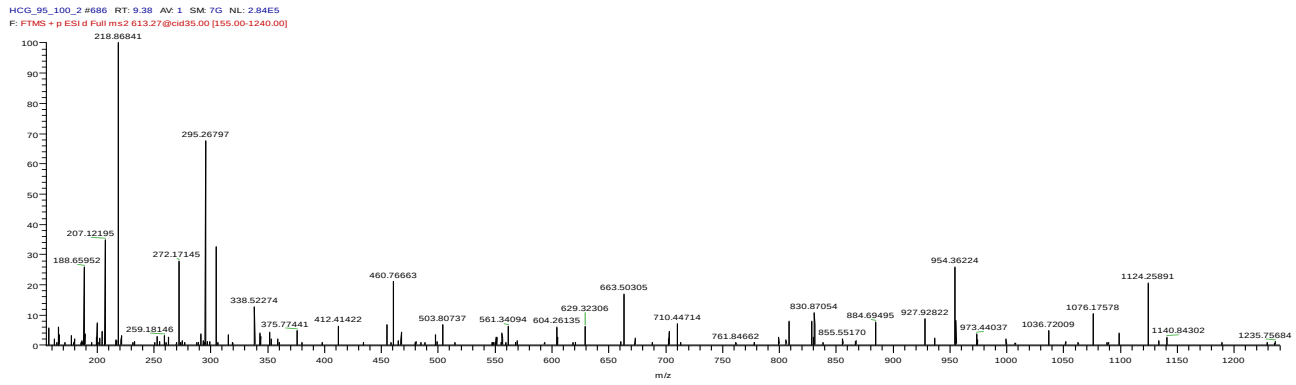

Fig.1. – Mass spectrum of fragment ions of hCG beta-subunit peptide DHPLTCDDPR, m/z 613.2626, protonation degree +2

Based on the data obtained, method for quantifying human chorionic gonadotropin using «bottom-up» proteomics based liquid chromatography – tandem mass-spectrometry in human urine for doping-control was developed.

THE FEATURES OF AP_4A IMPACT ON ADP-INDUCED PLATELET AGGREGATION IN PREGNANT WOMEN WITH PRE-ECLAMPSIA

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Pregnant women with pre-eclampsia have a significant increase in the degree of platelet aggregation in response to ADP, in comparison with a physiologically occurring pregnancy. In vitro experiments revealed that Ap4A inhibits ADP-induced platelet aggregation of pregnant women with pre-eclampsia.

Keywords: pre-eclampsia, platelets, ADP, Ap4A, aggregation.

Violations of the functional activity of platelets associated with their adhesion and aggregation lead to increase bleeding or increased thrombosis and development of circulatory pathology.

The addition of ADP to platelet-rich blood plasma in vitro leads to a change in the shape of the blood platelets and primary aggregation. By acting on P2-purinoreceptors, ADP activates phospholipase C, which leads to the formation of IP3, calcium mobilization from intracellular stores; inhibits adenylate cyclase, thereby reducing the level of intracellular cAMP, causing granule secretion and platelet aggregation. After primary aggregation, ADP activates phospholipase A2 and releases arachidonic acid from membrane phospholipids, which is converted to TxA2. TxA2 converts reversible aggregation into irreversible, also called the second wave of aggregation.

The experiment revealed that platelets of women with physiological pregnancy (n = 32) and pregnant women with pre-eclampsia (n = 32) reacted without showing any special differences in the responses to ADP in concentrations of $2{,}44\times10^{-5}$M and $2{,}44\times10^{-6}$M. With a further decrease of ADP concentration to $2{,}44\times10^{-7}$M, platelet aggregation was manifested exclusively in pregnant women with pre-eclampsia. Thus, the degree and rate of aggregation during physiological pregnancy was in the range of 0,8±0,69 % and 1,2 [0,35–2,2]%/min; whereas in case of pre-eclampsia – 5,46±1,72 % and 6,35 [3,7–10,7] %/min, respectively ($P < 0{,}05$). A slight increase in the concentration of ADP to $7{,}32\times10^{-7}$M cause platelet aggregation, both in women with physiological pregnancy and in pregnant women with pre-eclampsia. Satistical differences in the degree and rate of aggregation between norm and pathology (13,02±4,62 % and 13,65 [9,7–18,6] %/min; and 20,09±4,10 % and 21,4 [15,4–26,6]%/min, respectively; $P < 0{,}05$), made it possible to conduct further studies using antiplatelet agents on this model. There may be several reasons for increased platelet aggregation during pre-eclampsia: a decrease in the sensitivity of platelets to ADP and increased secretion of Ca^{2+} ions, ATP, and ADP from intracellular stores [1]; decreased intercellular levels of cAMP and cGMP.

