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Research Article

Development and evaluation of curcumin-loaded vesicular carriers: impact of formulation variables

Denitsa Momekova[1], Viliana Gugleva[2], Petar Petrov[3]

1 *Department of Pharmaceutical Technology and Biopharmaceutics, Faculty of Pharmacy, Medical University of Sofia, Sofia, Bulgaria*
2 *Department of Pharmaceutical Technologies, Faculty of Pharmacy, Medical University of Varna, Varna, Bulgaria*
3 *Institute of Polymers, Bulgarian Academy of Sciences, Sofia, Bulgaria*

Corresponding author: Denitsa Momekova (dmomekova@pharmfac.mu-sofia.bg)

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Abstract

Vesicular carriers are a well-established approach to improving the technological and biopharmaceutical characteristics of the loaded cargo. The current manuscript is focused on the development and evaluation in a comparative aspect of two types of vesicles—ethosomes and transfersomes loaded with the phytoconstituent curcumin. The formulation variables affecting their physiochemical and cytotoxic properties are outlined as well. A series of ethosomes and transfersomes based on Lipoid S75 and ethanol, or edge activator, were prepared using the thin film hydration method and subjected to comprehensive evaluation by dynamic light scattering (DLS) analysis, transmission electron microscopy (TEM), entrapment efficiency evaluation, *in vitro* release, and cytotoxicity studies. Ethosomes based on Lipoid S75 (4% w/w) and ethanol (30% v/v) showed suitable physicochemical characteristics (hydrodynamic diameter of 578.6 nm, monomodal size distribution, high curcumin entrapment efficiency (78.2%)), and superior antiproliferative activity compared to free drug and transfersomal nanocarriers.

Keywords

biological active compounds, curcumin, antineoplastic activity, topical delivery, ethosomes, transfersomes

Introduction

Bioactive compounds from natural origin exhibit a variety of advantageous effects when applied to skin; however, often their physicochemical characteristics, such as high molecular weight, strictly hydro-lipophilicity, and high degree of ionization, may hinder their successful dermal and transdermal delivery (Isopencu et al. 2023). Currently, the most exploited strategy to improve phytochemicals' biopharmaceutical and pharmacokinetic behavior is their inclusion into nanoscale drug delivery systems. In this regard, it is crucial to consider the proper design of the nanocarrier platform with respect to composition constituents' selection, method of preparation, and the resulting physicochemical properties (size, size distribution, entrapment efficiency, etc.), as well as conducting the experiments in physiologically relevant conditions.

Curcumin is a plant phenolic compound (curcuminoid) isolated from the roots of *Curcuma longa* and extensively used in traditional medicine and current therapeutics owing to its diverse pharmacological effects, such as antioxidant, anti-inflammatory, antimicrobial, antiviral, and

anti-proliferative (Urošević et al. 2022). Regarding its topical application, curcumin is efficient in the treatment of various skin diseases such as psoriasis, atopic dermatitis, skin infections, wounds of different etiologies, as well as basal cell carcinoma, melanoma, and cutaneous T cell lymphoma (Trochopoulos et al. 2020; Tang and Cao 2022; Kasprzak-Drozd et al. 2024). Cutaneous lymphomas include different types of lymphoproliferative diseases, the most common of which are mycosis fungoides and Sézary syndrome. Mycosis fungoides clinically manifests with erythema predominantly on the sun-protected body areas, patches, plaques, and ultimately tumor formation; the Sézary syndrome, in addition to the erythroderma (usually covering more than 80% of the body area), is characterized also by the presence of atypical T cells (Sézary cells) in the skin and in the blood, wherefore this syndrome is often referred to as the leukemic form of cutaneous lymphomas (Jonak et al. 2021). Curcumin's antiproliferative properties have been successfully reported in regard to cutaneous T-cell lymphomas, owing to the suppression of signal transducer and activator of transcription (STAT)-3 and IkappaB-alpha phosphorylation (Zhang et al. 2010); therefore, it was selected as the active agent in the current study. Aiming to maximize its therapeutic potential, the phytochemical was loaded into two types of vesicular nanocarriers: ethosomes and transfersomes.

