RESEARCH PAPER

Preparation and Characterization of Curcumin Niosomal Nanoparticles via a Simple and Eco-friendly Route

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ARTICLE INFO

Article History:
Received 02 June 2019
Accepted 07 August 2019
Published 01 October 2019

Keywords:
Curcumin
Entrapment efficiency
Nanoparticles
Niosomes
Thin film hydration

ABSTRACT

In this investigation, curcumin niosomal nanoparticles were prepared via a simple, efficient and eco-friendly route, thin film hydration (TFH), in the presence of different mixture of the surfactants (tween 60 and span 60). Cholesterol ratio to surfactant, as effective factor, was altered to obtain the optimal nanoparticles. The size, zeta potential, size distribution, entrapment efficiency of the prepared nanoparticles were examined and compared. The optimum nanoparticles were chosen to examine the release from the dialysis membrane. Ratio of cholesterol to surfactant was found to have key and notable influence on the size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles. The nanoparticles prepared with Formulations 3 and 5 as optimum nanoparticles were chosen to examine the release from the dialysis membrane. The results denoted that by increasing the ratio of cholesterol to surfactant, the rate of curcumin release was enhanced from the membrane. High quantities of cholesterol in the formulation 3, in addition to explosive release, can lead to slow release.

How to cite this article
Zinatloo-Ajabshir Z and Zinatloo-Ajabshir S. Preparation and Characterization of Curcumin Niosomal Nanoparticles via a Simple and Eco-friendly Route. J Nanostruct, 2019; 9(4): 784-790. DOI: 10.22052/JNS.2019.04.020

INTRODUCTION

Curcumin is reported as a natural and harmless compound that possesses a polyphenolic hydrophobic structure and can be extracted from the rhizomes of Curcuma longa (1-3). Curcumin as effective drug has been reported for the treatment of diverse diseases. However, the delivery of this drug has associated with several challenges; owing to low water solubility, low bioavailability, chemical instability and fast metabolism. Accordingly, many attempts have been made to improve the drug delivery of this noteworthy drug. Niosomes have been presented as one of the most appropriate carriers to improve the delivery of curcumin (4-7). A variety of techniques like sonication, ether injection method, micro fluidization, thin film hydration technique and bubble method have been applied for the production of niosome nanoparticles (8-15). Use of thin film hydration technique for preparation of niosome nanoparticles has been regarded as a facile and efficient way. In this approach, surfactants as well as cholesterol are dissolved in an organic solvent at a round bottom flask. Afterward the thin layer is formed on the flask wall by removing organic solvent with rotary and vacuum. A solution like water or PBS is added, and the dried layer is re-hydrated at a temperature higher than the transition temperature (T_c) of the surfactant. Niosomes are formed during hydration (10).

Till now variant methods have been applied to fabricate several kinds of the nanostructured compounds. However, the greatest interest is in green chemistry-based ways as a result of their affordability, nontoxicity, easiness and effectiveness (16-22).

Here, curcumin niosomal nanoparticles were prepared through a simple, efficient and eco-friendly route, thin film hydration (TFH), in the

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presence of different mixture of the surfactants (tween 60 and span 60). Cholesterol ratio to surfactant, as effective factor, was altered to obtain the optimal nanoparticles. The size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles were investigated and compared. The optimum nanoparticles were chosen to examine the release from the dialysis membrane. The results demonstrated that by increasing the ratio of cholesterol to surfactant, the rate of curcumin release was enhanced from the membrane.

MATERIALS AND METHODS

The chemicals utilized in this work were of reagent grade and were employed without extra purification. Cholesterol, span 60, dichloromethane, curcumin, tween 60, ethanol were obtained from Merck. Deionized water was employed for all the tests. The size, zeta potential and size distribution of the prepared nanoparticles was investigated with photon correlation spectroscopy (PCS), Zetasizer 3000 (Malvern Instruments, UK). To achieve optimum signal intensity, the prepared samples were diluted before measurements. FT-IR spectra of the prepared nanoparticles and curcumin have been recorded on a Thermo Scientific Nicolet 6700 FT-IR spectrometer. GC-2550TG (Teif Gostar Faraz Company, Iran) have been applied for all chemical analyses.

