Application of a 3-level full factorial experimental design for the synthesis of chlorogenic acid-loaded transethosomes

Ance Bārzdiņa[1,2], Dace Bandere[1,2], Agnese Brangule[2,3]

[1]Department of Applied Pharmacy, Faculty of Pharmacy, Riga Stradins University, Riga, Latvia
[2]Baltic Biomaterial Centre of Excellence, Headquarters at Riga Technical University, Riga, Latvia
[3]Department of Pharmacology and Pharmacotherapy, Faculty of Pharmacy, Riga Stradins University, Riga, Latvia

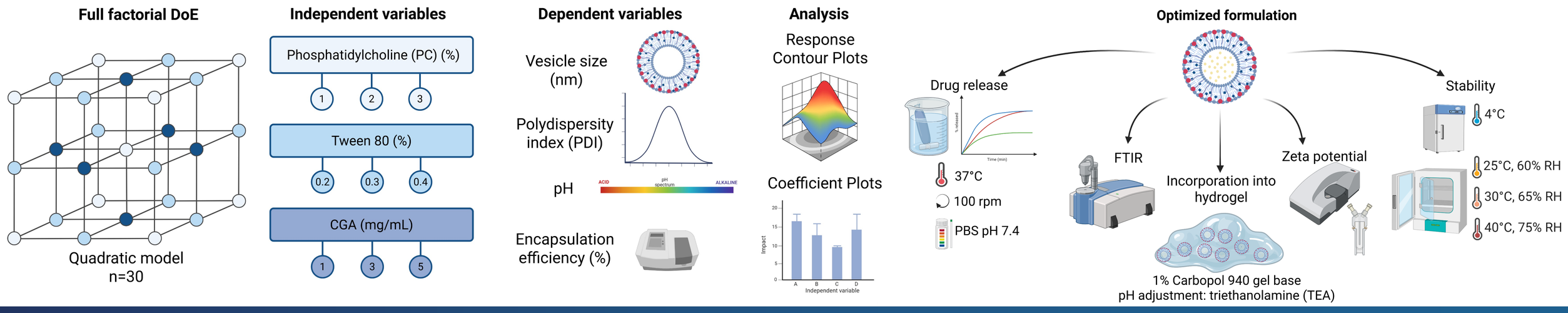
Introduction

Chlorogenic acid (CGA) is a natural phenolic acid known for a diverse pharmacological profile, including anti-inflammatory, anti-oxidative, antibacterial, and antiaging properties[1]. The biological activity spectrum makes this compound a candidate for various dermatological conditions. However, its wider application in the pharmaceutical industry is hindered by the physicochemical properties of the compound, such as a large topological polar surface area of 164.75 Å^2, pKa of 3.5, and log K_p of -8.76 cm/s, indicating poor skin permeation and subsequently limited transdermal delivery potential[2,3].

Transethosomes are ultra-flexible lipid nanoparticles designed to efficiently penetrate the stratum corneum and deliver various therapeutics to the deeper layers of skin.

The aim of this study was to apply a design of experiment (**DoE**) approach to optimize the synthesis of **CGA-loaded transethosomes** to achieve particles with parameters suitable for transdermal delivery.

Methods



Results

Figure 1. 4D Response contour plots

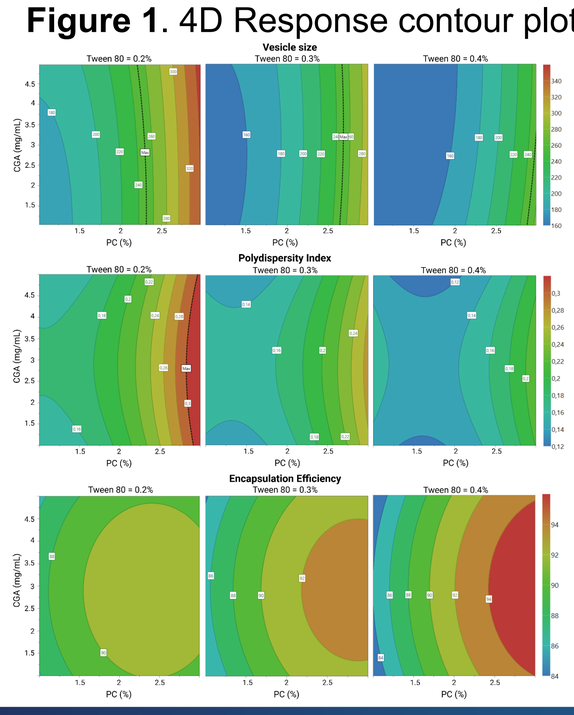


Figure 2. Coefficient plots (scaled and centered), multiple linear regression (MLR)

