CAOBO WORD
Accent Graphics
Publising & Communications

8th International youth conference

“Perspectives of science and education”

29th March 2019

New York
2019

SEARCH FOR BIOLOGICALLY ACTIVE SUBSTANCES AMONG NEW DERIVATIVES OF 1,3-THIAZOLE

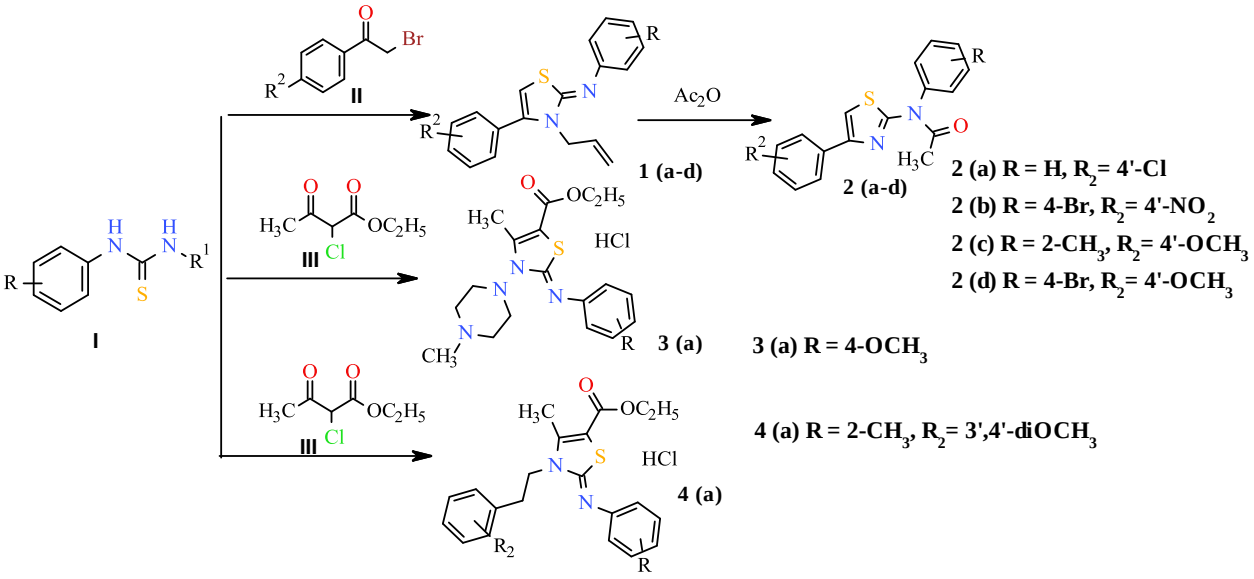
MAURURI I.
MURODOV Sh.
DRAPAK I.V.
YAREMENKO V.D.
SULEIMAN M.M.
PEREKHODA L.O.
Department of Medicinal Chemistry
The National University of Pharmacy
Kharkiv, Ukraine

Analysis of the scientific literature indicates that the derivatives of thiazole have a sufficiently wide spectrum of pharmacological activity and a large number of drugs is created on their basis. But despite a large number of publications, there is practically no information in the literature on the physical, chemical and biological properties of compounds that have piperazine, 1,3-thiazole cycles and phenyl fragments together in their structure. Since in modern medicine there are some examples of the successful use of medications based on these heterocycles, we considered it expedient to combine these known pharmacophores in one molecule [1-3]. In order to expand the arsenal of biologically active substances, it was planned to introduce an acetamide fragment into the structure of the derivatives of the R-phenylamine-1,3-thiazole.

