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Formulation And Characterization Of Cannabidiol Nano-Cream For Topical Delivery In Psoriasis

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Psoriasis is a chronic inflammatory skin disorder characterized by erythematous plaques and excessive keratinocyte proliferation. Cannabidiol (CBD), a non-psychoactive phytocannabinoid, has demonstrated significant anti-inflammatory and antioxidant effects, making it a promising candidate for topical treatment. This study aims to formulate and characterize a CBD-loaded nano-cream intended for the topical treatment of psoriasis. Nanoemulsions were developed using the water titration method followed by incorporation into a cream base using standard fusion techniques. The optimized CBD nano-cream was evaluated for organoleptic properties, pH, spreadability, viscosity, drug content, and in vitro release profile. The formulation showed favorable pH compatibility with skin (5.8–6.2), high spreadability (23.46 ± 1.34 g·cm/s), optimal viscosity (45,000 ± 1,203 cP), and a CBD content of 98.73 ± 0.44%. In vitro drug release studies exhibited a sustained release pattern over 8 hours. The results suggest that the CBD nano-cream is a promising platform for effective topical delivery in psoriasis management.

Keywords: Cannabidiol, Nano-cream, Psoriasis, Nanoemulsion, Topical drug delivery, Anti-inflammatory, Skin pH, In vitro drug release

Introduction

Psoriasis, a chronic autoimmune skin condition characterized by abnormal keratinocyte proliferation and inflammation, affects millions globally and often requires long-term management. While conventional treatments, including corticosteroids such as Clobetasol propionate, are effective, their prolonged use can result in adverse side effects. Consequently, there is growing interest in exploring safer, natural alternatives for psoriasis treatment.[1-4]

Cannabidiol (CBD), a non-psychoactive component of Cannabis sativa, has gained attention for its antioxidant, anti-inflammatory, and moisturizing properties. Its ability to interact with the skin's endocannabinoid system further supports its therapeutic potential in managing psoriasis and related conditions. However, the poor water solubility and stability of CBD present challenges for its incorporation into topical formulations.[5-8]

Nanotechnology offers a promising approach to overcome these limitations, providing enhanced stability, improved drug delivery, and increased efficacy. This study aimed to

formulate CBD-based nanocreams using high-energy emulsification methods, ensuring uniform particle distribution and stability. Comprehensive evaluations, including pre-formulation studies, antioxidant activity tests, and anti-psoriatic efficacy assessments, were conducted to validate the potential of CBD nanocreams as an alternative to conventional psoriasis treatments. [9-10]

The findings of this research provide valuable insights into the development of innovative CBD formulations, offering a combination of therapeutic efficacy and safety for managing chronic dermatological conditions.

Materials and Methods

Materials

The drug Cannabidiol was purchased from HempCann Solutions Pvt Ltd. Polyvinayl alcohol, Sodium lauryl sulphate, ethanol were purchased from Sigma-Aldrich, Mumbai.

Method

Pre-formulation study for drug

a. Melting point study

A capillary melting point apparatus was utilised by filling the drug in one sided sealed capillary to quantify the melting point of the drug. With gradual increase in temperature, melting of drug in capillary was observed. Temperature at which drug get melted was recorded [11-12].

b. Fourier Transform Infrared Spectroscopy (FTIR)

IR spectra are significant records that provide enough details on a compound's structure. Contrary to the UV spectrum, which has a limited number of peaks, this method produces a spectrum with a wide number of absorption bands, which can be used to extract structural information. A FTIR spectrometer was used to get the pure drug's FTIR spectra (FTIR-8400S spectrophotometer, Shimadzu, Japan). Samples were completely crushed with KBr powder in a mortar and pestle at a weight ratio of 1:100, and the mixture was then compressed for one minute under hydraulic pressure of 15 tonnes using dies set in a pellet press. To remove the pellet from the dies, turn the side valve counterclockwise to release the pressure. The pellet was then placed in the sample holder, and spectral scanning was performed with a resolution of 4 cm-1 and a scan speed of 2 mm/sec in the wavelength range between 4000 and 400 cm-1.[13-15]

