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DEVELOPMENT AND EVALUATION OF TOPICAL GEL FORMULATION CONTAINING MAGNESIUM CHLORIDE FOR CELLULITIS MANAGEMENT

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ABSTRACT

This research aimed to develop and evaluate topical gel formulations of magnesium chloride for the management of cellulitis, focusing on optimizing drug delivery through the use of the gelling agent hydroxypropyl methylcellulose (HPMC). The study commenced with comprehensive pre-formulation investigations, including organoleptic assessment, solubility profiling, and determination of the absorption maxima for magnesium chloride. Five gel formulations with varying HPMC concentrations were prepared using the cold mechanical method, with consistent drug levels across batches. The prepared gels were systematically characterized for physical appearance, pH, viscosity, spread ability, drug content uniformity, swelling index, antimicrobial efficacy, in vitro drug release, and stability. Experimental results revealed that increasing HPMC concentration produced gels with greater viscosity and reduced spread ability, with formulation F3 (3% HPMC) achieving an optimal balance for topical application. All formulations exhibited homogeneity, stability, and no phase separation. F3 demonstrated uniform drug distribution (97.6%), excellent swelling behaviour, and significant in vitro antimicrobial activity against Staphylococcus aureus, exhibiting the largest zone of inhibition. Drug release studies illustrated a sustained release profile, with F3 achieving the highest cumulative release (95%) over 5 hours, following zero-order kinetic behaviour. Stability studies confirmed that F3 maintained physical integrity, pH, viscosity, drug content, and release characteristics over a storage period. The findings underscore the pivotal role of HPMC as a gelling agent in modulating gel viscosity, drug release, and therapeutic performance. Formulation F3 was identified as the most promising candidate, providing robust physical stability, effective sustained drug release, and antimicrobial action. These results support the potential of HPMC-based magnesium chloride gel as an efficient topical delivery system, with meaningful implications for future clinical development and transdermal magnesium supplementation.

KEYWORDS: Magnesium chloride, Topical delivery, HPMC, Drug release.

INTRODUCTION

Cellulitis is an acute bacterial infection of the dermis and subcutaneous tissue, commonly caused by *Streptococcus* and *Staphylococcus aureus*. It presents with redness, warmth, pain, swelling, and fever, most often affecting the lower limbs. Risk factors include skin injury, oedema, obesity, diabetes, venous insufficiency, and immunosuppression. The infection arises when bacteria enter through a disrupted skin barrier. Treatment involves use of antibiotics usually penicillin or clarithromycin, for allergies and supportive care, such as limb elevation, wound cleaning, and hydration are employed. Prevention includes managing underlying conditions, protecting the skin, completing antibiotics, and seeking prompt medical attention for severe symptoms.[1,2]

Dead Sea therapy, practiced for centuries, is widely used to treat chronic inflammatory and skin conditions such as psoriasis, dermatitis, and arthritis. Its therapeutic benefits are primarily attributed to the high concentration of minerals, particularly magnesium salts, found in Dead Sea water. Magnesium plays a vital role in reducing inflammation, regulating ion transport, signal

transduction, cell proliferation, and energy metabolism. Deficiency in magnesium is linked to various disorders, including hypertension, type 2 diabetes, osteoporosis, and migraines. For topical magnesium to exert beneficial effects, it must effectively penetrate the stratum corneum, the outermost skin barrier. Transdermal absorption depends on factors such as skin hydration, integrity, and the presence of pathways like sweat glands and hair follicles. Substances cross the skin through diffusion and intercellular routes, allowing both lipid-soluble and water-soluble molecules to pass. However, the mechanisms and efficiency of magnesium ion absorption and its immunological effects remain not fully understood.[3,4]

The present research work aimed to develop and evaluate topical gel containing magnesium chloride for cellulites management.

The objectives of the present work were

- To perform pre-formulation studies: solubility studies by qualitative analysis,
- To determine the λ max & develop standard curve by atomic absorption spectroscopy.
- To formulate gel containing Magnesium chloride.
- To carry out the evaluation of prepared gel formulation for physical examination, viscosity, pH, spread ability, drug content, and drug release kinetics.
- To determine the Anti-Cellulitis Activity
- To carry out *In vitro* drug diffusion study
- To carry out stability studies of formulations.

MATERIALS AND METHODOLOGY

1. MATERIALS

Magnesium chloride obtained from Karnataka Fine Chem®, Bangalore. Hydroxypropyl methylcellulose (HPMC) purchased from Hi Media Laboratories Pvt. Ltd. Glycerine was supplied by Karnataka Fine Chem®, Bangalore. Propelene glycol was procured from Sisco Research Laboratories Pvt. Ltd, Mumbai. Triethanolamine was supplied by Karnataka Fine Chem®, Bangalore. Methyl paraben was supplied by Loba chemie Pvt Ltd, Mumbai. All chemicals and solvents used were of analytical grade.

2. METHODOLOGY

PRE-FORMULATION STUDIES

Pre-formulation is the initial stage of drug development focused on evaluating the physicochemical and biopharmaceutical properties of a drug. It provides essential data for rational formulation design through drug characterization and assessment of excipient properties and compatibility.

