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Yours sincerely,

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CENTRIFUGAL FORMATION OF FIBERS OF SOLID DISPERSED SYSTEM OF POLYMER WITH HESPERIDINE

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Hesperidin is a biologically active substance, a plant polyphenol that belongs to the class of flavonoids. Bioflavonoids have anti-inflammatory, antioxidant, immunomodulatory, antithrombotic, antiallergic, vasodilating effects [1]. The problem with their use is poor solubility in water, which means low bioavailability. That is why it is important to increase the solubility of hesperidin to expand the possibilities of application.

Method: to increase the solubility used centrifugal formation of a solid dispersed system (SDS) from a polymer melt (method of formation of "cotton candy"). To do this, we used a machine for making cotton candy "Cotton candy maker". The essence of the method is to melt the powder mass in the disk, which rotates with the subsequent force of the melt due to centrifugal force in the holes on this disk and solidification of the mass in the air in the form of thin fibers. As a pharmaceutically acceptable polymer used polyvinylpyrrolidone K-17 (PVP K-17), which is slower to form cotton wool, which allows the formation of an alloy with hesperidin.

To determine the coefficient of solubility increase, a method for studying the concentration of hesperidin in solution was developed. Usually, hesperidin in solution is determined by spectrophotometric method, because flavonoids have an absorption peak in the yellow region of the spectrum (284 nm). But during remelting, sugar and polyvinylpyrrolidone turn yellow, which interferes with the determination of hesperidin. That is why a method for determining the concentration of hesperidin in solution was developed and validated, the essence of which is the interaction of phenolic groups of hesperidin with ferric chloride (III) with the formation of a dark green compound with an absorption peak at 602 nm.

To check the solubility of the formed SDS in the form of cotton wool, it was weighed and dissolved in 1 ml of purified water. Then stirred for 30 minutes at 25 °C on a thermoshaker and centrifuged for 20 minutes. The supernatant formed was separated and 1 ml of 0.3 N ferric chloride solution (III) was added, left for 20 min and checked spectrophotometrically with 0.3 N ferric chloride (III) solution taken as reference.

Several samples were made with different ratios of polyvinylpyrrolidone to hesperidin 99:1, 95:5 and 90:10. According to the results of the solubility test, it was found that at a mass ratio of hesperidin to polyvinylpyrrolidone 90: 10, the coefficient of increase of the solubility of flavonoids increased 157 times. As the content of hesperidin in the SDS decreases, the coefficient of increase of solubility increases from 157 to 188 times. Also, with increasing content of hesperidin slightly decreases the final yield: at the lowest amount of hesperidin the yield is ~ 30%, about increased content of hesperidin to 5% yield is 27.5%, at 10% hesperidin - 26%.

To increase the yield, sugar was added, which in a mixture with polyvinylpyrrolidone allows to increase the final yield of cotton wool [2]. Samples were made in the ratios of hesperidin: sugar: polyvinylpyrrolidone 10:05:85, 10:10:80, 10:20:70, 10:30:60, 10:40:50, 10:50:40. When the amount of sucrose increases to 20%, the yield of the product increases, it is possible to increase the yield of cotton wool from 26% to 40%. However, when the sucrose content is more than 10%, the coefficient of increasing of solubility of hesperidin decreases by approximately 15%. The optimal content of components for the preparation of polymeric SDS by the method of "cotton candy" is the ratio of PVP K-17 and sucrose 80:10.

Infrared spectroscopic study of the components of SDS and complexes of polyvinylpyrrolidone K-17 and hesperidin suggests the formation of complexes mainly due to hydrogen bonds. The complexes formed are characterized by an increase in the number of hydrogen bonds by more than a third.

Therefore, a method for obtaining SDS by "cotton candy" technology has been developed, the essence of which is to alloy hesperidin with a polymer with subsequent centrifugal formation of "cotton candy" fibers. A method for detecting hesperidin based on the reaction with ferric chloride (III) was developed for the analysis of cotton wool. When testing the solubility of cotton wool, it was proved that this method increases the coefficient of solubility of hesperidin in 188 times. Also, there was a study of the effect on the solubility of the addition to the mixture of polymer and hesperidin sugar, which was able to increase the final yield to 40%.

[1] Effects of flavonoids on the release of reactive oxygen species by stimulated human neutrophils. Biochem Pharmacol. 1993. № 46. P. 1257– 1271.
[2] Nasir, Sidra, et al. “Improved Bioavailability of Oxcarbazepine, a BCS Class II Drug by Centrifugal Melt Spinning: In-Vitro and in-Vivo Implications.” International Journal of Pharmaceutics, vol. 604, 2021, p. 120775., https://doi.org/10.1016/j.ijpharm.2021.120775.