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Original Article

Formulation, Developing, and Assessment of Vitamin D3-Enriched Microsphere Cream for Anti-Aging Therapy

Shyam Nikethen Girivasan[3], Sabeel Salam[1,*], Mohammed Fazil Rayamarakkarveettil Musthafa[3], Zakir Hussain Kovval Peedikayil[3], Akza Marium Reji[2], Manojkumar Venkatesan[3]

[1]Department of Pharmaceutics, JSS College of Pharmacy, Ooty, Tamil Nadu, INDIA.
[2]Department of Pharmacy Practice, Grace College of Pharmacy, Palakkad, Kerala, INDIA.
[3]Department of Pharmacy Practice, JSS College of Pharmacy, Ooty, Tamil Nadu, INDIA.

ABSTRACT

Background: The aim of this paper is to describe the advancement in dermal drug delivery employing microspheres as the method, focusing on the synthesis of microspheres by solvent evaporation technique to be formulated in to a cream base foundation. **Materials and Methods:** The microspheres were prepared through a solvent evaporation method followed by incorporation into a cream base enriched with Vitamin D3 (Cholecalciferol) to improve the drug release rate. *In vitro/ex vivo* analytical practices were used to assess the permeation of the drug, with specific emphasis of the capability of the formulation of delivering the drugs across a membrane. **Results:** *Ex vivo* diffusion studies suggested the drug release kinetic followed zero order model, implying controlled and sustained release of the active compound. Additional characterization using FTIR spectroscopy revealed the absence of physical and chemical incompatibilities between the drug and formulation ingredients which enhance the stability of the product. **Conclusion:** Therefore a Vitamin D3 Anti-Aging Cream in the microsphere formulation demonstrates a great potential to be safe, efficacious and non-irritating drug delivery system. From this view, it is believed that this approach will reduce side effects of topical applications to a minimal level while at the same time enhancing therapeutic efficiency which will give an improvement of future topical drug delivery method in anti-aging therapies.

Keywords: Anti-aging, Cosmetics, Microsphere, Skin Care, Vitamin D3.

Correspondence:
Mr. Sabeel Salam
Department of Pharmaceutics, JSS College of Pharmacy, Ooty-643001, Tamil Nadu, INDIA.
Email: sabeelsalam1996@gmail.com
ORCID: 0009-0009-5323-2511

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INTRODUCTION

The modern trend for anti-aging products has increased as people have developed the desire to stay young. This would include fine lines, wrinkles, and even age spots. This is further enhanced by today's culture, which puts so much stress on looks and the development of a healthy and radiant complexion. With that in mind, skin care manufacturers are applying a range of formulations with newer active ingredients and technologies that have been advanced to address customer needs.[1]

Among the myriad active ingredients, there has emerged one of the highly valued anti-aging cream components known as vitamin D3 (Cholecalciferol). With several skin health-friendly properties, vitamin D3 therefore contributes to regulating various kinds of skin activities such as moisturisation and cellular repair mechanisms. Its excellent potential for skin health improvement and to counter the effects of aging; therefore, it is highly in demand in the formulation of skincare products. Therefore, it has become a key Vitamin for many customers in selecting appropriate anti-aging solutions.[2,3]

A new direction in which skincare formulators have been working is the use of microspheres. It consists of minute spherical particles that have the ability to encapsulate the active ingredients. With this technology, these agents are released slowly to maintain their continued action in the skin. More importantly, vitamin D3 can be effectively provided by the microspheres for an optimal penetration of the skin in a very long period of time. In this way, it substantially prolongs the effectiveness of anti-aging creams, making the action of vitamin D3 beneficial not only immediately but for a long time.[4-6]

An innovative approach explored by skincare formulators is the use of microspheres-tiny spherical particles that can encapsulate active ingredients.[7-9] This technology enables the gradual release of these substances, ensuring sustained benefits for the skin. In particular, microspheres can effectively deliver vitamin D3, facilitating its optimal penetration into the skin over an extended period. This method significantly enhances the efficacy of