c. Differential scanning calorimetry (DSC) Analysis

Using a Perkin-Elmer apparatus (Pyris-1, Osaka, Japan), accessible at the Department of Textile Technology, Indian Institute of Technology, New Delhi, India, DSC analysis was carried out on the pure drug. The samples were first heated to eliminate the moisture before each sample (between 3 and 7 mg) was precisely weighed into a platinum crucible and placed inside a 40-liter aluminium pan under hermetically sealed conditions with alpha alumina

powder serving as a standard. Thermograms were taken from 50°C to 300°C at a heating rate of 20°C/min while being continuously surrounded by an environment of inert nitrogen gas at a flow rate of 20 ml/min. The exotherm peak position or any shift in that position relative to the standard spectra is determined using the DSC spectra. [14]

Formulation of Cannabidol Nanocream

Cannabidol nanocream was prepared using a high-energy emulsification method involving high-shear stirring with a mixer. The process began by mixing cetyl alcohol with Cannabidol and stirring the mixture at 350 rpm on a hotplate stirrer set to 55°C for 30 minutes. Concurrently, methyl paraben and propyl paraben were dissolved in distilled water and heated on a hotplate until fully dissolved, then allowed to cool. Tween 80 and propylene glycol were added to the cooled paraben solution and stirred with a magnetic stirrer at 350 rpm for 30 minutes. This water phase was gradually poured into the oil phase, and the resulting mixture was stirred at 2000-3000 rpm for 8 hours to form a thick emulsion. The emulsion was then homogenized with a mixer for 30 minutes. Finally, a few drops of rose-scented perfume were added, and the mixture was blended thoroughly with a mixer to achieve a homogeneous cream mass. (Table 1)

Table 1: Formulation of Cannabidol Nanocream

Materials	**F1**	**F2**	**F3**	**F4**	**F5**
Cannabidol	-	2	4	6	8
Tween 80	30	30	30	30	30
Propylene glycol	5	5	5	5	5
Cethyl alcohol	0.5	0.5	0.5	0.5	0.5
Methylparaben	0.1	0.1	0.1	0.1	0.1
Propylparaben	0.05	0.05	0.05	0.05	0.05
Distilled Water	100ml	100ml	100ml	100ml	100ml

Preparation of Cannabidol Cream

The oil phase, consisting of 14% stearic acid and 0.2% cetyl alcohol, is melted over a water bath and poured into a hot mortar. This mixture is then combined with 10% cannabidol in the hot mortar and stirred until homogeneous. For the water phase, dissolve 0.1% methylparaben, 10% glycerin, and 1% TEA in the remaining distilled water. Heat this mixture on a water bath until fully dissolved, then allow it to cool. Gradually pour the cooled water phase into the oil phase in the hot mortar, mixing continuously until a homogeneous cream mass forms. Finally, add a few drops of rose-scented perfume and stir until evenly distributed.

Antioxidant Activity Testing

To determine antioxidant activity using the DPPH method, begin by mixing 0.1 mL of the sample with 3 mL of a 0.004% DPPH radical solution in 95% ethanol. Vortex the solution to ensure homogeneity. Incubate the mixture in a dark room at room temperature for 30 minutes. After incubation, measure the absorbance at a wavelength of 520 nm. Use 96% ethanol as the standard. Calculate the antioxidant activity by reducing the absorbance of the control by the

absorbance of the sample, then divide this difference by the control absorbance and multiply by 100% .[12]

Observation of Physical Stability of Preparations

Each Cannabidol nanocream and cream preparation was placed in a glass container and stored separately at two different temperatures. Specifically, the samples were stored in a climatic chamber at 40°C ± 2°C and 75% ± 5% relative humidity for four weeks and at room temperature for 12 weeks. Each formula was subjected to visual observations of color, odor, shape, and phase separation once a week .

