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## SYNTHESIS, DETERMINATION OF PHYSICO-CHEMICAL PARAMETERS, STRUCTURE CONFIRMATION, AND ANTIOXIDANT ACTIVITY OF COMPOUNDS BASED ON 3,5-BIS(5-MERCAPTO-4-R-4H-1,2,4-TRIAZOLE-3-YL)PHENOL

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*In this study, the potential of using 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol as a critical component for the synthesis of new compounds is considered, which may be of significant importance in various fields of science and technology. The relevance of the research is due to the fact that studying the properties of new synthetic derivatives of 1,2,4-triazole is a promising direction in modern chemistry. This study opens new opportunities for creating biologically active substances with antioxidant activity and the prospect of their further use as individual and combined drugs for correcting pathological processes associated with oxidative stress.*

**The aim of the study.** *The main objective of the research is to find new, low-toxic, and highly effective antioxidant compounds based on derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol, as well as to confirm the individuality, structure, and establish their physicochemical constants.*

**Materials and methods.** *The article investigates the synthesis and establishes the structure of a series of compounds, in particular, diacetic acids and dibenzoic acids, derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol, which were chosen as the material for the search for highly effective antioxidants. The methods used in this work are as follows: organic synthesis, physicochemical methods for determining the structure of synthesized substances (elemental analysis, UV spectrophotometry, <sup>1</sup>H NMR spectroscopy, mass- and chromato-mass spectrometry), and a biological method for determining antioxidant activity using the free radical method with DPPH.*

**Results of the study.** *The results showed that some of the synthesized compounds have significant potential as antioxidants, which may be important in the context of their application in various fields, particularly in medicine and the food industry. Among the obtained results, it is especially worth noting ethyl 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4-phenyl-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene))dibenzoate (compound 7c) and propyl 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4-methyl-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene))dibenzoate (compound 7d), which showed the highest level of antioxidant activity among all the studied compounds.*

**Conclusions.** *The obtained results indicate the possible application of the studied compounds as potential antioxidants in the production of materials and products, which may be of great significance for further research in this area*

**Keywords:** *1,2,4-triazole, synthesis, dibenzoic(diacetic) acids, esters, antioxidant activity, DPPH, physicochemical analysis*

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## 1. Introduction

Relevance of the topic. The development of new materials and compounds is a key direction in modern pharmacy [1–3]. In this case, the use of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol as a basis for the synthesis of new compounds can open new opportunities in the creation of materials with antioxidant properties, which are important in various fields of science and technology, which is proven by the works of scientists [4–6] who are engaged in the study of 1,2,4-triazole derivatives.

The research results may have practical significance for various fields, including pharmacy, catalysis, material science, and others. For example, new compounds may have antibacterial, antioxidant, or other beneficial properties, making them interesting for further research and development.

## 2. Research planning (methodology)

A detailed study of the physicochemical parameters of new compounds and derivatives of 1,2,4-triazole is an important stage in their understanding and further use. These data can be used to predict the behaviour of compounds in various conditions, which allows them to be used more effectively in practical applications.

Analysis and confirmation of the structure of new compounds is an important stage [7–9], as it allows us to make sure of their correct synthesis and to identify them in further research.

When planning our research, these key factors formed the goal of our research, namely the synthesis of new, not described in the literature, derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol, setting for physico-chemical parameters, confirmation of structure and individuality.

### 3. Materials and methods

The article investigated the synthesis and established the structure of a number of compounds, in particular, diacetic acids and dibenzoic acids, derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol, which were chosen as a material for the search of highly effective antioxidants.

The methods used in this work are as follows: organic synthesis, physicochemical methods for determining the structure of synthesized substances (elemental analysis, UV spectrophotometry, <sup>1</sup>H NMR spectrometry, mass and chromatography-mass spectrometry), a biological method for determining antioxidant activity using the free radical method using DPPH.

The bibliosemantic method was used for the analysis of literary sources, relying on the scientometric databases Google Scholar, PubMed, Scopus, Web of Science.