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anti-aging creams, ensuring that the benefits of vitamin D3 are not only immediate but also long-lasting.[10-13]

Creating an effective anti-aging cream containing vitamin D3 and microspheres involves a precise series of processes. Initially, it's essential to select appropriate polymers or polymer blends that can provide the desired release profile of vitamin D3. The microspheres must then be accurately loaded with the vitamin. Following this, the microspheres are integrated into a cream or lotion base specifically formulated to optimize skin absorption and penetration. This meticulous formulation process guarantees that the final product delivers maximum benefits to consumers.[14-16]

MATERIALS AND METHODS

Vitamin-D_3 (Cholecalciferol) were procured from Supreme pharmaceuticals, Mysore, and the Polyvinyl Alcohol Ethyl Cellulose, Ethanol and Dichloromethane were purchased from Yarrow chem products, Mumbai, India.

Development of microspheres

An alcoholic solution containing ethyl cellulose and vitamin D3 is prepared in dichloromethane. Slowly, the prepared mixture is slowly added dropwise in a solution made up of 1% polyvinyl alcohol and the surfactant Tween 80 of 0.3%. The final product as described above is then stirred at 500 rpm and then allowed to mix for 2 hr. After the stirring phase, the microspheres are then filter collected, washed, and lastly dried at room temperature.[15,16] The formulation chart for each formulation was mentioned in Table 1.

Preparation of Microsphere-Infused Cream

An oil phase chosen stearic acid and lanolin are weighed in two different vessels and the aqueous phase, glycerin, triethanolamine and water are also weighed separately. In both phases the temperature is maintained at 75°C, employing a water bath to heat the phases. After this temperature has been attained in both, phases they are mixed at high speed. That is followed by cooling the mixture at room temperature until all the ingredients form a smooth white cream. Thereafter, formulated microspheres are spread uniformly into the cream for 30 min to create microsphere loaded cream.[17]

FTIR study of Drug-Polymer Interaction

In order to analyze the interaction between the drug and the polymer, the drug is then weighed with potassium bromide, and pressed at 100 kgs per cm^2 for 1 min with a KBr press. The resultant spectra are then logged in the region of 4000 cm^{-1} to 400 cm^{-1}.[18]

Percentage yield

Practical yield percentage is computed to determine the efficiency of the microsphere preparation. This is established by the following formula, mass of microspheres obtained in the different batches/Mass of initial materials.[19] The percentage yield is computed using the following formula:

$$\text{Percentage yield} = (a \times 100)/ b$$

Where ‘‘a” represent Product weight and ‘‘b” represent Total weight of drug and polymer.

Entrapment efficiency

The percentage of drug encapsulated in the microspheres in each batch is determined by the formula indicated below. 10 mg of drug-loaded microspheres were dissolved in 10 mL of methanol for measurement of drug content by using UV spectroscopy.[20] The entrapment efficiency is quantified as follows:

$$\text{The percentage for entrapment efficiency} = y \times 100 \div c$$

Where ‘‘y” is Practical drug content and ‘‘c” represents Drug content.

pH Determination

This was prepared by mixing 0.5 g of cream with 5 mL of distilled water and then taking the measurement using an accurate digital pH meter maintained at a constant temperature. To allow a thorough mixing, the solution was stirred slightly before putting the calibrated pH meter in the cream-water solution.[21]

Spreadability

When evaluating spreadability, one gram of cream was placed on the middle of two glass slides and the cream was spread or layered uniformly between the slides. The time required to physically separate the two slides was measured and its value used to estimate the spreadability of the cream.[22]

Viscosity

The rheological values of the topical formulation give information about its flow properties of the formed formulation and changes give information about alteration in product stability and efficacy. The viscosity was determined at spindle number 4 to a rotational speed of fifty revolutions per minute.[23]