Physical Characterization

i. Organoleptic Characteristics

The sample of Magnesium chloride were studied for organoleptic properties such as colour, odour and taste.[5]

ii. Solubility

The solubility of the drug was determined by placing 5-10 mg of the sample in a cleaned, dried 10 ml volumetric flask. 10 ml of each solvent (purified water, ethanol, methanol, chloroform, DMSO, and pH 7.4 phosphate buffer) were added separately. The flasks were shaken and, if needed, sonicated for 30-60 min. Solubility was recorded at room temperature and measurements were performed in triplicate.[6]

ANALYTICAL METHOD USED IN DETERMINATION OF MAGNESIUM CHLORIDE

i. Determination of Absorption Maxima (λmax)

An accurately weighed 10 mg of Magnesium chloride was dissolved in 5 ml of water and diluted to 10 ml with phosphate buffer solution (pH 7.4) in a volumetric flask, yielding a stock solution of 1000 µg/ml. Different aliquots were taken from stock solution and diluted with phosphate buffer solution of pH 7.4 and analysed spect rophoto metrically to determine λmax.[7]

ii. Standard Calibration Curve

A calibration curve for Magnesium chloride was prepared by dissolving various concentrations (1–5 ppm) in phosphate buffer (pH 7.4). Absorbance was measured at 285 nm using an Atomic Absorption Spectrometer () with phosphate buffer as the blank. The calibration curve was plotted as absorbance versus concentration, and the regression equation was obtained.[8]

FORMULATION OF MAGNESIUM CHLORIDE TOPICAL GEL

Gel was prepared by cold mechanical method.[9]

Step 1- Required quantity of polymer (HPMC) was weighed and it was sprinkled slowly on surface of purified water for 2 hrs. After which it was continuously stirred by mechanical stirrer, till the polymer is dissolved in the water.

Step 2- Triethanolamine was added with continuous stirring to neutralize the gel and it maintains the pH of the gel. Then the appropriate quantity of Propylene Glycol was added to the gel, which acts as the penetration enhancer, followed by the required quantity of methyl paraben as a preservative.

Step 3- Finally the drug Magnesium chloride were added to the gel with continuous stirring till all the ingredients get dispersed in gel completely. The quantity of each formulation material is mentioned below in Table number 1,

Table 1: Formulation of Magnesium chloride gel.

SI. No	Ingredients	Formulations				
		F1	F2	F3	F4	F5
1	Magnesium chloride (%)	4	4	4	4	4

2	HPMC (%)	2	2.5	3	4	5
3	Glycerine(ml)	5	5	5	5	5
4	Propylene Glycol(ml)	5	5	5	5	5
5	Triethanolamine (ml)	0.23	0.23	0.23	0.23	0.23
6	Methyl Paraben	0.02	0.02	0.02	0.02	0.02
7	Distilled water up to 100 ml					

CHARACTERIZATION OF TOPICAL GEL

i. Physical appearance

The prepared formulation was systematically evaluated for their physical properties, including color, overall appearance, homogeneity, and presence of lumps by visual inspection after the gels is prepared.

ii. Determination of pH

Digital pH meter was used to determine the pH of the Magnesium chloride gel. The pH meter was calibrated previously with buffered solution pH 4.0, 7.0 and 10.0. In 25ml of distilled water 1m of gel was dispersed and electrode then become immersed in to the gel formulation for 30 minutes till the constant reading was attained. Each formulation pH was measured and replicated three times and calculated the average value.[10]

iii. Viscosity determination

Viscosity of the Magnesium chloride gel was measured at 25 ± 0.5°C using a Brookfield RV viscometer fitted with spindle RV-7. The gel was equilibrated to room temperature, carefully transferred to a 250 mL beaker, and the spindle was cantered without contacting the bottom. Apparent viscosity (cP) was recorded after stabilization at successive rotational speeds (0.5-20 rpm), maintaining instrument torque between 1090%. Measurements were performed in triplicate, and viscosity was reported as mean ± SD.[11]

iv. Spread ability detemination

Two glass slides were taken. Gel was placed on one slide and put another slide on gel in such way that gel get packed in between two slides to form thin layer. Removed the pressure and excess gel stick to the slides was scrapped off. The two slides were fitted to a stand in such a technique that lower slide was held firmly by means of opposite fangs of the clamp permitting allowing the upper slide to move freely along the surface through force of weight fixed to it. Twenty-gram weight was fixed to the upper slide with care. The time required for an upper slide to move the distance of 6cm and detached away from lower slide below the direction of weight was note down. Determined the spread ability of topical gel formulation which was calculated through following

$$S = \frac{M \times L}{T}$$

Where,
S- Spread ability
M = Weight fixed to upper slide
L = Slide length
T = Time required

The experiment was carried out in triplicate, and the average values were reported.

Higher spreadability values indicated better ease of application of the gel.[12]

v. Determination of drug content

Drug concentration in the gel was determined using an Atomic absorption spectroscopy. One gram of formulation was transferred into a 10 ml volumetric flask, dissolved in distilled water with frequent shaking, and the volume was made up to the mark with distilled water. The solution was filtered through filter paper to obtain a clear sample. The absorbance was recorded at 285 nm using an AAS. The experiment was carried out in triplicate to determine the average drug content of each formulation. The concentration of active ingredient present in 1 g of the formulation was calculated using the calibration curve by back-calculating drug concentration from the measured Absorbance.[13]
Drug Content = Concentration × Volume taken × Dilution factor x Conversion factor.

vi. Swelling Index

The effectiveness of polymers in pharmaceutical preparations improves when the macromolecule is fully swollen, as this enhances rheology modification, suspension stability in topical formulations.

