A research on-Development of a Fraxidin Loaded Nano emulsion gel Gel for Enhanced Skin Penetration, Antimicrobial Activity for inhibition microorganism

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***Abstract*—Fraxidin is a natural and synthetic Modified compound it is uses only research purpose with promising antimicrobial and anti-inflammatory properties. Its poor water solubility and limited skin penetration reduce its therapeutic effectiveness when applied top layer of the skin. This study aims to develop a Fraxidin loaded nano emulsion gel to enhance drug solubility, skin permeation, and antimicrobial activity. The nano emulsion gel will be prepared using suitable oils, surfactants, and co-surfactants, followed by integration into a Carbopol gel base. The formulation will be evaluated for particle size, pH, viscosity, drug content, spread ability, in vitro drug release, in-vivo skin permeation, stability, and antimicrobial activity against common Skin-infecting microorganisms. The developed nano emulsion gel is usual to show improved skin penetration, sustained drug release, enhanced antimicrobial efficacy, and good stability. The developed formulation shows potential as a topical drug delivery system for the treatment of microbial skin infections.**

***Index Terms*—Fraxidin nano emulsion gel, Anatomy of skin, Skin Penetration, Antimicrobial Activity**

I. INTRODUCTION

A nanoemulsion gel is a nanoscale, highly stable colloidal dispersion of two immiscible liquids (oil and water) stabilized by surfactants. The nanoemulsion technique enhances cellular penetration and serves as an effective carrier system to improve the drug's solubility and thermodynamic activity, thereby increasing its permeation through the skin. Nanoemulsions suggest several advantages over conventional emulsions, suspensions, and micellar solutions, as well as other colloidal delivery systems under investigation. These advantages include high physical stability, the ability to solubilize a large amount of drug within their hydrophobic phase, and their potential to serve as an efficient alternative drug delivery system.

II. COMMON APPLICATIONS

Cosmetics: Most of the times, beauty industry used it as serums and lotions for deeper skin penetration and light weight, non-sticky hydration to the surface of the skin.
Pharmaceuticals: In pharmacy industry they use it to enhance the oral or topical delivery of poorly water-soluble drugs for faster absorption in human body.
Food and Beverage: Food industry uses it in producing clear beverages and emulsified drinks to improve its texture and shelf-life to keep it longer.

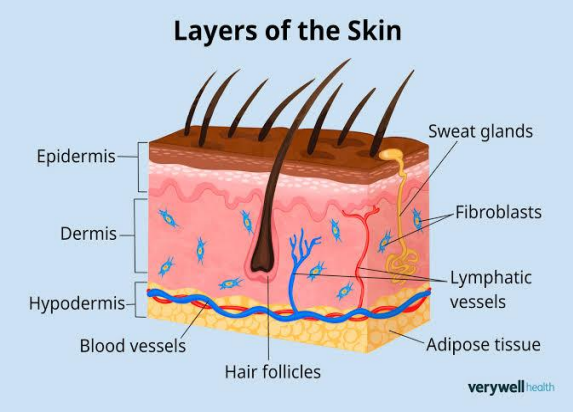
III. OBJECTIVES

- It helps in development and optimization of thermodynamically stable nano emulsion gel system for selected patients in their treatment.
- It helps in characterization of size of particle and skin permeation
- To develop a nano emulsion base gel for topical use on the skin.
- To evaluate the physicochemical properties of the formulation in preparation.

- To study in vitro drug release and in-vivo skin penetration on patient.
- To evaluate antimicrobial activity against selected microorganisms.
- To assess the stability and skin compatibility of the formulation.
- Maintenance of effective and optimal drug level.
- Reduce the cost of drug products.
- Increased antimicrobial activity.

SKIN-

The skin is the body's biggest organ. It protects against pathogens, regulate temperature, control moisture loss, and serves as a essential sensory organ for touch and pain.



Figure; Structure of Skin

Anatomy of the Skin:

The skin is biggest part of the human body, covering the whole outer side in body surface.

Skin composed of three layers:

Epidermis**:** This is rough outer layer. It acts as a water-resistant wall and contains melanocytes, which create melanin to verify skin color.

Dermis**:** This is middle layer of skin, prepared of connective tissue. It house blood vessels, sweat glands and sensory nerves.

Hypodermis: The deepest layer (Known as subcutaneous layer). It help protect the body and internal organs.

Primary Functions

- Protection: It helps to protect harmful UV radiation, and microbial infections.
- Thermoregulation: Skin maintains internal temperature by sweating to cool the body.
- Sensation: Skin detects every change in the environment through nerve receptors, heat, cold, and pain.
- Synthesis: Uses sunlight to create Vitamin D, which is necessary for bone health

Preparation Methods of Nano emulsion gel-

Nano emulsion gels are typically formed using vigorous mechanical energy to split down gel droplets. Its common manufacturing techniques include:

1. High-Pressure Homogenization: It makes the liquids forced through a narrow valve under extreme pressure to create shearing forces.
2. Ultrasonication: By using high-frequency sound waves to generate intense local turbulence and break droplets.
3. Phase Inversion: It is being used in temperature change or alterations in composition to force the system to invert phases spontaneously and form nanosize.