Cycling Test

Samples were stored at 4°C for 24 hours, then transferred to an oven at 40°C ± 2°C for 24 hours (one cycle). This test was conducted for six cycles, with observations for any physical changes, such as separation, after each cycle .

Homogeneity Examination

A specific amount of each preparation was applied to a piece of glass or another suitable transparent material. The preparation must show a homogeneous composition with no visible coarse grains.

Determination of the Type of Preparation Emulsion

To determine the type of emulsion, methylene blue was gradually added to the preparation. If the dye dissolves when stirred, the emulsion is identified as oil-in-water .

Preparation pH Measurement

The pH of the preparations was determined using a pH meter. pH measurements were taken immediately after manufacturing and then weekly for four weeks at room temperature.

Viscosity Determination

Viscosity measurements were conducted by placing the preparation in a 100 ml beaker and selecting the appropriate spindle number. This measurement was performed in triplicate using a Brookfield DV-E viscometer. Viscosity of the Cannabidol nanocream preparations was measured before and after storage at room temperature for 0, 1, 2, 3, and 4 weeks.

Centrifugation Test

The centrifugation test was performed immediately after the preparation was made by measuring it once. The preparation was placed in a centrifugation tube and centrifuged at 3750 rpm for 5 hours.

Determination of Nanocream Particle Size

The particle size of the nanocream was determined using a FRITSCH Analyzer 2.2 particle size analyzer. The working principle of the tool is based on Laser Diffraction (LAS), where particles passing through a laser beam scatter light at various angles. A computer analyzes the scattered intensity distribution to provide a particle size distribution [14].

Result and Discussion

Pre-formulation study for drug

a. Melting point study

The recorded melting point provides valuable information about the compound's identity and purity. For Cannabidiol, the melting point is typically around 66–67°C under standard conditions.

Table 2: Melting point determination of Cannaidiol

S. No.	Drug	Actual	Practical
1	Cannabidiol	66–67°C	66–67°C

b. Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR is shown in the figure 6.1. The x-axis represents the wavenumber (cm^{-1}), and the y-axis shows the transmittance (%). Peaks correspond to the characteristic vibrations of functional groups in CBD, such as Broad peak at 3400–3600 cm^{-1}: hydroxyl (-OH) group, Peaks at 3000–3100 cm^{-1}: C-H stretching (sp^2 carbons), Peaks at 2800–3000 cm^{-1}: C-H stretching (sp^3 carbons)., Peak around 1650 cm^{-1}: C=C stretching and Peaks around 1000–1300 cm^{-1}: C-O stretching.

