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FORMULATION AND CHARACTERIZATION OF VITAMIN D3 EMULGEL: A COMPARATIVE EVALUATION OF CARBOPOL 940 AND POLOXAMER 407

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ABSTRACT

This research focused on developing and characterizing a vitamin D3 emulgel using Carbopol 940 and Poloxamer 407 as gelling agents to enhance stability, skin permeation, and patient compliance in topical delivery. Eight formulations (F1-F8) were created with varying concentrations of the gelling agents and evaluated for multiple physicochemical properties. Vitamin D3 was characterized as an odorless, white crystalline solid, freely soluble in various solvents, with UV spectrophotometry confirming λ max at 265 nm in methanol. FTIR analysis showed no drug-excipient interactions, and microscopic evaluation revealed uniform oil droplet dispersion in the gel matrix. Higher concentrations of gelling agents increased gel strength, with Carbopol 940 forming stronger gels than Poloxamer 407. All formulations showed uniform drug distribution (95-105% content) and skin-compatible pH values (5.72-7.01). Rheological studies demonstrated non-Newtonian behavior with thixotropic properties, and spreadability decreased as polymer concentration increased. Carbopol 940 formulations exhibited higher swelling indices compared to Poloxamer 407. In vitro drug release studies showed 92.21% and 79.42% release after 8 hours for optimized formulations F3 and F7, respectively, following the Korsmeyer-Peppas model. The study successfully developed stable vitamin D3 emulgel formulations with controlled release properties, with Carbopol 940-based formulations showing particularly promising results for efficient topical delivery.

KEYWORD: Vitamin D3, Topical delivery, Drug release, Emulgel, Optimization.

INTRODUCTION

The pharmaceutical field has witnessed increased interest in developing innovative formulations to enhance therapeutic efficacy. Vitamin D3, a crucial fat-soluble vitamin, has gained prominence for its multifaceted health benefits, prompting a reevaluation of its delivery systems. This research explores emulgels, a versatile class of formulations combining the advantages of emulsions and gels, as a promising vehicle for the effective topical delivery of Vitamin D3.

Vitamin D3 (Cholecalciferol) is essential for maintaining calcium homeostasis and supporting bone metabolism, alongside various physiological functions within the human body. Traditionally, Vitamin D3 has been administered orally; however, there is growing interest in topical delivery methods.

This shift is largely due to the potential benefits of topical applications in treating localized conditions while circumventing the first-pass metabolism that occurs with oral administration. Despite these advantages, effective topical delivery of Vitamin D3 is hindered by its lipophilic nature and poor aqueous solubility, which complicates its formulation into effective topical products.

Vitamin D3 or cholecalciferol, plays a vital role in bone metabolism, phosphorus and calcium homeostasis, and various physiological processes, including immune function and cardiovascular health. While oral supplementation remains common, topical application presents an intriguing avenue for targeted delivery and potential therapeutic benefits, particularly for skin health.

The skin, as the body's largest organ, holds unique significance in the absorption and utilization of vitamin D3. Recent advancements in topical formulations offer potential for addressing vitamin D3 deficiency, which can lead to various skin problems such as psoriasis, atopic dermatitis, dry skin, acne, and impaired wound healing.

Topical vitamin D3 interacts with keratinocytes, influencing cellular proliferation, differentiation, apoptosis, barrier maintenance, and immune functions. It has shown promise in treating conditions like psoriasis, promoting wound healing, addressing skin aging and photodamage, and potentially benefiting those with ichthyosis, eczema, and vitiligo.

Emulgels, which are hybrid systems that combine the characteristics of emulsions and gels, have emerged as promising vehicles for delivering lipophilic drugs like Vitamin D3. These formulations can enhance skin permeation and stability while improving patient compliance compared to conventional topical formulations. The selection of a suitable gelling agent is pivotal, as it significantly influences the physicochemical properties and overall performance of emulgel formulations.

This study aims to develop and evaluate Vitamin D3 emulgels utilizing two commonly used gelling agents: Carbopol 940, an anionic polyacrylic acid polymer, and Poloxamer 407, a non-ionic triblock copolymer. Both agents are recognized for their superior gelling properties but exhibit distinct differences in molecular structure, gelation mechanisms, and interactions with skin barriers. The primary objectives of this research include:

- Formulating stable Vitamin D3 emulgels using both Carbopol 940 and Poloxamer 407.
- Characterizing and comparing the physicochemical properties of these formulations.
- Evaluating in vitro release kinetics and skin permeation characteristics.
- Assessing stability and rheological behavior of the prepared emulgels.

By understanding how different gelling agents affect emulgel properties, this study seeks to contribute to the rational design of more effective topical Vitamin D3 formulations. Such advancements could potentially enhance therapeutic outcomes for conditions that necessitate localized delivery of Vitamin D3.The relevance of this research is underscored by the increasing prevalence of Vitamin D deficiency globally, which affects an estimated one billion people, particularly during winter months when sunlight exposure is limited.

Furthermore, studies indicate that topical administration of Vitamin D can effectively manage conditions like psoriasis by blocking inflammatory processes.

By addressing the challenges in topical vitamin D3 delivery through an innovative emulgel formulation, this research seeks to contribute to the growing field of topical vitamin D therapy. The potential benefits include improved patient compliance, targeted delivery to the skin, and enhanced therapeutic efficacy for various dermatological conditions.