As initial substances to synthesize new derivatives of N1-(4-(4-R- phenyl)-1,3-thiazolyl-2)-N1-(4'-R'-phenyl)acetamide and ethyl-[2-[R-imin]-4-methyl-3-R^1-2,3-dihydro-1,3-thiazole-5-carboxylate the asymmetrical thioureas were used, which were synthesized by reaction between R-phenyl isothiocyanates and arylamines, alkylamines and substituted by piperazine amines in equimolar amounts in a dry dioxane medium [4-7]. A new series of N1-(4-(4-R-phenyl)-1,3-thiazolyl-2)

derivatives-N1-(4'-R'-phenyl)acetamide **2 (a-d)** is obtained by acetylation of hydrobromide derivatives 3-alyl-4-(R-phenyl)-N-(R^1-phenyl)thiazol-2-imine **1 (a-d)** with acetic anhydride while boiling under reflux for 1 hour. 3-Alyl-4-(R-phenyl)-N-(R^1-phenyl)thiazol-2-imine **1 (a-d)** hydrobromides were obtained by reacting asymmetric thiourea derivatives **I** with α-bromo-4-R-acetophenones **II** in equimolar amounts by boiling in ethanol. Ethyl-[2-[R-imin]-4-methyl-3-R^1-2,3-dihydro-1,3-thiazole-5-carboxylate hydrochlorides **3 (a)** and **4 (a)** were obtained under similar conditions by action of ethyl 2-chlor-3-oxobutanoate **III** on the corresponding thioureas **I** respectively (scheme 1).

Scheme 1



The structure of the synthesized compounds was confirmed by elemental analysis and by ^{1}H NMR spectroscopy.

Prediction of pharmacological activity for new derivatives of N1-(4-(4-R-phenyl)-1,3-thiazolyl-2)-N1-(4'-R'-phenyl)acetamide is made using the PASS program. According to the results obtained, the synthesized compounds have a wide range of pharmacological activity and act as inhibitor ACE, calcium channel N-type blocker, mucomembranous protector, insulin promoter, ubiquinol-cytochrome-c reductase inhibitor, transcription factor STAT3 inhibitor etc.

Pharmacological screening for ethyl-[2-[R-imin]-4-methyl-3-R^1-2,3-dihydro-1,3-thiazole-5-carboxylate hydrochlorides has shown that the obtained substances

possess cardiotropic activity. As can be seen from the results of pharmacological research, the cardiotropic activity of the obtained substances depends on the nature of the radicals at positions 3 and 5 of the thiazole cycle. The cardiotropic activity decreases with increase in the length of the aliphatic chain of substituents at position 3. The presence of alkyl radicals and a piperazine fragment in the structure of the 1,3-thiazole derivatives positively affects the activity index.

References

1. Perekhoda LO, Drapak IV, Suleiman MM, Sych IA, Yaremenko VD. Synthesis and in silico research of derivatives of 3-allyl-4-(R-phenyl)-N-(R1-phenyl)-thiazole-2-imine. Der Pharma Chemica 2017; 9(13): 95-98.
2. Richards D, Aronson J, Reynolds DJ, Coleman J. Oxford Handbook of Practical Drug Therapy: Edition 2, 2011.
3. Hernandez MA, Rathinavelu A. Basic Pharmacology: Understanding Drug Actions and Reactions, 2017.
4. Yeromina, HO, Drapak IV, Perekhoda LO, Yaremenko VD, Demchenko AM. Synthesis of 2-(4-aryl(adamantyl)-2-phenyliminothiazol-3-yl)-ethanol derivatives and prediction of their biological activity. Der Pharma Chemica 2016; 8(3): 64-70.
5. Venkatachalam TK, Uckun FM. Synthesis of Symmetrical and Asymmetrical Phenethyl Thiourea Compounds as Nonnucleoside Inhibitors of HIV-1 Reverse Transcriptase. An International Journal for Rapid Communication of Synthetic Organic Chemistry 2005; 35(15): 2039-2056.
6. Esteves-Souza A, Pissinate K, Nescient M, Grynberg NF, Echevarria A. Synthesis, cytotoxicity, and DNA-topoisomerase inhibitory activity of new asymmetric ureas and thioureas. Bioorganic & Medicinal Chemistry 2006; 14(2): 492-499.

7. Taha Muhammad et all. Synthesis and evaluation of unsymmetrical heterocyclic thioureas as potent β-glucuronidase inhibitors. Medicinal Chemistry Research 2015; 24(8): 3166–3173.