In vitro permeation studies

In the *in vitro* permeation studies, Franz diffusion cell was used together with the receptor medium of pH 6.8 phosphate buffer and 1 g of microsphere cream in the donor side. The receptor medium was sampled at 1, 2, 3, 4, 5 and 6 hr intervals by withdrawing 2 mL of the medium and analyzing it with a UV spectrometer.[24]

Ex vivo permeation study

The goat skin used in the *ex vivo* permeation study was thawed gently and then divided into circular disks. It was then made to hydrate in the receptor medium at 37°C for 1 hr as well following

the method described above. The goat skin was safely secured between the donor and the receiving compartments to allow the exchange of gas between the two compartments. A magnetic stirrer was used to ensure agitation in the receiving chamber that was composed of the pH 6.8 phosphate buffer. During the course of the experiment, aliquots were removed from the receptor solution and replaced with fresh pH 6.8 phosphate buffer at 37°C.[25,26]

RESULTS

The areas of the FT-IR spectra of Vitamin D3 before and after incorporation into the formulations shown in Figures 1 and 2 were compared to determine the excipients compatibility assessment. The percentage yield of microspheres was determined to be 84%, 86%, 90% and 92% for the formulations F1, F2, F3 and F4 respectively. The entrapment efficiency for the various batches outlined in Table 1. was as follows; F1=78.18%, F2= 80.01%, F3= 86.50%, F4=80.80%. The pH level of formulation F1, F2, F3 and F4 was 5.5, 7.1, 6.5, and 5.8 respectively, which shows that the formulations are slightly acidic, slightly alkaline, neutral and slightly acidic respectively of those studied with formulation F2 having the nearest pH level to that of human skin. Hence the pH of these formulations plays a decisive role as that determine the stability, skin permeability and effectiveness of the topical drug delivery system as depicted in Table 2.

Spreadability study

The results of the spreadability study of the formulations F1 through F4 are summarized in Table 1. The particular formulations F1 participants received a spread rate of 13.2 gm cm per second within 15 sec and the formulation F2 the spread rate of 13 g cm per second in 14 sec only. Compared formulation F3 had a highest spreadability of 14.5 gm cm/sec in 15 sec and formulation F4 spreadability of 14 gm cm/sec in 13 sec. These outcomes suggest that all the assessed formulations present different spreadability properties, and more specifically formulation F3 and F4 with the highest spreadability properties. It has been demonstrated that the spreadability of its topical formulation is one of the key characteristics that define its applicability and efficiency as a method of application or method of active ingredient delivery to the skin surface.

Viscosity

Table 1 affords the needed viscosity values of the formulations F1, F2, F3 and F4. The recorded viscosity levels for formulation F1 F2 F3 and F4 were 19567, 19887, 20415 and 18991 respectively. These data express the rheological rates of the formulations, and the formulation F3 has the highest rheological rate at 20,415 and the F2 formulation at 19;887. Spreadability is an essential attribute of texture and can impact the flow properties of a topical formulation and its stability. Modifications within the viscosity is possible to achieve the particular application requirements and anticipated product properties.

In vitro permeation studies

The extent of drug release from formulations F1 to F4 was measured using percentage cumulative permeation from permeation studies. These results show that formulation F3 supplied the highest drug release and with 6 hr SUP-10 was released up to 22.75% while formulation F4 had a release of 19.85% only. Formulations F1 and F2 had slightly lower percentage drug diffusion during the trial, but this remained fairly constant over the test period. These results point to the differences in the release profiles, where formulation F3 has the most efficient drug diffusion among the formulas described and depicted in the Figure 3 on the right side of the proposed workflow model in the Figure 4.

Ex vivo permeation study using goat skin

The *ex vivo* permeation of formulations utilizing goat skin in the experiment revealed that the drug diffusion ascendently rise within the 6 hr testing period. Determination of the extent of drug diffusion shows that formulation F3 had the highest diffusion rate at the end of the duration with 23.55% while formulation F4 had 19.01%. On the other, formulations F1 and F2; had comparatively lower percent drug diffusion, however, this percent had remained proportional throughout the time period. From these experiments, it emerges that formulation F3 enabled the most potent penetration of the drugs through the goat skin out of all the formations investigated, as demonstrated in Figure 5 above, making it desirable for transdermal drug delivery.