The successful development of a stable and effective vitamin D3 emulgel could pave the way for new approaches in skincare and dermatological treatments, offering a valuable alternative to traditional oral supplementation and expanding the therapeutic applications of topical vitamin D3.[1][2][3]

MATERIALS AND METHODS

a) Materials

Vitamin D3 was obtained as a gift sample from Supreme Pharmaceuticals Mysore Pvt. Ltd. Isopropyl myristate, Tween 80, Span 80, Carbopol 940, Poloxamer 407, Triethanolamine, Dimethyl sulphoxide, Methyl paraben, Butylated hydroxy anisole and methanol were purchased from Yarrow Chem products and Loba chemie Pvt Ltd, Mumbai. Double distilled water was used for the formulation. All chemicals were of pharmaceutical grade and used without further modification.

b) METHODOLOGY

1. Preformulation studies

1.1 Organoleptic evaluation

The drug was evaluated for sensory attributes including color, odor, taste, and texture.

1.2 Solubility studies

Solubility studies of Vitamin D3 were conducted using various solvents to assess its solubilization properties. Initially, 10 mg of Vitamin D3 was dissolved in 10 mL of several solvents, including ethanol, methanol, isopropyl myristate, DMSO, glycerol, and water. The mixture was stirred with a magnetic stirrer for 10 minutes to facilitate the dissolution process.[4]

1.3 Determination of Maximum Wavelength (λmax)

UV spectrophotometer (Shimadzu, UV-1900i Japan, UV-spectrophotometer) was used to determine λ max of Vitamin D3 in scan mode with the scanning range of 200-400 nm. Sample was prepared using methanol and placed in a quartz cuvette and read against blank at room temperature (25 ± 2ºC).[5]

1.4 Standard calibration curve preparation

The standard solutions with concentrations of 2, 4, 6, 8, and 10 µg/ml were analyzed using a UV-Visible spectrophotometer (Shimadzu, UV-1900i Japan) against a blank (methanol), measuring absorbance at 265 nm. A calibration curve was created by plotting absorbance against the concentration of the standard solutions, and the regression equation was derived. This experiment was conducted in triplicate to ensure accuracy.[6]

1.5 Compatibility study

In the formulation of Vitamin D3 emulgel, interactions among excipients can occur due to their close proximity, potentially compromising drug stability. The compatibility of Vitamin D3 with these excipients was assessed through infrared absorption spectral analysis (FTIR). The FTIR spectra of the drug and polymer were compared to the standard spectrum of pure Vitamin D3.

Both the pure drug and a physical mixture of the drug with excipients were prepared and analyzed over a frequency range of 4000 to 400 cm^{-1} using an FTIR spectrophotometer.[7]

2. Formulation development

2.1 Emulsion Preparation and Stability

The emulsion was formulated using the HLB system to determine the optimal proportions of components, with emulsifiers featuring hydrophilic and lipophilic segments. The balance between these segments defines the Hydrophile-Lipophile Balance (HLB), which can be calculated or experimentally determined.

Selection of Emulsifiers Suitable to RHLB of Oil Phase

The HLB System indicates that all fats and oils have a Required HLB, with Isopropyl myristate having an RHLB of 11.50, necessitating an emulsifier blend of Span 80 (RHLB=4.3) and Tween 80 (RHLB=15) to achieve this value for stable emulsion formulation. To determine the percentage composition of two emulsifying agents, A combination of high and low HLB emulsifier is usually used to get desired HLB (denoted by X). It can be calculated by using the formula,

$$\%A = \frac{(X - HLB_B)}{HLB_A - HLB_B} \times 100$$

$$\%B = 100 - \%A$$

Where, HLB_A = RHLB of Tween 80, HLB_B = RHLB of Span 80, X = Desired HLB value

Based on calculation, blend of Tween 80 = 67.92% and Span 80= 32.08% would be needed to emulsify an oil phase that has a required HLB of 11.5.

Preparation of emulsion with RHLB emulsifier blend ratio

Based on the emulsifier blend ratio, emulsions were prepared at concentrations of 0.5% to 5%, assessed for stability, and a single concentration was selected for further batches with various oil and Smix combinations.

Ternary phase diagram

The goal of this study is to provide an overview on the importance and assessment of ternary plot an essential tool for selecting appropriate formulations for the synthesis of stable emulsions. These emulsions are intended to enhance the stability of bioactive compounds or hydrophobic drugs. Establishing a ternary phase diagram is an essential tool for identifying and establishing the formulations of the components used in the production of emulsions.

Ternary plot

The ternary plot was constructed using an aqueous titration process with oil, surfactants/ co-surfactants (Smix) and double distilled water, resulting in a transparent mixture that was titrated dropwise to determine the point of turbidity; the phase diagrams with high emulsion regions were selected for formulation, and ternary plots were created using Ternaryplot.com based on ten combinations.

Table 1: Different combinations of oil and Smix.

