Hyalurosome-Based Delivery System for Bioactive Compounds in Cosmetic Applications

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Abstract

Berberine chloride (BC) and resveratrol (RES) are bioactive compounds with potent antioxidant activity and promising applications in cosmetic formulations. However, their utilization is limited by poor aqueous solubility, instability, and low delivery efficiency. This study aimed to develop hyalurosomes, nanoscale vesicular carriers composed of phospholipids and hyaluronic acid, for the encapsulation of BC and RES and to evaluate their antioxidant activity, physicochemical properties, and encapsulation performance. Antioxidant activity was assessed using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay, with vitamin C as a reference standard. The half-maximal inhibitory concentration (IC_{50}) values were 0.852 mg/mL for BC and 0.108 mg/mL for RES, and were used to guide concentration selection for formulation development. UV–visible spectrophotometry was employed for quantitative analysis. BC exhibited a maximum absorption wavelength (λmax) at 349 nm, while RES showed a λmax at 306 nm; these wavelengths were applied for the determination of encapsulation efficiency (%EE). The developed hyalurosomes exhibited particle sizes ranging from 97.67 ± 0.85 to 135.10 ± 2.76 nm, with polydispersity index (PDI) values of 0.38 ± 0.01 to 0.45 ± 0.01, confirming nanoscale formation with an acceptable and relatively narrow size distribution. The zeta potential values ranged from −23.17 ± 0.51 to −25.57 ± 1.00 mV, indicating moderate colloidal stability of the vesicular systems. Encapsulation efficiency ranged from 57.18–62.80% for BC and 51.15–59.77% for RES. The optimized systems were successfully incorporated into facial serum formulations with appropriate pH and desirable rheological characteristics for topical application, highlighting their potential as nanocarrier platforms for enhanced antioxidant delivery and improved applicability of bioactive compounds in cosmetic applications.

Introduction

- Hyalurosomes are phospholipid nanovesicles modified with hyaluronic acid that improve stability, hydration, and skin interaction for enhanced dermal delivery.
- Encapsulation in hyalurosomes may enhance the stability, protection and skin delivery of antioxidant compounds such as BC and RES.
- Berberine chloride (BC) is an isoquinoline alkaloid with a quaternary ammonium structure that exhibits antioxidant, anti-inflammatory and antimicrobial activities.
- Resveratrol (RES) is a polyphenolic stilbene with strong antioxidant, anti-aging and photoprotective properties.
- Hyalurosomes enhance skin interaction and retention of antioxidants, supporting their potential use in dermal and cosmetic formulations.

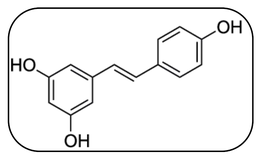


Figure 1 The structure of resveratrol

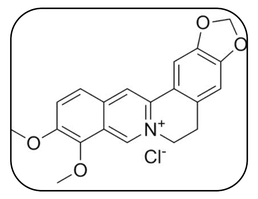


Figure 2 The structure of berberine chloride

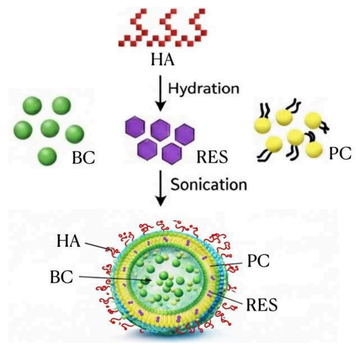


Figure 3 Graphical of hyalurosome delivery system

Methodology

1. Preparation of hyaluronic acid solution



15 mg of hyaluronate (Standard molecular, 1M Daltons)

Added of DI water →  Stirred 2 hrs. →  Hydration 5 hrs. → 

0.1% Hyaluronate solution

2. Antioxidant activity (DPPH assay)



0.1 mM DPPH mixed with ascorbic acid, resveratrol and berberine chloride

Incubated in the dark for 30 mins → 

Measured the absorbance at 515 nm → Calculated % Inhibition → Standard curve → Calculated IC50

