Preformulation and development of preliminary nanoemulsion carrier for patent protected compound GL-II-73

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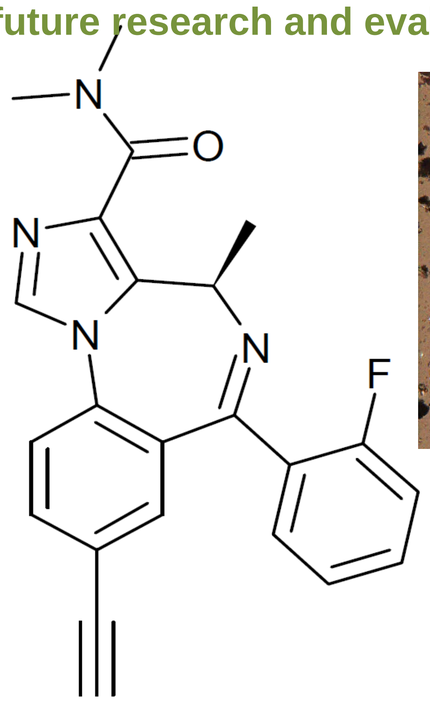
CONCLUSION

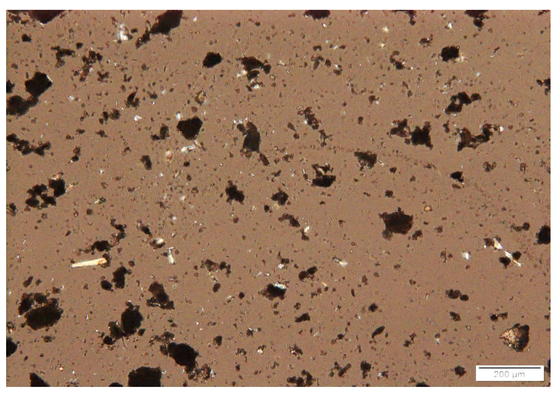
Preliminary studies suggest that nanoemulsions are good potential carriers for GL-II -73, but further research is needed to optimise stability.

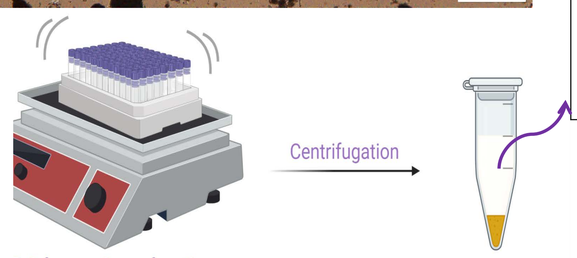
INTRODUCTION AND AIMS

Nanopharmaceuticals offer a good way to circumvent some of the difficulties faced by new drug candidates. They can be tailored to adjust their water solubility, half-life, and biodistribution or to control the release of the integrated drug. Due to the excipients used, lipid nanocarriers (liposomes, nanoemulsions (NEs), nanoparticles) were used to improve targeting to the brain (1,2). The investigated compound GL-II-73 is an imidazobenzodiazepine (IBZD) ligand that acts as a positive allosteric modulator at α-GABAA receptors and has been shown to have a combined antidepressant and cognition enhancing effect, making it a promising candidate for further research (3).

The aim of this work is to investigate the physicochemical properties of GL-II -73 to select the best parenteral nanodelivery system for future research and evaluate its parameters.