Sl. No.	Oil (%)	Smix (%)
1	19.5	0.5
2	19	1
3	18.5	1.5
4	18	2
5	17.5	2.5
6	17	3
7	16.5	3.5
8	16	4
9	15.5	4.5
10	15	5

2.2 Emulgel formulation

Figure 3 illustrates the steps in the formulation of an emulgel, with different formulations (F1-F8) prepared using varying concentrations of gelling agents. The preparation method remains consistent across all batches.[8][9]

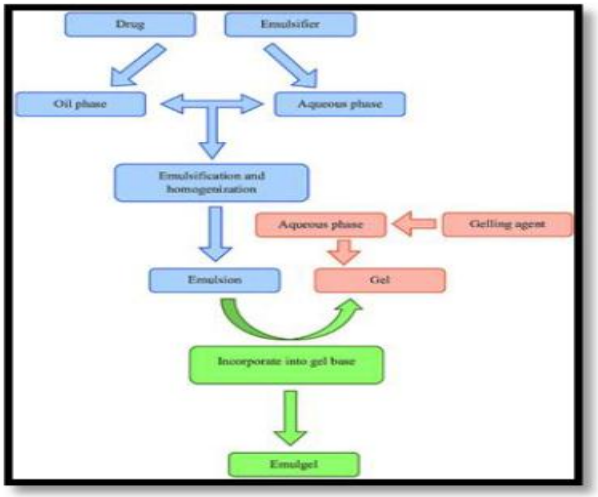


Fig. 1: Steps involved in emulgel formulation.

a) Preparation of emulsion

- **Oil phase:** BHA was dissolved in isopropyl myristate under slow stirring, followed by drug incorporation and DMSO addition to aid dissolution.
- **Aqueous phase:** Distilled water was mixed with Smix under continuous stirring until the surfactants were well dispersed.
- **Emulsification:** The oil phase was slowly added to the aqueous phase under homogenization.
  After the formation of stable emulsion, methyl paraben was added to the mixture and stirred well to ensure even distribution throughout the emulsion.

b) Preparation of Gel

Two different gel bases were formulated using Carbopol 940 and Poloxamer 407:

- **Carbopol Gels:** Concentrations of 0.5%, 1%, 1.5%, and 2% w/v were prepared by dispersing Carbopol 940 in distilled water, stirring continuously at moderate speed, and soaking the mixture overnight. The gel was formed by neutralizing the dispersion with triethanolamine and adjusting the pH to 6.5.
- **Poloxamer Gels:** Concentrations of 20%, 25%, 30%, and 35% w/v were prepared using the cold method, where Poloxamer 407 was slowly added to cold water while stirring. The solution was then stored at 50°C for 24 hours to allow full hydration and gel formation.

c) Preparation of emulgel

The resulting emulsion was combined with the gel base in a 1:1 ratio and homogenized using a dispersator to achieve a clear emulgel. The composition of the various formulations is detailed in Table 5.

Table 2: Composition of Emulgel (F1 – F8).

Ingredient (%w/w)	Formulation Code							
	F1	F2	F3	F4	F5	F6	F7	F8
	Emulsion							
Vitamin D3	0.0125	0.0125	0.0125	0.0125	0.0125	0.0125	0.0125	0.0125
Isopropyl Myristate	15	15	15	15	15	15	15	15
Span 80	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Tween 80	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39
Butylated Hydroxy Anisole	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Distilled Water	q.s							
Dimethyl sulphoxide	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Gel base								
Carbopol 940	0.5	1	1.5	2	-	-	-	-
Polaxamer 407	-	-	-	-	20	25	30	35
Distilled Water	q.s							
Methyl paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Emulsion : Gel	01:01	01:01	01:01	01:01	01:01	01:01	01:01	01:01
Triethanolamine was added to adjust the pH of F1 - F4 formulations from 5.5 to 6.5								

3. Characterization of emulgel

a) Physical evaluation: All the prepared formulations were examined visually for color, appearance, homogeneity, and phase separation.

b) Microscopic study: The emulgel was diluted, mounted on a glass slide, and examined under a light microscope at 40x magnification to study the globular structure within the gel base.

c) Determination of gel strength: The strength of the formulated gel at various concentrations was evaluated using the penetration method, where a weighted metal ball was dropped into the gel in a 100 ml graduated cylinder, and the time(sec) taken to penetrate a distance of 1 cm was recorded.[10][11]

d) Determination of drug content: Drug concentration in the emulgel was measured using a UV spectrophotometer. One gram of the formulation was placed in a 10 ml volumetric flask, mixed with methanol, and the volume was adjusted to 10 ml. The solution was filtered to obtain a clear liquid, and the absorbance was measured at 265 nm. This procedure was repeated three times to calculate the average drug content for each formulation, using the calibration curve to determine the concentration based on the absorbance.[12][13] The drug content was calculated using the formula:

Drug Content = Concentration × Volume taken × Dilution factor × Conversion factor.

e) pH determination: pH evaluation is crucial for topical formulations, with the emulgel's pH ideally between 5 and 7 to match skin conditions. If the pH is too acidic or basic, it may irritate the skin. The pH was measured using a digital pH meter at room temperature, calibrated with standard pH 4 buffers. Two methods were used:

- **Direct method:** 10 gm of the sample were placed in a glass vial and the pH meter electrode, previously rinsed with distilled water was immersed in the formulation to take three measurements for each sample and calculate the average.
- **Dilution method:** A 10% dispersion was prepared by diluting 1g of the formulation in 10ml of purified water. The pH electrode was placed in the dispersion, and the stabilized reading was noted. This test was conducted in triplicate to determine the average pH values.[14]

f) Spreadability: Good spreadability is a key criterion for dermatological preparations, indicating how well the gel spreads on the skin and affecting its therapeutic efficacy.