Diadenosine-5',5'''-P1,P4-tetraphosphate (Ap4A) is a content of platelet dense granules [2], which is a molecule that is included in the processes of recovery, correction and protection of the body, both on the cellular and organism level. Inside the cell, Ap4A acts as a secondary messenger, initiates DNA repair, participates in the

mechanisms of apoptosis and platelet aggregation / disaggregation by acting on P2Y1 and P2Y12 purinoreceptors, and acts as an alarmone in the cellular response to stress. Extracellular Ap4A acts through purinoreceptors and, possibly, through their own specific receptor structures.

The experiment revealed that the disaggregation properties of Ap4A are dose-dependent. At concentration of $2{,}44\times10^{-7}$M, Ap4A demonstrate a slight inhibition of the degree and rate of ADP-induced platelet aggregation to equal values in both groups (the degree and rate of aggregation during physiological pregnancy was 7,84±3,21% and 9,1 [6,1–12,6]%/min; during pre-eclampsia – 8,17±3,26 % and 8,8 [5,2–12,6]%/min, respectively). Adding Ap4A (7.32×10^{-7}M) significantly reduced the functional activity of platelets caused by ADP in women with physiological pregnancy, as well as in pregnant women with preeclampsia. Moreover, the degree and rate of aggregation were: during physiological pregnancy – 1,10 ±0,64 % and 1,4 [0,85–2,9] %/min; during pre-eclampsia – 0,76±0,50 % and 0,95 [0,55—1,25]%/min, respectively. The greatest inhibitory effect of diadenosine-5',5'"-P1,P4-tetraphosphate in ADP-induced platelet aggregation was achieved at a concentration of 2,44×10-6M (the degree and rate of aggregation during physiological pregnancy was 0,24±0,21 % and 0,35 [0,2–1,2]%/min; with preeclampsia – 0,33±0,26 % and 0,6 [0,4–0,95]%/min, respectively). The experimental data allow us to conclude that Ap4A can be used to correct increased platelet aggregation ability of pregnant women with pre-eclampsia.

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SYNTHETIC ANALOGS OF NATURAL PHENOLIC ANTIOXIDANTS AND ANTIMUTAGENS FROM RASPBERRY AND GINGER

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The object of the study is unsaturated ketones obtained by aldol-croton condensation of aromatic alde-hydes with acetone and pinacoline. The aim of the work is to develop a preparative method for obtaining raspberry ketone, ginger ketone and their structural analogues from unsaturated synthetic precursors.

Keywords: the raspberry ketone , zingerone, phenols, hydrogenation.

The problem of oncology diseases origin caused by various of factors, and particularly by radioactive chemical pollution is of vital importance. In view of this, the embrace of bio-effecting agents and examining their influ-ence on organism is growing. Two carbonyl compounds were considered and the synthesis technique was improved.

Raspberry ketone and zingerone are well-known natural substances isolated from raspberry and ginger which became the objects of both laboratory studies and commercial production. Investigations of the biological activity of these phenolic compounds, in particular antioxidant and anti-inflammatory actions, cancer prevention, influence on the mutagenesis and metabolism are still ongoing [1–2]. Zingerone can potentially be used for the se-lective protection of the normal tissues in the course of the radiotherapy of tumor diseases. Also zingerone and re-lated compound dehydrozingerone found to inhibit growth of the colon cancer cells [3–4].

Now we report an efficient synthetic way for the preparation of zingerone, raspberry ketone and different structural analogs of these natural compounds based on the aldol condensation. Simple procedure for the selective hydrogenation of the double bonds was developed [5].

Readily available products of the aldol condensation of 4-hydroxybenzaldehyde or vanillin with acetone were hydrogenated in the presence of cheap nickel boride to give raspberry and zinger ketones, respectively, in good yield. The advantage of the reported procedures is that a two-step sequence (preparation of catalyst and hydro-genation) can be carried out in a one pot reaction and in a short time.