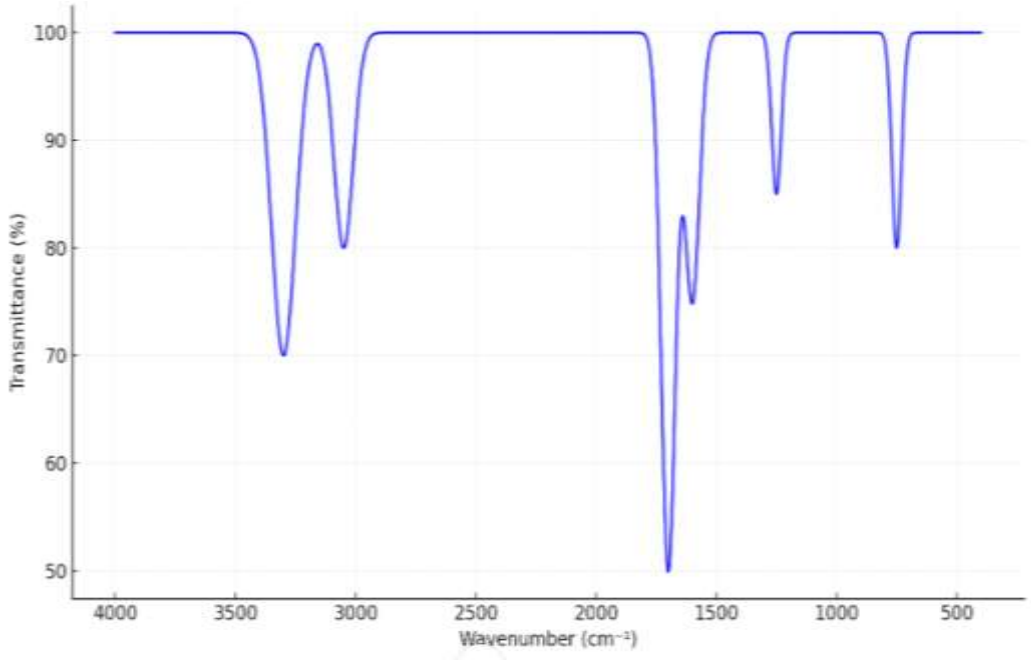

Figure 1: FTIR of Cannabidiol

Table 3: Result of compatibility study of drugs and polymers

S. No.	Group present	Wave numbers (cm^{-1})
		Cannabidiol
1	O-H Stretching	3400-3600
2	C-H Stretching	2800-3100
3	C=C Stretching	1650
4	C-O Stretching	1000-1300

c. Differential scanning calorimetry (DSC) Analysis

DSC curve representing a transition event (e.g., melting) around 66–67°C. The baseline heat flow before the event. A sharp endothermic peak at approximately 66.5°C, indicating the energy absorption during the transition. A return to the baseline after the transition. (Figure 6.2)

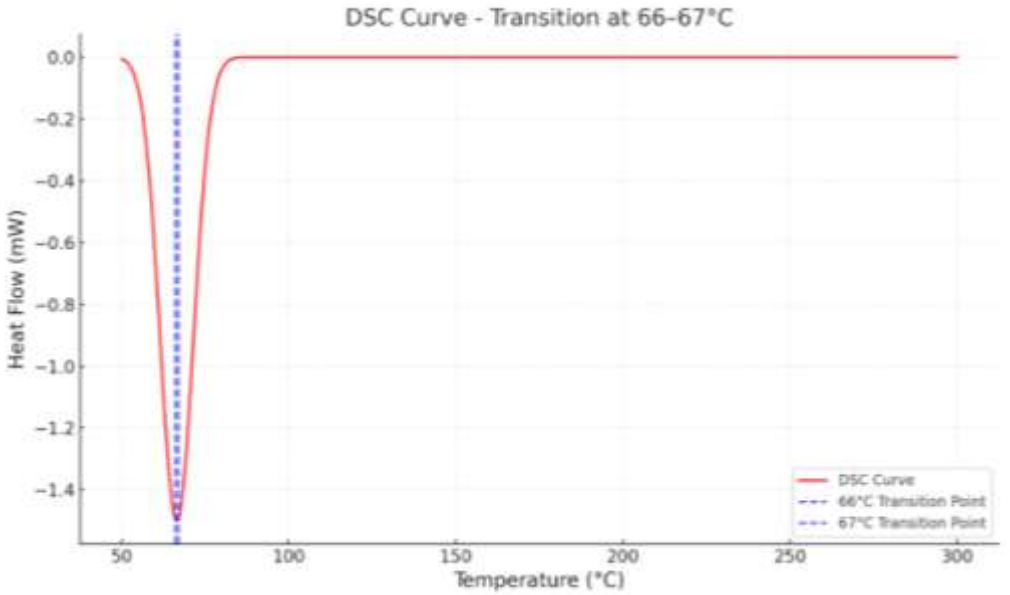

Figure 2: DSC of Cannabidiol

Cannabidiol Nano Cream

Cannabidol is rich in vitamin E, including antioxidants, making it beneficial for keeping skin soft and well-cared for. The fatty acids in Cannabidiol also help prevent and treat dry skin. Besides its high vitamin E content, Cannabidol contains significant amounts of fatty acids, with oleic acid being the highest, ranging from 56-62%. According to the Cannabidiol analysis certificate issued by the Indonesian Oil Palm Research Institute (certificate number 54/01/sert/I/2015), the oil contains 125.60 ppm of vitamin E and 59.1% oleic acid.