Preparation of curcumin niosomal nanoparticles

In this study, curcumin niosomal nanoparticles were prepared via a simple, efficient and eco-friendly route, thin film hydration (TFH), in the presence of different mixture of the surfactants (tween 60 and span 60). 50 mg of curcumin and certain amount of cholesterol, tween 60 and span 60 were dissolved in 24 mL of dichloromethane at a round bottom flask. Afterward, the thin layer was formed on the flask wall by removing dichloromethane with rotary and vacuum at 60 ˚C. 25 mL of deionized water was added, and the dried layer is re-hydrated at 100 ˚C using rotary. Afterward, the beaker involving formulation was placed in an ice-water bath under ultrasonic waves (with AM = 20%; 5 cycles of 2 minutes, intervals of each cycle 5 minutes). Schematic diagram of the preparation of the curcumin niosomal nanoparticles is demonstrated in Fig. 1. Cholesterol ratio to surfactant, as effective factor, was altered to examine its effect on the size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles (Table 1).

Curcumin loading

To examine the entrapment efficiency (23, 24) (EE) of curcumin, the prepared nanoparticles in four opendorfs of 2 mL was centrifuged at 15,000 rpm at 4 ˚C and afterward the supernatants were separately collected and diluted with distilled

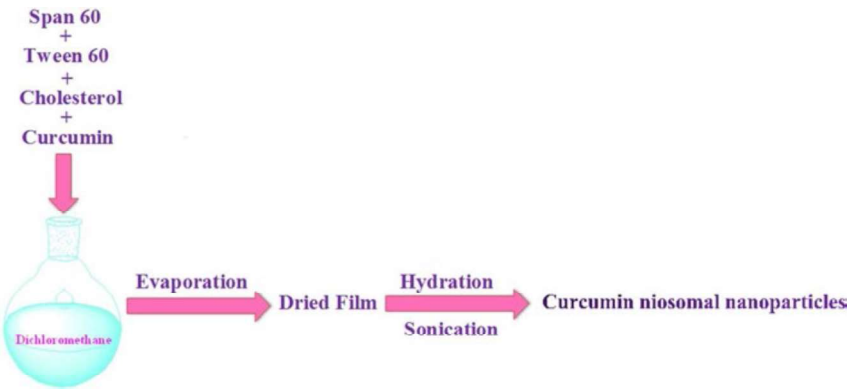

Fig.1. Schematic diagram of the preparation of the curcumin niosomal nanoparticles

Table 1. The preparation conditions for the all samples

F	Amount of cholesterol (mg)	Amount of S60 (mg)	Amount of T60 (mg)
F_1	450	450	450
F_2	450	225	225
F_3	300	225	225
F_4	300	150	150
F_5	150	225	225

water up to 50 times and their absorbance was recorded with UV–vis spectrophotometer at 428.6 nm. Next, by inserting the absorbance into the standard curve and computing the concentration in µg/ml, the concentration at dilution factor (50) was multiplied to an actual concentration. The actual concentration in supernatant volume was multiplied and the amount of unloaded drug was computed in µg per ependorph. The EE was subsequently computed as:

$$EE\,\% = \frac{Mass\ of\ curcumin\ in\ the\ nanoparticles}{Mass\ of\ total\ curcumin\ added} \times 100$$

Curcumin release from dialysis membrane

For this aim, the acetate cellulose membrane (MWCO 12 kDa) as well as cells similar to immersion cells was employed. The samples were placed in the cells and acetate cellulose membrane placed on the cells and afterwards the door of the cells was closed and they were inserted into the US Pharmacopoeia No. 2 dissolution unit. In order to modify the volume of the dissolution medium, the cells of device were replaced with 200 mL of beakers, and in each beaker 70 mL of ethanol were placed. The time of placing in the dissolution medium was considered to be t = 0. Sampling was performed at 2, 4, 6, 8 and 24 hours after cells was placed in the dissolution medium. For sampling, each time 5 cc were removed from the mixture in the dissolution medium, it was filtered with a 0.25 micron filter and its absorbance was obtained with HPLC at 430 nm. The absorbance was placed in the absorption-concentration equation of curcumin and the concentration of the drug was computed. To maintain the volume of the dissolution medium, 5 cc of ethanol was added into it after each removal of 5 cc from the medium.

