Eurasian Journal of Analytical Chemistry
ISSN: 1306-3057 OPEN ACCESS 2024 19 (1): 230-239

Formulation, Characterization, and Evaluation of Neomycin Sulphate Emulgel Incorporating Tea Tree Oil for Treatment of Bacterial Skin Infections

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ABSTRACT
Background: Skin infection caused by bacteria is common and can be range from mild to severe. It includes topical treatment of antibiotics such as neomycin sulphate. However increasing the antibacterial properties the tea tree oil is used for the skin infection
Aim: The research specifically concerns with the development of a unique Emulgel system containing Neomycin Sulphate and Tea Tree Oil for the treatment of bacterial skin infections.
Methods: Emulgel of Neomycin Sulphate were prepared using Carbopol 934, Liquid Paraffin, Tea Tree Oil, Span 20, Tween 20, Propylene Glycol, Methyl Paraben, Propyl Paraben and Triethanolamine in different ratio by incorporation method. Every Emulgel formulation underwent testing on a range of characteristics, including physical inspection, pH measurement, rheological studies, spreadability, Zeta potential, SEM, TEM, in vitro investigation, and stability research.
Results: The Neomycin Sulphate Emulgel prepared with tea tree oil and the various formulations are presented by the help of Incorporation method and the better formulations are given F4.The formulations are given better viscosity, pH and in vitro study was given in the result and discussion.
Conclusion: The developed Neomycin Sulphate Emulgel with Tea Tree Oil shows as an effective topical treatment for bacterial skin infections, offering enhanced antibacterial activity by increasing the concentration of Tea Tree Oil in the Emulgel formulation.

Keywords: Neomycin Sulphate, Tea Tree Oil, Emulgel, Incorporation Method

INTRODUCTION

Skin medications are pharmaceutical dosage form that is administered topically to the skin to treat skin condition. These are designed to reduce the medication pharmacological reaction on the skin's surface.[1] Topical medication administration is regarded as the simplest and most convenient method of delivering drugs to particular parts of the body through multiple paths (such as ophthalmic, rectal, vaginal, or cutaneous channels. These treatments treat healthy or injured skin using a variety of cosmetic and dermatological solutions. [2]
The method of treating a cutaneous aliment by directly putting a medication containing formulations to the epidermis is a "topical drug administration". Topical medicine is frequently utilized in cases of localized skin illness, such as a fungal infection, or when some technique of pharmaceutical administration such as mouth, tongue, stomach, or injection flop. Drug application allows immediate diagnosis and treatment on the skin, eliminating the risk of metabolism in the first place.[3]
Topical delivery products include: External topical are applied directly onto the affected site by spreading, spraying or dusting over the cutaneous surfaces and internal medication are applied orally, vaginally or topically to the stomach surfaces to produce local effect.[4]
Mix the lotion and gel to create emulgel. Emulgel is an emulsion where water is mixed with oil or oil with water combined by a gelling agent to produce a gel. Emulsifying gels are a reliable and effective medium for transporting hydrophobic or water-insoluble substances. For lipophilic drugs, oil-in-water formulations are used. The water-in-oil version is designed for use with hydrophobic chemicals. Because latex contains both aqueous and non-aqueous components, it can effectively transmit water-soluble and oil-soluble chemicals. They have recently been used to control the release of formulations. This system is biphasic and has increased drug utilization, capacity and stability. Latex has many cosmetic advantages, such as good spreading, thixotropic properties, oil-free, long life, odor-free and good visibility. Latex is a formulation that combines the properties of gel and emulsion to provide dual release. [5, 6]

Neomycin sulfate, an amino glycoside antibiotic, is widely used in the treatment of bacterial skin infections. Its broad-spectrum activity against Gram-positive and Gram-negative bacteria makes it an effective choice for managing superficial skin infections, wounds, and burns. However, the use of neomycin sulfate in conventional formulations is often associated with limitations such as poor patient compliance due to skin irritation and the potential development of antibiotic resistance with prolonged use. Therefore, there is a need to enhance the therapeutic efficacy of neomycin sulfate while minimizing its side effects.[7]

Tea tree oil (TTO), derived from the leaves of Melaleuca alternifolia, is a natural essential oil with well-documented antimicrobial and anti-inflammatory properties. Its effectiveness against a wide range of microorganisms, including bacteria, fungi, and viruses, makes it a valuable addition to topical formulations for skin infections. The incorporation of tea tree oil into a topical drug delivery system not only provides a synergistic antimicrobial effect when combined with conventional antibiotics like neomycin sulfate but also offers additional benefits such as reducing inflammation and promoting skin healing.[8]

The objective of this study is to develop and evaluate a topical drug delivery system in the form of an emulgel containing neomycin sulfate and tea tree oil for the treatment of bacterial skin infections. The formulation aims to leverage the potent antibacterial activity of neomycin sulfate and the broad-spectrum antimicrobial and anti-inflammatory properties of tea tree oil to create an effective and patient-friendly treatment option.

