

## DEVELOPMENT AND OPTIMIZATION OF PREPARATION PROCESS FOR NOVEL NADES-BASED ALGinate EUTECTOGELS AS CARRIERS FOR RESVERATROL

S. Kalafateli<sup>1</sup>, I. Pitterou<sup>1</sup>, E. A. Fragkonikolaki<sup>1</sup>, A. Tzani<sup>1</sup>, A. Detsi<sup>1,\*</sup>

<sup>1</sup>School of Chemical Engineering, National Technical University of Athens, Athens, Greece

(\*adetsi@chemeng.ntua.gr)

### ABSTRACT

Eutectogels have emerged as a new type of gel, formed via gelation of Deep Eutectic Solvents and promising as innovative drug delivery vehicles for poorly soluble bioactive ingredients (e. g. quercetin), due to their biocompatibility and tunable properties.<sup>[1, 2, 3]</sup> Natural Deep Eutectic Solvents (NaDESs) are mixtures of two or more compounds of natural origin, a hydrogen bond donor (HBD) and a hydrogen bond acceptor (HBA) at specific molar ratios, resulting in a significant reduction of the melting point compared to those of the initial components. NaDESs are distinct for their biodegradability, non-volatility, non-flammability, low toxicity and cost.<sup>[4]</sup> Resveratrol (*trans*-3,4',5-trihydroxystilbene) is one of the most common naturally occurring polyphenols with powerful antioxidant activity, but its hydrophobic nature results in its low solubility and bioavailability.<sup>[5]</sup>

The aim of the present work is the development and optimization of a green preparation process for novel non-toxic eutectogels using a NaDES for the encapsulation of resveratrol. The NaDES employed consists of betaine, glycerol and water and is synthesized using the heating and stirring method. The gelling agent is sodium alginate, a cheap, biocompatible, readily available, non-toxic, anionic biopolymer, commonly used as encapsulation matrix.<sup>[3]</sup> First, the solubility of resveratrol in an aqueous NaDES solution was studied and it was found that, when NaDES concentration in the solution is 900mM, the solubility is increased by 4.5 times compared to that in water. The impact of the factors (A) alginate content (% w/v), (B) water content (% v/v) and (C) resveratrol content (% w/v) on the responses (R<sub>1</sub>) water-retention capacity of eutectogels and (R<sub>2</sub>) resveratrol encapsulation efficiency, was investigated and the optimization process was accomplished through a 3-factor, 3-level Box–Behnken experimental design and statistical analysis of the results.

**KEYWORDS:** eutectogel, Natural Deep Eutectic Solvent (NaDES), alginate, resveratrol

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