RESULTS AND DISCUSSION

Cholesterol ratio to surfactant, as effective factor, was altered to examine its effect on the size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles. Fig. 2 depicts the influence of various ratios of cholesterol to surfactant on the mean diameter of curcumin niosomal nanoparticles. By varying ratio

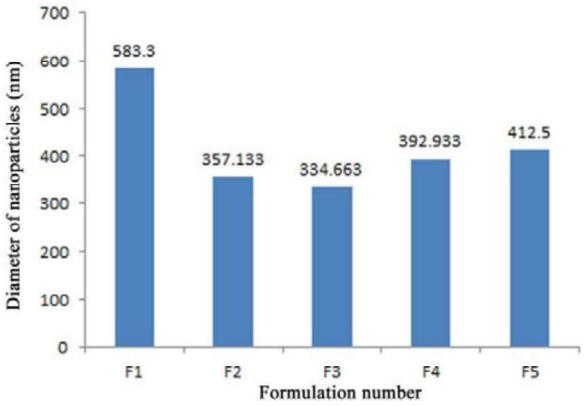

Fig. 2. The mean diameter of nanoparticles prepared with different Formulations

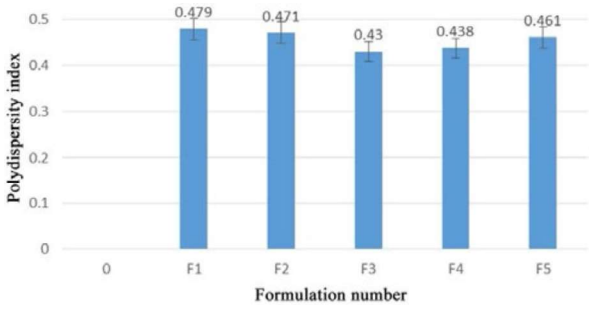

Fig. 3. The mean dispersity index of nanoparticles prepared with different Formulations

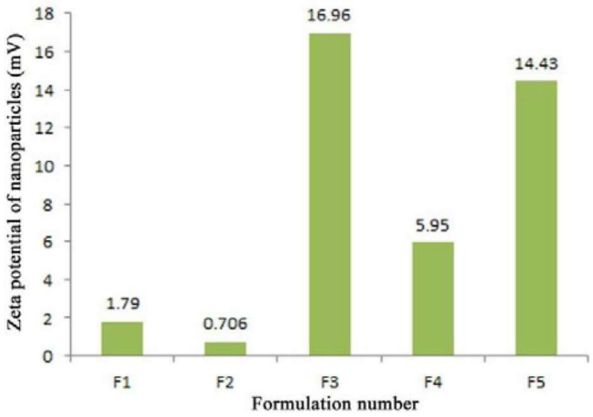

Fig. 4. The zeta potential of nanoparticles prepared with different Formulations

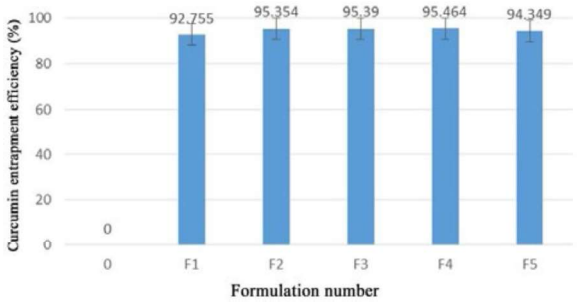

Fig. 5. The curcumin entrapment efficiency of nanoparticles prepared with different Formulations

of cholesterol to surfactant, the nanoparticles with different diameters can be produced. It is apparent that the nanoparticles prepared with Formulation 3 illustrate the smallest diameter compared to other nanoparticles.

The mean dispersity indexes of the prepared nanoparticles by various ratios of cholesterol to surfactant were compared, as depicted in Fig. 3. The nanoparticles with various dispersity indexes can be obtained with altering ratio of cholesterol to surfactant. Obviously, the nanoparticles prepared with Formulation 3 have the narrowest dispersity index compared to other nanoparticles. The influence of various ratios of cholesterol to surfactant on the zeta potential of curcumin niosomal nanoparticles is illustrated in Fig. 4. By changing ratio of cholesterol to surfactant, the nanoparticles with various zeta potentials can be produced. The results demonstrate that the nanoparticles prepared with Formulation 3 have the most zeta potential compared to other nanoparticles.

