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Усі матеріали збірника подаються в авторській редакції. Відповідальність за представлені результати досліджень несуть автори тез.

SEARCH FOR COMPOUNDS WITH DIURETIC ACTIVITY AMONG 7-(NAPHTHYL-1-METHYL) XANTHINE DERIVATIVES

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Introduction. An important problem of clinical nephrology is the medicinal correction of disturbances in the regulation of the stability of the osmotic concentration of physiologically active substances in the blood plasma. Regulation of the speed of these processes by reflex mechanisms ensures that the kidneys perform their renal function. An increase in the level of sodium in the blood and intercellular space leads to an increase in osmotic pressure, retention of water in the interstitial space and the formation of edema. Symptoms of a human disease reflect a violation of certain kidney functions as a result of pathological processes in the kidneys, which are manifested in hypertension, chronic heart failure, nephrotic syndrome, chronic renal failure, obesity, diabetes insipidus. In the treatment of arterial hypertension combined pharmacotherapy is used: β-blockers, angiotensin II blockers (valsartan, irbesartan) and thiazide diuretics (hydrochlorothiazide), which contribute to reducing the reabsorption of sodium ions in the proximal tubules of the kidneys, the excretion of sodium ions, magnesium sodium, calcium and uric acid.

In the treatment of violations of the water-electrolyte balance, pharmacological correction of the excretory function of the kidneys is carried out with the help of diuretic drugs. Along with the pronounced diuretic effect, diuretics have undesirable side effects: hypokalemia, hypochloremic alkalosis, metabolic acidosis, hyperlipidemia, hyperglycemia, azotemia, protein metabolism disorders, etc., which limit their use in clinical practice. The search for biologically active substances that improve the excretory function of the kidneys is conducted among various groups of organic compounds. Our attention was drawn to xanthine derivatives, which play an important role in correcting the activity of the human body.

In this regard, an important task is the creation of new effective drugs to improve kidney function and increase urination in pathological conditions. The search for new diuretics for pharmacological correction of kidney function is an important problem of modern pharmacology.

The purpose of this work is to develop simple laboratory methods for the synthesis of undescribed in the literature 7-(naphthyl-1-methyl)xanthine derivatives and to study their physical, chemical and biological properties.

Materials and methods of research. The temperature of melting was determined by the open capillary method on the PTP-M device. Elemental analysis was performed on the Elementar Vario L cube device, the PMR spectra were taken on the Bruker SF-200 spectrometer (operating frequency 200 MHz, DMSO solvent, TMS internal standard).

Molecular descriptors were calculated using the ALOGPS and DRAGON computer programs. Biological properties of synthesized compounds were calculated using the GUSAR and ACD/Percepta Platform.

Acute toxicity of synthesized compounds was studied by the Kerber method in experiments on white mice. The study of the diuretic action of the compounds obtained was carried out according to Berkhin's method. As a benchmark, hydrochlorothiazide was used in a dose of 25 mg/kg.

Results. The reaction of 8-bromotheophylline with 1-chloromethylnaphthalene in a DMF environment produced 8-bromo-7-(naphthyl-1-methyl)theophylline, the interaction of which with primary volatile amines in a steel autoclave in a methanol environment at 150 °C leads to the formation of the corresponding 8-amino-7-(naphthyl-1-methyl)theophyllines. Amino derivatives are also obtained by boiling 8-bromo-7-(naphthyl-1-methyl)theophylline with secondary heterocyclic amines in ethoxyethanol.

The structure of the compounds obtained is confirmed by the data of elemental analysis and PMR-spectroscopy. According in silico tests all the compounds obtained meet the

requirements of the «rules of five», which shows the expediency of further researches. We also calculated the acute toxicity rate for rats and mice with GUSAR and ACD/Percepta Platform computer software. According to this indicator, the synthesized substances belong to grade IV toxicity. The study of acute toxicity in vivo showed that the synthesized compounds belong to grade IV toxicity, which is consistent with the calculated data.

Research of the diuretic activity of synthesized 7-(naphthyl-1-methyl)xanthine derivatives showed that, according to the diuretic activity indexes, there were identified compounds that are not inferior to, and in some cases, are more active (175,5-268,5 %) than the comparison standard (176,2 %).

Conclusions. 8-Amino-7-(naphthyl-1-methyl)xanthines previously not described in the literature, were synthesized and their spectral characteristics were studied. The synthesized substances belong to grade IV toxicity according to in silico and in vivo tests. The obtained data on diuretic activity indicate the prospects for further research in the series of 7-(naphthyl-1-methyl)xanthine derivatives.

ANTIOXIDANT RADICAL SCAVENGING ACTIVITY STUDYING WITH COMPUTATIONAL QUANTUM CHEMISTRY

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Introduction. Nowadays the discovery of antioxidant agents is a recent problem that requires new methodological approaches development for the synthesis of novel compounds and their pharmacological activity screening, while it is also the society relevant task of life sciences, including pharmaceutical and medicinal chemistry.

The aim of the present research was to look through the current trends in computational quantum chemistry applications for free radicals scavenging activity mechanisms studying.

Materials and methods. Methods which were used included systematizing original articles approaches and results, analysis and comparison of information from various sources, generalization and allocation of new and promising directions of research.

Results. The main characteristic of an antioxidant is its ability to break or prevent a chain of oxidative propagation, by stabilizing the generated radical, thus helping to reduce oxidative damage in the human body. Antioxidant compounds act through several chemical mechanisms: hydrogen atom transfer (HAT), single electron transfer (SET), and the ability to chelate transition metals. The importance of antioxidant mechanisms is to understand the biological meaning of antioxidants, their possible uses, their production by organic synthesis or biotechnological methods, or for the standardization of the determination of antioxidant activity. According to the action mechanism antioxidants may by also classified as follows: Type I: chain breakers, which can directly interact with free radicals and create more stable and less hazardous specie. Type II: preventers, for which the unified mechanism of action is not specified, but it does not include interactions with radicals. Their activities may include metal chelation, and regulation of enzymes responsible for radical formation or those directly involved in oxidative stress development. Type III: substances that effectively repair oxidatively damaged biomolecules. However, any of these classifications are often artificial as most antioxidants exhibit multiple types of activity at the same time. So any conclusions concerning the mechanism of action is better to do on the basis of the chemical structure or origin.

Computational chemistry approaches including quantum chemistry methods may be applied to study the action mechanisms of Type I antioxidants only as chain breakers share similar reactivity patterns and mechanisms despite their diversity. The two main features of the initial structure namely selecting the appropriate conformer for the study and intramolecular hydrogen bond counts are known as a critical first step in theoretical elaborations. The level of theory chosen,