The swelling behavior of the gel was evaluated by weighing 1 g of the formulation and placing it on a porous aluminium foil, which was then immersed in a 100 ml beaker containing 20 ml of 0.1 N sodium hydroxide. At predetermined time intervals, the samples were removed, and excess surface fluid was carefully blotted using filter paper. The samples with aluminium foil were reweighed until a constant weight was achieved. The initial weight of the gel at zero time (Wo) and the corresponding swollen weight after immersion (Wt) were recorded.[14] The Swelling index was calculated using
Swelling index (SW%) = $[Wt - Wo / Wo] \times 100$

Where,
(SW)% = Equilibrium percent swelling
Wt = Weight of swollen emulgel after time,
Wo = Original weight of emulgel at zero time.

vii. Anti- microbial Activity

The nutrient agar plate is been made, then the plate is autoclaved for sterilization for 30 min then the plate is removed from the autoclave. The plate is then taken to under laminar air flow, there the bacteria is incorporated in the plates and allowed for solidification. Then with the bore wells are made and gel formulation is incorporated inside the wells and put it for 30 min and then this plate is put in the incubator for incubation. Readings were taken after 24 hrs, 48hrs.[15]

***IN VITRO* DRUG RELEASE STUDY**

The drug release study was carried out using a Franz diffusion cell. A pre-soaked dialysis membrane was mounted between donor and receptor compartments. The receptor chamber was filled with phosphate buffer pH 7.4, maintained at 37 ± 0.5°C, and stirred continuously. An accurately weighed amount of Magnesium chloride gel was placed in the donor compartment. At fixed intervals (0.5-5 hr), 1 mL samples were withdrawn and replaced with fresh buffer. Samples were filtered and analysed using Atomic Absorption Spectroscopy at 285 nm. The cumulative percentage drug release was calculated and plotted against time to study release kinetics. All tests were performed in triplicate.[8]

Diffusion protocol

- Diffusion membranes: Cellophane Membrane
- Sample Quantity: 1g (Equivalent to 125 mcg)
- Temperature: 35 ± 0.5°C
- RPM: 300
- Diffusion medium: Phosphate buffer (pH 7.4)
- Volume of Diffusion medium: 50 ml
- Volume of sample removed: 1 ml
- Sampling intervals: 30min, 1hr, 2hr, 3hr, 4hr, 5hr.

***In-vitro* drug release kinetics[16]**

Kinetic analysis of drug release was performed by fitting the in vitro release data to various mathematical models to identify the most appropriate release mechanism. The models applied included zero-order, first-order, Higuchi, and Korsmeyer–Peppas equations. The correlation coefficient (R^2) and release constant (k) values obtained from each model were compared to determine the best-fit model. This analysis was carried out to elucidate the drug release mechanism of the Magnesium chloride gel formulated using HPMC.

Zero Order Release

Zero-order drug release describes a profile in which the drug is released at a constant rate over time, independent of its concentration. This ensures that the same amount of drug is released per unit time, regardless of the remaining drug content in the formulation.

The drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be expressed by the equation: $Q = Q_o + Kot$

where Q is the amount of drug released at time t, Q_o is the initial amount of drug in solution (generally zero), and K0 is the zero-order release constant. A plot of cumulative percentage drug release versus time typically gives a straight line if the release follows zero-order kinetics.

First Order Release

First-order drug release is a commonly applied kinetic model used to describe the release pattern of drugs from topical and other pharmaceutical formulations. In this model, the rate of drug release is directly proportional to the amount of drug remaining in the formulation. Unlike zero-order release, the release rate decreases over time as the concentration of the drug in the dosage form diminishes.

The release data were analysed according to the first-order equation

$$Kt \log C = \log C_0 - \frac{\quad}{2.303}$$

where C is the concentration of drug remaining at time t, C_0 is the initial drug concentration, and K is the first-order release constant. A plot of log cumulative percentage of drug retained versus time typically indicates whether the release follows first-order kinetics.

Higuchi Model

The Higuchi model is widely used to describe drug release kinetics from matrix-based topical formulations such as gels, creams, and ointments. This model assumes that drug release occurs primarily through diffusion, with the drug molecules gradually migrating from within the polymeric matrix into the surrounding medium.

The model is mathematically expressed as: Q = Kt1/2 where Q is the cumulative amount of drug released at time t, and K is the Higuchi release constant that incorporates system-related design variables.

Korsmeyer-Peppas Model

The Korsmeyer–Peppas model is a versatile kinetic model that can describe a wide range of drug release mechanisms, particularly from polymeric matrix systems. It is especially useful when the release mechanism is not well defined or when multiple processes may be involved.

Korsmeyer et al. (1983) proposed the following equation

$$Mt / M\infty = Kt^n$$

Where F is fraction of drug released at time t, Mt is drug release at time t, M is the total amount of drug in dosage form, Km is a constant dependent on the geometry of the dosage form, n is diffusion exponent indicating the mechanism of drug release.

Stability testing

Stability studies were carried out to evaluate the influence of formulation additives on drug stability and

to assess the physical stability of the prepared gel under standard storage conditions of temperature and relative humidity. Real-time stability testing was performed on the optimized formulations over a period of three months under ambient storage conditions. This modern approach to quality control enables the monitoring of product stability during actual storage.

For this purpose, formulations F3 (10 g each) were stored in tightly sealed glass containers at room temperature for three months. At the end of the storage period, samples were withdrawn and evaluated for various parameters including physical appearance, pH, viscosity, spreadability, drug content, and in vitro drug release profile.

RESULTS AND DISCUSSION

PREFORMULATION STUDY

Organoleptic Characteristics

The organoleptic evaluation of magnesium chloride typically includes its general characteristics, odour, colour, taste. It was observed that magnesium chloride is colourless, Deodorized and appears as a White or Colourless Crystalline Solid and the results are shown in Table 2.

Table 2: Organoleptic properties of Magnesium chloride.

Properties	Results
Description	White or Colourless Crystalline Solid
Taste	Bitter and Salty
Odour	Odourless
Colour	Colourless

Solubility Study

Solubility studies of magnesium chloride show that it is very soluble in purified water and slightly soluble in ethanol and methanol. It is insoluble in DMSO and chloroform. And poorly soluble in glycerol and results are shown in the Table 3.

Table 3: Solubility Study of Magnesium chloride.

