

Development of Self-microemulsifying Lipid-based Formulations of Trans-resveratrol by Systematically Constructing Lipid-surfactant-water Phase Diagrams Using Long-chain Lipid †

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Abstract: Self-microemulsifying lipid-based formulations (SMLBF) are isotropic mixtures of oil, surfactant, and/or cosurfactant in which a drug is solubilized. In this work SMLBF of trans-resveratrol in cod liver oil (CLO), to increase its solubility, dissolution rate, and oral bioavailability was developed. Ternary phase diagrams of CLO with surfactant and water and of the same by mixing CLO with glycerol monooleate (GMO) were constructed to identify regions where microemulsions were formed. Kolliphor RH 40, Tween 80, and their 1:1 mixtures were evaluated. A 1:1 mixture of CLO and GMO was necessary to form the microemulsion, and Kolliphor RH 40 provided the maximum microemulsification effect. Several formulations containing 6:4, 1:1, and 4:6 w/w lipid/surfactant ratios using the 1:1 mixture of CLO and GMO as lipid components and Kolliphor RH 40 or its mixture with Tween 80 as surfactants were identified, and trans-resveratrol solubility was determined. Drug concentrations used in the formulations were 80% of saturation solubility, and no organic cosolvents were used to increase drug solubility or enable emulsification. *In vitro* dispersion testing in 250 mL of 0.01 N HCl (pH 2), according to the USP method 2 at 50 RPM, showed that the formulations dispersed rapidly in aqueous media, forming microemulsions with no drug precipitation.

Keywords: lipid-based formulations; microemulsion; SMEDDS; trans-resveratrol; cod liver oil; long chain lipid; glycerol monoglyceride; surfactant; phase diagram; solubility.

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Conflicts of Interest

The authors declare no conflict of interest.