Materials

Neomycin Sulphate and Tea Tree Oil are purchased from Yarrow chem. Product, Mumbai. Carbomer 934 is purchased from S.D Fine chem.pvt ltd, Mumbai. Span 20 and Tween 20 are purchased from Loba chemical. Liquid paraffin, Propylene Glycol and Triethanolamine are purchased from Thermo-Fisher Scientific, Pvt Ltd Mumbai. Methyl and Propyl Paraben are purchased from Hi-Media Laboratories Pvt Ltd, Mumbai

Preformulation Studies

Organoleptic Properties

The use of sight to evaluate neomycin sulphate by human senses expressed the qualities of neomycin sulphate. The sensory evaluation of neomycin sulfate was conducted which included testing the visual appearance of its overall condition, with respect to the color, odor, and homogeneity.[9]

Solubility Study

First, measure the neomycin sulfate powder with a balance and put it in a test tube with a volume of 10 ml, followed by 1 ml of methanol, acetic acid, dimethyl ether, DMSO, chloroform and water.[10]

pH Determination

Decide the pH of neomycin sulfate using a digital pH meter. Measure 25 mg of neomycin sulfate powder and dissolve it in 25 ml of purified water. Use distilled water to clean the pH meter electrode before placing it in the liquid. The electrode is then put in the solution and the pH value is recorded.[11]

Melting Point

Take 50 mg of neomycin sulfate and determine its melting point using the capillary method. The 1 mm diameter end of the capillary tube can be heated and sealed. The powder can be placed on a plate with a hole made of breathable porcelain and then allowed to flow into the capillary itself. Then place the open end of the capillary tube near the group. Some of the medicine will go into the tube. Slowly and carefully tap the perforated plate end of the sealed tube onto the top of the pile. The depth at the top of the pipe is 2-3 mm. The sample is continuously heated when the capillary is exposed to the molten medium.[12]

UV Spectroscopy

A quantity of 10mg of Neomycin sulphate was measured and put into a volumetric flask with a capacity of 10 ml. The solution is diluted with water to achieve a volume of 10ml, resulting in a concentration of 1000µg/ml.A volume of 1ml is removed from the prepared standard stock solution and then poured into a 10ml volumetric flask. The leftover level is reached by adding water. The sample was scanned by UV-spectrophotometer(UV-1800 Shimadzu, Japan) within the wavelength range of 200-400nm, with water used as the reference solution. The peak absorbance of the sample is registered.[13]

FTIR (Fourier Transform Infrared Spectroscopy)

The FT-IR spectra which will be taken at 400–4000 cm−1 at a resolution of 4.0 cm−1 and 20 co-added scans will have a thickness will be prepared by placing the mixtures in KBr disks using 1:100 of the mass ratio. The FTIR spectrometer-8400S will be used to get the samples FT-IR spectra.[14]

Method

Gel Preparation: In a 100-ml beaker, take about 40 ml of diminealized water and mix at a speed of around 800 rpm. A precisely measured amount of Carbopol 934 was added pinch by pinch to the stirring solution mentioned above and stirred for 10 minutes.[15]

Emulsion Preparation: 10 ml of distilled water was used to dissolve 0.5% w/w tween 20 in order to create an aqueous phase. Then propylene glycol was combined with methyl paraben and propyl paraben, and they were eventually mixed in with the aqueous phase. 1% w/w spam 20 was mixed with the liquid paraffin in order to create an oil phase, and in this oil phase, 0.25% of the medication was dissolved in ethanol. The oily and aqueous phases were warmed up independently in a water bath to 80 °C.The oil phase and aqueous phase were mixed to create the emulsion by using a mechanical stirrer for 20 minutes. The mixture was cooled to room temperature after being stirred.[15]

Emulgel Preparation: Add emulsion solution to the gel drop by drop, stirring continuously at a moderate speed. Triethanolamine (TEA) has been used to bring the pH down to 6 or 6.5.Continued stirring for 5 minutes, led to the creation of emulgels that were more consistent.[15]