### 4. Results

The structure of compounds based on 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols is a promising matrix for the search for biologically active substances [3, 4]. In particular, the presence of sulfur-containing functional groups in these compounds indicates their potential antimicrobial properties. The study of their effectiveness against various pathogens, including bacteria, fungi, and viruses, may lead to the development of new antimicrobial agents to combat infectious diseases and microorganisms that are resistant to treatment. Given the large number of electron-donating centers, the compounds should possess antioxidant activity [5]. Since oxidative stress and inflammation are closely related, compounds with antioxidant activity often exhibit anti-inflammatory properties. Studying the ability of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols to moderate inflammation may reveal their potential in the control of inflammatory diseases such as arthritis, inflammatory intestinal diseases and asthma. Some antioxidants have chemopreventive properties, thanks to which they can restrain the initiation, progress and development of carcinogenesis. Investigation of the effects of these compounds on cancer cell proliferation, apoptosis, and metastasis may reveal their potential as adjuncts in cancer prevention and treatment. The structural versatility of these compounds, combined with their potential biological properties, may make them promising candidates for drug delivery systems. Researching their ability to encapsulate and deliver therapeutics to specific targets in the body could improve drug efficacy and reduce side effects.

In view of the above, the study of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols can reveal their therapeutic potential in various diseases and contribute

to the development of new pharmacological agents and drug delivery systems. Therefore, at the first stage, we realized the synthesis of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols.

*Synthesis of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols.*

5-Hydroxyisophthalic acid was the starting substance for obtaining (3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol (compounds 4 a-c, Fig. 1). In the first 5-hydroxyisophthalic acid methyl ester was obtained (compound 1, Fig. 2). The esterification of the acid (compound 2, Fig. 1) was carried out in the presence of sulfuric acid in a catalytic amount. In the next step, under the influence of hydrazine hydrate, methyl ester (compound 2, Fig. 1) is transformed into 5-hydroxyisophthalic acid hydrazide (compound 2, Fig. 1). At the next stage, the interaction of 5-hydroxyisophthalic acid hydrazide (compound 3, Fig. 1) with methyl, ethyl, or phenylisothiocyanate in an acidic environment, the corresponding 2,2'-(5-hydroxyisophthaloyl)bis(oxy)bis(N-R-hydrazino-1-carbothioamides) were obtained (compounds 3 a-c, Fig. 1). The last stage of the synthesis of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols was the stage of cyclization of compounds 3 a-c under the action of a two-normal aqueous solution of sodium hydroxide, while after filtration and drying gave compounds 4 a-c (Fig. 1, Table 1).

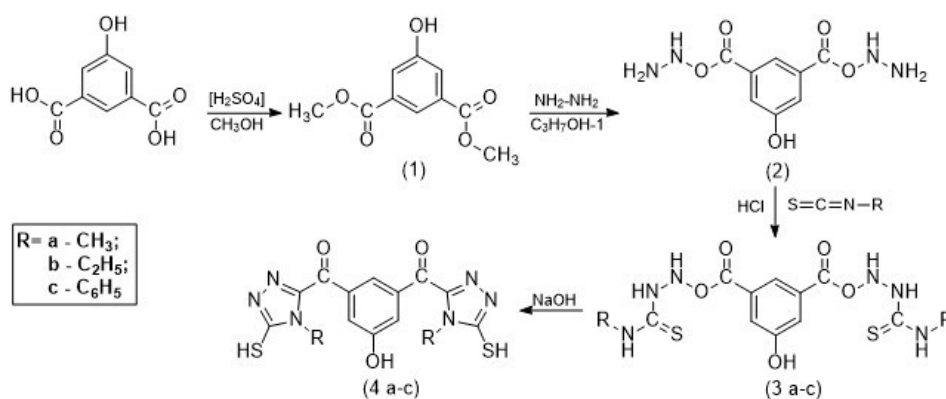


Fig. 1. Step-by-step production of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazole-3-yl)phenols

The obtained compounds 4 a, b are white crystalline substances, soluble in alkaline and polar solvents, poorly soluble in organic, non-polar solvents. For purification, the compounds were recrystallized from a 1:2 mixture of ethanoic acid and water.

The obtained compound 4c is a grey crystalline substance, soluble in alkaline and polar solvents, poorly soluble in alcohols, diethyl ether and chloroform, non-polar solvents. For purification, the compound was recrystallized from a 1:2 mixture of ethanoic acid and water.