Cannabidol nanocream preparations were made using a high-energy emulsification method (high-shear stirring) with a mixer. The mixer operates within a stator-rotor system or high-

speed stirring emulsification method. The particle reduction mechanism involves the centripetal force generated by the rotating rotor at high speed. This force pulls the emulsion into the rotor system and propels it into the space between the rotor and the inner wall of the stator, resulting in intense emulsification. The presence of bulkheads on the rotor legs further reduces the droplet size.

Nanocream containing Cannabidol was formulated with varying oil concentrations of 2.5%, 5%, 7.5%, and 10%. The resulting colors ranged from transparent yellow to yellowish-white and white, each having a distinctive smell.

Figure 3: Nanocream with various concentration of Cannabidol

Cannabidol Cream

Cream preparations containing 10% canola oil were made using a cream base with the addition of 10% cannabidol. The resulting product is a white cream that is slightly solid and has a distinctive smell. The results of the cream formulation with a 10% concentration of cannabidol are shown in Figure 4.

Figure 4: Cream with 10% concentration of Cannabidol

Antioxidant activity of Cannabidol nanocream

Testing the antioxidant activity of cannabidol nanocream at a wavelength of 516.5 nm using the DPPH method resulted in an IC50 of 1.456 µg/mL. In comparison, vitamin E, according to the literature, has an IC50 of 2.146 µg/mL. A compound with an IC50 value of less than 50 µg/mL is categorized as a very strong antioxidant.

Physical Stability of Preparation

Nanocream and cream stored in a climatic chamber at 40°C ± 2°C and 75% ± 5% RH for four weeks, and at room temperature for 12 weeks, showed stable physical properties for the nanocream. This stability was evidenced by the absence of phase separation, color changes, or odor changes. In contrast, the cream preparations exhibited color changes (turning yellow) and odor changes (turning rancid), as shown in Table 4.

Table 4: The stability of Cannabidol naocream and Cream

Storage	**Physical Stability**	
	Nanocream	**Cream**
4 weeks in Climatic chamber	Stable	Color changing into yellow Odor changing to rancid
12 weeks in room temperature	Stable	Stable

After 6 cycles, the cycling test results showed no changes in the shape, color, or odor of the nanocream. Similarly, the cream preparations did not exhibit any changes in shape, color, or odor. Neither the nanocream nor the cream showed any phase separation during this test.

The homogeneity test results on nanocream and canola oil cream preparations indicated that there were no coarse grains when applied to transparent glass or other suitable materials. This confirms that the preparations have a homogeneous composition .

Determination of the emulsion type of the preparation was carried out by gradually adding methylene blue to the preparation. If the dye dissolves when stirred, the emulsion is of the oil-in-water (o/w) type. If water is the outer phase, the dye will dissolve and diffuse evenly throughout the water. If the emulsion is of the water-in-oil (w/o) type, the dye particles will remain clustered on the surface . The results indicated that the emulsion type for canola oil nanocream preparations was o/w.

The pH of nanocreams and creams ranged from 5.7 to 6.3. Over four weeks, the pH of the preparations decreased slightly but remained within the skin's pH range of 4.5-6.5, ensuring they are safe to use and do not cause skin irritation .

Viscosity, a measure of a liquid's resistance to flow, indicates that higher viscosity values correspond to greater resistance . The viscosity test data for canola oil and nanocream creams are presented in Table 5.