Table 1: Composition of neomycin sulphate emulgel

Ingredient	F1	F2	F3	F4	F5
Neomycin sulphate	250mg	250mg	250mg	250mg	250mg
Carbopol 934	0.30g	0.50g	0.50g	1g	1.5g
Liquid paraffin	3ml	3ml	3ml	3ml	3ml
Tea tree oil	1ml	2ml	3ml	4ml	5ml
Span 20	0.5ml	0.5ml	0.5ml	0.5ml	0.5ml
Tween 20	1ml	1ml	1ml	1ml	1ml
Propylene glycol	3ml	3ml	3ml	3ml	3ml
Methyl paraben	0.03g	0.03g	0.03g	0.03g	0.03g
Propyl paraben	0.02g	0.02g	0.02g	0.02g	0.02g
Triethanolamine	q.s	q.s	q.s	q.s	q.s
Purified water	q.s	q.s	q.s	q.s	q.s

Evaluation of Emulgel Formulations

Physical examination

The emulgel compositions were visually inspected to determine their color, homogeneity, and consistency.[16]

pH determination

The pH of the formulation was measured with a digital pH meter. The pH meter electrode was cleaned with distilled water before being dipped into the liquid, and this process was repeated three times.[17]

Rheological studies

20g of the prepared emulgel is put in a 25-ml beaker, and the viscosity of the various emulgel formulations is measured with a Brookfield viscometer (cone and plate) with spindle numbers 55, 63, or 64. [18, 19]

Spreadability

It may be calculated by applying Mutimer's slip and drag approach. Apply 2 grams of emulgel on the bottom side. Attach one side to a wooden block and form a sandwich with another glass slide of the same size bound with a hook and weighing 500 milligrams. After five minutes, the pan attached to the second slide received more weight. The time taken to cross a 5cm distance with the top slides was recorded. [20]The spreadability was calculated using the formula:

Spreadability (S) = M * L / T

Where, M = Weight tied to upper slide

L = Length of glass slides

T = Time taken to cover distance by upper slide

Skin irritation test

Human volunteers' skin is frequently checked for skin irritation in accordance with their written informed consent agreement. The created drug is put to the skin of the hand, and any unfavorable effects are observed. [21]

Zeta potential

Zetasizer (malvern zetasizer) determines the zeta potential of an emulgel formulation. The formulation is put in a transparent, disposable zeta cell, and the outcome is determined. Curvettes are washed with methanol before being put in the sample.[22]

TEM microscopy
Transmission electron microscopy validated the emulgel composition following hydration. To prepare the samples, phosphate buffer (pH 5.5) was added to the emulgel and manually shaken for 1 minute. After 15 minutes, a drop of the sample was put on a carbon-coated copper grid and negatively stained with a 1% aqueous solution of phosphotungstic acid. After air drying the grid, samples were inspected using a TEM (FEI TecnaiTM G2)

SEM microscopy
Morphology and structure of sample will be examined using scanning electron microscopy (SEM JSM-6360 (JEOL Inc. Japan) from the samples a small drop of sample will be air dried by oven drying and sprinkled on SEM stub (pins) using double side adhesive tape and coated with aluminium at 20mA for 6minute through sputter-coater (Ion-Sputter JFC100). A scanning electron microscope with secondary detector will be used to obtain digital images of samples at an accelerating voltage of 15kV.

In Vitro drug release study
In vitro drug release study is done with a Franz diffusion cell in emulgel. It aids in figuring out the medication release [23]

Stability studies
The emulgels were stored in hard conditions and packed in aluminum collapsible tubes, and their stability was investigated. [24]

Results and Discussion

Organoleptic Properties
Neomycin sulphate is odourless, which makes it suitable for dermatological formulations where it is important to minimize potential irritating effects by avoiding fragrances. Neomycin sulphate exhibits an absence of odour, rendering it appropriate for dermatological formulations where it remains crucial to reduce possible irritation by the exclusion of fragrances.

Table 2: Organoleptic properties of Neomycin Sulphate

S.No	Properties	Outcome
1.	**Color**	White to slightly yellow
2.	**Shape**	Powder
3.	**Odour**	Odourless
4.	**Texture**	Fine and grainy
5.	**Taste**	Bitter taste

Solubility Study
Neomycin is Very soluble in distilled water because neomycin sulphate comes under BCS III classification.

Table 3: Solubility of neomycin sulphate in different solvents

S.No	Parameters % w/w	Solubility
1.	**Methanol**	Slightly soluble
2.	**Distilled water**	Very soluble
3.	**Chloroform**	Slightly soluble
4.	**DMSO**	Insoluble
5.	**Acetic acid**	Insoluble
6.	**Dimethyl ether**	Soluble

Melting Point
Neomycin sulphate, in its crude drug form, does not exhibit a distinct melting point. The capillary method is used to determine the melting point of neomycin sulphate. The melting point was found to be 192º C which are well within the range. Consequently, neomycin sulphate should be stored in a cool, dry environment, protected from excessive heat and light, to maintain its stability and therapeutic effectiveness throughout its shelf life.