The curcumin entrapment efficiencies of the prepared nanoparticles by various ratios of cholesterol to surfactant were also compared, as exhibited in Fig. 5. The nanoparticles with different entrapment efficiencies can be prepared with varying ratio of cholesterol to surfactant. It is clearly seen that the nanoparticles prepared with Formulation 4 indicate the best efficiency compared to other nanoparticles. Based on the above results, ratio of cholesterol to surfactant is found to have key and notable influence on the size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles.

The nanoparticles prepared with Formulations 3 and 5 were stable under long storage conditions. The size, zeta potential, size distribution of these nanoparticles remained approximately unchanged after 4 weeks storage under refrigeration conditions at 4 ˚C. Thus, these optimum nanoparticles were chosen to examine the release from the dialysis membrane.

Diagrams of release from the membrane for the nanoparticles prepared with Formulations 3 and 5 are illustrated in Fig. 6. It is observable that up to 8

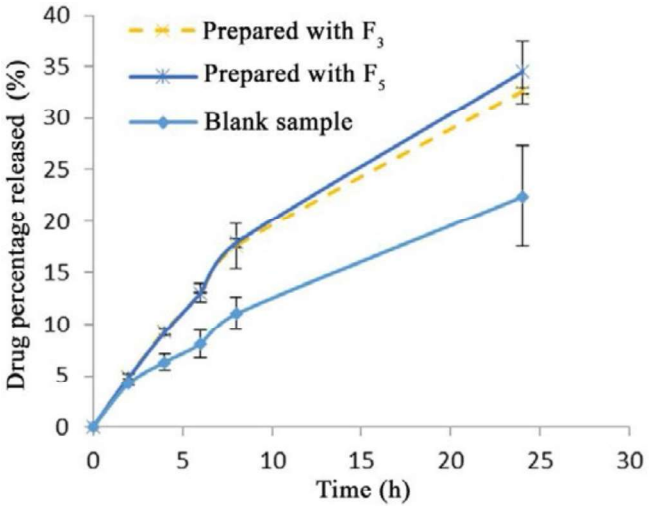

Fig. 6. Diagrams of release from the membrane for the nanoparticles prepared with Formulations 3 and 5

h after the release of the dialysis membrane, there is no remarkable relationship between the ratio of cholesterol to surfactant and release from the membrane, but from 8 to 24 h, the nanoparticles prepared with Formulation 5 illustrate the higher release (34.49% ± 3.06) and the nanoparticles produced with Formulation 3 indicate slower release (32.65% ± 0.3). The release of curcumin from niosomal nanoparticles has a 2-phase: the initial phase, a slow release, and the next phase is an explosive release. Based on the above results, it is found that by enhancing the cholesterol ratio to the surfactant from 0.33 to 0.66, slower release from the membrane can be occurred. It seems that cholesterol can play a double role in the niosome membrane (25). High quantities of cholesterol in the formulation 3, in addition to explosive release, can lead to slow release.

The mixture of water and curcumin as blank sample was used to release from the membrane. It is apparent that within 24 hours, the release from the nanoparticles prepared with Formulations 3 and 5 was remarkably higher than blank sample. Cholesterol existing in these nanoparticles resulted in an explosive release from them and also a notable gain in the percentage of released curcumin during 24 hours compared with the blank sample (Fig. 6).

The FT-IR data was employed to identify possible interactions and potential bonds between carrier and curcumin. The FT-IR spectra of the nanoparticles prepared with Formulations 3 and 5 with pure curcumin spectrum were compared to examine the interactions (Fig. 7). The characteristic peaks of the pure curcumin appear at 3509, 1601, 1509, 1278, 1026, 962 and 810 cm^{-1}. It is observable from the FT-IR spectra of the nanoparticles prepared with Formulations 3 and 5 that the characteristic peaks of drug did not have notable shift, demonstrating no interaction between the formulation components. These results demonstrate that the nanoparticles prepared with Formulations 3 and 5 have high potential to be employed effectively for drug delivery applications.