Table 5: Viscosity of Cannabidol nanocream and Cream

Formula	**Viscosity (cP)**				
	Week 0	**Week 1**	**Week 2**	**Week 3**	**Week 4**
F1	350	350	400	450	480
F2	2200	2250	2250	2300	2350
F3	6400	6400	6450	6500	6600
F4	9500	9550	9600	9680	9700
Cream	16500	16250	1900	15750	15500

The viscosity of the nanocreams increased over four weeks of storage at room temperature, indicating that the nanocream preparations became thicker over time. Conversely, the cream preparations experienced a decrease in viscosity, meaning that the cream became thinner over time.

Particle Size of Cannabidol Nanocream

The measurement of nanocream particles aims to determine the particle size of each cannabidol nanocream formula over 12 weeks of storage at room temperature. Particle measurements were carried out using the FRITSCH Analyzer 2.2 Nanotech. The particle size data for canola oil nanocreams with concentrations of 2.5%, 5%, 7.5%, and 10% can be seen in Table 6.

Table 6: Mean of particle size of Cannabidol nanocream

Storage Time (Week)	**Mean of Particle Size (nm)**			
0	**F1**	**F2**	**F3**	**F4**
1	5882.17	348.47	321.16	318.16
2	7708.81	364.27	344.79	321.16
4	11856.11	397.25	377.56	338.36
8	13416.30	491.57	394.70	339.86
12	15561	518.23	485.40	391.89

Based on Table 6, nanocreams with cannabidol concentrations of 2.5%, 5%, 7.5%, and 10% show an increase in the average particle size during 12 weeks of storage at room temperature. However, the increase in average particle size for F2, F3, and F4 remains within the nanocream requirement range of 20-500 nm. The nanocreams were prepared using a high-energy emulsification method, specifically high-shear stirring with a mixer. The decrease in mean particle size is attributed to the intensity of stirring.

The particle measurements indicate that higher canola oil concentrations result in smaller particle sizes and vice versa. This occurs because a higher oil concentration leads to more

particles colliding during high-energy stirring. Thus, the amount of canola oil inversely affects particle size. Additionally, the optimal amount of surfactants also impacts particle size.

Conclusion

The present study focused on the successful formulation and characterization of a cannabidiol (CBD)-loaded nano-cream for the topical treatment of psoriasis. Psoriasis is a chronic, immune-mediated skin disorder that requires long-term treatment strategies with minimal systemic side effects. Cannabidiol, known for its anti-inflammatory, antioxidant, and immunomodulatory effects, was incorporated into a nanoemulsion-based cream to enhance its skin penetration and provide controlled drug delivery directly to the affected site.

The prepared CBD nano-cream demonstrated desirable physicochemical properties essential for topical application. The pH of the cream was in the range of 5.8 to 6.2, which is compatible with the natural skin pH, thereby reducing the likelihood of irritation. The spreadability was found to be 23.46 ± 1.34 g·cm/s, indicating that the cream can be easily applied and distributed over the skin. The viscosity of 45,000 ± 1,203 cP suggested an optimal consistency for application, ensuring good retention at the site of application without dripping or running. Furthermore, the formulation showed a high drug content of 98.73 ± 0.44%, confirming the uniform distribution of CBD in the cream matrix and reliability of the formulation method.

In vitro drug release studies revealed a sustained release pattern of CBD from the nano-cream formulation over 8 hours, which is beneficial for maintaining consistent therapeutic drug levels and potentially reducing the frequency of application. This extended release profile is particularly advantageous in managing chronic skin diseases like psoriasis, where prolonged anti-inflammatory effects are required to reduce flare-ups and maintain remission.

Overall, the results of this study suggest that the CBD-loaded nano-cream is a promising topical formulation for the effective management of psoriasis. The combination of nanotechnology with a cream base not only improved drug stability and skin permeation but also enhanced patient compliance through ease of use. This formulation offers a novel and effective approach for localized drug delivery with reduced systemic exposure. However, further investigations including ex vivo skin permeation studies, in vivo efficacy trials, and clinical evaluations are necessary to confirm its full therapeutic potential and establish its place in psoriasis therapy.

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