Vesicular systems such as liposomes and niosomes have been widely investigated as drug delivery platforms capable of preserving the chemical stability of the encapsulated cargo and improving its bioavailability for various routes of administration (Ahmad et al. 2017). However, with respect to dermal and transdermal delivery, the next generation of nanocarriers, such as ethosomes and transfersomes, has attracted more attention owing to the superior drug permeation they provide (Cristiano et al. 2019). Ethosomes are vesicular systems composed of phospholipids, water, and ethanol (between 20 and 40% v/v), first reported as a feasible drug delivery platform in 2000 by Touitou et al. (Touitou et al. 2000; Sakdiset et al. 2019). The beneficial effect of ethosomes on the skin can be attributed to a variety of factors, such as their elastic nature, the ethanol fluidizing effect on the lipids of stratum corneum, as well as the formation of novel pathways following the fusion of the carriers with epidermal lipids (Singh et al. 2014; Shinde et al. 2023). Similar to ethosomes, transfersomes are also phospholipid-based vesicles whose permeation-enhancing properties and deformability are attributed to "edge activators" instead of ethanol. Edge activators in the composition have often included non-ionic surfactants (Span, Tween series) or bile salts (e.g., sodium cholate/deoxycholate). They are known to decrease the interfacial tension, thereby increasing the elasticity of the bilayer membrane (Guillot et al. 2023). The ultradeformability of transfersomes allows them to penetrate through skin pores even up to 10 times smaller than their own dimensions (Opatha et al. 2020).

The aim of this study was to develop curcumin-loaded vesicular carriers—transfersomes and ethosomes—and to evaluate in a comparative manner the impact of the composition variables on their physicochemical, drug release, and cytotoxic characteristics.

Materials and methods

Materials

Curcumin, Tween 20, Tween 60, and Tween 80 were obtained from Sigma-Aldrich (St. Louis, MO, USA). Lipoid S75 (Soya phosphatidylcholine) was a generous gift from Lipoid GmbH (Ludwigshafen, Germany). All other solvents and reagents used were of analytical grade.

Methods

Preparation of curcumin-loaded ethosomes and transfersomes

Ethosomes and transfersomes (blanc and curcumin-loaded) were prepared by the thin film hydration method (Malviya and Alexander 2023). For the preparation of ethosomes, lipid-soluble components—lipoid S75 (2%, 3%, and 4% w/v) and curcumin (0.0025% w/v)—were dissolved in 10 mL chloroform and subjected to rotary vapor evaporation (Buchi, Germany) at 52 °C. The thin lipid film was subsequently hydrated for 45 minutes using purified water containing different ratios of ethanol (20%, 30%, and 40% v/v). The obtained ethosomal dispersions were stored in the refrigerator (4–6 °C) for further analysis.

Transfersomes were prepared following the same procedure and maintaining the constituents' concentrations (Lipoid S75 3% w/v, curcumin 0.0025% w/v) constant. After the formation of the lipid film, it was hydrated for 45 minutes with purified water containing different edge activators (Tween 20, Tween 60, and Tween 80) in concentrations of 0.3% and 0.60% (w/v). The obtained transfersomal dispersions were further sonicated for 10 minutes in a sonication bath (ArgoLab DU-32, Capri, Italy), then transferred into vials and stored at 4 ± 2 °C for subsequent studies.

Characterization of the developed vesicular carriers

Size, size distribution pattern, and zeta potential measurements

The hydrodynamic diameter (D_h) and polydispersity index (PDI) of the nanocarriers were determined by applying the dynamic light scattering technique. The experiment was performed at 25 °C using Zetasizer Ultra (Malvern Panalytical Ltd., Malvern, UK), equipped with a 633 nm laser. The samples were properly diluted (1:300 v/v) with distilled water and measured using a back-scattering angle of detection of 173°. The zeta potential of the formulations was assessed via electrophoretic light mobility using Zetasizer Ultra (Malvern Panalytical Ltd., Malvern, UK) following the same dilution protocol. The values are presented as mean ± standard deviation (SD) from three measurements.

Transmission electron microscopy (TEM)

The morphology of optimal ethosomal and transfersomal formulations was assessed by transmission electron

microscopy. A drop of nanovesicles' suspensions was placed onto a carbon-coated copper grid and allowed to dry at ambient temperature for 10 minutes. A solution of phosphotungstic acid (1% w/v) was used as a staining agent, placed onto the formulations, and after excess' removal, the samples were analyzed with a transmission electron microscope (JEOL JEM-2100), equipped with a digital camera, at an accelerating voltage of 200 kV and proper magnification.

