

### МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я ЗАПОРІЗЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

## **МАТЕРІАЛИ**

# ВСЕУКРАЇНСЬКОЇ НАУКОВО-ПРАКТИЧНОЇ КОНФЕРЕНЦІЇ З МІЖНАРОДНОЮ УЧАСТЮ

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As we conduct the introduction of medicinal plants, a special place is given to the most important features of the chemical composition in view of its possible variability at the new conditions of existence. The countries population with a high standard of living today consumes from 23 mg to 1-2 g of flavonoids daily with food.

Flavonoid preparations are powerful antioxidants, immunomodulators, and anti-inflammatory pharmacologically active compounds. They have attracted the attention of phytochemical researchers due to their wide range of pharmacodynamics and lowly toxicity. Dietary plants containing flavonoids are reported to be functional foods that provide a wide range of protection against different organ-induced oxidative damage and protects from various lethal disorders by increasing antioxidants and suppressing inflammation and apoptosis in various tissues including the brain, liver, kidney and the heart. It vides prescribe as a potential inhibitor of COVID 19 and other viruses.

Medicago sativa L., Fabaceae is known as perennial herbaceous leguminous plant species that originated in southwestern Asia and is used as a folk medicine for the treatment of various ailments. The upper ground part of Lucerne contains phenolic compound such as flavonoids etc. contributes to its biological activities. We are determined widely known flavonoids in extracts 20 alfalfa varieties herb at the Ukrainian steppe growing. We selected 50 seeds of the same size from twenty alfalfa cultivars from different countries, were cultivated under controlled areas of the southern part of the Ukrainian left-bank at the border of forest-steppe and steppe zones (Zaporizhzhya, Ukraine) from April to June, with 15 °C/07 °C (day/night), 14 h/10 h (light/dark) and 60–65% relative humidity. The content of flavonoids was found unequable in ethanol extracts. The chemical compositions and their content were assessed by ultrahigh-performance liquid chromatography. The content of flavonoids was different in the 20 alfalfa varieties raw materials. Umbelliferone was found high in ethanol extract of Mongolian colorful hybrid (Mongolia, 0.23 mg/g). Four sorts have not contained umbelliferone: Kisvardai (Hungary), Nizona (Cuba), Tanhuato (Mexico), and Mesopotamian (Iraq). The leader from cinaroside content was sort Commercial 2-52-75 of UK origin. Routine has been found in the highest quantities in WL 50 from the USA. Ferganska 700 from Uzbekistan was the leader in luteolin content and Kisvardai, Hungary was the leader in an average of kaempferol content (0.030 mg/g). Have been followed by hierarchical clustering analysis the link from sorts origin and similarities in their flavonoids composition in Ukrainian growing. We performed a tree structure containing a k-block set partition for each value of k between 1 and n, where n is the number of data points to cluster. Note have been connectioned the sorts origin only to the five flavonoids composition in clusterig analysis.

## SYNTHESIS AND PROPERTIES OF S-ALKYL 5-R-4-PHENYL-1,2,4-TRIAZOLE-3-THIOL DERIVATIVES

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Azaheterocyclic compounds are of considerable interest to scientists as a source of creation of various biologically active substances. Compounds that combine pyrazole, 1,2,4-triazole and indole fragments in their structure attract considerable attention in this aspect. The mentioned heterocyclic systems belong to the group of compounds, the use of which is associated with significant successes in the field of creating new medicines.

The aim of the work was to optimize the synthesis conditions and study the properties of S-alkyl derivatives of 5-R-4-phenyl-1,2,4-triazole-3-thiol, which contain 5-methylpyrazole and (indol-3-yl)propyl fragments in their structure.

Methods and results. Diethyl oxalate, acetone, sodium methylate and 4-(indol-3-yl)butanoic acid were used as key starting reagents. The target intermediate with a pyrazole fragment was

obtained through the stage of formation of ethyl 5-methylpyrazole-3-carboxylate and 5-methylpyrazole carbohydrazide. The synthesis of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazole-3-thiol was previously accompanied by the interaction of the potassium salt of indole-3-butanoic acid with bromoethane, which made it possible to obtain the corresponding ester. The next stages of chemical transformation included reactions of hydrazinolysis, addition of phenylisothiocyanate and alkaline cyclization. Subsequently, S-alkylation reactions were implemented. Ethanol turned out to be the optimal medium for their implementation. The reaction was carried out with the participation of potassium hydroxide.

The structure of the obtained compounds was confirmed by the data of elemental analysis, <sup>1</sup>H NMR spectroscopy and IR spectrophotometry. The individuality of substances is established using high-performance liquid chromatography with electrospray ionization mass spectrometry.

**The results.** Synthesized S-alkyl derivatives of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazol-3-thiol and 4-phenyl-5-(pyrrol-2-yl)-1,2,4-triazole-3-thiol, their structure was proven and their physical properties were investigated.

The biological potential of the synthesized compounds was previously determined using docking studies. A possible effect on anaplastic lymphoma kinase was obtained using the 2XP2 model, lanosterol  $14\alpha$ -demethylase using the 3LD6 model and cyclooxygenase-2 using the 4Z0L model, which were obtained from the Protein Data Bank.

**Conclusions.** Conducted *in silico* studies on a number of S-alkyl derivatives of 5-(3-(indol-3-yl)propyl)-4-phenyl-1,2,4-triazole-3-thiol and 4-phenyl-5-(pyrrole-2-yl)-1,2,4-triazole-3-thiol demonstrated the possibility of creating biologically active compounds that can affect the activity of anaplastic lymphoma kinase, lanosterol  $14\alpha$ -demethylase and cyclooxygenase-2.

#### CREATION OF PROMISING DIURETICS BASED ON THE XANTHINE CORE

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An important problem of modern pharmacology, nephrology and pharmacy is the search for new pharmacological agents for the correction of homeostasis and vital functions of the body.

A change in the water-electrolyte composition of intracellular and extracellular fluids can cause various pathological conditions. Violation of renal excretion of electrolytes plays a significant role in the development of hypertensive conditions.

Renal transport of electrolytes and water is a complex multicomponent process that is implemented at various levels and is under the control of numerous regulatory factors: nervous, hormonal, humoral, physicochemical, etc. Diuretic drugs can affect the leveling of the water-electrolyte balance in the body.

Despite the high therapeutic effectiveness of diuretic drugs: hydrochlorothiazide, furosemide, clopamide, ethacrynic acid, etc. can cause unwanted side effects: hypokalemia, dizziness, headache, metabolic acidosis, hyperlipidemia, hyperglycemia, and others, which limit their practical use.

For the treatment of hypertensive conditions, combined pharmacotherapy is used, which includes the diuretic hydrochlorothiazide and the hypotensive drug losartan, valsartan, irbesartan, which affects the cardiovascular system and kidney function.

Thus, the search for new compounds that have diuretic activity is a relevant and promising direction in the development of original domestic drugs.

The purpose of this work is the synthesis of undescribed in the literature 8-aminosubstituted of 7-(2-hydroxy-3-p-methoxyphenoxy-)propyl-3-methylxanthine and to study their physical, chemical and biological properties.