CONCLUSIONS

This work describes a simple, efficient and eco-friendly route, thin film hydration (TFH), to prepare curcumin niosomal nanoparticles in the presence of different mixture of the surfactants (tween 60 and span 60). Cholesterol ratio to surfactant, as effective factor, was altered to obtain the optimal nanoparticles. The size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles were examined and compared. Ratio of cholesterol to surfactant was found to have key and notable influence on the size, zeta potential, size distribution and entrapment efficiency of the prepared nanoparticles. The nanoparticles prepared with Formulations 3 and 5 as optimum nanoparticles were chosen to examine the release from the dialysis membrane. The results denoted that by increasing the ratio

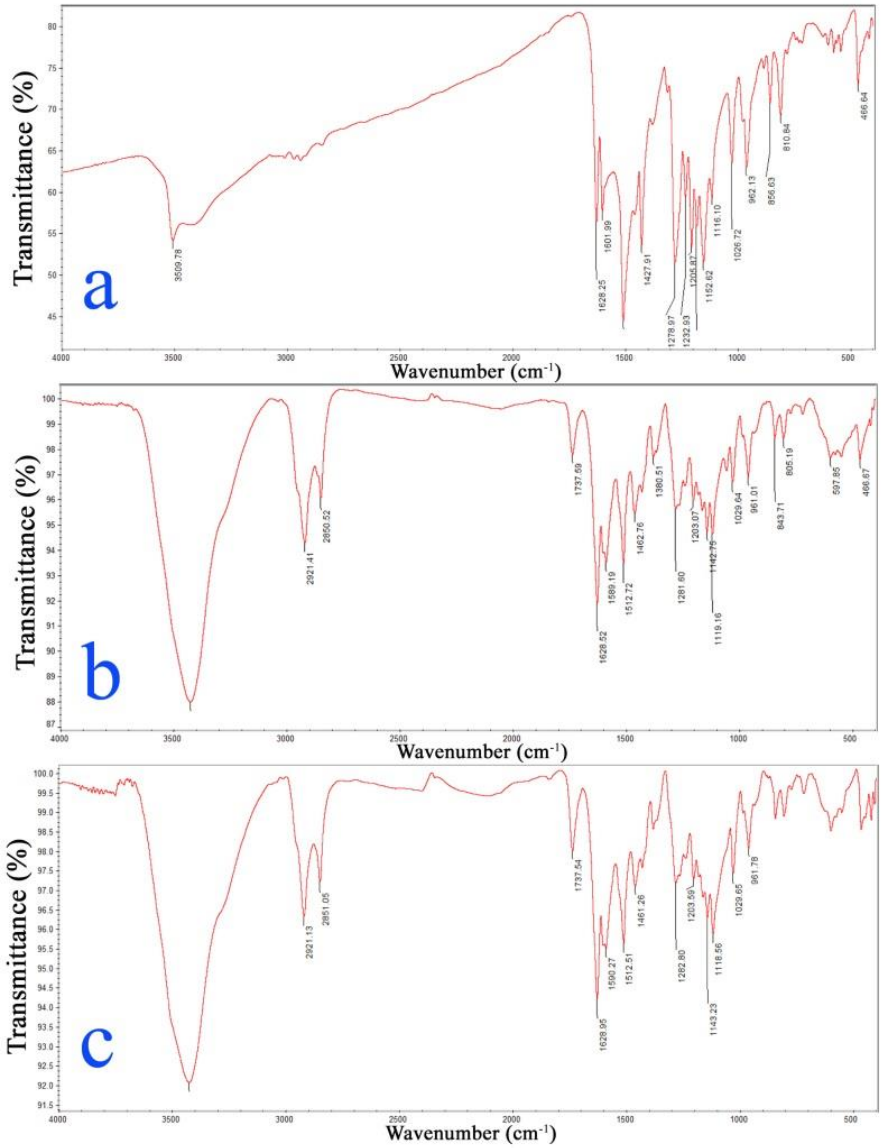

Fig. 7. FT-IR spectra of pure curcumin (a) and the nanoparticles prepared with Formulations 3 (b) and 5 (c)

of cholestrol to surfactant, the rate of curcumin release was enhanced from the membrane. High quantities of cholesterol in the formulation 3, in addition to explosive release, can lead to slow release.

ACKNOWLEDGEMENTS

This research was financially supported by Mazandaran University of Medical Sciences.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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