Determination of curcumin entrapment efficiency (EE%)

Curcumin entrapment efficiency in the vesicular carriers was evaluated by the ultracentrifugation method (El-Shenawy et al. 2019). In brief, the curcumin-loaded vesicular carriers (ethosomes and transfersomes) were centrifuged for 1 hour at 10 000 rpm using a microcentrifuge (D2012 Plus, DLAB Scientific, Rowland St. City of Industry, CA, USA). The obtained supernatant was divided, diluted (1:1 v/v) with ethanol, and analyzed using a UV/Vis spectrophotometer (Reileight UV-9200, China) at 427 nm. Curcumin entrapment efficiency was determined by applying the following formula:

$$EE\,(\%) = \frac{\text{Total amount of Curc} - \text{free Curc}}{\text{Total amount of Curc}} \times 100 \quad (1)$$

In vitro *release of curcumin from vesicular formulations*

Curcumin release from ethosomes and transfersomes was evaluated by the dialysis method against phosphate-buffered saline (PBS) of pH 5.5 at 32 °C (Abd El-Alim et al. 2019). To secure curcumin spectrophotometric detectability, the medium (100 mL) also contained 10% (v/v) ethanol. Vesicular dispersions were pipetted in the dialysis bag (12 400 Mw cut-off), tightly sealed, and placed in the dissolution medium, which was continuously stirred (100 rpm) throughout the experiment. At predetermined time points, 2 mL aliquots of the medium were withdrawn and analyzed for curcumin at $\lambda = 427$ nm. Sink conditions were maintained through replenishment with an equal volume of fresh medium. The experiment was conducted three times.

Drug release kinetic studies

To evaluate curcumin release kinetics from the prepared ethosomes and transfersomes, *in vitro* release data was fitted with different mathematical models (zero order, first order, Higuchi, and Korsmeyer-Peppas models). The highest values obtained for the coefficient of determination (R^2) indicated the most suitable kinetic model.

Physical stability evaluation

The stability of optimal curcumin-loaded ethosomal and transfersomal formulations was investigated in terms of alterations in the physicochemical properties (D_h, PDI, zeta potential, EE%) of the vesicles after one-month storage in the refrigerator (4 ± 2 °C). A macroscopic evaluation of the appearance of vesicular dispersions was also performed.

Cell line and culture conditions

The cytotoxic activity of curcumin and its nanovesicular formulations was evaluated against HUT-78 cells (cutaneous T-cell lymphoma, CTCL Sézary syndrome). The cell lines were purchased from the German Collection of Microorganisms and Cell Cultures (DSMZGmbH, Braunschweig, Germany). The growth medium was 90% RPMI-1640 + 10% FBS. The cells were cultivated in a controlled environment—cell culture flasks at 37 °C in an incubator 'BB 16-FunctionLine' Heraeus (Kendro, Hanau, Germany) with a humidified atmosphere and 5% CO_2.

Evaluation of cytotoxicity

The cytotoxicity of free or loaded curcumin into ethosomes and transferosomes was evaluated by an MTT-dye reduction assay against HUT-78 (cutaneous T-cell lymphoma, CTCL-Cesary syndrome). In brief, exponentially growing cells were plated in 96-well flat-bottomed plates (100 µL/well) at a density of 1×10^5/mL and were incubated for 24 h at 37 °C. Afterwards, cells were exposed to varying concentrations of the tested formulations and the free drug for 72 h. At least 8 wells were used for each concentration. After the needed time for exposure, 100 µL of MTT solution (10 mg/mL in PBS) were added to each well. Afterwards, the samples were incubated for 4 h at 37 °C, and the MTT-formazan crystals that had formed were then dissolved by adding 5% formic acid-acidified 2-propanol. The MTT formazan absorption was recorded using a LabeximLMR-1 microplate reader at 580 nm. Cell survival fractions were calculated as a percentage of the untreated control. In addition, IC_{50} values were derived from the concentration-response curves.

