RESEARCH ARTICLE

Preparation, Characterization and *In-vitro* Evaluation of Nano Encapsulated 1-Octacosanol for Solubility Enhancing by using Various Polymers through Spray Drying Approach

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Received: 14th October, 2023; Revised: 08th November, 2023; Accepted: 22th November, 2023; Available Online: 25th December, 2023

ABSTRACT

This research aimed to develop a nano-encapsulated free-flow powder of 1-octacosanol for functional food application. We had prepared stable green nano-emulsion oil in water by Dyno Mill and spray dryer for free flow powder by using different polymers (Hydroxypropyl methylcellulose, polyvinylpyrrolidone, octenyl succinate starches) as hydrophilic polymers in different ratios for enhancing the solubility. Zeta potential, X-ray diffraction (XRD), fourier transform infrared spectroscopy (FTIR), encapsulation efficiency, particle size distribution, surface morphology, differential scanning calorimetry spectroscopy and *in-vitro* dissolution research were used to analyze 1-octacosanol.

The optimized nano-emulsion preparation F15 consists of an average particle size 720.9 nm, zeta potential -24.5 mV shows stable nano-emulsion oil in water type, and encapsulation efficiency was found to be 96.76%, FTIR studies did not show any evidence of interaction between the herbal extract and the polymers. XRD shows the conversion of crystalline to amorphous nature of powder. In differential scanning calorimetry (DSC), spectroscopy studies found three major peaks in standard herbal extract peaks is 60.21, 67.16, 81.27°C and nano-encapsulated spray dried powder peaks are 58.18, 66.44, 79.25°C with minor moisture absorbed by the polymer in formulation.

This evaluation shows significant improvement between normal herbal extract of 1-octacosanol and encapsulated spray-dried powder of 1-octacosanol for functional food application successfully improving the water solubility without changing a structural and chemical properties of the 1-octacosanol crystal.

Keywords: 1-Octacosanol, Nano-emulsion, Hydrophilic polymers, Encapsulation, Functional food.

International Journal of Drug Delivery Technology (2023); DOI: 10.25258/ijddt.13.4.36

How to cite this article: Singh AK, Kharb R, Kandpal JB. Preparation, Characterization and *In-vitro* Evaluation of Nano Encapsulated 1-Octacosanol for Solubility Enhancing by using Various Polymers through Spray Drying Approach. International Journal of Drug Delivery Technology. 2023;13(4):1347-1353.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

A total of 28 carbon atoms make up the 1-octacosanol, a naturally higher aliphatic alcohol, which is extensively derived from natural sources including wheat-germ oil, beeswax, and wax from rice bran. Numerous physiological characteristics of 1-octacosanol include the ability to decrease cholesterol, protect cells, and have antibacterial actions.[1]

Since it was detected in the greatest amount, 1-octacosanol was thought to be the main active policosanol liable for effectiveness. Octacosanol increases oxygen consumption by bolstering the heart, maintaining high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels, and preserving normal cardiac function.[2]

The 1-octacosanol is readily available on the market due to its safety for usage in people. The weak solubility of 1-octacosanol in water restricts its use, however, several technological solutions have been used to address this issue.[3]

Herbal products have a lower bioavailability since they are water-insoluble. To increase solubility, stability, and bioavailability in final products, intermediate formulation was thus done on the original extract form.[4]

It has been demonstrated that encapsulation, a strategy for protecting the natural active ingredient and developing delivery mechanisms, improves the action of functional ingredients in gastrointestinal tract (GIT) and produces the desired release profile.[5]

The core and wall materials are combined in the main solution for microencapsulation utilizing spray drying. These substances must thus be manufactured as dispersions or emulsions or be soluble in water. In some circumstances, it is

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preferable to use the main solution with low viscosity to avoid adhesion nozzle and clogging, as well as to ensure consistent spraying.[6]

The choice of the proper wall material or polymer is crucial since it is essential to the encapsulation process. Sometimes, during the encapsulation process, it is challenging to achieve the intended result with just one polymer; thus, the use of two polymers in combination might be advised to obtain the necessary products.[7]

This study's major goal was to create a novel nano-encapsulated 1-octacosanol for improving solubility utilizing a variety of hydrophilic polymers and a spray drying method. In this work, the stability and solubility of the nanoemulsion between the herbal extract of 1-octacosanol and nano-encapsulated 1-octacosanol were comprehensively examined particle size, fourier-transform infrared spectroscopy (FTIR), zeta potential, X-ray diffraction (XRD), encapsulation effectiveness, differential scanning calorimetry (DSC), surface morphology, and *in-vitro* dissolution investigation were all used to describe nano complex.