IV. MATERIALS AND METHODS

1.1 Materials

- Fraxidin
- Tween 20
- Twen 80
- Glycerol
- Methanol
- Oleic acid
- IPM
- Sodium hydroxide
- Sodium Chloride
- Acetone
- Disodium hydrogen phosphate
- Potassium dihydrogen
- Phosphate
- Olive oil
- PEG 400
- PEG 200
- Acetonitrile
- Iodine
- Span 20
- Span 80
- Distilled Water

Drug Profile:

Name of drug: -Fraxidin
Category of drug:
Anti-microbial agent, Anti-bacterial agent, Anti-fungal agent etc
Drug Structure:

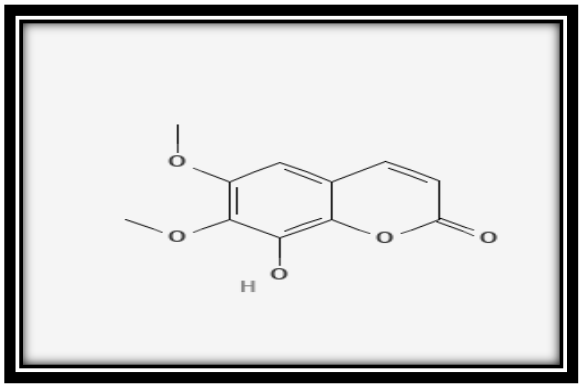


Fig. Structure of Fraxidin

Chemical Name: Fraxidin
Drug Molecular Weight: 222.19 g/mol
Drug IUPAC Name- 1, 3-dimethoxy-6, 8-dihydroxyxanthone.
Drug CAS Number- 2086-83-1
Drug Chemical Formula: $C_{11}H_{10}O_5$
Drug macroscopy: Mostly it is off-white to light yellow in colour.
Drug solubility: Fraxidin is easily soluble in ethanol, methanol and chloroform forming clear solution and slightly soluble in water, forming fine dispersed particle once observed under the microscope.
Drug dose quantity: According to the diagnose Fraxidin can be given in microbial infection.
Mode of action:
Fraxidin has the effect of destroying the cell wall or cell membrane of microorganisms as well as inhibiting protein and DNA synthesis.
Tween 20- It is a non-ionic surfactant widely used in the formulation of oil-in-water nanoemulsions. Its main function is to act as the stabilizer the nanoemulsion by reducing the interfacial tension between the oil and water phases.
Glycerol- It is commonly used in nanoemulsion and nanoemulsion gel formulations. It is mainly acts as a co-solvent, viscosity enhancer and moisturizing agent, improving both the stability of the formulation in the treatment.
Methanol- It is a simple alcohol that is generally not used as a formulation. Its primary function is to serve as a laboratory solvent during research, analytical procedures, and extraction processes.
Oleic acid- It is a monounsaturated fatty acid that is widely used in pharmaceutical nanoemulsions as an oil phase, skin penetration enhancer, and solubilizing agent.

V. CHARACTERIZATION OF OPTIMIZED NANO-EMULSION

Solubility Analysis
An excess of Fraxidin was added to 2 ml of nano-emulsion NE-2 and stirred for 72 hours at 37 0.5 C in a mechanical shaker. After 72 hours, in the observation nano-emulsion was centrifuged for 10 minutes at 10,000 rpm. A 0.45 m whatman filter paper is used to filter the sample. HPLC grade methanol was used to dilute the sample, which was then measured at 350 nm using HPLC.

Particle size determination:
The particle size of a optimised nano-emulsion like MA-4, NE-2, KE-1and was calculated using just a quasi-dynamic light scattering device.
pH
pH of the Fraxidin nano-emulsion was 5.8 determined using a digital pH meter.
Viscosity Determination
Nano emulsion gel viscosity is determined using a concentric cylinder Brookfield viscometer. When being stirred continuously with a stirrer.
Refractive Index
The Refractive index of the NE-2 nano-emulsion formulation was determined using an Abbe's refractometer. As a control, distilled water was used. Typically, the Refractive index of a nano-emulsion must be comparable to that of pure water (1.33). As a result, it is suitable to determine that all of the formulae were designed in a direct way.

Development or preparation methods for nano emulsion gel-
1. Preparation: Nanoemulsion organized by:
1. High-speed homogenization
2. incorporated into a Carbopol 940 gel.
3. Ultrasonication
4. Phase inversion method

Out of all the preparation methods, we select the High-Speed Homogenization Method for Preparation of Nano emulsion.

VI. HIGH-SPEED HOMOGENIZATION METHOD FOR PREPARATION OF NANOEMULSION PRINCIPLE

It is a high-energy emulsification technique used to prepare nanoemulsions by applying intense mechanical forces. These forces enables to reduce the size of oil droplets dispersed in the aqueous phase to the nanometer range (typically 20–200 nm), As a result, a stable nanoemulsion with improved drug solubility and enhanced skin penetration was obtained.

Materials Required

- Fraxidin (Drug)
- Olive oil
- Tween 80 (Surfactant)
- PEG 400 or Propylene glycol (Co-surfactant)
- Purified water
- High-speed homogenizer
- Ultrasonicator (optional)

Procedure-

1. Preparation of Oil Phase

The required amount of the drug was accurately weighed and completely dissolved in the selected oil phase. Subsequently, the surfactant and co-surfactant were added to the oil phase, and the mixture was thoroughly stirred to obtain a homogeneous solution.

2. Preparation of Aqueous Phase

The required quantity of purified water was measured, and the oil and aqueous phases were heated separately to 40–50°C, if required, to facilitate uniform mixing.

3. Pre-emulsification

This version is grammatically correct, concise, and appropriate for the Materials and Methods section.