Table 1: Table includes all the formulation charts for each batch.

Ingredients	F1	F2	F3	F4
Drug (VIT d3) (mg)	1.25	1.25	1.25	1.25
Ethyl Cellulose(mg)	200	400	600	800
Dicloromethane(mL)	20	20	20	20
Ethanol	20	20	20	20
Polyvinyl alcohol (%)	1	1	1	1
Tween 80(%)	0.3	0.3	0.3	0.3

Table 2: **Table includes all the results of Spreadability study, Viscosity, Percentage Drug Entrapment and Determination of pH.**

Formulation	Time (sec)	Spreadability (gm cm/sec)	Viscosity	Entrapment efficiency (%)	pH
F1	15	13.2	19567	78.19	5.5
F2	14	13	19887	80.80	7.1
F3	15	14.5	20415	86.50	6.5
F4	13	14	18991	84.52	5.8

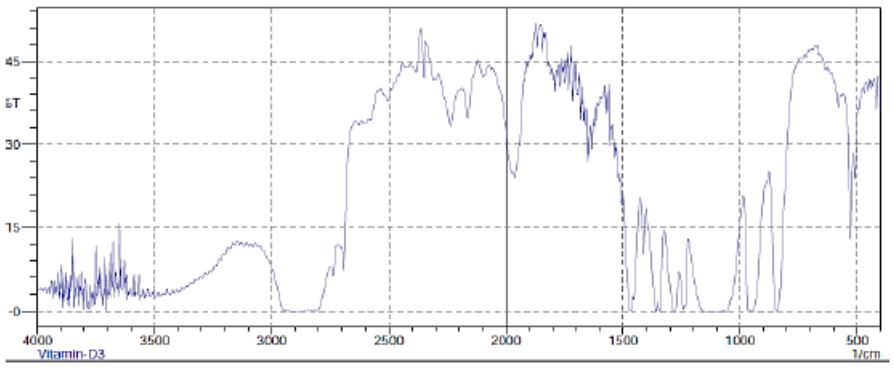

Figure 1: Shows the FTIR spectrum of Pure vitamin D3.

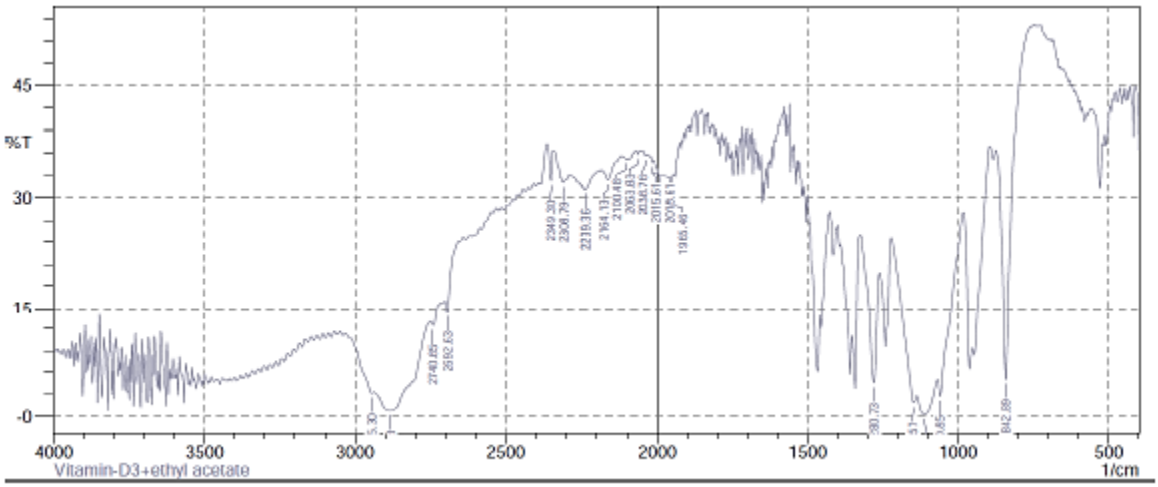

Figure 2: Shows the FTIR spectrum of vit d3+ethyl cellulose and results showed that there is no obvious interaction between the Vitamin D3 and the excipients.