Solvents	Solubility
Purified water	Very soluble
Ethanol	Slightly soluble
Methanol	Slightly soluble
Chloroform	Insoluble
DMSO	Insoluble
Glycerol	Poorly soluble

Determination of Absorption Maxima (λ max) of Magnesium chloride

An atomic absorption spectroscopy analysis established that the maximum absorption wavelength (λ max) for magnesium chloride is 285.2 nm, as shown in Figure 1. This peak closely matches values reported in the literature, confirming its accuracy. Therefore, this wavelength was selected for further quantitative analysis.

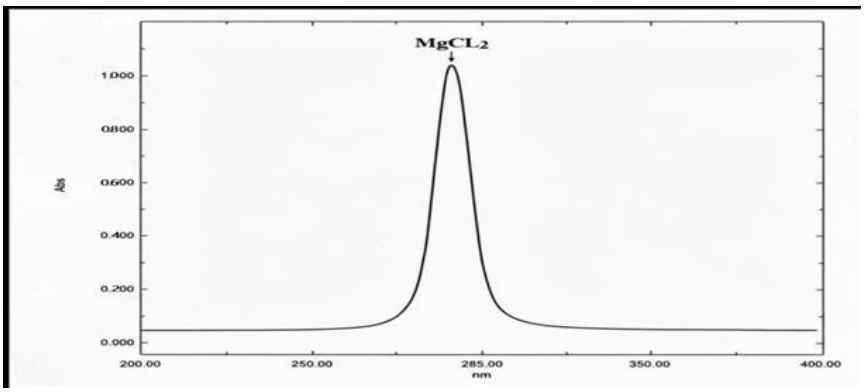

Fig 1: Determination of absorption maxima of Magnesium chloride.

Standard Calibration plot

A series of drug solutions with concentrations ranging from 2 µg/mL to 10 µg/mL were prepared using phosphate buffer (pH 7.4). Absorbance measurements were conducted at the absorption maximum (λ max) of 285.2 nm using atomic absorption spectroscopy, with a blank as reference. A calibration curve was constructed

by plotting concentration on the x-axis against absorbance on the y-axis, as depicted in the Figure 2.

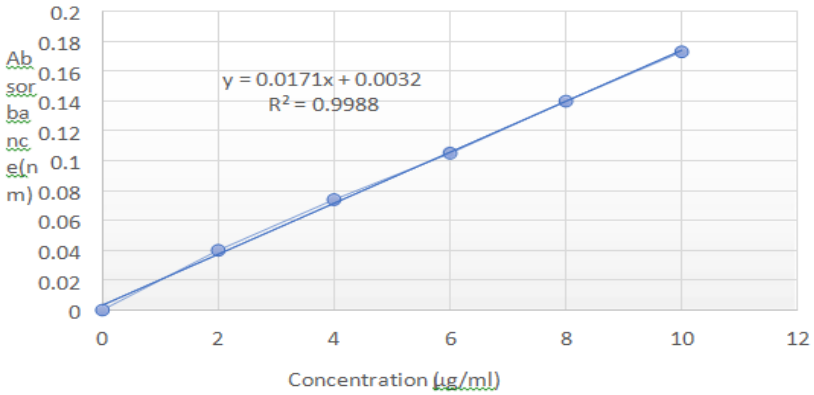

Fig 2: Standard calibration curve of Magnesium chloride.

The absorbance data was plotted against the concentration of the drug solution. The absorbance values showed linearity in the concentration range of 0–10 µg/ml, with the regression equation y = 0.0171x + 0.0032 and a correlation coefficient (R^2 = 0.9988) the corresponding standard calibration plot is depicted in Figure 2.

Preparation of Magnesium Chloride Topical Gel

Topical gels containing magnesium chloride were prepared by the cold mechanical method, magnesium chloride topical gels were successfully prepared by dispersing different concentrations of gelling agents while keeping the drug concentration constant across all formulations. Following the procedure outlined in the methodology section, a total of five gel formulations were developed.

Characterization of Magnesium Chloride Gel

i. Physical Parameters of Prepared Formulations

The formulations were evaluated for their appearance colour, homogeneity, and consistency.

- F1 and F2 formulation with lower HPMC concentrations were fluid in consistency due to the lower polymer content. F3 Formulation exhibited a clear transparent appearance, while F4 and F5 formulations with higher HPMC concentrations appeared thick and white due to the increased polymer content.
- All the formulations showed homogenous and consistent physical appearances. No phase separation was observed in any of the formulated gels.
- The results of the evaluation of various physical parameters are provided in Table 4, and the photographic representations of the formulations are displayed in Figure 3.

Table 4: Physical Parameters of a Magnesium chloride gel.

Formulation	Colour and appearance	Homogeneity	Phase separation
F1 (2% HPMC)	Clear, light, fluid	Excellent	None
F2 (2.5% HPMC)	Clear, light, fluid	Excellent	None
F3 (3% HPMC)	Clear, stable, uniform	Excellent	None
F4 (4% HPMC)	Clear, thick white	Excellent	None
F5 (5% HPMC)	Very thick white	Excellent	None

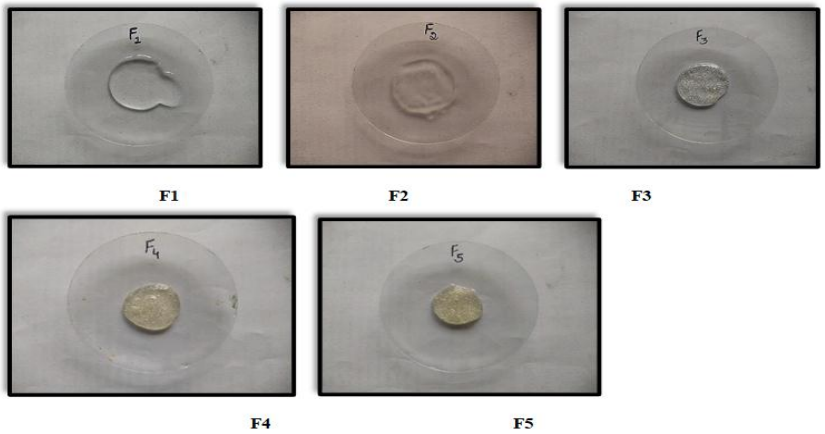

Fig 3: Photographic representations of magnesium chloride gel formulations (F1-F5).

ii. Determination of pH

The pH values of all prepared magnesium chloride gel formulations ranged approximately from 6.5 to 7.2. The pH stability across the formulations supports their suitability for use, these values fall within the acceptable range for topical formulations (5.5-7.0). Maintaining a near-neutral pH minimizes the risk of irritation while ensuring gel stability and compatibility and graphical representation of pH is shown in Figure 4.