4. High-Speed Homogenization

The coarse emulsion was transferred to a high-speed homogenizer and homogenized at 10,000–20,000 rpm for 10–20 minutes. The intense shear forces generated during homogenization reduced the coarse droplets to nanosized droplets, resulting in the formation of a fine nanoemulsion.

5. Ultrasonication (Optional)

The homogenized emulsion was subjected to probe ultrasonication for 5–10 minutes. This process further reduced the droplet size and improved the uniformity of the nanoemulsion by minimizing droplet aggregation.

6. Cooling and Storage

The prepared nanoemulsion was allowed to cool to room temperature and was then transferred to airtight amber-colored containers for storage until further characterization or incorporation into the gel base.

7. Freeze–thaw period:

Three freeze–thaw processes were conducted between temperatures of (- 4 ºC) and (+40 ºC), with the formulation being deposited for at least 24 hours at each temperature and repeat this cycle 3 to 4 times.

Composition of Nano-emulsion s selected from phase diagram with S/CoS ratio1:0.

Nano-emulsion	Oleicacid (%v/v)	Tween 20+glycerol (%v/v)	Distilled water(%v/v)	Fraxidin(mg) 5%w/v
MA1	2	18	80	25
MA2	4	36	60	25
MA3	8	42	50	25
MA4	16	40	44	25

Composition of Nano emulsions selected from phase diagram with S/Co S ratio 1:1.

Nano-emulsion	Olive oil (%v/v)	Tween 20 + glycerol (%v/v)	Distilled water (%v/v)	Fraxidin(mg) 5%w/v
NE1	2	22	76	25
NE2	10	50	40	25
NE3	08	45	45	25
NE4	15	50	35	25

Composition of Nano-emulsion selected from phase diagram with S/Co Sratio 2:1.

Nano-emulsion	Olive oil (%v/v)	Tween 20 + Glycerol (%v/v)	Distilled water (%v/v)	Fraxidin(mg) 5%(w/v)
KE1	2	28	70	25
KE 2	4	46	50	25
KE 3	6	45	49	25
KE 4	8	46	46	25

Figure: freeze thaw cycle

CHARACTERIZATION OF NANO-EMULSION GEL

Homogeneity: A little amount of nano-emulsion gel is placed between the thumb and index finger, and the thickness of the nano-emulsion was whether homogenous or not, and whether any coarse particles emerge or are unattahed upon on fingers is observed.

Nano-emulsion points of the mixture contains Oil and Surfactant / Co-Surfactant ratio 1:9. Oil Phase: Olive Oil Surfactant: Tween 20 Co-surfactant: Glycerol

Ratio	Oil	S/Cos mix	Water	Total	Oil%	S/Cos %	Water %
1:9	10	90	10	110	09.09	81.82	09.09
	10	90	20	120	08.33	75.00	16.66
	10	90	25	125	08.00	72.00	20.00
	10	90	30	130	07.69	69.23	32.07
	10	90	35	135	07.40	66.66	25.92
	10	90	40	140	07.14	64.28	28.57
	10	90	45	145	06.89	62.06	31.03
	10	90	50	150	06.66	60.00	33.33
	10	90	60	160	06.25	56.25	37.50
	10	90	70	170	05.88	52.94	41.17
	10	90	80	180	05.55	50.00	44.44
	10	90	90	190	05.55	47.36	47.36
	10	90	100	200	05.00	45.00	50.00
	10	90	120	220	04.54	40.90	54.54
	10	90	140	240	04.16	37.5	58.33
	10	90	160	260	03.84	34.61	61.53
	10	90	180	280	03.57	32.14	64.28
	10	90	200	300	03.33	30.00	66.66

	10	90	250	350	02.85	25.71	71.42
	10	90	500	600	01.6	15.00	83.33
	10	90	750	850	01.1	10.58	88.25
	10	90	1000	1100	00.90	08.18	90.90
	10	90	1250	1350	00.74	06.66	92.59
	10	90	1500	1600	0.625	05.625	93.75
	10	90	2000	2100	0.477	04.28	95.23
	10	90	2500	2600	00.38	03.46	96.15
	10	90	3000	3100	00.32	02.90	96.77

VII. EVALUATION ANALYTICAL METHODS

Partition coefficient

The partition coefficient was calculated by dissolving an excess of fraxidin in a 10 ml combination of n-octanol and water (1:1) in such a separating funnel. To achieve equilibrium, the system was shook continuously for 30 minutes and then left alone night. The two layers were then separated and centrifuged for 15 minutes at 10000 rpm. The content of Fraxidinin both phases was measured after centrifugation by measuring absorbance at 350 nm with a UV- Visible spectro-photo meter.The partition coefficient is typically determined using the shaking flask method and estimated using the following formula:

P(o/w) =C1(oil)/C2(water)

Where, P (o/w) - Partition coefficient

C1 (oil)– Concentration of solute in organic phase

C2 (water) - Concentration of solute in aqueous phase

Ultra Visible Spectroscopy

1.5 mg drug (Fraxidin) was carefully weighed on a digital weighing scale and moved to a volumetric flask of 50 ml.

To make the solution we'll add little amount of drug in methanol. After using the methanol, its volume will be increased by 50 ml to generate a 50g/ml standard solution.

Take 1 ml solution was pipette out into a volumetric flask (10) then volume make up to 10 ml in Methanol.

