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Short communication

Preparation of the ascorbic acid and ferulic acid loaded niosomes

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Introduction

Using niosomes as nanocarriers offers several advantages. The foremost benefit lies in their amphiphilic nature, allowing for the loading of both lipophilic and hydrophilic active pharmaceutical ingredients (APIs). To enhance niosome rigidity, steroid-based compounds like cholesterol are commonly employed (Bhardwaj et al., 2020). Antioxidant APIs such as ferulic acid and ascorbic acid have been shown to synergistically enhance each other's antioxidant activity. Moreover, ferulic acid has been reported to improve the stability of the formulation. This study aims to optimize the surfactant ratios necessary to achieve a stable niosome formulation containing both ascorbic acid and ferulic acid. (Lin et al., 2005).

Materials and methods

Materials used in niosome formulation studies, cholesterol, curcumin, Brij 35, Span 20, Span 60, Span 85, Tween 20, were all purchased from Sigma Aldrich and used as received. Chloroform used as organic solvent, ethyl alcohol is used to prepare ferulic acid stock solution and purified water was used to dissolve the formed thin film layer. Ascorbic acid and ferulic acid were used as active ingredients.

Thin Film Hydration Method was used to prepare niosomes. Figure 1 illustrates the schematic depiction of the method. API is dissolved in the aqueous or organic phase.

Vesicle size distribution analyzes were performed with Malvern Nanosight NS300 (UK) device on 50-fold diluted formulation at room temperature and 40 °C using Nanoparticle Tracking Analysis (NTA) method. The samples are collected at 15, 30, and 45th minutes and 1, 2, 3, and 6th hours with the membrane diffusion test. Briefly, 4 ml of the sample was introduced into the membrane, which was subsequently immersed in a 500 ml PBS solution. The samples were then collected at the designated time intervals. The chromatographic analysis of those samples is performed on the Agilent 1260 HPLC-DAD (Germany) device.

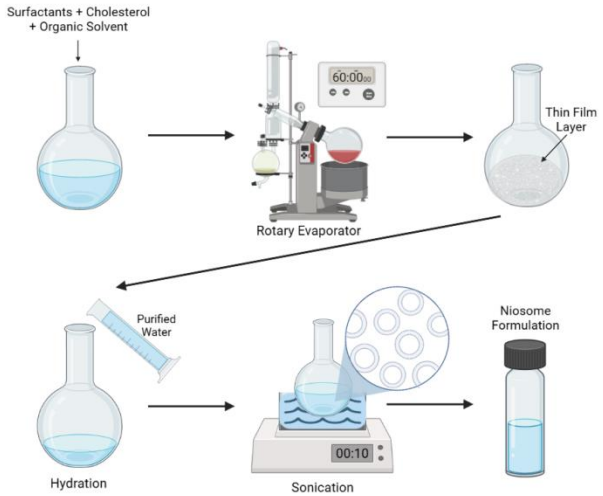

Fig. 1. Schematic Representation of Thin Film Hydration Method.

The percentage of API that has been loaded into the vesicles is calculated by the following equation.

Equation 1: $X = \frac{l-f}{l} x\ 100$

l = the amount of API loaded to the formulation f = free API in the formulation

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Results and discussion

The thin film-forming properties and physical stability of the formulations were observed for periods ranging from 1 week to 1 month. It was observed that Brij 35 did not form a thin film layer when used alone, due to its high HLB value and long chain linear structure. The use of curcumin as a cholesterol substitute was attempted. However, a stable formulation could not be obtained.

It has been determined that the stability of the sample containing Brij 35, Span 20, and Cholesterol in a molar ratio of 0.25:2:1 is acceptable. However, localized formation of a thin film layer was observed, as circled in Figure 2. The reason for the local formation of the thin film layer could be the low amount of material. By increasing the amount of material, a better thin film layer and a more concentrated formulation can be obtained.

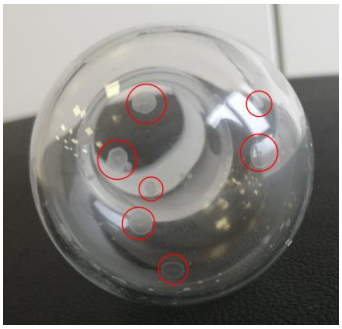

Fig. 2. Thin Film Layer of the Final Formulation

The final formulation contains 1 mg ferulic acid in the organic phase and 100 mg ascorbic acid in the aqueous phase.

The vesicle size of the formulation was measured by NTA with an average of 215nm. The measurements made in 25°C and 40°C are compared as in Figure 3 and it is seen that the number of vesicles decreases with the increase in temperature, but there is no significant change in the average vesicle size. Vesicles of the final formulation can be seen in Figure 4.

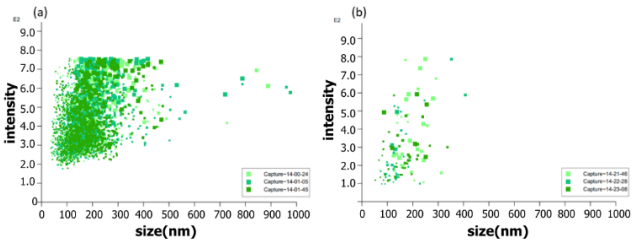

Fig. 3. Vesicle size distribution of the final formulation in 25°C (a) and 40°C (b)

According to the calculations made with equation 1, 76% of ascorbic acid and 43% of ferulic acid added to the formulation were loaded into the vesicles. It has been seen that the release of ferulic acid occurs in the first 15 minutes and a total of 96.4% of the loaded ferulic acid is released. The concentration of ascorbic acid was stable during the first 30 minutes, the release occurred between the 30th and 45th minutes, and a total of 97.8% of the loaded ascorbic acid was released.

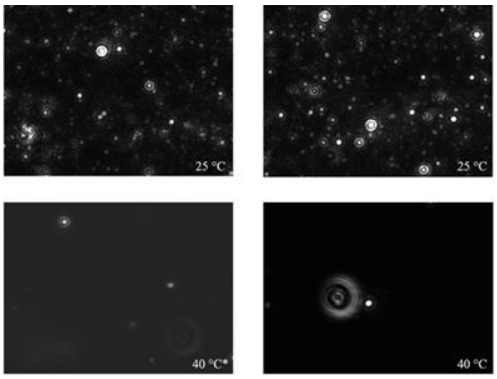

Fig. 4 Frames captured with NTA

Conclusion

Based on the pre-formulation studies, a formulation exhibiting favorable characteristics was achieved. Due to inadequate physical stability, curcumin was not chosen. Ascorbic acid and ferulic acid used as APIs in this study. Nevertheless, the developed formulation holds promise for exploration in novel domains featuring diverse active ingredients. The inclusion of ferulic acid in the final formulation did not impact the 3-month stability; however, extended observations or accelerated stability tests are warranted for further investigations. Furthermore, an inquiry into the antioxidant, photoprotective, anticancer, and antiscar/wound healing effects of ferulic acid and ascorbic acid is imperative.

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