Solubility of GL-II-73

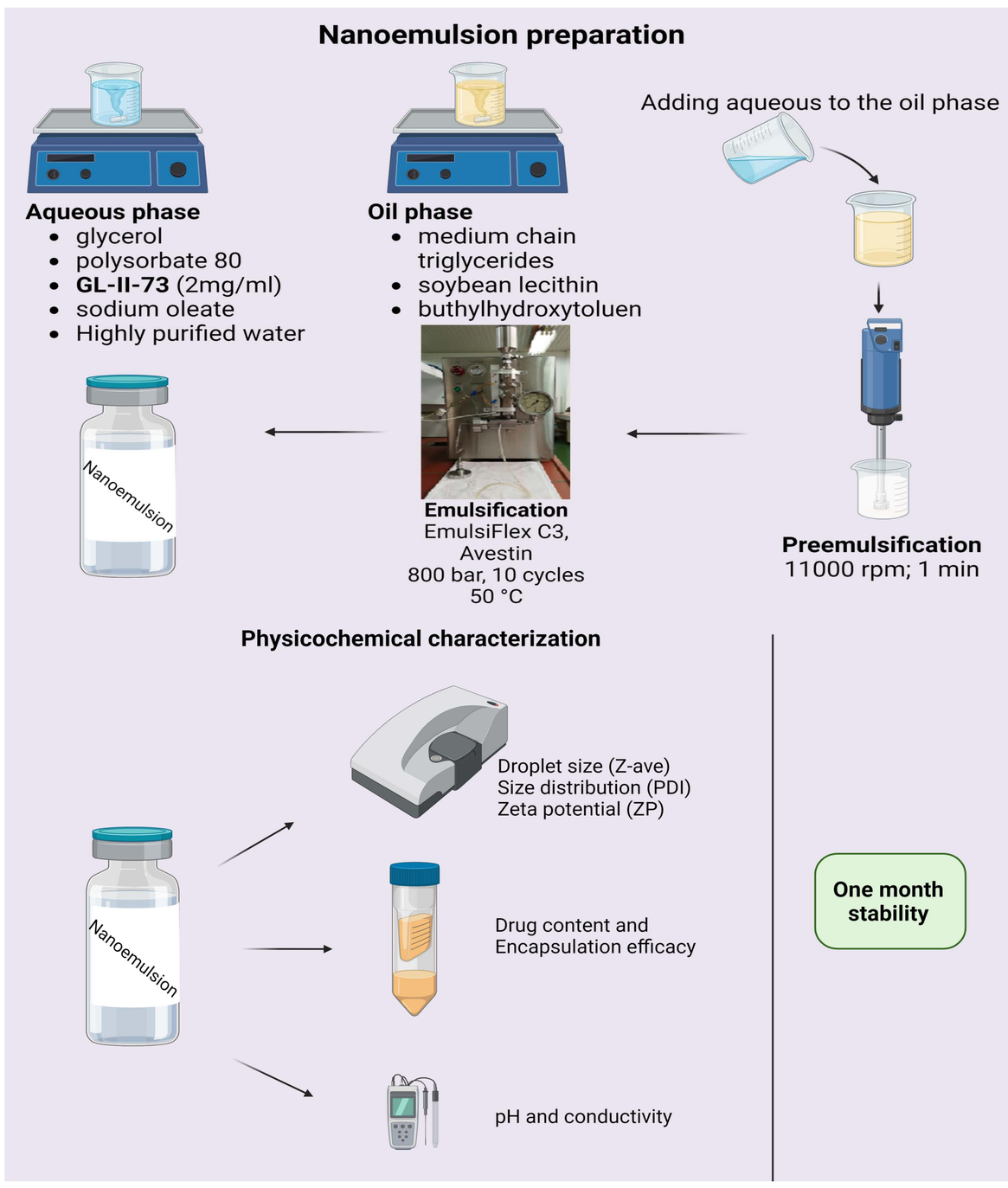
Solvent	Solubility (µg/ml)
Phosphate buffer (pH 7.4)	951.37 ± 41.38
Water (pH 5.2)	1,001.10 ± 39.94
0.1 M HCl (pH 1.2)	5,370.70 ± 195.26
Medium-chain triglycerides	4,489.70 ±148.32
Soybean oil	3,055.05 ± 137.42
Castor oil	2,820.65 ± 183.68
Fish oil	2,395.07 ± 331.00
Isopropanol	131,047.81 ± 6,902.35
Methanol	> 1,469,735.25 ± 93,891.20