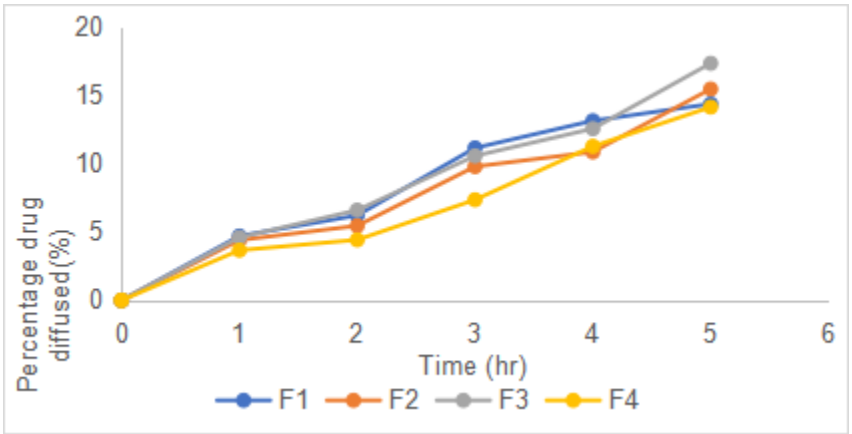

Figure 3: This Figure shows the *in vitro* Drug Diffusion of the formulation.

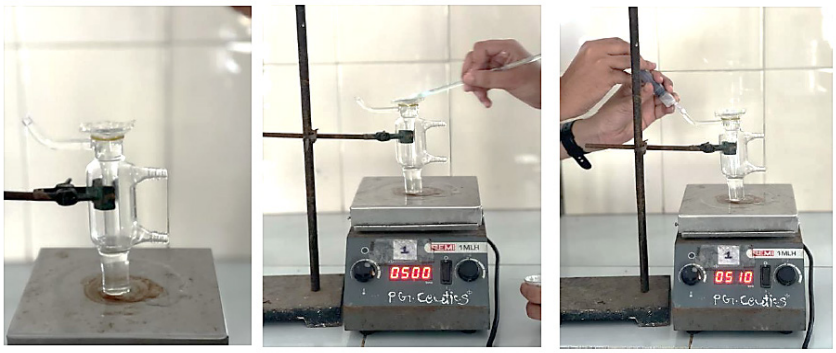

Figure 4: This Figure shows the model of work of *In vitro* Permeation studies done.

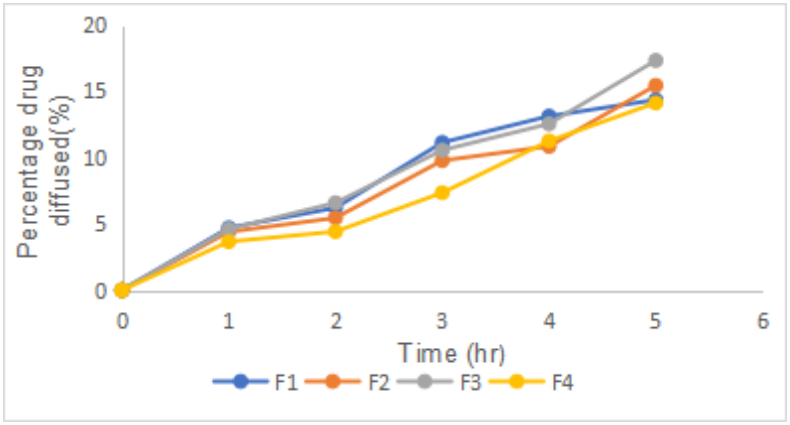

Figure 5: This Figure shows the *Ex vivo* drug diffusion of the formulation.