MATERIAL AND METHODS

Materials

The 1-octacosanol (50% purity) was supplied by India Glycols Ltd., India, Hydroxypropyl methylcellulose (HPMC) was supplied by Signet excipients Pvt. Ltd., India, Polyvinylpyrrolidone (PVP) was supplied by Anshul Life Sciences Ltd., India, Octenyl succinate starches (OSS) was supplied by Ingredion Pvt. Ltd., India, Tocopherol was supplied by Matrix Life Sciences Pvt. Ltd., India, Polysorbate 80 was supplied by BASF Pvt. Ltd., India, Medium Chain Triglycerides C8 (MCT-C8) was supplied by AAK Pvt. Ltd., India. The remaining other chemicals were analytical grade.

Methods

Preparation of spray-dried nano-encapsulated 1-octacosanol

There were prepared a total of two series of formulations, the specifics of which are displayed in Table 1. Three formulations from the first series were created using a mixture of HPMC 1-octacosanol, PVP, and OSS. Three formulations were included in the second series, which was likewise made with 1-octacosanol and various ratios of HPMC, PVP, and OSS. In all of the formulations, tocopherol was utilized as an anti-oxidant, Polysorbate 80 served as a surfactant, and MCT C8 served as an emulsifier. Each formulation required 500 mL of liquid o/w nano-emulsion in total. 1-octacosanol and polymer were added to water, which was then prepared and ground in a bead mill (DYNO®-MILL Research Lab, Switzerland) for 20 minutes at 6 tip speed.

The nano-emulsions were produced in a laboratory-scale using a spray dryer (SPD-P-111, Techno Search Process, India) equipped with 0.5 mm atomizer, compressed auto jet deblocking system, compressed spray atomizer, drying chamber, and cyclone. Throughout the experiment, an air velocity of approximately 2.5 Bar was maintained. 180 ± 1 and 90 ± 1°C were chosen as the intake and exit temperatures. The nano-emulsions were introduced into dryer using a peristaltic pump with 10 mL/min flow rate. Samples of dried powder were collected using a cyclone separator and Schott bottle attached to the bottom of the drying chamber. Next, an aluminum zip-lock bag was used to store the powder samples, who were then maintained at 24°C.

Table 1: Batches of formulation spray-dried 1-octacosanol emulsion

Ingredients	*Series-I*			*Series-II*		
	F11	*F12*	*F13*	*F14*	*F15*	*F16*
1-Octacosanol (g)	42	42	42	42	42	42
HPMC (g)	42	0	0	21	21	0
PVP (g)	0	42	0	21	0	21
OSS (g)	0	0	42	0	21	21
Polysorbate 80 (g)	2	2	2	2	2	2
Tocopherol (g)	2	2	2	2	2	2
MCT C-8 (g)	12	12	12	12	12	12
Distilled water (g)	400	400	400	400	400	400
Solid content (wt. %)	20	20	20	20	20	20

Characterization of 1-octacosanol Emulsion

Distribution of particle size and zeta potential

Using DLS technique, particle size distribution and zeta potential were examined, droplet size of the produced emulsions was appropriately diluted. With a little modification, the Malvern Zetasizer Nano ZS (Malvern, UK) was utilized to ascertain DLS characteristics. [8] Particle size distribution and Zeta potential average count rates were correctly adjusted using distilled water to be around 366 and 107.5 kcps, respectively. At a constant temperature of 25°C and a fixed angle of 90°C, all measurements were made. Each sample was examined three times, and the usual results were presented.

