Після введення карбацетаму вміст ТБКАП знижувався на 28,2 %. Водночас спостерігали зменшення вміст ОМБ. Зокрема, вміст кетодинітрофенілгідразонів нейтрального характеру, знижувався на 16,9 % та альдегідодинітрофенілгідразони основного на – 15,4 %.

Отже, на основі отриманих результатів дослідження, можна припустити, що модуляція ГАМК-рецепторів сприяла зниженню процесів пероксидного окиснення ліпідів та білків нейронів гіпокампа щурів із метаболічним синдромом.

Висновок. Отримані результати свідчать про корегувальний вплив карбацетаму через модуляцію ГАМК-рецепторів нейронів гіпокампа на маркери оксидативного стресу у щурів із метаболічним синдромом.

COMBINED USE OF THE SUBSTANCES OF HERBAL ORIGIN WITH XANTHINE OXIDASE INHIBITORS: EXAMPLE OF *AEGOPODIUM PODAGRARIA* L.

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Introduction. Xanthine oxidase (XOD) is not only a significant target for antigout interventions, but a pathogenetically important enzyme for overcoming of cardiovascular and renal diseases, limiting of oxidative stress, normalization of the CNS function [1, 2]. Search of the new biologically active substances is being actively conducted among plant sources. High massive of evidence has been collected about XOD inhibitors of plant origin as well as herbal substances able to influence renal excretion of uric acid [3, 4]. Less data are available about possibilities of such inhibitors combinations with currently used XOD inhibitors, namely allopurinol and febuxostat. These aspects are important because of the possibility of the reducing of the dose of the latter thus increasing their safety or broadening pharmacodynamics with additional favourable effects.

Goutweed (*Aegopodium podagraria* L., GW) is wide-spread in temperate climates including northern and western Ukraine and as evidenced by Latin, English and Polish names of the plant, has been used in traditional medicine for gout treatment since time immemorial. Our previous studies have confirmed favourable influence of GW aerial part tincture and extract on uric acid metabolism realized through xanthine oxidase (XOD) inhibition, enhancement of the renal uric acid excretion or combination of both mechanisms [5, 6]. Further studies were directed towards verifi-

cation of the results of combined administration of GW preparations with commonly used drugs [7].

The aim of the study. This study aimed to provide a summary of the own results concerning herbal drugs combinations with XOD inhibitor and explore new research areas based on the data found in the literature.

Results. A number of important data on the possibilities of GW combined use with allopurinol (ALL) as the widely used and commonly available hypouricemic drug were obtained [7]. Namely, the effects of such combinations were as follows:

– combination of GW tincture (1 ml/kg) or GW extract (1 g/kg) with a subtherapeutic dose of ALL of 2.5 mg/kg enabled statistically significant XOD inhibition under conditions of potassium oxonate induced hyperuricemia in mice (after single administration);

– complete inhibition of XOD by ALL (10 mg/kg) was maintained when it was combined with the tincture (1 ml/kg) or the extract (1 g/kg) during the prolonged (3-weeks) hyperuricemia induced by potassium oxonate in mice;

– absence of the increase in toxicity of ALL at a high dose (50 mg/kg) combined with the tincture (1 ml/kg) and moderate nephroprotective effects of the latter (decrease in proteinuria, maintenance of sodium reabsorption as well as normokalemia, urea clearance normalization) in rats against the background of an excess of purine derivatives and proteins;

– decrease in the acute toxicity of ALL in mice against the background of the extract and the tincture.

The studied GW preparations main components are hydroxycinnamic acids and flavonoids. In the literature available, there are reports about in vivo studies of herbal extracts and ALL combinations efficacy, still these herbal preparations are of different chemical composition [8, 9]. And as for the mechanism of XOD inhibition by plant polyphenols, it has been studied for the numerous compounds and it is important that both competitive and non-competitive inhibitors were revealed [3, 4]. There are also robust data about chlorogenic acid as XOD inhibitor [10] as well as data about the benefits of coffee as a source of hydroxycinnamic acids for gout prevention [11].

Proceeding from the beforementioned data, the next logical step is the assessment of the possible mechanisms of interaction of these polyphenols and ALL (or other XOD inhibitors) which could be realized at the level of XOD active site or allosteric sites. Besides, there is a lack of data of the changes of prooxidant-antioxidant status under the influence of such combinations, given the role of XOD in generation of free radicals.

Thus, it could be expedient to take the following steps in the research of XOD inhibitors combinations: *in silico* modeling of the interaction with the enzyme; *in vivo* assessment of enzyme activity with individual substances combinations as well as their influence on the prooxidant-antioxidant processes, especially the superoxide generation under the influence of XOD; *in vitro* verification of the most promising combinations activity and safety.

Other aspect that may seem to be unexpected, still possessing sufficient evidence base, is the positive influence of XOD inhibitors on the CNS function [12, 15]. This influence is possibly realized through the mechanism other than hypouricemic action (since uric acid is neuroprotective itself at the certain range of concentrations) and can include (being not limited to) the reducing of the prooxidant role of XOD mentioned above especially that localized within the cerebral vascular bed. In this context, flavonoids are discussed as promising XOD inhibitors with the possible benefits for mental disorders treatment [13]. For chlorogenic acid there are data both on the normalizing influence on uric acid metabolism (also mentioned above) and experimentally established ability to decrease anxiogenic and depressive processes in the laboratory animals [14].

Thus, it is of great interest, how these effects of chlorogenic acid (or those of flavonoids) will be modulated in their combined use with ALL or other XOD inhibitors. Interactions results could proceed from changes of uricemia, from the limiting of oxidative stress during XOD functioning and from the changes of specific mechanisms of these herbal compounds mentioned above.

Partially we addressed these issues in studies of GW combinations with ALL [7]. Importantly, on the model of hyperuricemia, when uric acid level was normalized by ALL combined with GW extract or the tincture, no negative changes of the CNS functional state were registered. Moreover, when combined with ALL, GW preparations counteracted the increase in depressive signs, the tincture also reduced anxiety signs.

Conclusions. The data presented elucidate the prospects of the combined use of the substances of herbal origin with xanthine oxidase inhibitors.

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THE TOPICAL ISSUES ASPECTS OF CHARACTERISTICS OF ENDOVASCULAR SURGERY AND PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT CHALLENGES FOR GASTROINTESTINAL AND DUODENAL ULCER BLEEDING WITH BRIEF CASE REPORT

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Abstract. Acute gastrointestinal bleeding is a common medical emergency that ranges from minor to potentially life-threatening bleeding. Endoscopy is the first-line diagnostic procedure for upper and lower gastrointestinal bleeding. Treatment options for acute GI bleeding include conservative management, therapeutic endoscopy, transcatheter embolization, and surgery. Transcatheter embolization and surgery are both options for recurrent GI bleeding when therapeutic endoscopy fails; However, both options are associated with several complications and risk of bleeding. The choice of management depends on the patient's status. Emergency surgery is usually associated with high rates of morbidity and mortality. Recently, superelective