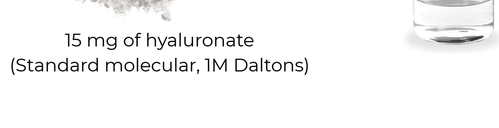
3. Preparation of formulations

Formulation	Ingredients
F0	0.1% Hyaluronic acid
F1	0.1% Hyaluronic acid and 0.07% Berberine chloride
F2	0.1% Hyaluronic acid and 0.03% Resveratrol
F3	0.1% Hyaluronic acid, 0.07% Berberine chloride and 0.03% Resveratrol

→  Sonication → 

BC/RES-loaded hyalurosome (F0-F3)

4. Vesicle size analysis



BC/RES-loaded hyalurosome (F0-F3) → Zetasizer

5. Encapsulation efficiency



Disruption → 70% ethanol →  measured the abs. at λ max

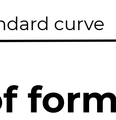
Standard curve → Calculated encapsulation efficiency (%)

Centrifugation 20 min at 3000 rpm at 25° C →

6. Prototype of formulation

 $MgSO_4$ Solution + Mild preservative + 



Hyalurosome-based serum ← Stirred ←  Serum base +  Cyclopenta-siloxane

7. Stability test



Hyalurosome-based serum → Stability test at different temperature 4 °C, room temp and 40 °C for 7 days

Results and Discussion

Table1 Mean Vesicle Size, Zeta Potential, Polydispersity Index and Encapsulation Efficiency of Formulation. Measurements are expressed as mean ± SD

Formulation Code	Vesicle size (nm) ± SD	PDI ± SD	Zeta potential (mV) ± SD	pH	Encapsulation efficiency (%)	
					BC, 349 nm	RES, 306 nm
F0 (HS blank)	122.97 ± 1.10	0.39 ± 0.01	-24.7 ± 0.52	7.39	62.80	59.77
F1 (BC-HS)	97.67 ± 0.85	0.39 ± 0.00	-23.17 ± 0.51	6.61	62.27	54.94
F2 (RES-HS)	135.10 ± 2.76	0.45 ± 0.01	-25.57 ± 1.00	6.91	57.18	51.15
F3 (BC-RES-HS)	112.47 ± 3.00	0.38 ± 0.01	-23.23 ± 1.42	6.58	60.02	52.97

Vesicle size
- Mean diameter of vesicles affecting skin penetration and formulation stability.
- Typically 50–300 nm for topical nanocarrier systems.
- Obtained sizes (97–135 nm) fall within the acceptable range, indicating suitable nanoscale vesicles.

Zeta Potential
- Surface charge of vesicles reflecting colloidal stability.
- Stable systems typically show -20 to -30 mV, though moderate stability may occur at lower values.
- Values (−23 to −26 mV) indicate moderate electrostatic stability.

Polydispersity Index (PDI)
- Indicates the uniformity of particle size distribution.
- PDI < 0.5 acceptable; < 0.3 considered highly uniform.
- Values (0.38–0.45) suggest acceptable homogeneity of vesicle size.

Encapsulation Efficiency (%EE)
- Percentage of active compounds successfully entrapped within vesicles.
- Standard >50% generally considered acceptable for nano-delivery systems.
- %EE values (~51–63%) demonstrate satisfactory encapsulation of both BC and RES.

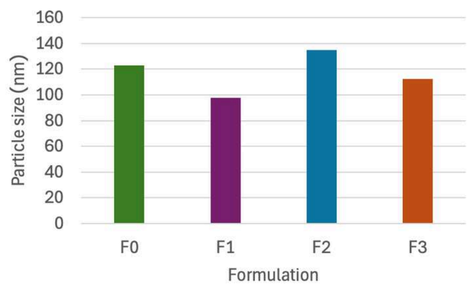


Figure 4 Vesicle size of formulation



Figure 5 Hyalurosome-based serum

Conclusion

Berberine chloride and resveratrol were successfully encapsulated in hyalurosomes. The developed vesicles showed suitable physicochemical properties, indicating their potential as nanocarriers for antioxidant delivery.

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