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WPŁYW NOWEGO SOLUBILIZATORA ROFAM 70 NA ROZPUSZCZALNOŚĆ OCTANU MEGESTROLU

Rozprawa na stopień doktora nauk farmaceutycznych

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SUMMARY

The appropriate choice of solubilizer can improve the solubility of poorly soluble substances. Drugs with greater solubility provide more efficient treatment while avoiding the use of increased doses or frequent administration to patients, as higher concentrations in blood can be obtained in a shorter period of time, resulting in greater convenience for patients. Furthermore, the use of surface active agents to reduce the surface tension of particles allows greater dispersal of oil-soluble substances in water to create stable solutions, suspensions or emulsions what allows to use from the new products for a longer time.

The present study examines ethoxylated fatty acid methyl esters of rapeseed oil. These compounds were synthesized in The Institute of Heavy Organic Synthesis "ICSO Blachownia" in Kędzierzyn-Koźle. The aim of this study was to make studies and analyzes of new substances as a solubilizers on the solubility of megestrol acetate, a substance belonging to the II Biopharmaceutical Classification System (BCS), characterized by low solubility.

Firstly, a cytotoxicity assay was performed for compounds belonging to Rofam's group and commonly-used compounds including Tween 80, PEG 40 and Poloxamer 188. The results showed that at a concentration of 200 μM , neither Rofam 70 nor the other tested compounds had any significant effect on A549 cell viability.

For Rofam 70 – solubilizer showed cytotoxicity comparable to commonly uses surfactants which are general called Tween was carried out structural analysis using mass spectrometry, gel permeation chromatography (GPC) and high performance chromatography (HPLC). Rofam 70 was found to consist of two fractions: the first having the formula $\text{C}_{17}\text{H}_{33}\text{COO}(\text{CH}_2\text{CH}_2\text{O})_n\text{CH}_3$ where $n = 22 - 29$ (ethoxylated fatty methyl esters) representing 64% of total, and the second with the formula $\text{C}_{17}\text{H}_{33}\text{COO}(\text{CH}_2\text{CH}_2\text{O})_n\text{OCC}_{17}\text{H}_{33}$ where $n = 35 - 50$ (diesters of fatty acids and polyglycols) representing 36% of total.

To determinate the surface tension which allowed to the estimation of the critical micelle concentration (CMC), Rofam 70 was dissolved in 0.1 M HCl, and with phosphate buffer pH 6.8, and with addition of megestrol acetate (a substance belonging to the II biopharmaceutical classification system).

Following this, megestrol acetate was solubilized by the addition of Rofam 70, with the tested solubilizer in two different concentrations and at three different pH values. Two methods were used: the first with a centrifugation step and the second without. Commonly-used compounds (Tween 80, Pluronic F68) were used as reference surfactants. Rofam 70 gave more effective solubilization than Pluronic F68. Samples treated with Rofam 70 gave the best results when centrifugation was not used, and for samples with higher surfactant concentrations and pH 5.0.

The hydrophilic-lipophilic balance (HLB) was calculated for the Rofam 70 by the Griffin method, which is recommended for nonionic surfactants. The obtained value 15.6 indicates that the tested compound was hydrophilic and a solubilizer.

Our results indicate that Rofam 70 can be used as a surfactant. All tests and analyzes clearly indicate that it may potentially be used in both the pharmaceutical and cosmetics industries.