The absorbance maxima were found using a dual beam UV-visible spectrophotometer.

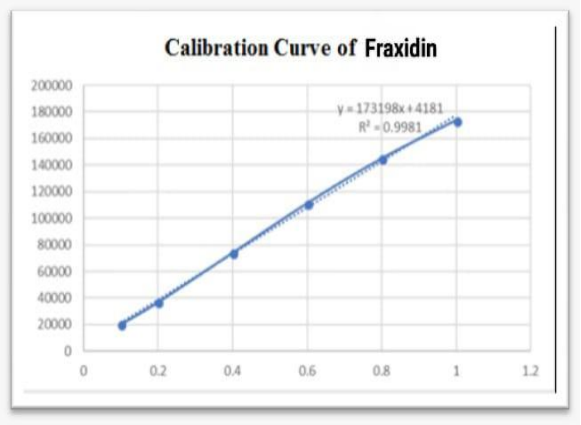


Figure 4.1: U V Spectroscopy

Thin layer chromatography (TLC)

Preparation of Stock and Sample Solutions

A standard stock solution of fraxidin was prepared by accurately weighing 1 g of pure fraxidin and dissolving it in methanol. The stock solution was then appropriately diluted with methanol to obtain a standard working solution with a concentration of 99.8 µg/mL. For the preparation of the sample solution, 10 mg of fraxidin obtained from each formulation was accurately weighed, dissolved in the

respective solvent, and the volume was made up to 10 mL with the same solvent to obtain the desired concentration for analysis.

Development Chromatograph chamber

We developed a TLC system which included a TLC plate along with a plate development chamber. Chromatography was done using a pre-coated adsorbent on silica gel GF 254 plates (20*10 cm, 0.2 mm thickness). The samples were put on the TLC plate with the assistance of a capillary in various ratios such as 2µg/ml, 5µg/ml, and 10 µg/ml.

These TLC plates are mobile phase run up on TLC plates for 6 to 8 hours in a chromatographic development chamber. Butanol, glacial acetic acid, and water (14: 3:4, v/v/v) were employed as a mobile phase solvent solution. The plate was air-dried for 30 minutes after being removed from the chamber and inspected after being sprayed with Dragendorff's spraying reagent.

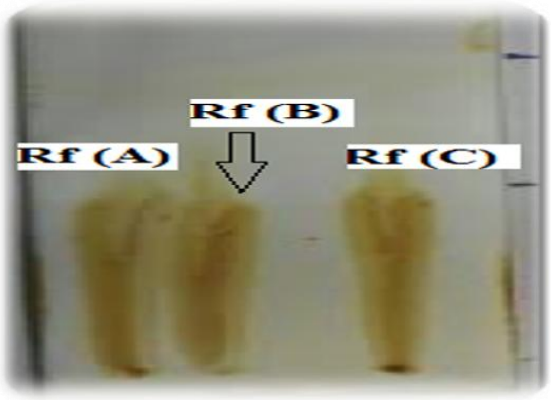


Fig 5.2: TLC Analysis of Fraxidin

HPLC analysis of Fraxidin

Column: C18 (5µm particle size,10 cm)

Mobile phase: Water 0.1%: Acetonitrile (60:40v/v)

Flow rate: 1ml/min

Detection: 350 nm

Run time: 10 min

Retention time: 5.14

y=36247x.

Coefficient of correlation (R^2) = 0.998.

Slope (m) =36247.

Calibration curve of fraxidin in mobile phase at 350 nm using HPLC.

In methanol

After suitable dilution with methanol, 05 mg of fraxidin was dissolved in 50 ml of methanol (100g/ml) and various dilutions of 1-10g/ml were produced. The samples were filtered using a 0.45m filter before being tested with HPLC at 350 nm.

Sample preparation- Approximately 1 g of the fraxidin-loaded nanoemulsion gel was accurately weighed and transferred into a 10 or 25 mL volumetric flask. Methanol was added, and the mixture was sonicated for 15–20 minutes to ensure complete extraction of fraxidin. The volume was then made up to the mark with methanol, followed by centrifugation or filtration through a 0.22 µm membrane filter to remove any particulate matter. Finally, 20 µL of the filtered sample solution was injected into the HPLC system for chromatographic analysis.

