change	No Change	No Change
pH	7.2	7.1	7.00	6.96
Viscosity (cps)	138.6±0.5	138.6±0.5	138.6±0.5	138.6±0.5
% drug release	98.90	98.10	97.00	96.50

All the prepared micro-emulgel formulations were found to be unchanged upon the storage for 3months; no change was developed in their physical appearance but various changes in pH, viscosity and % drug release.

Conclusion:

Microemulgel as a delivery system is advantageous to use such as ease of administration, increased residence time at applied site, steady drug release with improved bioavailability, better thermodynamic stability and high transdermal permeability over simple conventional formulations. The microemulgel of Trolamine Salicylate were prepared, using Carbopol-940 and Liquid Paraffin as a gelling agent, oleic acid as oil, parabens as preservative, Tween-20 as emulgent and penetration enhancer. The prepared microemulgel formulation was inspected visually for Appearance, Spreadability, Viscosity, pH, % Drug Release and In vitro diffusion studies. Results obtained has proved that development of Trolamine Salicylate containing microemulgel will be more effective however its clinical efficacy must be understood using clinical trials. So Trolamine Salicylate microemulgel can be used as pain reliever that treatment of muscle and joint pain for topical drug delivery.

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