Characterization of Encapsulated 1-Octacosanol

Moisture content

By heating around 10 mg of the collected samples on a hotplate for 10 minutes at 100°C, the water content of the samples was ascertained.[9] The samples' weights before and after heating were noted. After 10 minutes of heating at 100°C, the percentage of weight loss was calculated as a function of the sample's water content.

Particle surface morphology

Field emission scanning electron microscopy (JEOL JSM-IT200, Japan) was used to examine the morphological structure of 1-octacosanol-encapsulated powder particles.[10] The specimen stubs were coated with dry powder, which was attached using carbon tapes with double-sided adhesive. With magnifications ranging from 50X to 20,00, a specimen was coated in platinum, studied at 1-30 kV.

Determination of microencapsulation efficiency

With a little modification, GC-FID was used to determine [11]how much 1-octacosanol was contained inside the inclusion complex. Using the following equations, the drug loading (DL) and encapsulation efficiency (EE) of FMT were determined:

% EE = (weight of Active in complex/theoretical weight of Active) × 100

Bulk and tapped density of powder

For bulk density (ρ_{bulk}).[12] the 1-octacosanol encapsulated powder was carefully poured into 50 mL tared glass cylinder until it reached 50 mL mark, then weight (w) was recorded. Based on the connection illustrated below, volume (v) acquired nonstop from the glass cylinder was utilized to compute bulk density:

$$\rho_{bulk} = w / v_{untapped}$$

For tapped density (ρ_{tapped}), 50 mL tared glass cylinder was gently filled with the 1-octacosanol encapsulated powder to the 30 mL mark, and then the cylinder was weighed (*w*). After physically tapping a 50 mL tared glass cylinder filled with powder 100 times, there was no discernible variation in the volume (V_{tapped}) between the consecutive measurements. Then the following formula was used to get the tapped density:

$$\rho_{tapped} = w / v_{tapped}$$

Flowability of powder

These were determined using the modified method.[13] Carr index (*CI*) and Hausner ratio (*HR*). Both were calculated from value of bulk and tapped density of powder using the below formula, respectively:

$$CI = (\rho_{tapped} - \rho_{bulk})/\rho_{tapped} \text{ X } 100$$
$$HR = \rho_{tapped} / \rho_{bulk}$$

Scale of flowability and cohesiveness of powder particles based on *CI* and *HR* values.

Wettability

The modified method[14] was used to measure powder wettability. At room temperature, 1-gram of powder sample was added to 100 mL of distilled water in a beaker without stirring. The wettability of formulations was used to gauge how quickly powder particles sank and disappeared from the water's surface.

Powder X-ray diffraction

Using a PANalytical Empyrean Powder Diffractometer (PANalytical, Almelo, Netherlands) and Ni-filtered Cu K radiation (λ = 1.5406Å), materials' powder X-ray diffraction (P-XRD) patterns were captured[15] at room temperature. 30 mA of current and 45 kV of acceleration. The scan step duration was 67.945 seconds, with step size of 0.033, and data were composed across a scanning 2 range of 3° to 40°.

Differential scanning calorimetry

This (TA Instruments, New Castle, USA) was used to perform DSC. Tzero aluminum pans and Tzero lids were used to weigh powder samples [16] that ranged in size from 2 to 4 mg. The milled samples were subjected to analyses utilizing a linear heating rate 2°C/min, an amplitude 0.21°C, and a duration of 40 seconds under nitrogen flow of 50 mL/min and variable temperature mode. Samples were heated to 180°C after a 1-minute isothermal step at -10°C. Using the Trios v3.3.0.4055 software (TA instruments, New Castle, USA), glass transition temperatures (Tg, midway) were calculated from reverse heat flow signal of 3 separate replicates.

