PREFORMULATORY STUDIES ON ROSMARINIC ACID-NLC FOR ORAL ADMINISTRATION

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INTRODUCTION

Rosmarinic Acid (RA), a natural polyphenol from *Rosmarinus officinalis*, has antioxidant, anti-inflammatory, antidiabetic, antitumor, antimicrobial and antiviral properties. However, its pharmaceutical application is limited due to poor water solubility, low bioavailability, and rapid degradation in the gastrointestinal tract. Fast metabolism and elimination further reduce its efficacy[1]. This study aims to develop nanostructured lipid carriers (NLCs) to enhance oral bioavailability, protect RA from gastric degradation, and allow for prolonged intestinal release, thereby improving its overall therapeutic potential.

EXPERIMENTAL METHODS

NLCs containing Tristearin:Miglyol® or Tristearin:Vitamin E (2:1 w/w) and 2.5% Poloxamer were produced by hot homogenization and ultrasonication. RA was dispersed in the molten lipid phase, at different concentrations (0.5, 1, 2 mg/ml). Formulations were characterized by encapsulation efficiency, loading capacity, size distribution, morphological and charge properties by mean of different techniques including HPLC, Transmission Electron Microscopy (TEM), PCS and zeta potential.

RESULTS AND DISCUSSION

The preformulation study selected TM-RA1 and TV-RA1 (1 mg/ml RA) that remained stable up to 90 days post-production in terms of encapsulated RA (80%) and size, without significant variations in size distribution and polydispersity. Antioxidant activity, assessed by photochemiluminescence (PCL), was preserved.

In vitro release study by equilibrium dialysis showed a controlled, time-dependent release of RA, following second-order kinetics consistent with the Higuchi model.

Permeability tests using the PermeaPad® Plate[2] revealed a five-fold reduction in RA diffusion compared to aqueous suspension, supporting sustained release. Static *in vitro* digestion confirmed that NLCs protect RA from gastric degradation, enabling intact delivery to the intestinal environment and promoting absorption.

To improve mucosal adhesion, further studies will be conducted including NLC in gel-based systems.

REFERENCES

1. MK Azhar et al., *Nutrients*. **2023** (doi: 10.3390/nu15194297)
2. M Sguizzato et al., *Int J Pharm.* **2025** (doi:1 0.1016/j.ijpharm.2025.125170)