Determination of Lamda max and Calibration curve
The λmax of standard neomycin sulphate was measured by UV-VIS double beam spectrophotometer (Shimadzu-1800, Japan). The λ max of standard neomycin sulphate was found to be of 268nm. UV spectrum of standard neomycin sulphate shown in Fig .1

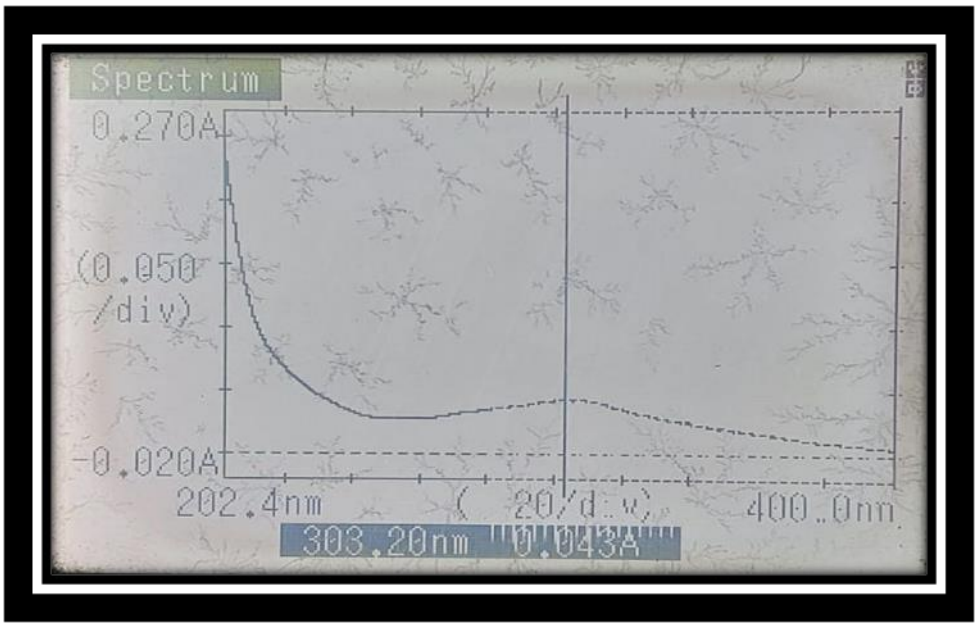

Figure 1. Lamda max of Neomycin sulphate

A standard calibration curve was created; data of standard neomycin sulphate against various concentrations versus absorbance was plotted. The graph showed linear relationship between absorbance and concentration (Fig. 7.2)

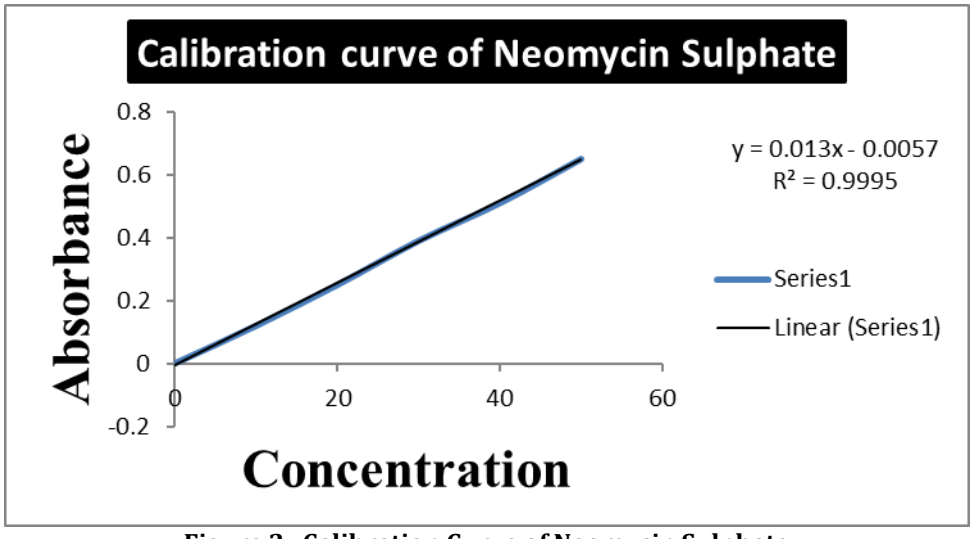

Figure 2. Calibration Curve of Neomycin Sulphate

FTIR (Fourier Transform Infrared Spectroscopy)

A FTIR spectrum of neomycin sulphate gives an idea about different specific functional groups in the molecule which is responsible for absorbing infrared radiation at particular wavelengths. The FTIR spectra of samples will be taken by an FT IR spectrometer 8400S (Shimadzu, Japan).