Fourier transform infrared spectroscopy analysis

Agilent Cary 630 FTIR spectrometer, Microlab PC software, and ATR sampling device with resolution 8 cm^{-1} and scan range 4000 to 650 cm^{-1} were used to analyze extracts.[17]

Analysis of 1-octacosanol encapsulated powder by GC-FID

The 1-octacosanol encapsulated powder was analyzed using an Agilent 8890 GC FID system, N2 gas chromatograph (Tokyo, Japan), equipped with a flame-ionization detector and an automatic injector[18] with a few minor adjustments. Agilent 122-7032 (DB-WAX; 30 m x 250 m x 0.25 m); 0.1 µL of injection volume; nitrogen carrier gas moving at 3 mL per minute. The temperature of the column was set to rise at rate of 1°C/min from 50 to 260°C after being held at 190°C for two minutes. Temperatures for the injector and detector were both set to 280°C.

RESULTS AND DISCUSSION

Particle Size Distribution and Zeta Potential of 1-octacosanol Emulsion

The z-average diameter and zeta potential of 1-octacosanol Emulsion nanocomplexes are given in Table 1. The F15 formulation's average particle diameter ranged from 720.9 to 736.1 nm, and the majority of the particles were uniformly sized nanoparticles.

Since the surface charge of the core-shell nanocomplexes in the F15 formulation had a stable and homogenous emulsion, the zeta-potential for 1-octacosanol emulsion nanocomplexes was between -24.5 and -23.3 mV.

Moisture Content

As a result of the product's deterioration, lipid oxidation may be enhanced by high moisture content, making it a significant criterion for water-based powder. In this study, all formulations' moisture contents ranged from 2.85 to 5.32% (Table 2). Prior to spray drying, there was a proportionate link between the emulsion's viscosity and the powder's moisture content. Formulations F15 and F12 both displayed moisture contents of 2.85 and 5.32%, respectively.

Microencapsulation Efficiency

The polymer composition had a substantial impact on efficiency, ranging from 76.92 to 96.75% for the powder that was enclosed. The effectiveness of 1-octacosanol encapsulation improved with the ratio of HPMC and OCC content (Table 2). Additionally, the drying temperature for each formulation was set at 180°C. The droplets dried more quickly due to the greater drying temperature, which resulted in crust development on the particle surface. This crust served

Table 2: Characteristics of various formulations of encapsulated powder

Formulation	*Moisture (%)*	*Microencapsulation efficiency (%)*	*Bulk density (gmL)*	*Tapped density (gmL)*	*Carr index (%)*	*Hausnerratio*	*Wettability (min)*
F11	4.51	86.44	0.285	0.332	14.16	1.16	11.14
F12	5.32	76.92	0.228	0.339	32.74	1.49	19.67
F13	3.75	82.11	0.328	0.394	16.75	1.20	9.92
F14	3.12	79.89	0.383	0.469	18.34	1.22	14.08
F15	2.85	96.75	0.478	0.528	9.47	1.10	7.21
F16	3.30	91.26	0.364	0.472	22.88	1.30	12.72

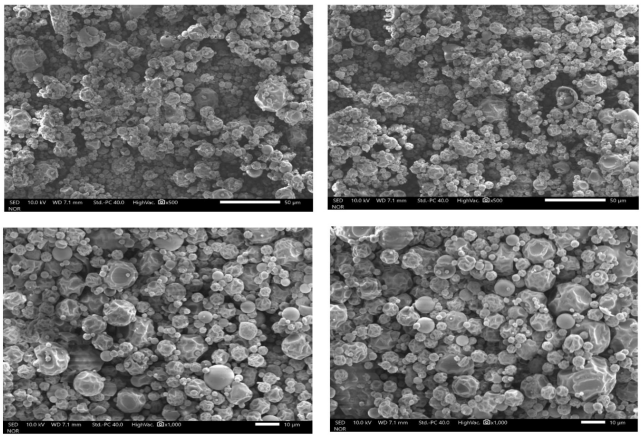

Figure 1: Morphology of F15 formulations' encapsulated powder

as a strong barrier surrounding particles, preventing active droplets from evaporating. discovered the beneficial effects of increased drying temperatures in the spray-dried encapsulation of 1-octacosanol. Higher emulsion viscosity, caused by a concentration ratio of several types of water-soluble polymer, improves encapsulation efficiency.