log P = 2.09

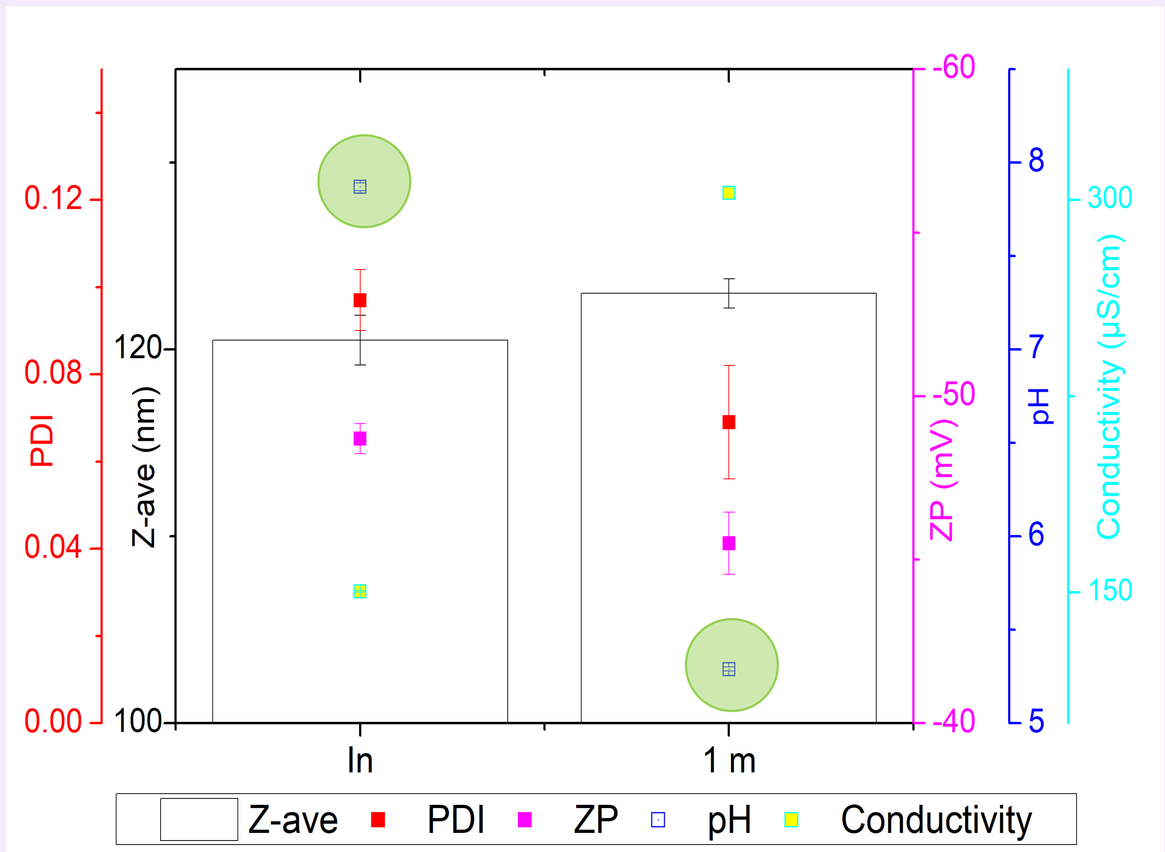
- The relatively good oil solubility of GL-II -73 in oils suggests that NEs act as promising carriers pH-dependent solubility (increases with decreasing pH)
  - ionizable functional groups
  - multiple H-bond acceptors
- Solubility in organic solvents revealed that methanol is the best solvent for GL-II -73 (higher polarity index compared to isopropanol).

GL-II-73 (4R)-8-Ethynyl-6-(2-fluorophenyl)-N,N,4-trimethyl-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxamide

MATERIALS AND METHODS



RESULTS



The values are shown as mean ± sd, n = 3

The values of physicochemical parameters: Z-ave, PDI, ZP, pH, conductivity, drug content, and encapsulation efficiency, measured both at baseline and after one month of storage, indicate suitability for parenteral administration. For the stabilization of the pH, further optimization is required.

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