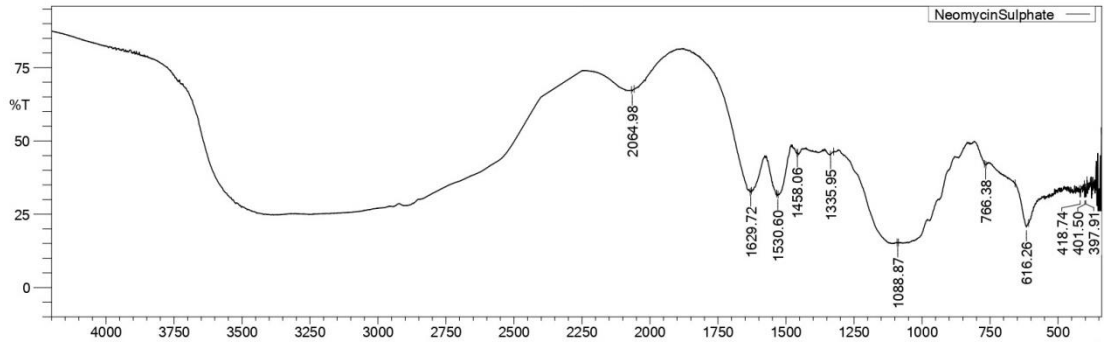

Figure 3 FTIR spectrum of Neomycin sulphate

Table 4: Peak and functional groups of Neomycin sulphate

	Peak (wavelength) cm^{-1}(observed)	Peak (wavelength) cm^{-1}(standard)	Functional Group	Vibration Type
1	766.38	900 -700	C-H (Aromatic)	C-H bending
2	1088.87	1000 – 1300	C-O (Ether), C-N (Amine)	C-O and C-N stretching
3	1458.06	1400 – 1460	C-H (Alkane)	C-H bending
4	1530.60	1550 – 1500	N-H (Amide)	N-H bending
5	1629.72	1650 – 1550	C = O (Amide)	C=O stretching

Evaluation of Emulgel Formulations

Physical Appearance

The physical appearance of neomycin sulphate emulgel formulations involves evaluating several key attributes, including color, consistency, homogeneity, and phase separation.

Table 5. Physical Appearance of the formulation

Formulation	Color	Texture	Homogeneity	Phaseseparation
F1	White	Viscous, Gel-like	Homogeneous	None
F2	Off- white	Smooth , Gel-like	Homogeneous	None
F3	Off- white	Thick, Creamy	Homogeneous	None
F4	White	Viscous, Gel-like	Homogeneous	None
F5	Off- white	Smooth, Fluid	homogeneous	None

pH determination

The pH determination of neomycin sulphate emulgel formulations ensures that the product is within the desired pH range for optimal performance and safety. Regular pH monitoring helps in maintaining the quality and efficacy of the formulations.Desired pH range for the emulgel formulation to ensure skin compatibility and stability. Typically, the pH range for Neomycin sulphate emulgel formulations is around 5.5 to 7.0, which are similar to the ph of skin.

Table 6. pH of the formulations

Formulations	pH			Average (n = 3)
F1	6.5	6.9	7.0	6.5
F2	6.5	7.0	7.5	7
F3	5.9	6.5	6.7	6.5
F4	6.0	6.9	7.5	6.9
F5	5.5	6.0	6.7	6.0

Rheological studies

The viscosity of neomycin sulphate emulgel formulations is a critical parameter impacting both pharmaceutical formulation design and therapeutic efficacy. The Brookfield viscometer is used to measure the viscosity of neomycin sulphate emulgel formulations at 100 rpm with spindle no 64 at room temperature.

Table 7. Rheological studies of formulations

Formulation	Average viscosity (cP)	Standard Deviation (cP)	ReportedViscosity (cP)
F1	6400	141.42	6400 ± 141.42
F2	5960	86.02	5960 ± 86.02
F3	6800	79.05	6800 ± 79.05
F4	7050	70.71	7050 ± 70.71
F5	6200	81.24	6200 ± 81.24

Spreadability

Spreadability measures the ability of a gel formulation to spread evenly over a surface. Formulations F1 to F5 demonstrate spreadability values ranging from 4.7 to 6.6 g.cm./sec. Higher spreadability values indicate that the gel can spread more easily, facilitating uniform application and coverage over the skin or affected area.

