

POSTER PRESENTATIONS

A NEW DOSAGE FORM OF TEFESTROL BASED ON LOW-MOLECULAR-WEIGHT OLEYL-HYALURONAN

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The ability of low-molecular-weight oleyl-hyaluronan to form polymeric micelles was used to design a new dosage formulation of Tefestrol (TF). The Tefestrol substance was provided by the Institute of the Chemistry of Plant Substances named after Academician S.Yu. Yunusov and is a mixture of sesquiterpene alcohol esters, the main components of which are ferutinin and tenuiferidin. It is known that TF has a pronounced estrogenic effect. One of the challenges in developing a dosage formulation of TF is its poor solubility; therefore, it is necessary to select suitable solubilizing agents.

A conjugate of low-molecular-weight hyaluronan with oleic acid (oleyl-hyaluronan, 15 kDa, 9% degree of substitution) can form self-assembling structures (polymeric micelles) with a hydrophobic core and a hydrophilic shell. An ultrasonic homogenization method was used to load TF into the oleyl-hyaluronan micelles. Technological parameters required for the maximum possible loading of TF into this micellar system (1.23 mg/mL) were optimized. Transmission electron microscopy established that TF is loaded into the hydrophobic cores of the oleyl-hyaluronan micelles. It is shown that the combination of a micellar phase (15 kDa, 1 wt.%) with a gel of high-molecular-weight hyaluronan (800 kDa, 2.5 wt.%) makes it possible to develop a dosage form of TF for topical application. Such a gel is proposed for intravaginal use or for external application to the skin in the breast area. The cytotoxicity of the micellar form of TF was evaluated by MTT assay in the BJ-5ta human fibroblast cell line. It was found that the IC₅₀ values of the micellar form and TF itself are close (15 and 21 µM, respectively); therefore, loading TF into micelles does not increase the cytotoxicity of TF for this fibroblast cell line. The release profiles of TF in stimulated vaginal fluid established that TF is unstable in such conditions; however, encapsulation in oleyl-hyaluronan micellar structures stabilizes it and prolongs its release rate (68% of TF was released over 48 hours). Thus, the described approach can be used to develop TF dosage formulations with prolonged action.

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