The parallel-plate method, valued for its simplicity and low cost, was used to assess the spreadability of emulgel formulations 48 hours after preparation. To measure, 1 g of emulgel was placed within a 1 cm diameter circle on a glass plate, covered with a second glass plate weighing 75 g, and subjected to an additional 425 g weight for 5 minutes to facilitate spreading. The increase in diameter was recorded.[15][16]

Spreadability ($g.cm.min^{-1}$) was calculated using the formula: $S = M \times L / T$, where S is spreadability, M is the weight of the upper plate (g), L is the diameter of the spreading emulgel (cm), and T is the time taken (min).

g) Rheological study: The emulgel formulation was rheologically characterized using a Manual Brookfield viscometer (spindle No. 7) to measure viscosity in centipoises at room temperature. A graph of apparent viscosity versus speed (RPM) was plotted. The spindle was positioned in the center of the emulgel without touching the bottom and rotated at various speeds. [17] Viscosity values were recorded after measuring the resistance to rotation for 5 minutes.

h) Swelling Index: The effectiveness of polymers in pharmaceutical preparations improves when macromolecules are fully swollen, enhancing rheological properties and emulsification in topical formulations.

To evaluate the swelling behavior of the emulgel, 1 g was placed on porous aluminium foil and immersed in 20 ml of 0.1N sodium hydroxide (NaOH) in a 100 ml beaker.[18] Samples were taken at various intervals, and the emulgel was blotted to remove excess water before reweighing until a constant weight was reached. The original weight (Wo) and the swollen weight (Wt) were recorded.

The swelling index was calculated using: Swelling Index (SW)% = [(Wt – Wo) / Wo] × 100.

where,

(SW)% = Equilibrium percent swelling, W_t = Weight of swollen emulgel after time,

W_o = Original weight of emulgel at zero time.

i) *In vitro* diffusion study: An in vitro release study was performed over 8 hours to evaluate the drug release profile of Vitamin D3 from the emulgel using a dialysis membrane diffusion model. A glass cylinder (10cm height) acted as the permeation cell, with a cellophane membrane fixed at one end after soaking in distilled water for 24 hours.

An emulgel equivalent to 125 mcg was placed in the donor compartment, while the receptor compartment contained 50 ml of phosphate buffer (pH 5.5) and ethanol (9:1). The assembly was configured so that the lower end of the emulgel cell touched the diffusion medium (1-2 mm deep). The diffusion medium was stirred continuously at 50 rpm. Samples (2 ml) were withdrawn at intervals of 0.5, 1, 2, 3, 4, 5, 6, 7, and 8 hours from receptor medium and maintained the sink condition. The sample was analyzed using a Shimadzu UV-visible spectrophotometer at λmax 265 nm, and the active amount was determined from a previously prepared calibration curve.[19][20]

j) *In-vitro* drug release kinetics: Kinetic analysis of drug release was performed by fitting the release data to various models, including zero order, first order, Higuchi and Korsmeyer-Peppas to identify the best-fit model based on R and k values. This analysis aimed to understand the release mechanism of Vitamin D3 from the emulgel formulated with Carbopol 940 and Poloxamer 407.[21][22]

k) Stability testing: Stability studies were conducted to evaluate the effects of formulation additives on drug stability and the physical stability of the prepared formulation under normal storage conditions (temperature and humidity). Real-time stability testing was performed on optimized formulations F3 and F7, each containing 10 g, stored in glass containers at room temperature for three months. After this period, samples were withdrawn and assessed for physical appearance, pH, viscosity, spreadability, drug content, and in vitro drug release.

RESULTS AND DISCUSSION

i) Preformulation studies

a) Organoleptic evaluation: The organoleptic evaluation of Vitamin D3 revealed it to be odorless, with no discernible scent, and it appeared as a white crystalline solid.

b) The solubility study: The solubility study of Vitamin D3 in various solvents showed that it is freely soluble in methanol, ethanol, isopropyl myristate (IPM) and dimethyl sulfoxide (DMSO), soluble in liquid paraffin, olive oil but insoluble in distilled water and glycerol.

c) Compatibility study: FTIR spectra of pure Vitamin D3 and its mixtures with excipients were analyzed to assess drug-excipient compatibility. Characteristic peaks for hydroxyl (O-H), aromatic and aliphatic C-H, as well as C=C and C=O stretching vibrations were observed, aligning with the molecular structure of cholecalciferol. No changes in existing peaks or the appearance/disappearance of peaks indicated compatibility between the drug and excipients

d) Standard calibration plot: The absorbances of all solutions with concentrations ranging from 2 µg/ml to 10 µg/ml were measured at 265 nm against a blank (methanol). A calibration curve was then constructed by plotting concentration on the x-axis and absorbance on the y-axis, as illustrated in the figure. Absorbance value remained linear and obeyed Beer's Lamberts law in the range of 0-10µg/ml with the slope value as y = 0.0741x+ 0.0891 and R^2 value of 0.9996.

e) Determination of λ max of Vitamin D3: A UV spectrophotometric analysis established that the maximum absorption wavelength (λ max) for vitamin D3 in methanol is 265 nm, as illustrated in Fig. 1.

