Approach to the determining release of low-soluble substances in water

Nataliia Khanina*, Victoria Georgiyants , Vadim Khanin

National Pharmaceutical University, Kharkiv, Ukraine
**Corresponding author e-mail: lucky820.ua@gmail.com*

Introduction. Solubility plays an essential role in drugs activity, especially for those which are primarily intended for oral using. As many new active pharmaceutical ingredients are poorly soluble in water, there is a need for a new approach to assessing the dissolution of low- soluble substances. In order to overcome the problems associated with bioequivalence studies and clinical trials for generic drugs. This is a particularly urgent problem for most domestic manufacturers, because the study of bioequivalence «in vitro» for low-soluble substances is impossible according to Guidelines for clinical trials [1], and «in vivo» research is not always feasible as it requires large financial investments and other material factors.
Materials and methods. The studies were performed using high performance liquid chromatography Agilent 1290 using a three-quadrupole time fly mass analyzer.
Results and discussion. The object of the study is quercetin substance - a substance that belongs to the II-IV class of Biopharmaceutics Classification System, because has very low solubility and moderate permeability [1]. The experiment was divided into three stages. In the first, the true value of the solubility limit was established, for which such parameters as the degree of size reduction of substance, the amount of moisture and the degree of purity were necessarily recorded. The second part of the experiment is devoted to determining the time of complete dissolution of the sample of the active substance. In the third stage was studied, the release of the substance «in vitro» according to the requirements of the Guidelines for clinical trials [1]. Dissolution was performed for the time period that was established during previous stage of the experiment. This ensured that factors such as diffusion and wetting were not affected on quercetin concentrations that were determined. Because of low level measured concentrations which are make up ppb, it was necessary to develop a method for determining such low concentrations in solutions for various substances. Using of a mass spectrometric detector made it possible not only to identify the substance by the mass of the molecular ion, but also to quantify the substance. Using of a mass detector significantly increased the selectivity of the developed analytical technique.
Conclusions. In current time there is an economically justified need for «in vitro» studies for insoluble substances, the developed approach of study the bioequivalence of substances of this class allows to obtain objective data about kinetics of its drugs release, without further «in vivo» studies. Thus, using of the developed approach of study of bioequivalence of low-soluble substances allows to assess the similarity of the original drug and generic drug before clinical trials and to guarantee the same degree of release during clinical trials.

References

1. Настанова з клінічних досліджень. Лікарські засоби. Дослідження біоеквівалентності (Настанова 42–7.2:2018). – К. : Міністерство охорони здоров'я України, 2018.
2. Державна Фармакопея України: в 3 т. / Державне підприємство «Український науковий фармакопейний центр якості лікарських засобів». 2-е вид. – Харків:2015. Т. 1. 1128 с.