Zeta potential

Zeta potential reflects the electrostatic stability of colloidal dispersions, indicating the magnitude of repulsive or attractive forces between particles. The formulations exhibit zeta potentials 24.1,zeta deviation to be 4.36 (mV) and the conductivity (mS/cm) 0.0188 indicating good stability of the formulation. These values suggest that all formulations possess relatively stable dispersions, with repulsive forces predominant, thereby mitigating particle aggregation and ensuring formulation stability.

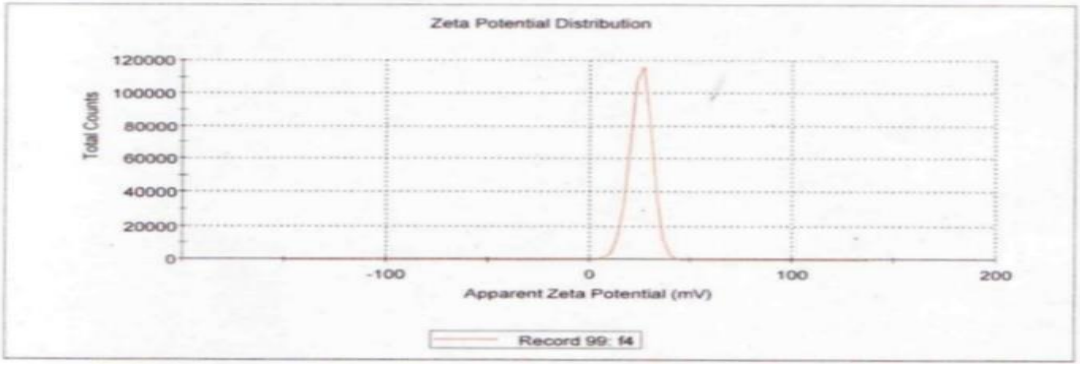

Figure 4 : Zeta potential of Neomycin sulphate Emulgel

TEM microscopy

Transmission Electron Microscopy (TEM) is a powerful imaging technique used to analyze the microstructure and morphology of neomycin sulphate emulgel formulations at the nanoscale level. This technique provides detailed information about the size, shape, distribution, and organization of particles within the emulgel matrix, offering insights into its physical properties and stability.

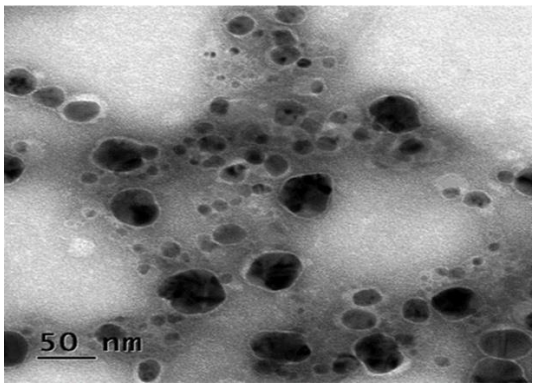

Figure 5: TEM of Neomycin sulphate Emulgel

SEM microscopy

Scanning Electron Microscopy (SEM) is an invaluable tool for examining the surface morphology and microstructure of neomycin sulfate emulgel formulations. This technique provides high-resolution images that reveal details about the physical characteristics, particle size, distribution, and interactions within the emulgel matrix**.**

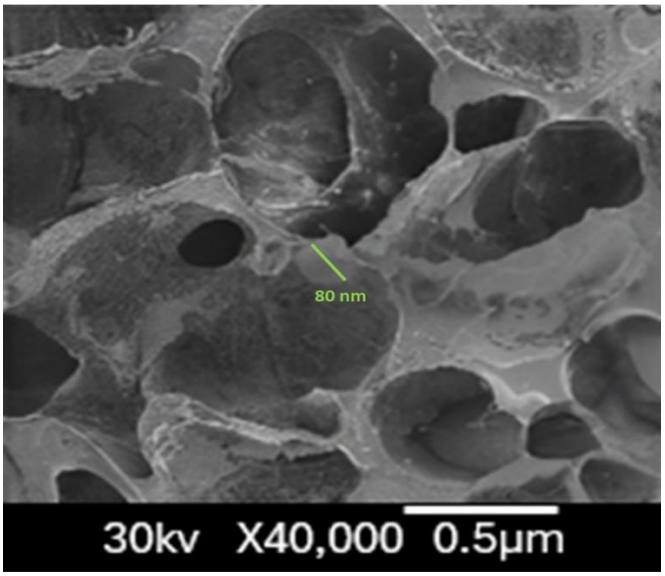

Figure 6: SEM of Neomycin sulphate Emulgel

In Vitro drug release study

It was performed using franz diffusion cell and egg cell membrane. Resultant solution within the chamber was examined in UV- spectroscopy