*Synthesis of 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))diacetate acids and 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene) dibenzoic acids.*

Thioacetate acids [3, 7] are widely used in chemical reactions as catalysts and intermediates in the syn-

thesis of organic compounds. They are also used in biochemistry to modify proteins and study their functions. In pharmaceuticals, thioacetate acids can be a component of drugs such as antifungal agents. In addition, they are used in materials science to modify polymers and create new materials with improved properties. They have significant applications in chemical and biological disciplines.

Representatives of substituted benzoic acids are used in the synthesis of organic compounds as intermediates and catalysts, which makes them important in the chemical industry. In biology, benzoic acids can interact with biological macromolecules such as proteins and DNA and affect their functioning. They may also have medical applications, for example, as antimicrobial agents or anti-inflammatory agents. It is important to note that benzoic acids can also be used in pharmaceuticals for the synthesis of drugs with various therapeutic properties. Taking into account the relevance, the synthesis of 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl)) diacetate acids and 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl)) bis(methylene)dibenzoic acids (5 a-c and 6 a-c) was realized.

The target acids 5 a-c and 6 a-c (Fig. 2, Table 1) were obtained by the interaction of the corresponding 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazole-3-yl)phenols with 3-(chloromethyl)benzoic or 1-chloroacetate acid in dimethylformamide with an equimolar amount of alkali. The solutions were boiled in an acidic medium, filtered, and water was added and left for a day. Product precipitates were filtered and dried.

The obtained compounds 5a and 6a are light pink crystalline substances, compounds 5b and 6b are white crystalline substances, all soluble in alkalis and in organic solvents, sparingly soluble in aqueous solutions. For purification, the compounds were recrystallized from a 3:1 DMF-water mixture.

The obtained compounds 5c and 6c are grey crystalline substances, soluble in alkalis and in organic solvents, sparingly soluble

in aqueous solutions. For purification, the compounds were recrystallized from a 3:1 DMF-water mixture.

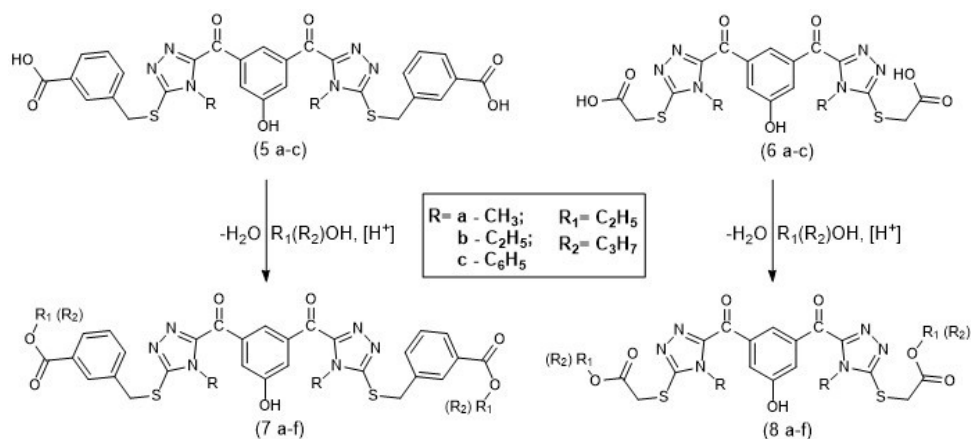


Fig. 3. Preparation of ethers of 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))diacetate acids and ethers 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acids

*Synthesis of ethers of 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))diacetate acids and ethers of 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acids.*

The further stage of synthetic research was the study of the esterification reaction for acids 5 a-c and 6 a-c, which were obtained at the previous stage of synthesis. Esters 7 a-f and 8 a-f (Fig. 3, Table 1) were obtained by the esterification reaction of 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acids (5 a-c) and 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))diacetate acids (6 a-c) in the medium of the appropriate alcohol with the addition of a catalytic amount of concentrated sulfuric acid (Fig. 3).

The obtained compounds 7 and 8 a-f are white crystalline substances, all soluble in alcohols and in organic solvents, sparingly soluble in aqueous solutions. For purification, the compounds were recrystallized from a 5:1 ethanol-water mixture.

