INVESTIGATION OF THERMAL STABILITY OF 4-METHYLPHENYL-O-B-D-GLUCOPYRANOSIDE BY TG-DTSCDTA-MS

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ИССЛЕДОВНАИЕ ТЕРМИЧЕСКОЙ СТАБИЛЬНОСТИ 4-МЕТИЛФЕНИЛ-О-В-Д-ГЛЮКОПИРАНОЗИД, МЕТОДОМ ТГ-ДСК-ДТА-МС

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Аннотация. *Были получены данные о термической стабильности 4-метилфенил-О-β-Д-глюкопиранозид. Данная субстанция обладает диуретическим эффектом сравнимым с современными диуретиками. Исследование термической стабильности проводили методом ТГ-ДСК-МС в инертной атмосфере аргона, в интервале температур 25–600 С°. Из полученных дериватограмм можно сделать вывод, что термическая стабильность субстанции соизмерима с термической стабильностью современных диуретиков. Был предположен механизм термического разложения субстанции и выявлены химические маркеры данного процесса.*

Introduction. Nowadays diuretics take important place in clinical practice for various diseases treatment. Diuretics is a group of pharmaceutical products used for excretion of water and salts from an organism[1]. Diuretics are ordered not only for chronic disease treatment, but also in emergency conditions for a patient. In addition, most of diuretics enter into the composition of complex medication for comorbidities treatment [2]. However, all diuretics have many side effects including a fatal outcome [3].

Russian scientists took out a patent 4-methylphenyl-O-β-D-glucopyranoside, which possesses diuretic activity and does not increase daily excretion of natrium and potassium ions. This compound differs significantly from modern diuretics. It is worth noting that the thermochemical properties of the compound have not been studied, and the thermal stability is the most important parameter when developing the technology for producing solid dosage forms. Thus, the aim of our research is to investigate the thermal stability of the 4-methylphenyl-O-β-D-glucopyranoside substance (Fig.1).

Materials and methods. Glycoside has been obtained from the corresponding tetraacetate. Deacetylation was perfomed by the Zempman method using sodium methoxide in methanol [4]. Acetate glycoside was obtained by fusion of α-glucose petaacetate with the corresponding aluminum phenolates.

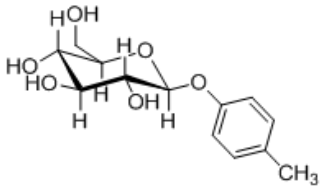

Fig. 1. Constitutional formula of 4-methylphenyl-O-β-D-glucopyranoside

Investigation of thermal stability was conducted using TG-DSC-MS on SDT Q600 V20.9 Build 20 synchronous analyzer. The analysis was performed in the temperature range of 25–600 C° under an inert argon atmosphere (100 ml / min). The heating rate was 5°C / min. Sample weight for TG-DSC-MS was 15,76 mg.

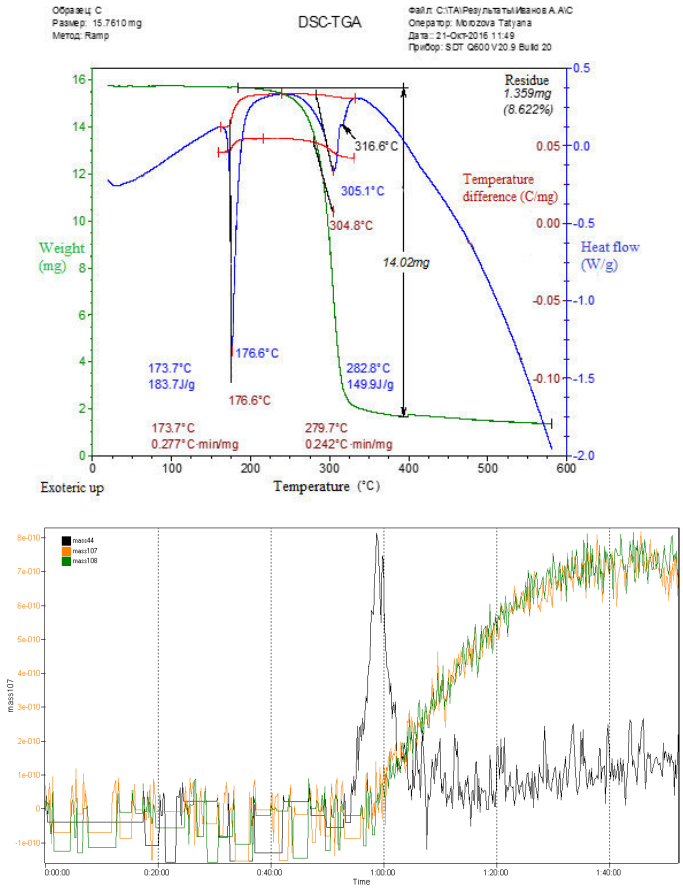

Fig. 2. TG-DSC and MID result of 4-methylphenyl-O-β-D-glucopyranoside

Experimental part. TG-DSC method provides defining the change in the sample mass and registers the effects of thermal processes at the same time. Also the tandem system of thermogravimetric equipment with mass detector allows us to determine simultaneously molecular ions of gaseous products. This allows us not only to determine the qualitative composition of the gaseous products, but also to know the temperate of the thermal decomposition of the substance.

It is shown in the thermograms that the decomposition process goes in one stage. It is obvious from the compound thermogram (Fig.2) that in the temperature range of 25–100°C the variability of mass indicating the

absence of crystal water is observed. The decomposition process starts immediately after melting the sample at 177°C (T_{melt}=178°C [5]). The decomposition process goes in one stage in the temperature range of 230–330°C. It should be said that the process is registered in the gaseous phase p-cresol (M_r=108 g/mol) and acetic aldehyde (M_r=44 g/mol). This fact indicates the simultaneous decomposition of the glycoside to the corresponding p-cresol and levoglucosan. Simultaneously p-cresol exhale with decomposition of the glycoside (T_r=201°C[6]) and levoglucosan at this temperature rapidly decomposes to form acetaldehyde (M_r=44 g/mol). Because of this fact the glycoside has rather high decomposition temperature of all of these processes are very intensely and simultaneously, does not allow dividing them into graphs.

Conclusion.

- The thermal stability of the compounds was studied by thermogravimetric analysis and differential scanning calorimetry, equipped with a mass detector (DSC-TG-MS). From the obtained date we can draw a conclusion, that the substance is heat-proof to a temperature of 177°C. Compound decomposition temperature is quite comparable to the decomposition temperature of modern diuretics: furosemide (T_{dec} = 200 ° C), amiloride (T_{dec} = 135 ° C) and spiranolacton (T_{dec} = 200 ° C [7]) indicating a sufficient stability of the studied substances to pharmaceutical products.
- Summarizing data will help develop an optimal process scheme for producing pharmaceutical shape. Also dates allow the development of methods for quality control and authenticity of the substance of TG method [8]. Assumptions mechanism of thermal decomposition can help ascertain chemicals markers, which allows developing the analytical approaches for quality control of substance during storage.

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