Table 8: Results of In Vitro drug release

Time (min)	F1	F2	F3	F4	F5
15	9.5	10.76	15.1	13.5	10.55
30	17.23	15.78	30.2	22.4	15.87
45	25.6	25.87	45.1	33.5	24.56
60	34.78	34.87	52.56	45.6	34.44
120	44.65	45.87	55.45	60.4	43.67
180	45.56	55.76	55.77	60.4	55.45
240	45.58	56.78	55.78	61.5	56.45
300	45.62	56.78	55.79	61.4	56.45
360	45.65	56.79	55.78	61.7	56.44
420	45.66	56.79	55.78	61.9	56.45

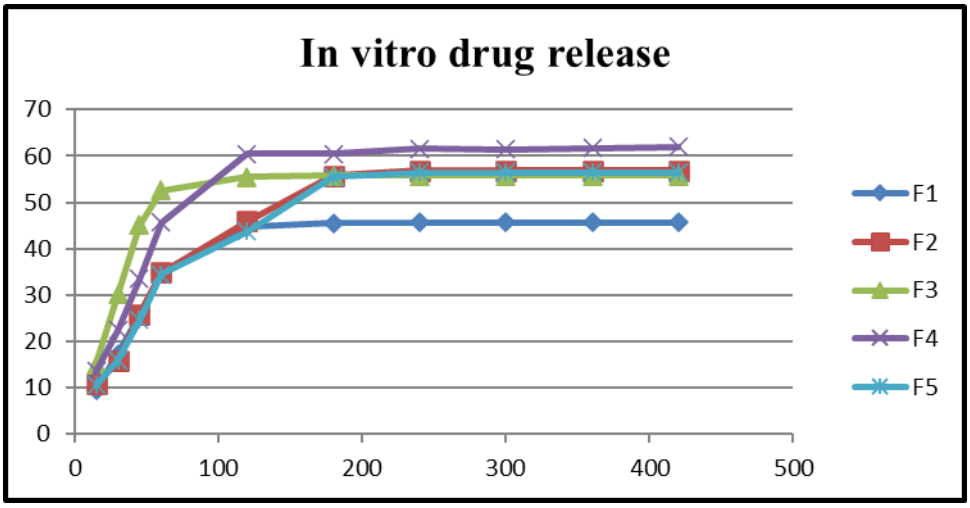

Figure 7: Graphical representation of drug release

Stability studies

Stability studies were conducted at 25^{0}C±2 ^{0}C temperature and 60 ±5% Relative Humidity. It was found that formulation was stable physically as well as chemically. There was no change in the evaluation parameters, such as the viscosity and pH.

Table 9: Stability studies of formulations, based on viscosity and pH

Viscosity(25^{0}C±2 ^{0}C and 60 ± 5% RH)					
Time (Days)	**F1**	**F2**	**F3**	**F4**	**F5**
0	6401	6400	6401	6400	6400
30	5962	5962	5960	5960	5960
45	6806	6805	6804	6803	6803
60	7053	7054	7053	7051	7052
90	6202	6202	6201	6202	6201

pH Study					
Time (Days)	**F1**	**F2**	**F3**	**F4**	**F5**
0	6.8	6.7	6.8	6.9	6.8
30	7.1	7.0	7.3	7.0	7.2
45	6.6	6.5	6.4	6.5	6.5
60	6.8	6.8	6.4	6.6	6.9
90	6.1	6.3	6.2	6.3	6.1

Conclusion

The Neomycin Sulphate Emulgel prepared with tea tree oil and the various formulations are presented by the help of Incorporation method and the better formulations are given is F4.The formulations are given better viscosity, pH and in vitro study was given in the result and discussion The neomycin sulphate emulgel with tea tree oil shows promise as an effective topical treatment for bacterial skin infections, offering enhanced antibacterial activity and potentially reducing the risk of resistance development. Further clinical studies are warranted to confirm these findings.

Acknowledgement

I would like to express my sincere gratitude to all those who have supported and contributed to this research project. I am grateful to Kailash Institution of Pharmacy and Management, Gida, Gorakhpur for providing the facilities and resources necessary to carry out this study. Special thanks to Dr. J.N Mishra and Amerendra Singh for their guidance, insightful feedback, and encouragement throughout the research process.