DISCUSSION

The formation of microspheres through solvent evaporation and the subsequent application of the obtained microspheres in a cream base for transdermal drug delivery represents a breakthrough in methods of medication administration. This formulation containing Vitamin D3, was aimed at improving the diffusivity of the base drug and, therefore, resulted in considerable drug penetration *ex vivo*/*in vivo* models. This dermal drug delivery system proved its efficiency while delivering the ability to enhance membrane penetration. *In vitro* release kinetic analysis revealed zero order release kinetics for the drug, pointing to good control and sustained delivery of the system. In addition, physicochemical characterization of the formulated product through FTIR spectroscopy showed that there was no interaction among the components of the formulated product hence laying credence to stable formulated product. By slowly releasing the medication from the microspheres it is expected that the amount of topical side effects may be minimized while maximizing the therapeutic benefits hence making the administration strategy more controlled and precise.

CONCLUSION

The development of a microsphere-based Vitamin D3 Anti-Aging Cream poses non-irritating, safe and effective approach for dermal anti-aging drug delivery. The successful preparation of microspheres and incorporation into a cream base demonstrates a possibility for enhanced drug diffusion and penetration that points to the potential for the formulation to deliver localized, controlled and sustained release of medication. It has great potential for improving both effectiveness and safety of dermal drug delivery in general and anti-aging therapies in particular, opening a new opportunity for further refining and individualizing skin care interventions.

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ABBREVIATIONS

FTIR: Fourier Transform Infrared Spectroscopy.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

This work gai for the preparation of microspheres using solvent evaporation technique where they are integrated in a cream matrix for the delivery of dermatological agents. The newly formulated improve drug diffusion parameters having Vitamin D3 chocking; the results have better permeation for dermal drug delivery across membranes through *in vitro* and *ex vivo* from higher

increase. Moreover, in the *ex vivo* diffusion analysis it was obvious that the release of the drug follows a zero order model which this means that the controlled release of the drug is sustained. Further physicochemical characterization through Fourier Transform Infrared (FTIR) spectroscopy analysis precluded the possibility of interactions between the formulation components, and thus stability. It is believed that the controlled release systemizes will reduce the topical side effect, while increasing the therapeutic effect at the same time. As a result, the Vitamin D3-enriched Anti-Aging Cream is considered safe, efficacious, and non-irritating, and thus potential for future application of topical drug delivery systems in anti-aging treatments. The introduction section focuses on the fact that the current trend for skin anti-aging products is increasing due to societal expectations concerning youth. The paper also elaborates on the importance of Vitamin D3 for skin functioning enhancing the hydration process and promoting the processes of cell regeneration, as well as the options for utilizing microsphere approach to stimulate active ingredients. This technology provides for consistent and effective delivery of Vitamin D3 to the dermis to complement the benefits of any anti-aging creams. The process includes a selective process of the choice of polymers in order to regulate the rate of the Vitamin D3 release, then an elaborated procedure to prepare the polymer formulation for skin permeability. Stability testing, skin irritation, and testing for the effectiveness regarding various signs of skin aging evidence the cream's efficacy and safety.

The experimental data revealed a wide range of microsphere yield percentages for different formulations, and different entrapment efficiencies. The formulations obtained in this study showed differences in pH and high spread values for all the formulations and therefore could best be described for topical use. The rheological values provided a basis for the stability of the formulations and the diffusion studies showed a great extent of drug releasing ability that was demonstrated in the most efficient formulation among the test formulations.

This research supports the practicality of microsphere-based Vitamin D3 formulations to improve the delivery of the drug as a new approach in eradicating skin aging. It is therefore safe and effective for use as presented in the formulation of the cream; it also emphasizes the capability of the embodiment to enhance the refinement of anti-aging therapies through intervention by controlled, localized and sustained drug delivery, thus improving skin care treatments.

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