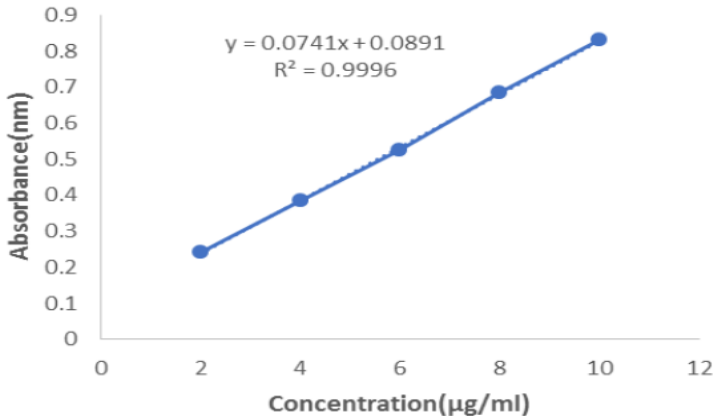


Fig. 2: Standard Calibration curve of Vitamin D3.

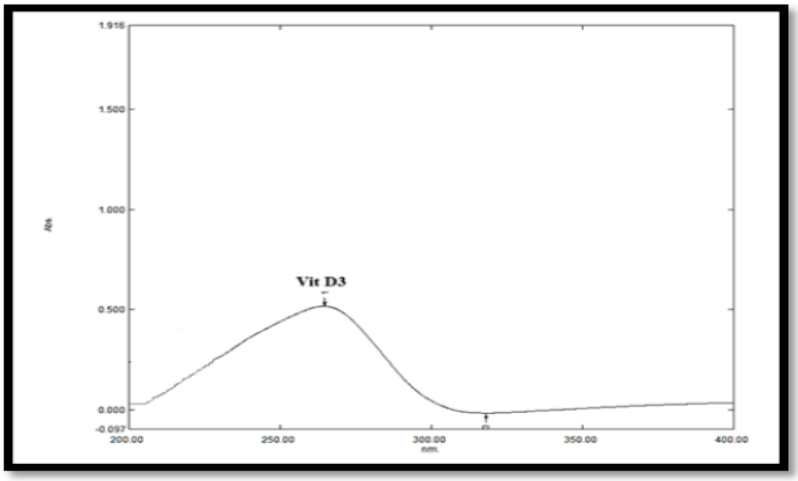


Fig. 3: Absorption maxima of Vitamin D3 in methanol.

ii) Formulation development

a) Preparation of Emulsion and Stability

- **Selection of oil phase:** Isopropyl myristate was selected as the oil phase for the emulsion formulation due to its excellent solubilizing properties for vitamin D3, enhancing the drug's bioavailability in the emulgel. Comparative studies with other oil phases, such as liquid paraffin and olive oil, demonstrated that isopropyl myristate provided superior drug solubility, confirming its suitability as the preferred oil phase for this formulation.
- **Selection of emulsifiers:** The Required Hydrophile-Lipophile Balance (RHLB) for isopropyl myristate was determined to be 11.50. To achieve this, a blend

of Span 80 (RHLB = 4.3) and Tween 80 (RHLB = 15) was selected to create a stable emulsion.

- **Emulsion preparation:** Emulsions were prepared using a blend ratio of 67.92% Tween 80 and 32.08% Span 80 at Smix concentrations of 0.5% to 5%. Their stability was assessed, resulting in the selection of a specific concentration for further formulation batches.
- **Optimization of emulsion:** Figure 2 displays the ternary phase diagram illustrating the relationship between Smix, oil, and water components in the emulsion system. The selected phase diagram, featuring a high emulsion region, was used to formulate emulsions, with ternary plots created via Ternaryplot.com. Based on visual estimation, the mixture consists of : Water: 80%, Oil: 15%, Smix: 5%

The diagram shows a single data point near the bottom right corner, indicating a water-dominant system and representing the optimal formulation identified through aqueous titration. This suggests a highly diluted oil-in-water (O/W) emulsion system, aligning with the goal of achieving a stable emulsion with minimal surfactant concentration. The optimized ratio for the emulgel was determined based on phase separation, creaming, and other visual assessments.

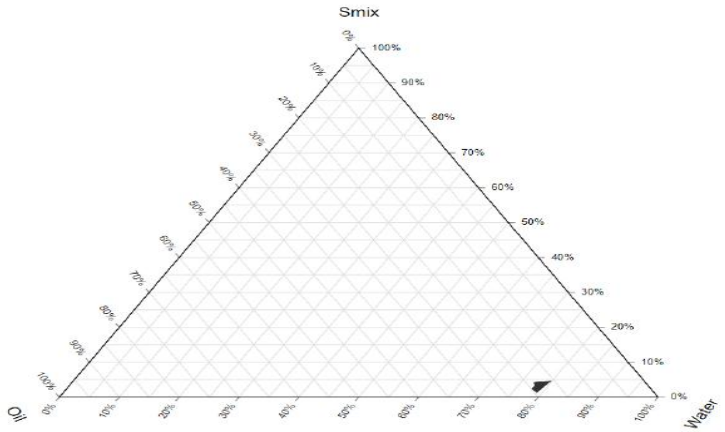


Fig. 4: Ternary plot.

b) Preparation of emulgel: The optimized emulsion containing Vitamin D3 was incorporated into two distinct gel bases at various concentrations, maintaining a 1:1 ratio of emulsion to gel. Following the procedure outlined in the methodology section, a total of eight emulgel formulations were developed. These formulations comprised four variations using Carbopol 940 and four using Poloxamer 407 as gelling agents, each at different concentrations.