Results and discussion

A series of ethosomes and transfersomes were prepared via the thin film hydration method, and the impact of constituents on their physicochemical characteristics was assessed. Next, optimal formulations were selected for further cytotoxic investigation. Although the thin film hydration method is the most established technique for the preparation of vesicular carriers, it may often determine the formation of non-uniform-size vesicles, unless followed by subsequent sonication or extrusion steps. Therefore, the initial aim of our study was to optimize the process parameters in order to obtain formulations with suitable physicochemical parameters. The ethosomes prepared via the thin film hydration method were characterized by sizes ranging between 578 and 871 nm, high zeta potential values, and curcumin entrapment efficiency ranging within 69–81%. The subsequent sonication of curcumin-loaded vesicles (E2) was not found to exert a beneficial effect on their properties; therefore, this step was not included in the ethosomes' preparation protocol. Opposite results were evident in the case of transfersomes, where the sonication process led to a decrease in vesicles' size and PDI values without compromising the colloidal stability of the dispersions (Table 1).

Table 1. Composition and physicochemical properties of curcumin-loaded ethosomes (E) and transferosmes (T). In each drug-loaded formulation, the curcumin concentration was maintained constant (0.0025% w/v).

Vesicular nanocarrier code	Lipoid S75 (% w/v)	Ethanol (% v/v)	Edge activator (% w/v)	D_h (nm) ± SD	PDI ± SD	ζ-potential (mV) ± SD	EE (%) ± SD
E1	3	20	-	871.1 ± 16.34	0.16 ± 0.06	-42.14 ± 4.67	69.1 ± 2.21
E2	3	30	-	722.2 ± 7.70	0.22 ± 0.01	-53.24 ± 1.15	81.5 ± 1.61
E2 sonicated	3	30	-	552.6 ± 14.48	0.30 ± 0.02	-50.23 ± 1.35	76.2 ± 0.86
E2 blanc	3	30	-	786.9 ± 3.18	0.08 ± 0/03	-30.72 ± 1.26	-
E3	3	40		627.7 ± 15.25	0.41 ± 0.03	-59.28 ± 1.32	75.1 ± 1.19
E4	2	30	-	778.1 ± 4.47	0.29 ± 0.01	-44.49 ± 0.40	73.7 ± 2.23
E5	4	30	-	578.6 ± 4.54	0.20 ± 0.02	-65.96 ± 3.60	78.2 ± 1.76
T1 sonicated	3	-	Tween 20 0.3%	881.1 ± 43.21	0.57 ± 0.03	-69.78 ± 1.69	59.4 ± 0.95
T2 unsonicated	3	-	Tween 60 0.3%	1383 ± 58.62	0.75 ± 0.14	-62.65 ± 1.31	70.7 ± 2.35
T2 sonicated	3	-	Tween 60 0.3%	1245 ± 65.27	0.55 ± 0.04	-60.11 ± 1.14	63.5 ± 2.39
T2 blanc sonicated	3	-	Tween 60 0.3%	817.6 ± 29.5	0.56 ± 0.1	-55.16 ± 1.78	-
T3 sonicated	3	-	Tween 80 0.3%	808.1 ± 31.75	0.50 ± 0.06	-70.31 ± 1.45	64.8 ± 2.76
T4 sonicated	3	-	Tween 20 0.6%	796 ± 21.19	0.41 ± 0.01	-56.12 ± 1.18	57.5 ± 2.17
T5 sonicated	3	-	Tween 60 0.6%	802.4 ± 13.93	0.31 ± 0.05	-59.81 ± 1.13	65.4 ± 1.15
T6 sonicated	3	-	Tween 80 0.6%	787 ± 10.46	0.46 ± 0.03	-57.38 ± 1.15	60.9 ± 1.89