REFERENCES

1. Bansal MO, Jamil SH. Micellar micro particles: A novel approach to topical drug delivery system. Int. J. Appl. Pharm. 2018; 10:1-5.
2. Panwar, A., Upadhyay, N., Bairagi, M., Gujar, S., Darwhekar, G., & Jain, D. (2011). Emulgel: A review. Asian J Pharm Life Sci, 2231, 4423.
3. Vishwakarma, G., & Panwar, A. S. (2022). Emulgel emergent systems: at a glance for topical drug delivery. Asian J Pharm Clin Res, 15(3), 8-14.
4. Sultana SS, Parveen P, Rekha MS, Deepthi K, Sowjanya CH, Devi AS. Emulgel-a novel surrogate approach for transdermal drug delivery system. Ind Am J Pharm Res. 2014; 4:5250-65.
5. Kute SB, Saudagar RB. Emulsified gel A Novel approach for delivery of hydrophobic drugs: An overview. Journal of Advanced Pharmacy Education and Research. 2013; 3(4):368-76.
6. Lakshmi SS, Divya R, Rao SY, Kumari KP, Deepthi K. Emulgel-novel trend in topical drug delivery system-review article. Research journal of pharmacy and Technology. 2021; 14(5):2903-6.
7. Martindale: The Complete Drug Reference. 39th Edition. Pharmaceutical Press.
8. Garson, C.F., Hammer, K.A., & Riley, T.V. "Melaleuca alternifolia (Tea Tree) Oil: a Review of Antimicrobial and Other Medicinal Properties," Clinical Microbiology Reviews, 2006.
9. Wehrle, Pascal, Daniel Korner, and Simon Benita. "Sequential statistical optimization of a positively-charged submicron emulsion of miconazole." Pharmaceutical Development and Technology 1.1 (1996): 97-111.
10. Eccleston J. Microemulsions. In: Swarbrick J, Boylan JC, eds. Encyclopedia of Pharmaceutical Technology. vol. 9. New York, NY: Marcel Dekker; 1994:375-421
11. Gossel TA, "Topical Antifungal Products,"U.S. Pharmacist 10 (June), 44–46 (1985).
12. Pedersen, Morten, and Margrethe R. Rassing. "Miconazole chewing gum as a drug delivery system test of release promoting additives." Drug development and industrial pharmacy 17.3 (1991): 411-420.

13. Lawrence, M. Jayne, and Gareth D. Rees. "Microemulsion-based media as novel drug delivery systems." Advanced drug delivery reviews 45.1 (2000): 89-121.
14. Srivastava, A., Desai, S., Jain, H., & Meshram, D. B. (2020). Formulation and evaluation of fusidic acid emulgel. Journal of drug delivery and Therapeutics, 10(3-s), 169-175.
15. Sainy J, Atneriya U, MAHESHWARI R. Development of an Aloe vera-based Emulgel for the Topical Delivery of Desoximetasone. Turkish Journal of Pharmaceutical Sciences. 2021 Aug;18(4):465.
16. Ambhore NP, Dandagi PM, Gadad AP, Mandora P. Formulation and characterization of tapentadol loaded emulgel for topical application. Indian J. Pharm. Educ. Res. 2017 Oct 1; 51:525-35.
17. Yadav SK, Mishra MK, Tiwari A, Shukla A. Emulgel: a new approach for enhanced topical drug delivery. Int J Curr Pharm Res. 2016; 9(1):15-9.
18. Redkar MR, Patil SV, Rukari TG. Emulgel: A modern tool for topical drug delivery. World Journal of Pharmaceutical Research. 2019 Jan 29; 8(4):586-97.
19. Hyndari N, Koorapati S, & Mamidibathula L. "Formulation and evaluation of aceclofenac lycopene transemulgel". World J.pharm Res 2,4 (2013) ; 1036-1045.
20. Singh RP, Parpani S, Narke R, Chavan R. Emulgel: A recent approach for topical drug delivery system. Asian Journal of Pharmaceutical Research and Development. 2014 Mar 1:112-23.
21. Inamdar SN, Nirmal S, Londge D, Manmode P. A review on emulgels drug delivery system. International Journal of Pharmacy & Pharmaceutical Research (2023) 26(4); 78-94.
22. Dhokale NN, Sangle SJ, Rajole SR, Rajput SU. "Emulgel – novel drug delivery system. Journal of emerging technologies and innovative research. Vol.9, Issue 5, page no.b390-b399, May-2022
23. Sreevidya VS. An overview on emulgel. International Journal of Pharmaceutical and Phytopharmacological Research. 2019; 9(1):92-7.
24. Jain A, Gautam SP, Gupta Y, Khambete H, Jain S. Development and characterization of ketoconazole emulgel for topical drug delivery. Der Chemica Sinica. 2010.