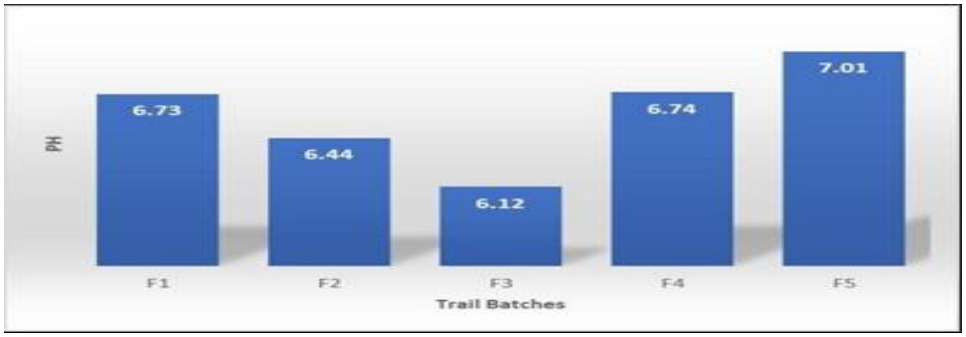

Fig 4: Graphical representation of Ph.

iii. Determination of Viscosity

Viscosity of the gel formulations from F1 to F5 was determined using a Brookfield RV viscometer. The study revealed that the formulation F1- F5 has viscosities ranging from 5,000 to 33,000. The gel was rotated at different speeds (rpm) with spindle no. 7, which is suitable for measuring high-viscosity gels. The viscosities demonstrate that formulation F1 and F2 showed too low viscosity and F3 exhibited moderate-high viscosity, providing an optimal balance of thickness and spread ability, which is ideal as it provides a smooth, easily spreadable gel with adequate consistency to stay on the skin without being too runny. while formulation F4 and F5 showed higher viscosity resulting in a thicker gel with reduced spread ability, graphical representation of Viscosity is shown in Figure 5.

iv. Spreadability Determination

Spreadability values ranged approximately from 6.54 g.cm/sec to 20.14 g.cm/sec across formulations F1 to F5. It was observed that spreadability decreased with increasing HPMC concentration.

F1 and F2 formulation exhibited higher spreadability values, indicative of softer gels that spread easily on application. F3 formulation showed moderate spreadability (10.29 g.cm/sec), which is considered acceptable for topical formulations, ensuring sufficient

consistency without being too runny. The formulation with the highest polymer concentration F4 and F5 resulted in a very stiff gel with reduced spreadability values and the Graphical representation of Spread ability is shown in figure 6.

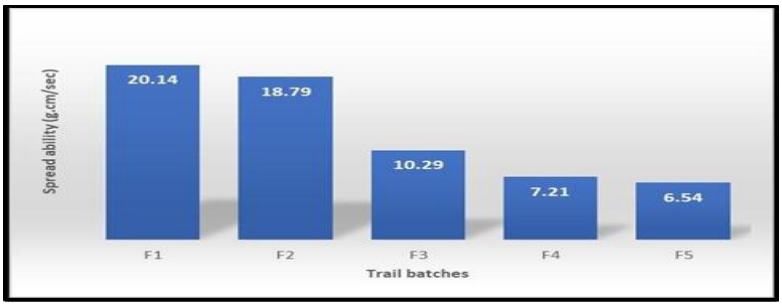

Fig 6: Graphical representation of Spread ability.

v. Drug Content Determination

The gel formulation was analysed for drug content by Atomic absorption spectroscopy in order to estimate the percentage of drug incorporated in the formulation. The Graphical representation of Drug Content is shown in figure 7.

The drug content of magnesium chloride gel was found to be in the range of 90.2% ± 0.521 to 97.6% ± 0.612. The results indicate that the drug was uniformly distributed throughout the gel formulations. The drug content values of formulation were within the specified acceptance range of 95–105%, indicating uniform distribution of drug in the formulations. The highest drug content was observed in F3 (97.6 ± 0.612 %), suggesting better entrapment efficiency and minimal drug loss during preparation.

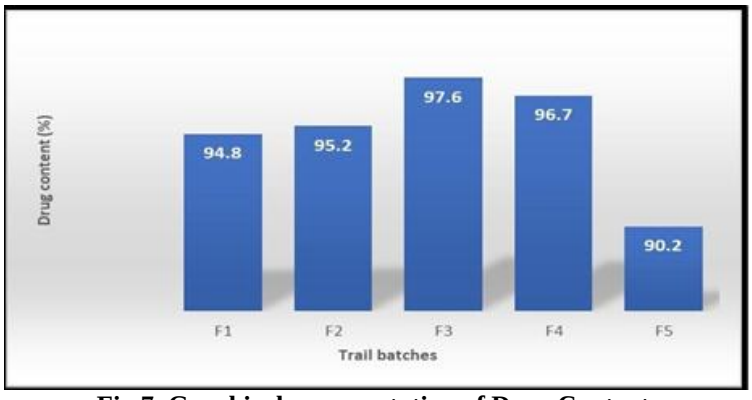

Fig 7: **Graphical representation of Drug Content.**

vi. Swelling index

The swelling index of Magnesium chloride gel for all the five formulation (F1-F5) was determined. The formulation exhibited a progressive increase in swelling index over 4 hours, reaching nearly 100% at the end of the study. The results confirm that F3 demonstrated excellent swelling behaviour, which may contribute to improved drug release performance compared to other formulations. The results of the swelling index are shown below in figure 8.