Effect of formulation variables on ethosomal physiochemical characteristics

Besides the preparation techniques, the formulation constituents also have a major impact on the physicochemical properties of the nanocarriers. As evident from the presented data (cf. E1, E2, and E3), increasing ethanol concentration determines a reduction in vesicles' size, which may be attributed to a decrease in the ethosomal membrane thickness following interpenetration of the alcohol hydrocarbon chain at higher concentrations (Abdulbaqi et al. 2016). Additionally, ethanol imparts a net negative charge to the vesicular carriers (Mombeiny et al. 2021), which contributes towards their steric stabilization, hence the observed smaller sizes at higher alcohol concentrations. This hypothesis is further supported by the results obtained from zeta potential analysis, which indicate superior colloidal stability at higher ethanol concentrations. Increasing ethanol concentration leads to a rise in curcumin entrapment efficiency, but only up to a certain extent. At 40% ethanolic content, a lower amount of curcumin was accommodated in the vesicles, probably due to the drug leakage that occurred following the solubilization of Lipoid S75 in ethanol and the subsequent derangement of the vesicular structure. Curcumin is a lipophilic compound, predominantly accommodated within the lipid membrane of the ethosomes, whereby the impact of phospholipid content was also evaluated. As evident from the presented data, increasing phospholipid content resulted in a decrease in the size of the vesicles, which may be explained by the increased rigidity of the nanocarriers. A similar tendency is also reported by Aljohani et al. (2023), elaborating ketoconazole-loaded conventional and binary ethosomes. Increasing phospholipid content corresponds to higher zeta potential values, but in the case of curcumin entrapment efficiency, the observed tendency was not linear. The highest curcumin entrapment (81.5%) was estimated at 3% Lipoid S75, as above this point, curcumin's saturation limit was probably reached. Taking into account the complexity effects of the physicochemical parameters on the biopharmaceutical and therapeutical behaviors of nanocarriers, an optimal ethosomal formulation was selected, composition E5, characterized by the lowest size, monomodal size distribution (PDI 0.2), highest zeta potential, and relatively high (78.2%) curcumin entrapment efficiency.

Regarding transfersomal formulations, the impact of type (Tween 20, Tween 60, and Tween 80) and concentration (0.3% and 0.6%) of edge activators on the main physicochemical parameters was studied. As evident from the obtained results, both of the investigated variables strongly affect the properties of the vesicles. There is an inverse relationship between the hydrophilic-lipophilic balance (HLB) values of edge activators and the obtained entrapment efficiency data. The highest curcumin encapsulation was estimated in the vesicles comprising Tween 60 (vs. Tween 20 and Tween 80-based ones), irrespective of the concentration (0.3 or 0.6% w/v). The obtained results also correlate with the molecular weight (Mw) of the surfactants; higher Mw values correspond to a higher percentage of entrapped curcumin. Tween 60-transfersomes are characterized by larger sizes, whereas Tween 80-based ones exhibit the smallest dimensions. As both edge activators (Tween 60 and Tween 80) have the same chain length (18C) and close HLB values (14.9 and 15, respectively), the obtained outcomes may be related to the presence of a double bond in the Tween 80 chain, which probably determines the formation of a more compact vesicular structure. A further decrease in transfersomal size was estimated by increasing the concentration of edge activators. The results may be attributed to surfactants' ability to reduce the interfacial tension; hence, higher edge activators' concentration contributes to size reduction. A slight decrease in curcumin entrapment efficiency was estimated in the compositions containing 0.6% (w/v) edge activators; however, the obtained values are still considered high (between 57.5% and 65.4%). Based on the obtained results, the optimal transfersomal composition for further studies was selected as composition T5. The size distribution curves of the selected curcumin-loaded ethosomes and transfersomes are illustrated in Fig. 1.

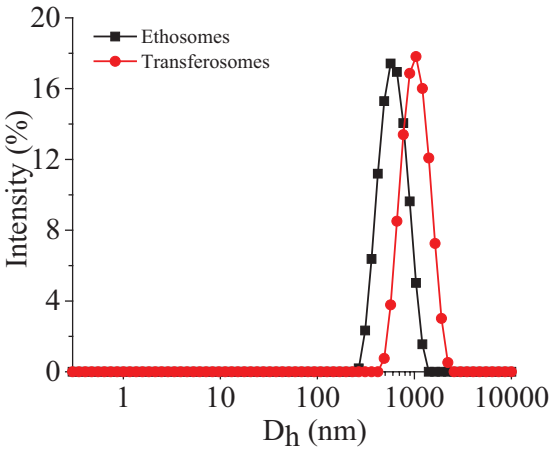

Figure 1. Size distribution plots of curcumin-loaded ethosomes (E5) and transfersomes (T5).