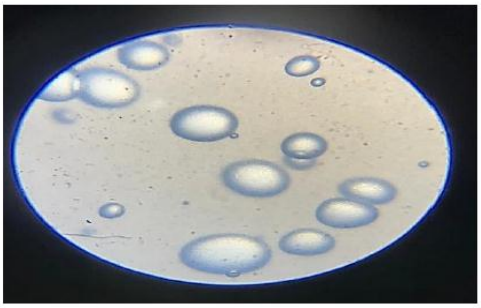
iii) Characterization of Vitamin D3 emulgel

a) Physical parameters of prepared formulations

The formulations were assessed for color, homogeneity, and consistency. Formulations F1 and F2 were fluid due to low carbopol concentrations, while F4 was thick and white due to a higher carbopol concentration. F3, containing 1.5% carbopol, appeared creamy white. Formulations F5, F6, F7, and F8 used a Poloxamer 407 gel base; F5 and F6 were fluid, whereas F8 was thick and white from a higher Poloxamer concentration. F7 had a creamy white appearance with 30% Poloxamer. All formulations were homogeneous and consistent, with no phase separation observed.

b) Microscopic study

Photomicroscopic evaluations revealed spherical globules, indicating a uniform dispersion of oil droplets within the gel matrix of the emulgel formulation. This structure suggests stability and good potential for the controlled release of Vitamin D3.



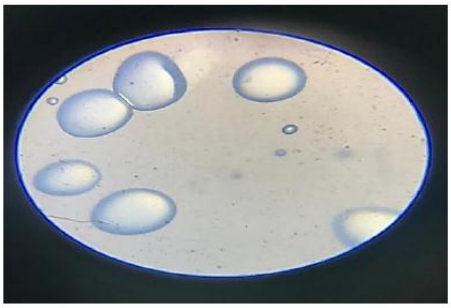


Fig. 5: Emulgel formulated with Carbopol 940. Fig 6: Emulgel formulated with Poloxamer 407.

c) Gel strength

Gel strength was directly related to the concentrations of both Carbopol 940 and Poloxamer 407. As the concentrations of either increased, penetration time also rose, indicating greater gel strength. Carbopol 940 consistently showed longer penetration times, demonstrating its superior effectiveness in forming stronger gels compared to Poloxamer 407, likely due to a more interconnected gel structure. Table 11 presents the data on gel strength.

Table 3: Gel strength.

Gelling agent	Concentration (%w/w)	Penetration Time (s)
Carbopol 940	0.5	25 ± 1
	1	38 ± 2
	1.5	52 ± 1
	2	74 ± 3
Poloxamer 407	20	12 ± 4
	25	20 ± 2
	30	41 ± 1
	35	59 ± 5

d) Drug content determination

The average percentage drug content present in 1 gm of emulgel formulation was found to be 99.3% ± 0.418 for F3 and 96.4% ± 0.596 for F7. It was noted that the API was evenly distributed throughout the formulation. The drug content of the formulations were found to be within the specified range of 95% - 105%.

e) Determination of pH

The pH values of all prepared emulgel formulations ranged from 5.72 to 7.0. These levels are deemed acceptable, as they minimize the risk of skin irritation, considering the average pH of adult skin is 5.5.

f) Spreadability studies

The spreadability of the Vitamin D3 emulgel formulations (F1-F8) ranged from 11.19 g.cm/min to 22.14 g.cm/min (Table 2). Higher concentrations of gelling agents significantly reduced spreadability, with Carbopol 940 formulations showing better spreadability than those with Poloxamer 407. Formulations F1, F2, F5, and F6 were classified as soft gels with higher spreadability, while F3 and F7 were semi-stiff, and F4 and F8 were very stiff due to higher gelling agent concentrations. Overall, increased gelling agent concentration led to decreased spreadability. The values of spreadability indicate that the emulgel is easily spreadable with minimal shear.

Formulation	Spreadability (gm.cm/sec) (Mean ± SD)
F1	22.14 ± 0.05
F2	21.52 ± 0.07
F3	19.79 ± 0.12
F4	15.42 ± 0.03
F5	19.41 ± 0.09
F6	17.45 ± 0.06
F7	14.58 ± 0.02
F8	11.19 ± 0.14

Table 4: Data for Spreadability.

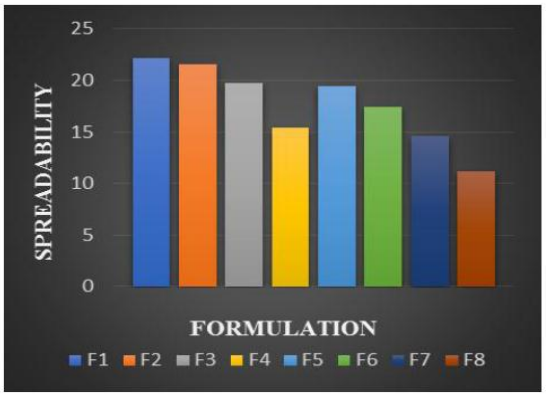


Fig.7: Graph of Spreadability.

g) Rheological study

The viscosity of the optimized emulgel formulations, F3 and F7 was measured using a Brookfield RV viscometer. The emulgel was rotated at various speeds (rpm) with spindle number 7. A comparative graphical representation of the viscosities is displayed in Fig 18.