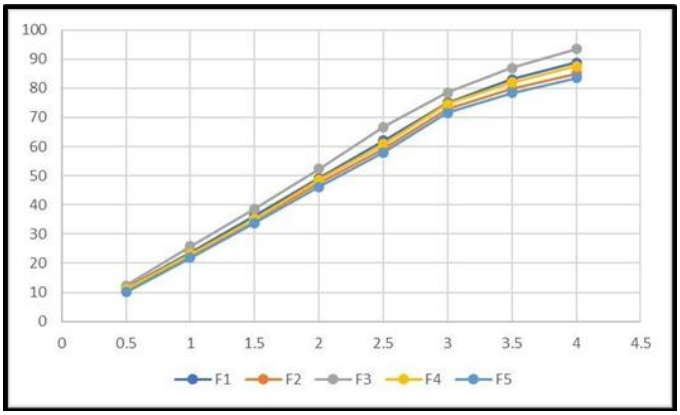

Fig 8: **Graphical representation of Swelling Index.**

vii. Anti-microbial activity

The antibacterial activity of the magnesium chloride gels against Staphylococcus aureus was evaluated using the agar well diffusion method. The zones of inhibition were measured for all the formulation, respectively and results are shown in Table 5. The larger inhibition zone exhibited by the F3 gel (21.5 mm) indicates a significantly stronger antibacterial effect compared to other formulation and graphical representation of Zone of Inhibition by Antimicrobial Activity shown in figure. This enhanced activity of the F3 formulation may be attributed to its optimized polymer concentration and viscosity, which could facilitate better drug release and diffusion. These results suggest that the F3 gel formulation not only provides favourable physicochemical properties but also superior antimicrobial efficacy, making it more effective for topical antibacterial applications.

Table 5: Antimicrobial activity data.

Formulation	Zone of Inhibition (mm)
F1	13.2
F2	14.8
F3	21.5
F4	15.6
F5	14.2
Standard	24.5

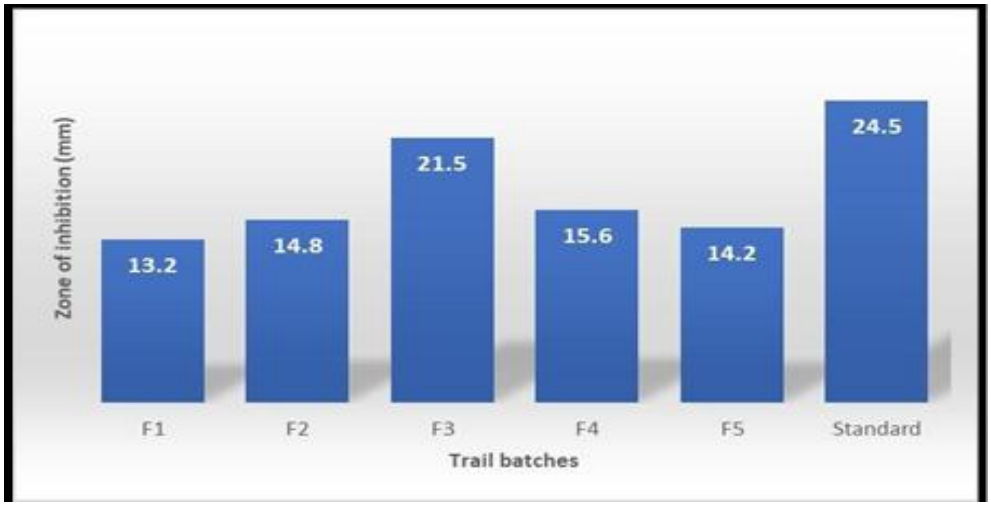

Fig 9: **Graphical Representation of Zone of Inhibition by Antimicrobial Activity.**

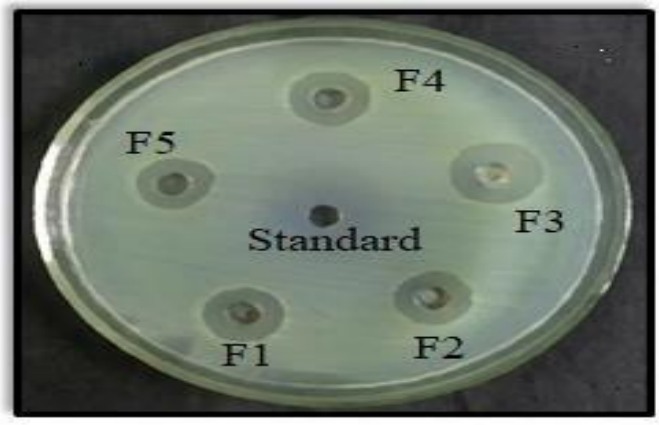

Fig 10: **Image of Antimicrobial Activity.**

***In Vitro* Drug Release Study**

In vitro drug release studies of gels were carried out using a Franz diffusion cell apparatus using 7.4 pH phosphate buffer. Samples were withdrawn at predetermined time intervals of 0.5, 1, 2, 3, 4 and 5 hours and analysed using atomic absorption spectroscopy. The results are summarized in Table 6, while the comparative drug release profiles are illustrated graphically in Fig 11, respectively.

Table 6: Cumulative % drug release of Magnesium chloride Gel.