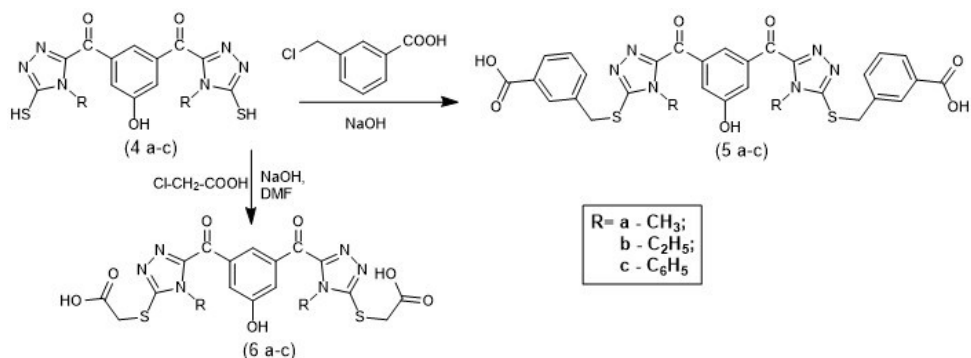


Fig. 2. Preparation of 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))diacetate acids and 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acids

Table 1

Physico-chemical constants of 4-6 a-c; 5 a-c; 6 a-c; 7,8 a-f compounds

Compound	R	R <sub>1</sub>	R <sub>2</sub>	Yield, %	M.p., °C
4a	CH <sub>3</sub>	–	–	92	105–107
4b	C <sub>2</sub> H <sub>5</sub>	–	–	90	99–101
4c	C <sub>6</sub> H <sub>5</sub>	–	–	94	271–273
5a	CH <sub>3</sub>	–	–	85	123–125
5b	C <sub>2</sub> H <sub>5</sub>	–	–	74	365–367
5c	C <sub>6</sub> H <sub>5</sub>	–	–	84	194–196
6a	CH <sub>3</sub>	–	–	90	232–234
6b	C <sub>2</sub> H <sub>5</sub>	–	–	90	165–168
6c	C <sub>6</sub> H <sub>5</sub>	–	–	88	155–157
7a	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	–	84	138–140
7b	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	–	78	117–119
7c	C <sub>6</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	–	80	212–214
7d	CH <sub>3</sub>	–	C <sub>3</sub> H <sub>7</sub>	74	151–153
7e	C <sub>2</sub> H <sub>5</sub>	–	C <sub>3</sub> H <sub>7</sub>	90	157–159
7f	C <sub>6</sub> H <sub>5</sub>	–	C <sub>3</sub> H <sub>7</sub>	77	228–230
8a	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	–	79	132–134
8b	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	–	90	113–115
8c	C <sub>6</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>	–	77	221–233
8d	CH <sub>3</sub>	–	C <sub>3</sub> H <sub>7</sub>	92	161–163
8e	C <sub>2</sub> H <sub>5</sub>	–	C <sub>3</sub> H <sub>7</sub>	87	132–134
8f	C <sub>6</sub> H <sub>5</sub>	–	C <sub>3</sub> H <sub>7</sub>	75	258–260

#### 4. 1. Determination of antioxidant activity

The antioxidant activity of the synthesized compounds was assessed using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical test [10], the DPPH method is a simple, fast and highly sensitive way to determine antioxidant activity. Its advantages include ease of use, high reproducibility of results and the possibility of applica-

tion to different types of samples. This method allows easy standardization of the procedure and provides reliable results even when analyzing small amounts of active compounds.

Indicators of antioxidant activity for synthesized derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol are shown in Table 2.