Based on the rheogram findings, It was observed that the viscosity of the emulgel decreased as the rotational speed of the spindle increased, which further reinforces the shear thinning effect with of both the formulations exhibit gel-sol-gel conversion.

The apparent viscosity of the emulgel decreased with increasing speed, indicating that the optimized formulations behave as non-Newtonian (pseudo-plastic) fluids.

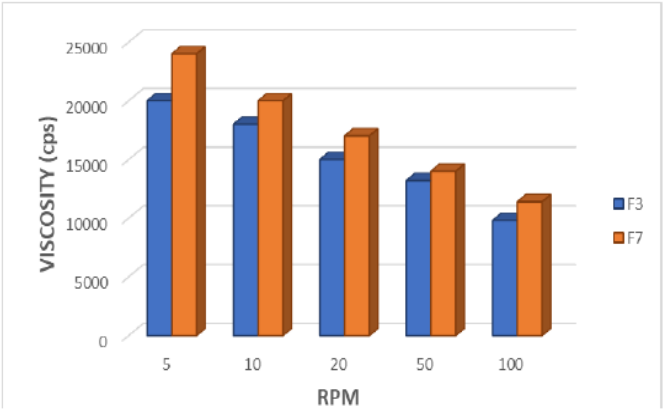


Fig. 8: Graphical representation of rheogram.

h) Swelling index

The swelling index of the optimized emulgel formulations was evaluated using the methodology outlined in the study. Formulations F3 and F7 were tested, showing that the emulgel with Carbopol-940 (F3) had significantly higher swelling indices than the one with Poloxamer 407 (F7). This superior swelling behavior of Carbopol-940 is vital for the performance and drug release characteristics of the emulgel formulations. The results are presented below.

Table 5: % Swelling Index of F3 and F7.

Time (hr)	% Swelling Index (Mean ± SD)	
	F3	F7
0.5	19.3 ± 0.25	15.2 ± 0.29
1	36.2 ± 0.48	28.4 ± 0.47
1.5	49.9 ± 0.62	39.6 ± 0.84
2	58.8 ± 0.98	48.4 ± 0.91
2.5	71.7 ± 0.39	62.3 ± 0.57
3	87.4 ± 0.87	79.6 ± 0.98
3.5	92.6 ± 0.66	86.4 ± 0.36
4	99.5 ± 0.85	89.3 ± 0.73

i) *In vitro* drug release

The therapeutic efficacy of a drug relies on its release from pharmaceutical dosage forms. After developing the formulations, F1, F2, F3, F5, F6, and F7 were evaluated for in vitro drug release over 0.5 to 8 hours. The percentage release of Vitamin D3 from the optimized emulgel formulations F3 and F7 was 92.21% and 79.42%, respectively, after 8 hours. The in vitro drug release data and percentage release from the formulations are presented in Tables 16 and 17, and Figures 22 and 23.

Table 1: *Invitro* drug release data of F1– F3. Table 7: *Invitro* drug release data of F5- F7.

Time (hr)	*In vitro* drug release (%) (Mean ± SD)		
	F1	F2	F3
0.5	9.92 ± 0.09	15.54 ± 0.24	21.52 ± 0.05
1	15.34 ± 0.12	24.12 ± 0.39	32.95 ± 0.45
2	24.86 ± 0.18	30.52 ± 0.48	41.59 ± 0.89
3	31.12 ± 0.29	37.82 ± 0.91	52.85 ± 0.52
4	36.45 ± 0.58	45.21 ± 0.82	63.45 ± 0.28
5	41.52 ± 0.48	58.52 ± 0.54	71.63 ± 0.11
6	45.59 ± 0.62	67.52 ± 0.15	76.45 ± 0.92
7	59.85 ± 0.75	73.53 ± 0.69	83.24 ± 0.39
8	68.22 ± 0.48	81.52 ± 0.72	92.21 ± 0.64

Time (hr)	*In vitro* drug release (%) (Mean ± SD)		
	F5	F6	F7
0.5	14.91 ± 0.28	15.82 ± 0.48	17.25 ± 0.35
1	21.25 ± 0.89	23.93 ± 0.92	31.46 ± 0.19
2	34.63 ± 0.12	37.52 ± 0.23	42.61 ± 0.88
3	37.85 ± 0.76	41.45 ± 0.35	51.25 ± 0.47
4	42.19 ± 0.98	49.25 ± 0.51	59.42 ± 0.72
5	48.52 ± 0.34	56.45 ± 0.56	64.28 ± 0.24
6	52.64 ± 0.53	59.85 ± 0.17	69.12 ± 0.53
7	55.49 ± 0.45	63.64 ± 0.84	73.55 ± 0.97
8	59.68 ± 0.34	68.52 ± 0.72	79.42 ± 0.62