Morphology of ethosomes and transfersomes

The representative TEM micrographs of the elaborated nanocarriers (blank and curcumin-loaded) are illustrated in Fig. 2. As evident from the TEM images, both vesicles exhibit spherical shapes with well-preserved membranes. The obtained sizes on the micrographs are smaller compared to the data from DLS analysis, which may be related to the differences in sample preparation: in TEM analysis, the samples are dehydrated, which determines the shrinkage of their dimensions, while in DLS they are in a hydrated state, which contributed towards larger sizes. This shift is reported elsewhere in the literature (Alaaeldin et al. 2021).

Curcumin release from ethosomes and transfersomes

Curcumin release from the selected ethosomal and transfersomal formulations was evaluated in a comparative manner under physiologically relevant conditions (Fig. 3). The observed biphasic pattern—faster drug release at the beginning and a subsequent slower stage—is characteristic for most of the vesicular systems, including transfersomes and ethosomes. The sustained release profile may be explained by the role of the nanocarrier as a "reservoir," gradually releasing the encapsulated cargo after the initial "burst" effect, owing to the unentrapped or located vesicular surface curcumin. Regarding the type of nanocarriers, faster curcumin release was estimated from ethosomes. This fact may be due to the presence of ethanol, which affects membrane permeability and facilitates curcumin release. The obtained *in vitro* release data were fitted to different kinetic models. The highest regression coefficient (R^2) values for the two vesicular nanocarriers were obtained for the Higuchi kinetic model, indicating a diffusion-controlled process with "n" values lower than 0.5 corresponding to the Fickian diffusion mechanism (Table 2). Our results are in agreement with the studies performed by other authors (AL Shuwaili et al.,2016; Ferrara et al. 2024).