Bulk and Tapped Density of Powder

The bulk and tapped density are influenced by the grades & content of the polymer as well as the moisture content. In this investigation, bulk density ranged from 0.228 to 0.478 g/mL (Table 2). The bulk density of powder was found to decrease as the polymer content rose in the formulations from series II, but to rise as the concentration ratio of various types of water-soluble polymer content increased. For the purpose of transporting and packing powder, tapped density is a crucial factor. The tapped density ranged from 0.332 to 0.528 g/mL.

Powder Flowability

The primary variables for determining flow characteristics of encapsulated spray-dried powder are CI and HR. The bulk density has an impact on the CI of the powder. The hydrophilic properties of the water-soluble polymer demonstrated very good flow characteristics. In this research, the formulations' *CI* values ranged from 9.47 to 32.74%. When *HR* is low, the powder is less cohesive and flows freely capability. Based on (Table 2), a value from I and II batches of formulations was between 1.10 to 1.49, which is considered an outstanding and good flow quality.

Wettability

One of the essential physical characteristics related to binding with water is the capacity of spray-dried powder to dissolve in water. A powder's wettability refers to its capacity for water absorption and rehydration. The time it took for a powder to evaporate from the surface of the water was used in this investigation to gauge the degree of wettability (Table 2). In 7.21 minutes was the ideal wetting time for the F15 formulation. According to this, reducing the amount of polymer and combining two distinct types of water-soluble polymer shortens the wetting time. Therefore, when the polymer content was decreased, it made it easier for water to reach and enter the powder particles. The powder's wettability is also influenced by the encapsulated powder's flowability and particle density. Powder clumping can enhance wettability because the liquid can more readily pass through the powder's pores.

Particle Surface Morphology

The use of FESEM, showed spray-dried encapsulated 1-octacosanol powder comprising HPMC and OCC had a more granular structure (Figure 1). It was shown that the particle surface shape is significantly influenced by kind and concentration of polymer. Shrinking of particles during drying process is what causes the surfaces of spray-dried particles to become wrinkled.

Powder X-Ray Diffraction

Figure 2 illustrates the XRD patterns of pure 1-octacosanol, 1-octacosanol that has been encapsulated, PVP, OCC, and HPMC. Sharp peaks in the Pure 1-octacosanol XRD patterns demonstrated the crystalline nature of active substance. Diminution in these crystalline peaks in encapsulated 1-octacosanol reveals the drug's amorphous nature following complexation. This diminished intensity denotes a reduction in 1-octacosanol's crystallinity.

It was established that the entrapped active was disseminated monomolecularly in encapsulated 1-octacosanol by the change in Pure 1-octacosanol's nature from crystalline to amorphous.

Differential Scanning Calorimetry

DSC graph of pure 1-octacosanol in (Figure 3) show an onset value start from 57.55 to 78.49°C and a peak value from 60.21 to 81.27°C, encapsulated 1-octacosanol shows an onset value start from 56.02 to 75.37°C and peak value from 58.18 to 79.25°C which shows there is no change in enthalpy of molecules.

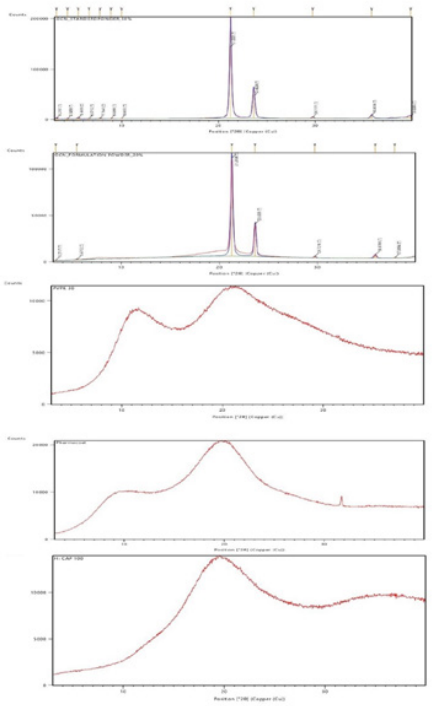

Figure 2: PXRD of pure 1-octacosanol, encapsulated 1-octacosanol, PVP, OCC and HPMC