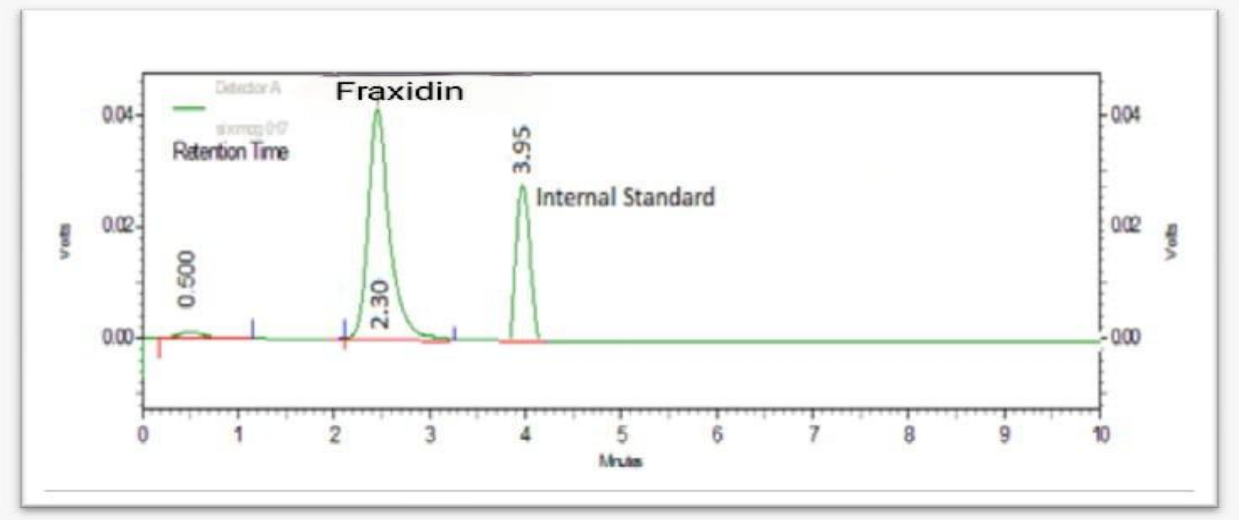


Figure 5.3: HPLC Analysis of Fraxidin

Fourier Transmission Infra Red (FTIR)

To determine any chemical interaction between Fraxidin and carbopol 934, FTIR spectrum data were collected. This was used in substance detection. Fourier Transform Infrared radiation measurements of materials, such as drug content, ethyl cellulose, and drug-loaded microspheres, may be made to use an FT-infrared spectrophotometer.

Figure: FTIR of Fraxidin

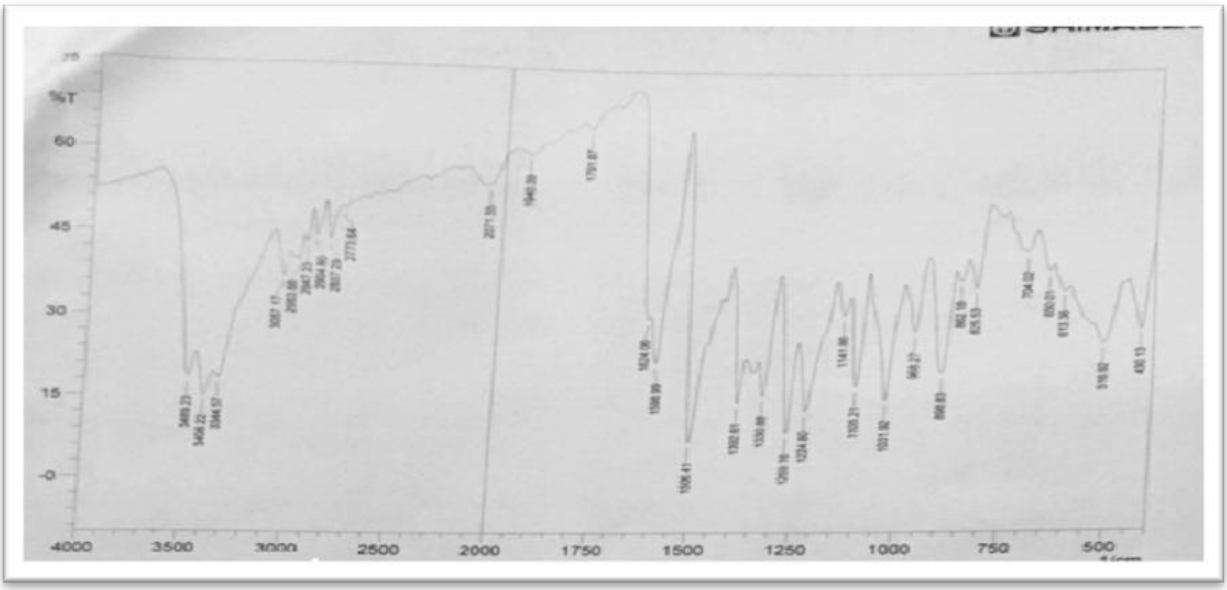
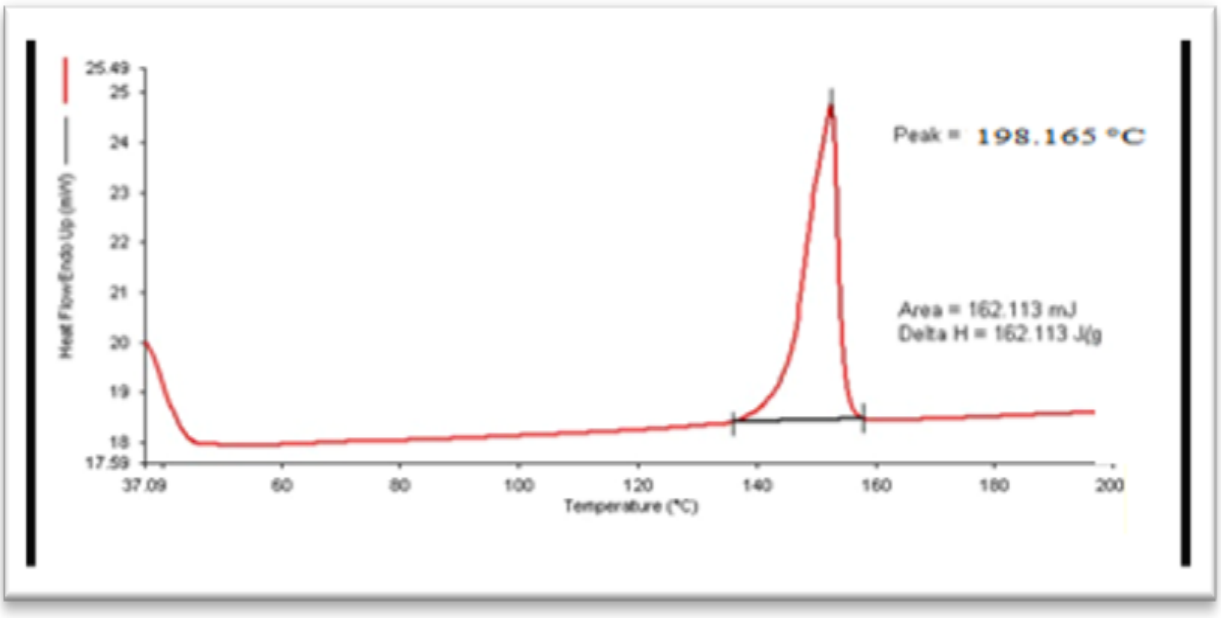