Time (hr)	% Cumulative Drug Release (Mean ± SD)				
	F1	F2	F3	F4	F5
0.5	13.5 ± 1.6	11.0 ± 2.2	18.0 ± 1.5	12.5 ± 1.3	10.0 ± 1.2
1	22.0 ± 2.4	19.0 ± 2.6	28.0 ± 1.9	20.0 ± 1.6	15.5 ± 1.4
2	35.5 ± 2.7	31.0 ± 2.9	44.0 ± 2.0	30.5 ± 2.1	22.0 ± 1.6
3	49.0 ± 3.0	42.0 ± 3.2	62.0 ± 2.5	40.0 ± 2.6	30.0 ± 1.8
4	64.0 ± 3.3	55.0 ± 3.6	79.0 ± 3.0	50.0 ± 3.0	38.5 ± 2.0
5	82.0 ± 3.7	68.0 ± 3.9	95.0 ± 3.4	60.0 ± 3.4	45.0 ± 2.3

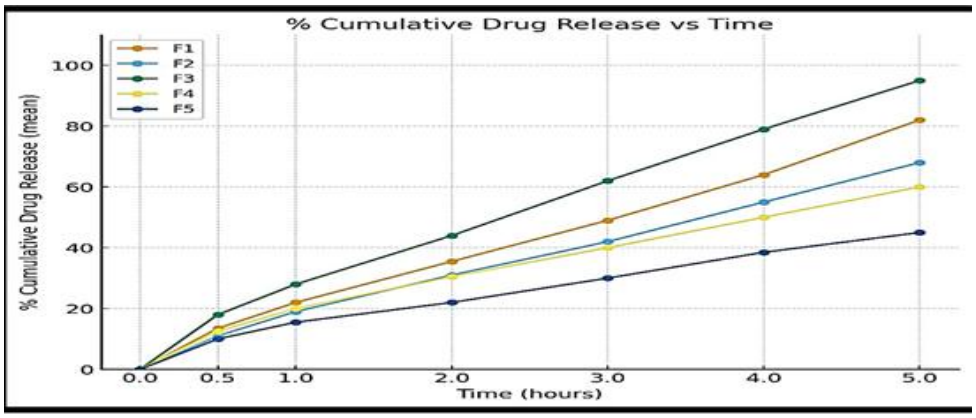

Fig 11: *In vitro* drug release study of Magnesium chloride gel.

The *In vitro* drug release study was conducted for all five gel formulations F1, F2, and F3, F4, F5 over a period of 5 hours. The results demonstrated a sustained and gradual release pattern for all formulations, indicating the ability of gel to prolong drug release. Among the five, F3 exhibited the highest cumulative drug release of 95.0 ± 3.4% at the end of 5 hours, which reflects appropriate gel consistency that favour enhanced drug diffusion. F1 and F2 showed moderate release (82.0 ± 3.7, 68.0 ± 3.9%), while F4 and F5 displayed the lowest release (60.0 ± 3.4, 45.0 ± 2.3%), which may be attributed to its higher viscosity, leading to slower drug diffusion. These results suggest that F3 is the most efficient formulation for sustained and enhanced drug delivery.

Drug Release Kinetics

Different kinetic models were applied to describe the release kinetics of Magnesium chloride gel. Data of percentage drug released from the F3 formulation batches were fitted in Kinetic models and equation. For zero order cumulative (% drug released versus time plot) and for first order (log cumulative % drug remaining versus time plot) and for Higuchi kinetic plot (cumulative % drug remaining versus square root time) and log cumulative percent drug retained vs. log time (Korsmeyer peppa's) were plotted separately as shown in Figure 12-15 respectively. For various kinetics models calculated regression coefficient (R2) were represented in Table 7. Result indicates that regression coefficient (R2) values of each formulation were greater for Zero order. In this study prepared formulations were best expressed through Zero order kinetics, which means constant release over time. All plots were linear, hence specified that, process of drug release was concentration independent release.

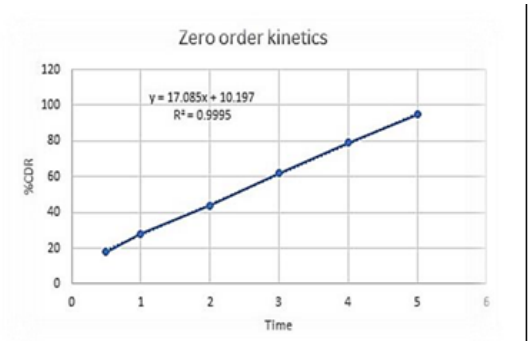

Fig 12: Zero order plot of F3 formulation.

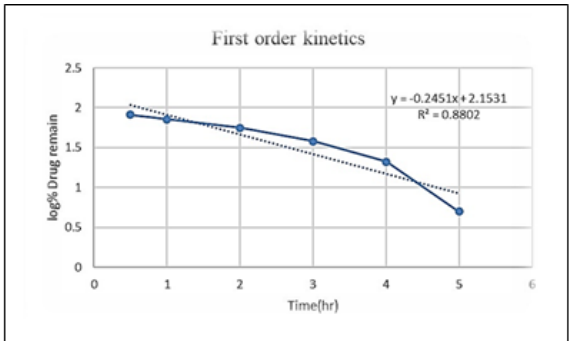

Fig 13: First order plot of F3 formulation.

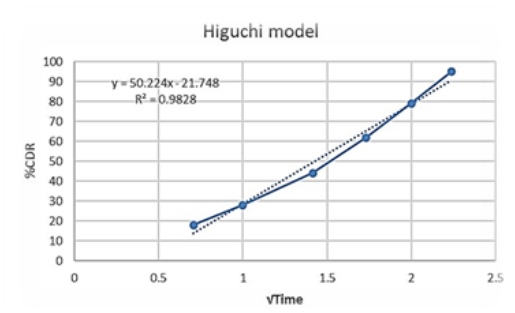

Fig 14: Higuchi Model for F3 Formulation.