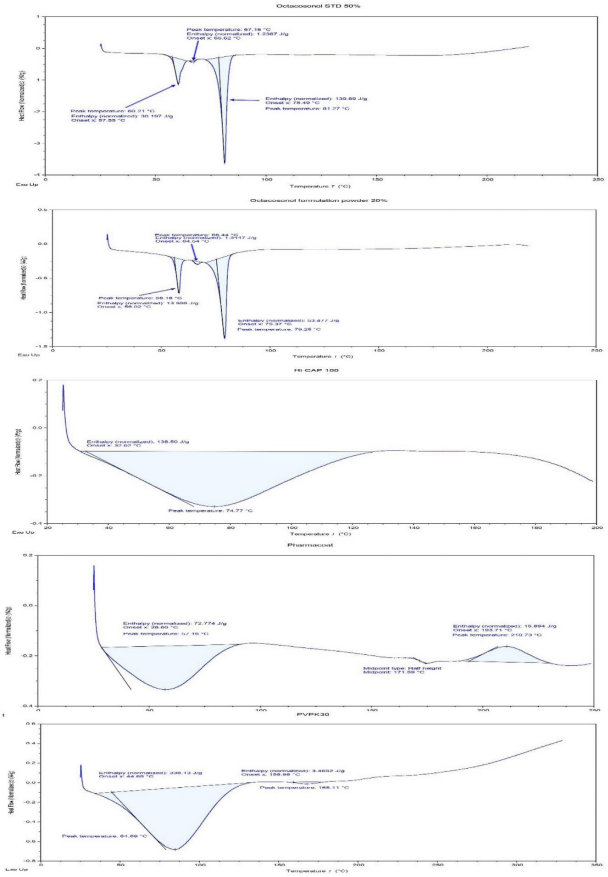

Figure 3: DSC of pure 1-octacosanol, encapsulated 1-octacosanol, PVP, OCC and HPMC. The fact that the entrapped active was disseminated monomolecularly in encapsulated 1-octacosanol was also verified.

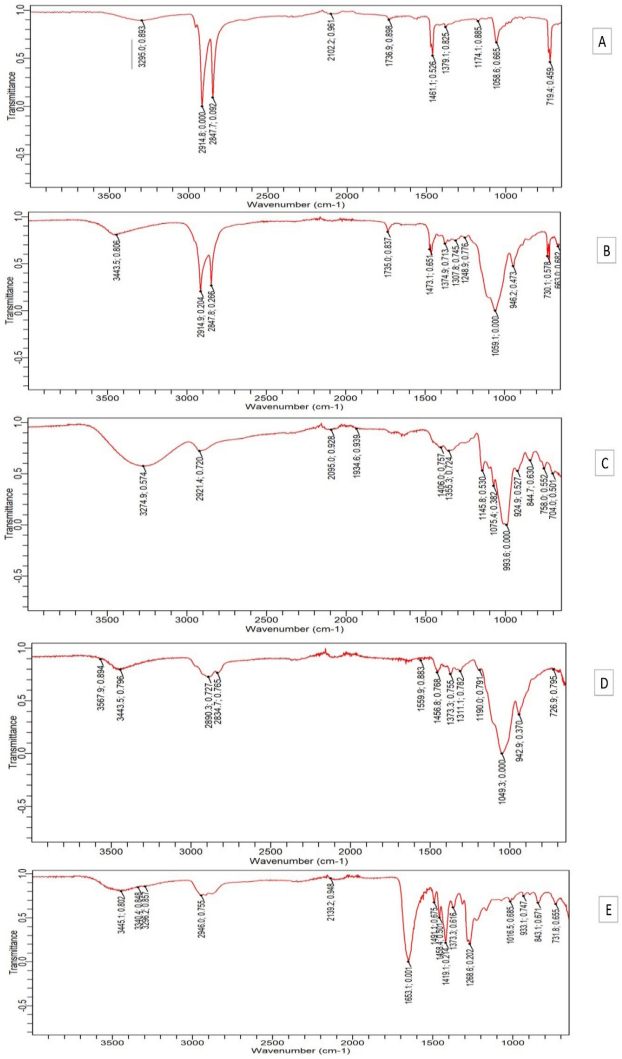

Figure 4: FTIR spectroscopy analysis of (A) Pure 1-octacosanol, (B) encapsulated 1-octacosanol, (C) OCC, (D) HPMC and (E) PVP.