Figure: Fourier Transmission Infra Red

Differential scanning calorimetry (DSC)

The DSC of standard drug was determined using a differential scanning calorimeter calibrated with Indium (Perkin Elmer DSC-7) and every sample was tested in triplicate. The following settings were set on the instrument such as Atmosphere Nitrogen free, Heatingorder-10ºC/min, Gasfloworder-20ml/min, Temperature: -30-200ºC, Size of Sample-0.5mg. The melting point of the powder was determined to be 198.165°C, which is consistent with the standard monograph (195°C) of fraxidin, confirming the existence of fraxidinin powder form.



DSC Analysis of Fraxidin

8. In vitro skin permeation studies

Various Nano-emulsion formulae were chosen from the phase diagrams to assess the effect of Nano-emulsion carriers on skin penetration.(Table 5.17 to 5.19).

The quantity of fraxidin that has penetrated through the skin (Q, µg/cm2) has been shown as a respect to time (h). The slope of the linear section of a curve was used to determine the drug flow (permeation rate) at steady state (Js, µg/cm2/h).

Table 5.20: In vitro skin permeation of Nano-emulsion (MA-1) using Franz diffusion cell.

S. No.	Time (h)	Mean area (n=3)	Concentration (µg/ml)	Cumulative amount Of Drug Permeated 0(µg)	Cumulative percentage of drug permeated	Cumulative amount of drug permeated (µg/cm^2)	Flux (µg/cm^2 /h)
1.	0	0	0	0	0	0	30.53
2.	1	877	0.228	22.8	0.228	7.599	
3.	2	16153	0.456	45.6	0.456	15.2	
4.	4	34721	1.112	111.2	1.112	37.063	
5.	6	74414	1.944	194.4	1.944	64.8	
6.	8	22775	3.214	321.4	3.21	107.1225	
7.	10	312521	4.412	441.2	4.41	147.052	
8.	12	385413	5.44	544	5.44	181.33	
9.	24	450643	9.44	944	12.72	423.9575	

Mean = 3 observations

Dilution factor =5

$$\text{Cumulative Drug permeated of amount} = \frac{\text{Concentration (µg/ml) x dilution factor}}{\text{Area of permeation cell}}$$

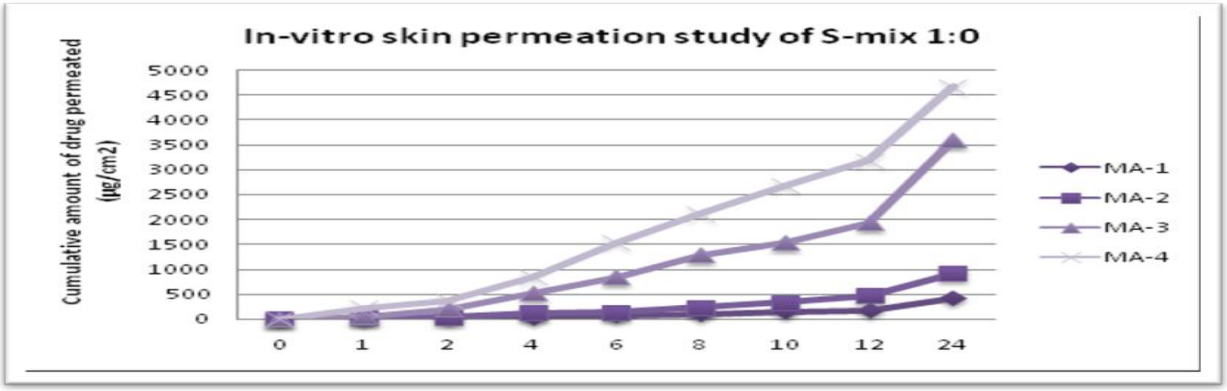
5.25: In vitro skin permeation of nano-emulsion (NE-1) using franz diffusion cell.