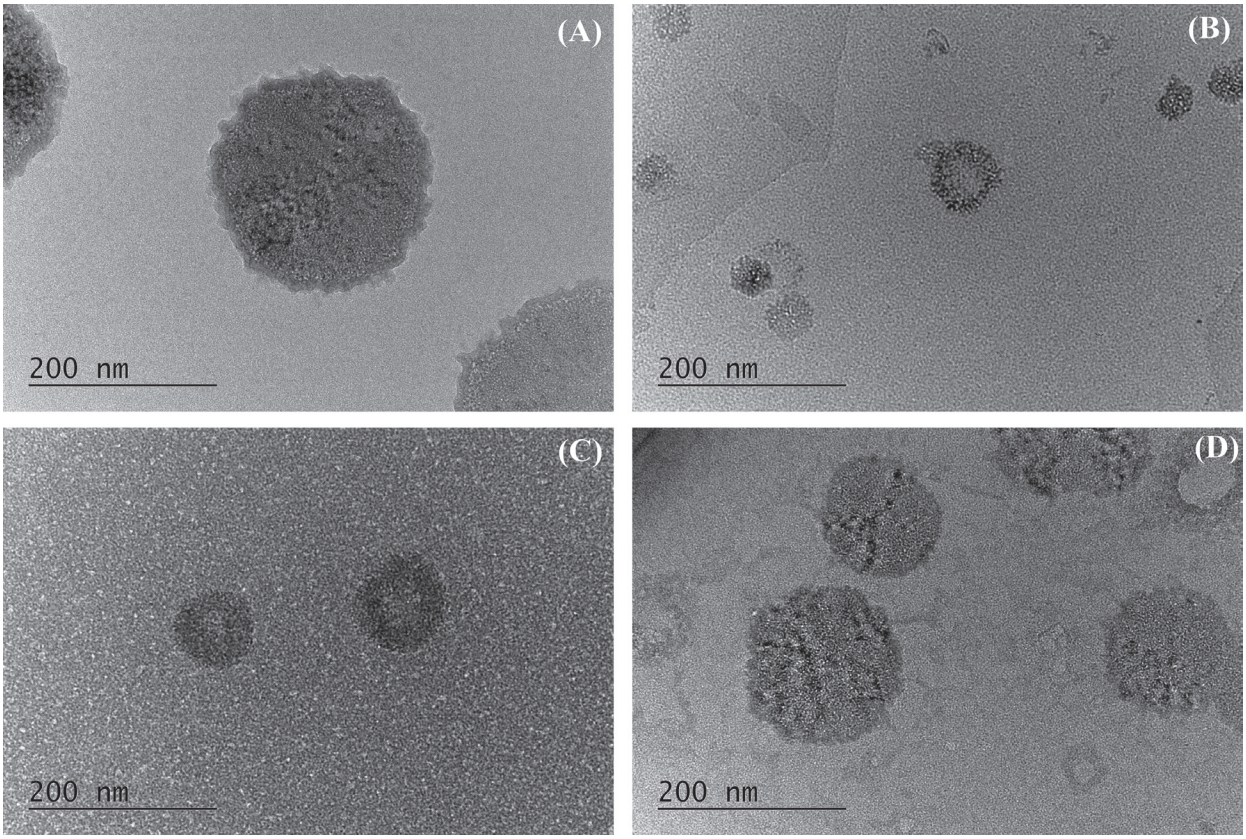

Figure 2. Representative TEM micrographs of **A.** Blank; **B.** Curcumin-loaded ethosomes, blank (**C**), and curcumin-loaded (**D**) transfesomes.

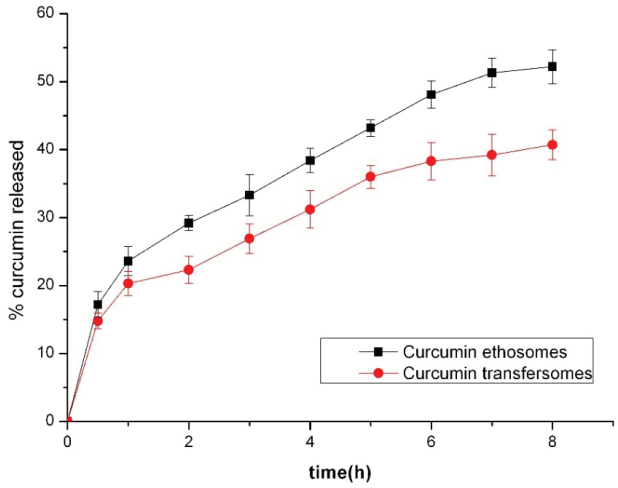

Figure 3. Curcumin release from ethosomes (E5) and transfersomes (T5) at pH 5.5.

Table 2. Release kinetic data for optimal ethosomal and transfersomal formulations.

Formulation	Zero order	First order	Higuchi	Peppas	
	R^2	R^2	R^2	R^2	N
E	0.887	0.946	0.990	0.985	0.404
T	0.858	0.907	0.978	0.959	0.373

Stability studies

The physical stability of the selected ethosomes and transfersomes expressed in terms of alterations in size, size distribution pattern, zeta potential, and curcumin entrapment efficiency was evaluated by storing the formulations at 4–6 °C for 1 month. As evident from Table 3, the elaborated vesicles preserved the entrapped curcumin and their colloidal stability during the test period. A slight increase (ca. 10% and 17%) in the vesicles' size was observed, accompanied by a decrease in the PDI values, following the formation of larger vesicles. At the end of the tested period, no significant changes in the physical appearance of the vesicular dispersion were observed; they maintained their yellowish color and homogenous appearance without the occurrence of any precipitation.

Cytotoxicity studies

Cytotoxic effects after treatment of malignant HUT-78 cells with free or formulated curcumin ethosomes or transfersomes were investigated. Succeeding 72-h exposure to the free drug and its formulations showed a noticeable concentration-dependent reduction of cell viability, causing almost 82% eradication of treated cells at the highest tested concentrations of curcumin (0.05 mg/mL) (see Fig. 4A). It is worth mentioning that the encapsulation of curcumin inside both types of elaborated vesicles proved to significantly augment its antineoplastic activity. Thus, the equieffective IC_{50} values derived from non-linear regression analysis of concentration-effect curves for formulated curcumin were lower as compared to free agents (Table 4). The transferosomal curcumin had 1.25 lower IC_{50} values as compared to the free curcumin. The entrapment of phytochemicals inside ethosomes, however, led to an additional enhancement of its cytotoxicity relative to the free drug by a factor of ca. 1.6. These results correspond very well to preceding studies with liposomes, showing enhanced anticancer activity (Peram et al. 2019) as compared to free curcumin. The observed higher antiproliferative activity of curcumin encapsulated in ethosomes as compared to transferosomal curcumin is probably due to the smaller size of the vesicles and the presence of ethanol in the formulation, leading to increased permeation and internalization of the drug. However, in order to prove this, it is necessary to carry out additional analyses.