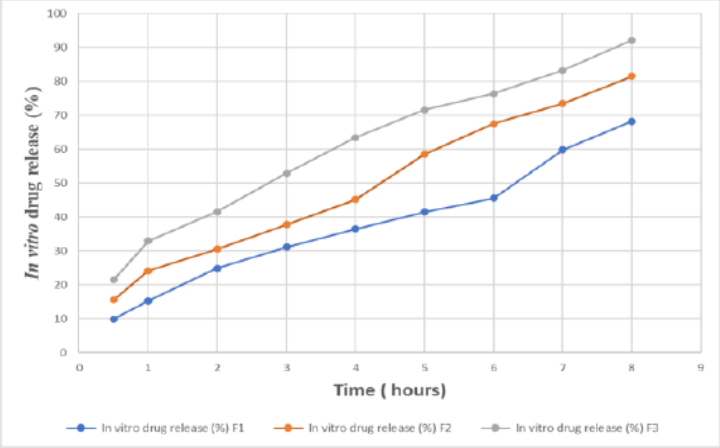


Fig. 9: *Invitro* drug release profile of F1 – F3 formulation.

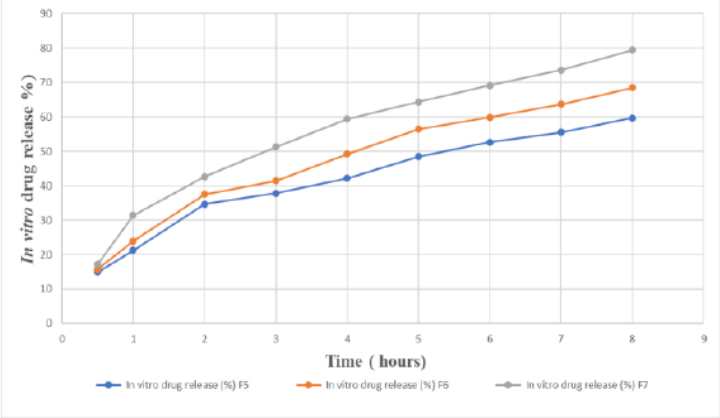


Fig. 10: *Invitro* drug release profile of F5 - F7 formulation.

j) Drug release kinetics

The in vitro release studies of emulgel were analyzed using various mathematical models, as summarized in Table 7. The most suitable model was determined by the highest regression coefficient (R^2) value close to 1, indicating a constant drug release over time.

The results showed that formulations F3 (R^2 = 0.994) and F7 (R^2 = 0.992) had the highest R^2 values in the Korsmeyer-Peppas model, suggesting both followed this model. Thus, the optimized formulation indicated that the drug release follows the Korsmeyer-Peppas model, representing release from a polymeric network.

Table 8: Drug release kinetics data for F3 and F7.

FORMULATION	ZERO ORDER		FIRST ORDER		HIGUCHI		KORSMEYER- PEPPAS	
	K	R^2	K	R^2	K	R^2	K	R^2
F3	8.9487	0.9796	-0.1181	0.9458	23.094	0.9002	0.5109	0.9949
F7	7.6299	0.9459	-0.0931	0.9677	19.349	0.8574	0.5171	0.9798

k) Stability studies

The F3 and F7 formulations successfully passed the stability studies, with no significant changes observed in physical appearance, pH, drug content, viscosity, spreadability and *in vitro* drug release. The stability study data for formulations F3 and F7 are presented in Tables 19 and 20, respectively.

Table 9: Data of stability studies for F3 formulation.

Formulation	Time (Days)	Physical appearance	pH	Viscosity (Centipoise)	Spreadability (gmcm/sec)	*Invitro* drug release (%)	Drug Content (%)
F7	Day 1	No phase separation	6.21 ±0.07	11400 ± 39.85	14.58 ± 0.02	79.42 ± 0.62	96.4 ± 0.59
	After 90 days	No phase separation	6.21 ±0.07	11050± 32.96	16.25 ± 0.08	75.98 ± 0.49	93.1 ± 0.23

Table 10: Data of stability studies for F7 formulation.

Formulation	Time (Days)	Physical appearance	pH	Viscosity (Centipoise)	Spreadability (gmcm/sec)	*Invitro* drug release (%)	Drug Content (%)
F3	Day 1	No phase separation	5.87 ± 0.03	9800 ± 21.63	19.79 ± 0.12	92.21± 0.64	99.3± 0.41
	After 90 days	No phase separation	5.87 ± 0.03	9250 ± 25.35	20.59 ± 0.25	90.35± 0.52	96.9± 0.36

CONCLUSION

The aim of this research was to develop a Vitamin D3 emulgel utilizing various gelling agents. The study effectively highlighted the potential of emulgels as an innovative topical delivery system for Vitamin D3. Although both gelling agents yielded emulgels with satisfactory physicochemical properties, Carbopol 940 proved to be more efficient, forming stable gels at significantly lower concentrations compared to Poloxamer. Furthermore, formulations using Carbopol 940 exhibited enhanced gel strength, spreadability, and swelling index. These attributes, along with its positive influence on formulation characteristics, suggest that Carbopol 940 is the preferred gelling agent for Vitamin D3 emulgel formulations. The improved stability, favorable rheological properties, and enhanced skin permeation seen in our optimal formulations could lead to better patient compliance and therapeutic outcomes. In summary, this research advances the field of topical Vitamin D3 delivery systems and offers valuable insights for the creation of innovative therapeutic formulations.

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