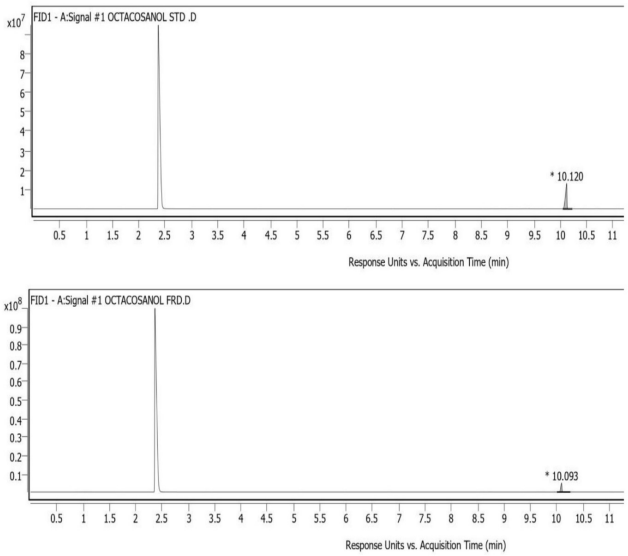

Figure 5: GC-FID chromatogram of encapsulated 1-octacosanol and standard 1-octacosanol.

Fourier Transform Infrared Spectroscopy Analysis

There was no interaction between pure 1-octacosanol and encapsulated 1-octacosanol in the FTIR spectra (Figure 4), which included bands of both compounds that overlapped. The distinctive peaks of pure 1-octacosanol may be seen at 3294.97 cm^{-1} for the alkane C-C bond, at 3200 to 2700 cm^{-1} for the presence of the alcohol group, and at 1000 to 650 cm^{-1} for C=C bond. During complexation, encapsulated 1-octacosanol with a C=O group can create H_2 bonds with the N-H group of the water-soluble polymer,

This suggests that the active and the water-soluble polymer have complexed.

1-octacosanol Encapsulated Powder by GC-FID

In various formulation combinations performed in which F15 shows acceptable physical and physicochemical properties, after quantification by GCFID it will show maximum encapsulated efficiency and potency.

1-octacosanol content in the spray-dried powder was found to be 23.32 g/100 g. The GC-FID (Figure 5) results revealed the presence of the 1-octacosanol (RT: 2.5 minutes) in the encapsulated spray dried powder of 1-octacosanol with the standard of 1-octacosanol at (RT: 2.5 minutes) taken as internal standard.

CONCLUSION

It was discovered that the varying proportions of the 1:1 combination of two water-soluble polymers had beneficial impacts on the creation of the 1-octacosanol emulsion and encapsulated powder. When manufacturing the 1-octacosanol emulsion and encapsulated powder, it was discovered that HPMC PVP and OCC may be employed as single carrier material for encapsulation with negligible impacts. Our main objective was to ascertain impact of a 1:1 combination of water-soluble polymers on the encapsulation of 1-octacosanol. Our findings show that high solid concentration causes low moisture content, big particle size, and considerable dented surfaces, all of which may increase particle flowability. We found that the F12 of formulations with greater concentrations of a single PVP carrier had lower quality than formulations with a 1:1 combination of two water-soluble polymers. However, an effective substitute for spray drying to microencapsulate 1-octacosanol is to employ a combination of HPMC and OCC. Due to this polymer's low cost, wide availability, and the fact that F15 is the optimum formulation composition according to current research, it is conceivable to create novel materials using this combination.

ACKNOWLEDGEMENT

The authors would like to acknowledge NIPER-Hyderabad, the Department of Research and Development of India Glycols Limited and Amity University for supporting research project.

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