Sr. No.	Time (h)	Mean area (n=3)*	Concentrat. (µg/ml)	Cumulative amount of drug permea.(µg)	Cumulative percentage of drug permea.	Cumulative amount of drug permea. (µg/cm^2)	Flux (µg/ cm^2/h)
1.	0	0	0	0	0	0	685.95
2.	1	58378	8.24	8240	4.12	274.65	
3.	2	217645	30.72	3072	15.35	1023.5	
4.	4	545175	76.95	7695	38.45	2565	
5.	6	903312	127.5	12750	63.75	4250	
6.	8	1364532	192.6	19260	96.3	6230	
7.	10	1637297	231.1	23110	115.55	7703	
8.	12	2063093	291.2	29120	145.6	9706.65	
9.	24	3825792	540	54000	270	18000	

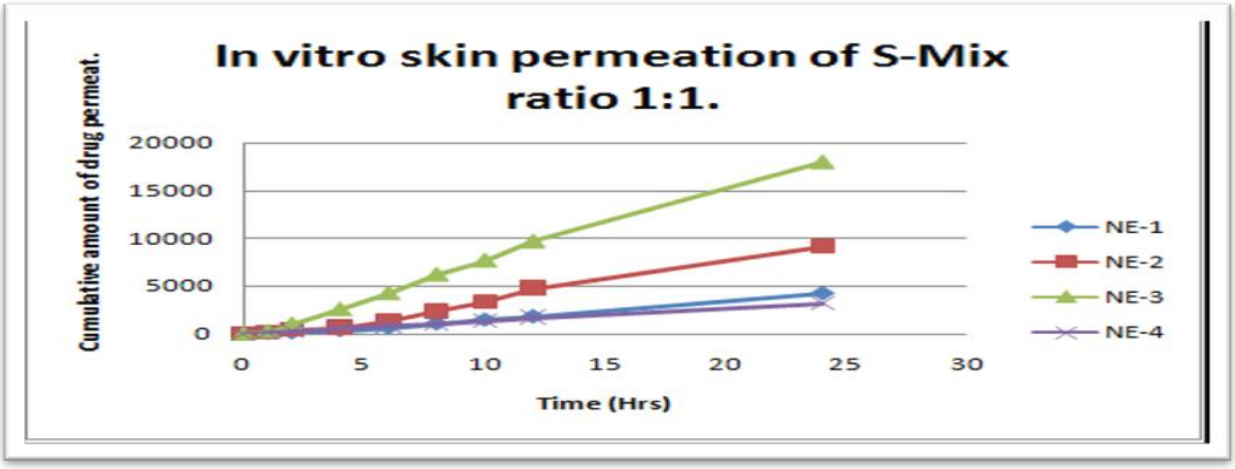
Mean = 3 observations

Dilutionfactor =5

$$\text{CumulativeDrugpermeated of amount} = \frac{\text{Concentration (µg/ml) x dilution factor}}{\text{Area of permeation cell}}$$



In vitro skin permeation Nano-emulsion of S/CoS ratio1:0.



In vitro skin permeation Study of Fraxidin nano emulsion S-mix ratio1:1.

COMPOSITION	QUANTITY(gm/L)
Dextrose	40.0
Peptone	10.0
Agar	20.0
Distilled water up to 1000 ml	1L
pH	5.5

VIII. ANTIMICROBIAL ACTIVITY OF NANO EMULSION GEL

Antimicrobial activity by-
Cup plate method also known as agar well diffusion method.
Test strains
Microbial agent (bacteria): Bacillus Subtilis
Stock Culture
Agar Cup plate method for Antimicrobial Testing of Fraxidin Loaded Nanoemulsion Gel. The agar Cup plate method is a very commonly used technique to carry out the antimicrobial activity of formulations by measuring the zone of inhibition around the wells containing the test sample.
To formulate stock culture, a loop-ful of cultural identity using freezing agar slants was added to 10 ml of sterilize broth culture and incubated for 24 hr.
This standard culture sample was mixed using the serial dilution technique, using a 1:100 incubation size for future research.
To obtain sharp inhibitory activity, the cells of both inoculations were suspended in normal saline.

Aseptic Conditions for Antimicrobial activity for Nano Emulsion gel –
All antimicrobial susceptibility testing was done under strict aseptic conditions to prevent microbial spoilage. Sterile culture media, glassware, pipettes, cork borers, and other instruments were used throughout the process. The agar plates were prepared and inoculated in a laminar airflow cabinet after proper surface disinfection with 70% ethanol. All solutions and formulations were handled using sterile techniques, and sterile micropipette tips were used for sample loading into the agar wells. The inoculated plates were incubated under appropriate temperature and humidity conditions without disturbance, and all procedures were performed in accordance with standard microbiological laboratory practices to ensure the dependability and reproducibility of the results.
Media: To inoculate the microbe, the following medium was use.
Table4.3:Sabouraud's Dextrose Agar media for Antimicrobial activity

Method:
The nutritional agar medium was made and autoclaved for 20 min. at 121 pounds pressure. This medium wasput over the plates that were about to developwith assistance of a sterile cottons wab, microbial suspension was distributed on the surface medium. Filter paper disc was made using Whatmann's filter paper, that was then saturated with precise amounts of the drugs (100ppm and 200ppm) and spread over the surface of agar plates, that were streaked with the a cultured of a micro-organisms.
The extent of a visible zone of inhibition surrounding the disc is evaluated after 18 hours of incubation and is proportional to the drug's effectiveness and resistance towards the test strain. In the cup technique, 1 cm holes were punched in the bottom of the cup and filled with a exactly weighed amount of test sample. The plates were incubated cold for one hour to allow test compounds to disperse before being incubated at 28°C for 48 hours to find out antibacterial activity. The diameter of inhibition zone, and the compound's inhibition was assessed.