Table 3. Physical stability assessment of optimal curcumin-loaded ethosomes and transfersomes.

Sample	Size (nm) ± SD		PDI ± SD		ζ potential (mV) ± SD		EE (%)	
	Initial	One month	Initial	One month	Initial	One month	Initial	One month
E5	578.6 ± 4.54	682 ± 12.74	0.20 ± 0.02	0.13 ± 0.03	-65.96 ± 3.60	-63.57 ± 2.27	78.2 ± 1.76	76.5 ± 1.98
T5	802.4 ± 13.93	889.7 ± 11.65	0.31 ± 0.05	0.30 ± 0.07	-56.12 ± 1.18	-54.98 ± 1.96	65.4 ± 1.15	63.2 ± 2.1

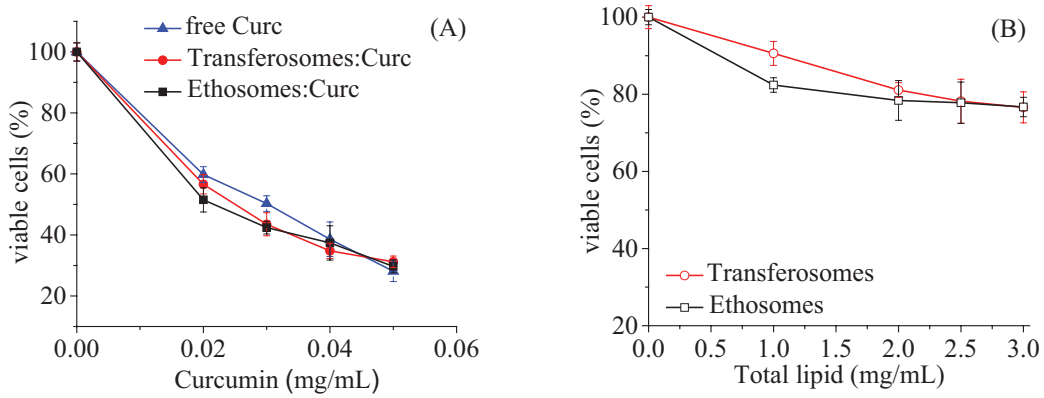

Figure 4. Cytotoxicity of free vs. formulated curcumin (**A**) and of empty nanovesicles (**B**) against human malignant HUT-78 cells after 72 h exposure. The concentration of total lipids in loaded vesicles equals that of non-loaded ones.

Table 4. Equivalent concentration (IC_{50}) and modulation indices (MI) of free curcumin and its formulations against the human tumor HUT-78 cell line after 72 h exposure.

Sample	IC_{50} (mg/mL)	MI*
Free Curc	0.031	-
Transferosomes:Curc (T5)	0.025	1.24
Ethosomal:Curc (E5)	0.020	1.55

*MI – modulation index = IC_{50} (free curcumin)/IC_{50} (curcumin formulation).

To investigate whether the observed enhanced cytotoxic activity of nanoformulated curcumin is due only to the inherent cytotoxicity of the drug (not to the carrier itself), we performed an analogous study on HUT-78 cells treated with empty vesicles at equivalent concentrations of the lipid carrier as in the analogue-loaded counterparts. The data shown in Fig. 4B unequivocally show that the unloaded carriers are virtually devoid of intrinsic toxicity, as only slight (less than 25%) suppression of cell viability was detected.

Conclusion

Curcumin-loaded ethosomes and transferosomes were elaborated and evaluated as nanoplatforms for dermal curcumin delivery. Both nanovesicular systems are characterized by high curcumin loading efficacy and controlled drug delivery, governed by the Fickian diffusion mechanism. In addition, both formulations are characterized by favorable storage stability. The bioassay data showed that the formulated curcumin was superior in terms of cytotoxic activity as compared to the free drug. The ethosomal formulation constrained the viability and proliferation of HUT-78 cells at lower micromolar concentrations as compared to free drugs and curcumin formulated in transferosomes. These findings give us the reason to conclude that the presented nanovesicles are feasible platforms to ensure augmentation of curcumin antiproliferative activity with a concomitant anticipated beneficial modulation of the skin permeation ability, based on the well-known generic properties of both types of vesicles, especially ethosomes.

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