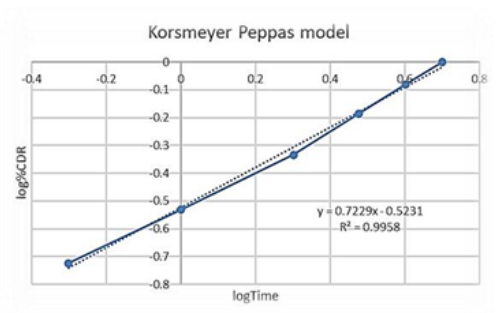

Fig 15: Korsmeyer-peppas model.

Table 7: Drug release kinetics data for F3 Formulation.

Formulation	Correlation coefficient of model fitting(R2)			
	Zero order	First order	Higuchi model	Korsmeyer Peppas model
F3	0.9995	0.8802	0.9828	0.9958

Stability studies

F3 formulation successfully passed the stability studies, showing no significant changes in physical appearance, pH, drug content, viscosity, spreadability and invitro drug release. Data of stability studies for the formulation F3 are shown in table 8.

Table 8: Data of stability studies for F3 formulation.

Formulation	Time (Days)	Physical appearance	PH	Viscosity (centipoise)	Spreadability (gm.cm/sec)	*In Vitro* drug release %	Drug content %
F3	Zero month	No phase separation	6.12±0.02	16,000±170	10.29±0.14	95.0±3.4	97.6±0.61
	After one month	No phase separation	6.12±0.02	16,000±170	10.29±0.14	95.0±3.4	97.6±0.61
	After two months	No phase separation	6.12±0.02	15,000±170	11.29±0.14	92.82±2.8	94.8±3.5
	After three months	No phase separation	6.12±0.02	14,000±158	11.84±0.42	90.35±0.52	92.9±0.36

CONCLUSION

The study successfully developed a Magnesium chloride gel using HPMC as the gelling agent. Among the tested formulations, HPMC-based gel (F3) exhibited optimal viscosity, homogeneity, and stability, forming a cohesive matrix that ensured ease of application and consistent performance. Viscosity and spreadability analyses confirmed its suitable firmness and shear-thinning behavior, while the drug release profile indicated sustained and effective release characteristics. These findings highlight HPMC as a preferable gelling agent for Magnesium chloride topical formulations, offering enhanced stability, favourable rheological properties, and potential for improved therapeutic efficacy and patient compliance. Overall, the optimized formulation shows promise for further development as a topical delivery system in both therapeutic and cosmetic applications.

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REFERENCE

1. Cranendonk DR. Cellulitis: current insights into pathophysiology and clinical management. Lavrijsen APM, editor. The Netherlands Journal of Medicine; 2017.
2. Wingfield C. (2012). Diagnosing and managing lower limb cellulitis. Nursing times, 108(27): 18–21.
3. Mazur, A. et al., 2007. Magnesium and the inflammatory response: potential physiopathological implications. Archives of biochemistry and biophysics, 458(1): 48–56.
4. Brisson, P., 1974. Percutaneous absorption. Canadian Medical Association journal, 110(10): 1182–5.
5. Liang R, Bao Z, Su B, Xing H, Ren Q. Solubility of vitamin D3 in six organic solvents at temperatures from (248.2 to 273.2) K. Journal of Chemical & Engineering Data. 2012 Aug 9; 57(8): 2328-31.
6. Pradhan M, Alexander A, Singh MR, Singh D, Saraf S, Saraf S. Understanding the prospective of nano-formulations towards the treatment of psoriasis. Biomedicine & Pharmacotherapy. 2018 Nov 1; 107: 447-63.

7. Thomas MA. Formulation and evaluation of ethosomal gel of tazarotene for topical delivery. Asian journal of pharmaceutics (AJP). 2019 Feb 9; 13(01).
8. Sang-ngern Mayuramas. Preliminary study of Transdermal Permeation of Magnesium Cream Formulations across Skin Department of Pharmaceutical Science, College of Pharmacy, University of Hawaii at Hilo, 200 W. KawiliSt., Hilo, HI 96720, USA.
9. Lalit K, Ruchi V. In vitro evaluation of topical gel prepared using natural polymer. International journal of drug delivery 2010; 2: 58-63.
10. Ranga PM, Sellakumar V, Natrajan R, Mohan KK. Formulation and In Vitro Evaluation of Ciprofloxacin Loaded Topical Emulgel. Int J Pharm Chem Sci., 2012; 1(1): 237-242.
11. Khan, A.; Yasmin, H.K.; Tariq, Q.; Mughal, M.A.; Sultan, K.K.M. Novel insight into potential leishmanicidal activities of transdermal patches of nigella sativa: Formulation development, physical characterizations, and in vitro/in vivo assays, Assay. Drug Develo. Technol, 2021; 3: 2335–2341. [CrossRef]
12. Navaneetha K, Asma B, Sumalatha P, Vinita D, Sravan J, Chinnala MK. Formulation and in-vitro evaluation of capsaicin emulgel for topical delivery. Scholars Academic Journal of Pharmacy. 2017; 6(6): 281-7.
13. Aher SD, Banerjee SK, Gadhave MV, Gaikawad DD. Emulgel: A New Dosage Form for Topical Drug Delivery. IJIPLS, 2013; 3: 1-10.
14. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. Journal of advanced research, 2015 Mar 1; 6(2): 105-21.
15. Formulation and Evaluation of Topical Herbal Cream for Cellulitis Harshal Sheth*1, Sharav Desai1, Dhara Patel1, Dhruvi Patel1, Priyanka Patel1, Snehal Patel2, Kartik Pandya2, Chainesh Shah2.
16. Trivedi P, Verma AM, Garud N. Preparation and characterization of aceclofenac microspheres. Asian Journal of Pharmaceutics (AJP). 2008; 2(2).