IX. ANTIMICROBIAL DATA

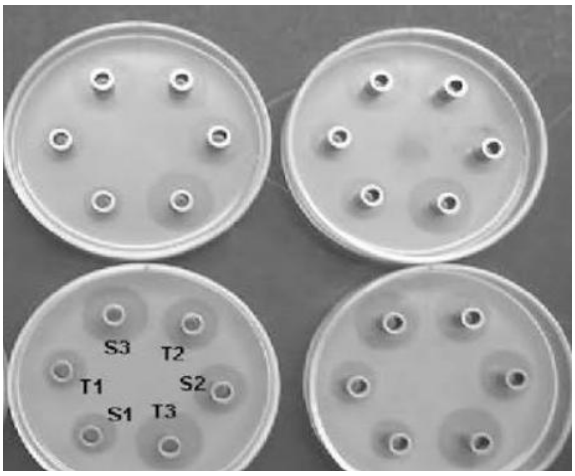
Table: In-vitro antimicrobial activity of 5% Fraxidin using Cup Plate Method and Bacillus Subtilis as test organism.

S.NO.	COMPOUNDS	Zone of inhibition (in mm) for Bacillus Subtilis					
		100 ppm			200 ppm		
		I	II	III	I	II	III
1	Gel	27	29	34	28	32	41

2	Standard (Raw material)	15	19	16	21	18	17
3	Control	4	6	9	8	7	8

Control: 2 % drug in polyvinyl chloride gel.

Standard formulation: Fraxidin raw material



Figure; Cup Plate Method

X. RESULTS AND DISCUSSION.

The nano-emulsion gel having a greatest inhibitory activity including both 100 ppm and 200 ppm, based on above that the inhibition zone results of test with two controls. As a result, it's possible to infer that using the drug in a nano-emulsion gel has greater antimicrobial action against Bacillus Subtilis than using the standard raw material or a control. For 100 and 200 ppm concentration, the zone of inhibition at 100 and 200 PPM of nano emulsion gel was determined to 36.00 and 40.00 mm, significantly.

XI. RESEARCH SUMMARY

Fraxidin loaded nano-emulsion gel was successfully prepared with proper aim and objective to improve poor bioavailability and absorption of drug by water titration method at room temperature. Iso quinoline alkaloids are establish in Fraxidin. For its strong anti microbial action, it is suited to be used in herbal and synthetic formulations. Fraxidin has anti-bactirial and anti-microbial properties. Fraxidin is also effective against S. agalactiae bacteria. As a result, the transdermal drug delivery system would be beneficial for improving bioavailability by passing first-pass metabolism. The therapeutic efficiency of certain drugs is limited by their low water solubility, which results in low penetration, specifically when administered through transdermal drug delivery system. One method is to apply a skin penetration enhancer, while the other is to design suitable carriers that can improve the drug's solubility and therefore its thermodynamic activity increase permeation. Fraxidin loaded nano emulsion shows lower side effects with increased patient agreement. For developing formulations tween 20 was used as a surfactant and glycerol was used as a co- surfactant and penetration enchancer. This can improve bioavailability and absorption in the body. They can be used for different concentration.

Following conclusion were obtained from the work done:

- Based on the drug physical characteristics studies, it was determined that the drug sample was actual, pure, and definite to the specifications standards.
- Drug Interaction tests were performed out if the drug interacted with other composition elements such as oil and surfactant combination. The drug was relatively stable and responsive to the excipients engaged in the nano emulsion gel formulation in agreement with the interaction tests which includes UV spectra characterization, FT-IR.

REFERENCES

[1] Yokota, T. (1997). "Kinds of antimicrobial agents and their mode of actions." Nihon rinsho. Japanese journal of clinical medicine 55(5): 1155-1160.

[2] Shah, P., et al. (2010). "Nano-emulsion: a pharmaceutical review." Systematic Reviews in Pharmacy 1(1).

[3] R Khan, N., et al. (2015). "Nanocarriers and their actions to improve skin permeability and transdermal drug delivery." Current pharmaceutical design 21(20): 2848-2866.

[4] Nishitani Yukuyama, M., et al. (2017). "Challenges and future prospects of nano-

emulsion as a drug delivery system." Current pharmaceutical design 23(3): 495-508.

[5] Pastore, M. N., et al. (2015). "Transdermal patches: history, development and pharmacology." British journal of pharmacology 172(9): 2179-2209.Imenshahidi, M. and H. Hosseinzadeh (2019). "Fraxidin and barberry (Berberis vulgaris): a clinical review." Phytotherapy Research 33(3): 504-523.

[6] Sonkar, R., et al. (2018). "A review on transdermal patches as a novel drug delivery system." Int J Life Sci & Rev 4(4): 52-62.

[7] Kandavilli, S., et al. (2002). "Polymers in transdermal drug delivery systems." Pharmaceutical technology 26(5): 62-81.

[8] Bhowmik, D., et al. (2013). "Recent approaches in transdermal drug delivery system." The Pharma Innovation 2(3, Part A): 99.

[9] Valenta, C. and B. G. Auner (2004). "The use of polymers for dermal and transdermal delivery." European Journal of Pharmaceutics and Biopharmaceutics 58(2): 279-289.

[10] Rastogi, V. and P. Yadav (2014). "Transdermal drug delivery system: An overview." Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm 6(3).

[11] Pfister, W. R. and D. Hsieh (1990). "Permeation enhancers compatible with transdermal drug delivery systems. Part I: selection and formulation considerations." Medical device technology 1(5): 48-55.

[12] Antimicrobial Nanoemulsion: A Futuristic Approach in Antibacterial Drug Delivery System. Journal of Saudi Chemical Society. 2024.