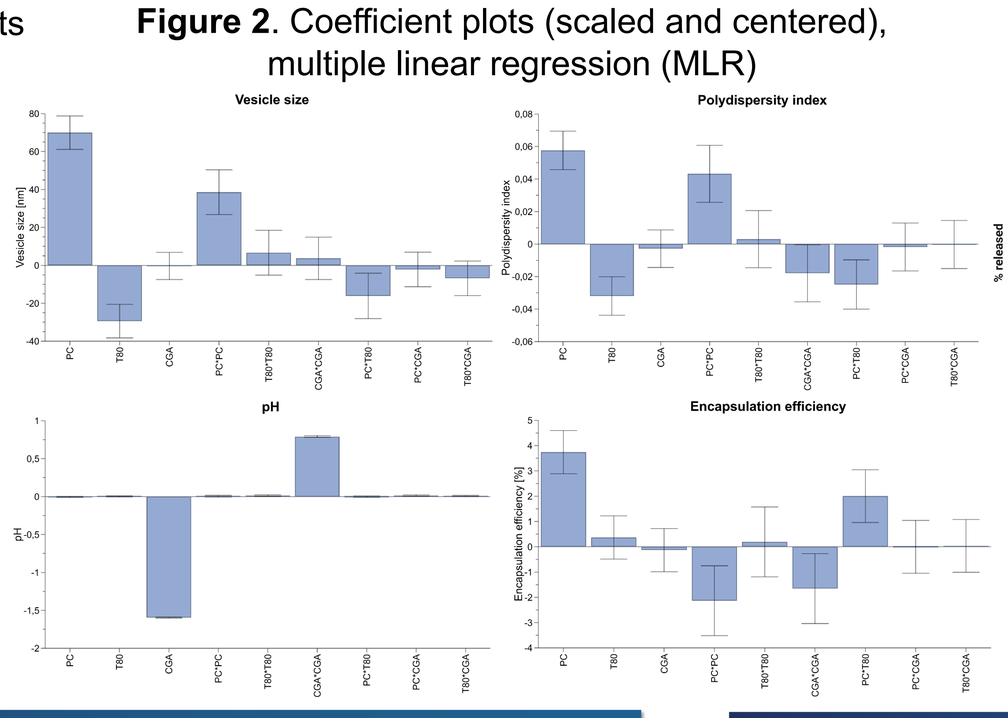


Figure 3. Drug release profiles of prepared formulations

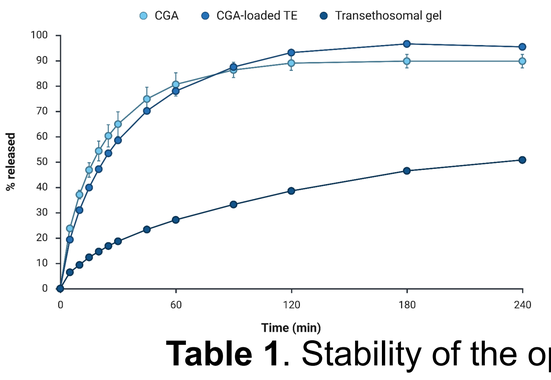


Figure 4. ATR-FTIR

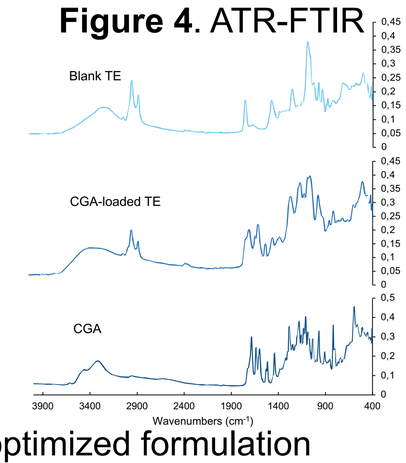


Table 1. Stability of the optimized formulation

Storage conditions	Mean diameter (nm ± SD)		PDI ± SD		Zeta potential (mV ± SD)	
	Day 1	Day 90	Day 1	Day 90	Day 1	Day 90
+4 °C	185.4 ± 3.7	175.5 ± 0.8	0.09 ± 0.01	0.08 ± 0.03	-7.8 ± 0.2	-8.4 ± 0.5
+25 °C, 60% RH	192.0 ± 4.9	197.6 ± 3.1	0.07 ± 0.02	0.08 ± 0.01	-9.3 ± 0.9	-13.5 ± 1.6
+30 °C, 65% RH	179.8 ± 2.2	194.2 ± 10.2	0.09 ± 0.01	0.09 ± 0.02	-9.1 ± 0.2	-13.7 ± 1.4
+40 °C, 75% RH	173.3 ± 2.8	178.9 ± 8.2	0.09 ± 0.02	0.08 ± 0.03	-10.1 ± 1.0	-16.7 ± 0.4

Conclusions

CGA-loaded transethosomes with the most suitable parameters for transdermal delivery can be synthesized using 2% phosphatidylcholine, 0.4% Tween 80, and 3 mg/mL CGA. Phosphatidylcholine concentration is the most influential factor impacting vesicle size, PDI, and encapsulation efficiency. The optimized transethosomal formulation is stable under refrigerated conditions for over 3 months. Transethosome incorporation into a Carbopol gel is needed to achieve a sustained release of CGA.

[1]doi:10.3390/nu16070924; [2]SwissADME online tool; [3]PubChem database – Chlorogenic acid

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Contact information

Ance Bārzdiņa - ance.barzdina@rsu.lv

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