Table 2

Indicators of antioxidant activity of derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazole-3-yl)phenol

No.	Compound structure	Absorption coefficient, A	% of antioxidant activity
1	Control (DPPH)	1.4054	–
2	Ascorbic acid	0.6847	51.28
3	4a	0.6873	51.10
4	4b	0.5993	57.36
5	4c	0.4750	66.20
6	5a	0.6807	51.57
7	5b	0.8814	37.28
8	5c	0.7673	45.40
9	6a	0.9008	35.90
10	6b	0.6807	51.57
11	6c	0.7896	43.82
12	7a	0.6503	28.63
13	7b	0.6666	26.84
14	7c	0.2517	72.38
15	7d	0.2625	71.19
16	7e	0.6900	24.28
17	7f	0.5418	40.54
18	8a	0.7955	12.70
19	8b	0.7548	17.16
20	8c	0.7319	19.68
21	8d	0.8284	41.06
22	8e	0.8318	40.81
23	8f	0.7319	19.68



## 4. 2. Experimental part

### 4. 2. 1. Synthetic part

<sup>1</sup>H NMR spectra were recorded using a Varian VXR-300 spectrophotometer (USA manufacturer), dimethylsulfoxide-D6 solvent, and tetramethylsilane was used as an internal standard. The spectra of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol and their derivatives were decoded using the ADVASP 143 computer program.

The chromat-mass spectra of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol and their derivatives were recorded on an LC MS instrument: Agilent 1260 Infinity HPLC System (production USA) (degasser, binary high-pressure pump, autosampler, column thermostat, diode-matrix detector; Agilent 6120 single-quadrupole mass spectrometer with electrospray ionization (ESI).

Calculations of molecular structures were carried out using the AM1 method (MOPAK 2003), with preliminary optimization of the geometric structure using the computer program Hyper Chem® 10.0.

The melting points data for synthesized compounds were obtained by the open capillary method with the MPA100 (OptiMelt, USA) device with a range of temperature measurements of 30-400 °C and 1 °C resolution.

Elemental analysis of (3-thio-4-R-1,2,4-triazol-5-yl)(phenyl)methanols and their derivatives was established on the ELEMENTAR vario EL cube analyzer (made in Germany) (standard – sulfonamide).

**Compound 1** (methyl ester of 5-hydroxyisophthalic acid). A mixture of 1.0 mol of 5-hydroxyisophthalic acid (compound 1), 500 ml of methyl alcohol and 40 ml of concentrated sulfuric acid is boiled for 15 hours, the excess methanol is evaporated, the residue is treated with a solution of sodium hydrogen carbonate to a neutral medium.

**Compound 2** hydrazide of 5-hydroxyisophthalic acid. A mixture of 0.5 mol of methyl ester of 5-hydroxyisophthalic acid (compound 1), 3 mol of hydrazine hydrate in the form of a solution in 50 ml of propanol-1 is boiled for 5 hours. Excess solvent is evaporated, the product is crystallized from ethanol.

**Compounds 3 a-c** (2,2'-(((5-hydroxyisophthaloyl)bis(oxy))bis(N-R-hydrazino-1-carbothioamides))). To a solution of 1 mol of hydrazide of 5-hydroxyisophthalic acid (compound 2) in 100 ml of propanol, 1 mol of methyl-, ethyl- or phenylisothiocyanate, respectively, is added upon cooling, the mixture is left for 24 hours, the precipitates of the reaction products are filtered.

**Compounds 4 a-c** 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols. 1 mol of hydrazinocarbothioamide (compounds **3a-c**), 2 mol of sodium hydroxide and distilled water are loaded into a 1-liter flask equipped with a reflux condenser. The mixture is boiled for 2 hours until a solution is formed, concentrated acetic acid is added to pH 6.9-7.1, cooled, and thion precipitates (compounds **4 a-c**) are filtered.

**4a** <sup>1</sup>H NMR (300 MHz, DMSO) δ 13.12 (s, 2H, SH), δ 9.38 (s, 1H, OH), δ 7.43 (t, 1H, Ar), δ 7.15 (s, 2H, Ar), δ 3.66 (s, 6H, N-CH<sub>3</sub>). Calculated: C-44.99, H-3.78, N-26.23, S-20.01. Found: C-45.07, H-3.79, N-26.20, S-20.16. M/z=321.

**4b** <sup>1</sup>H NMR (300 MHz, DMSO) δ 13.10 (s, 2H, SH), δ 9.41 (s, 1H, OH), δ 7.48 (t, 1H, Ar), δ 7.12 (s, 2H, Ar), δ 4.15 (qu, 4H, CH<sub>2</sub>), 1.33 (t, 6H, CH<sub>3</sub>). Calculated: C-48.26, H-4.63, N-24.12, S-18.40. Found: C-48.20, H-4.73, N-24.20, S-18.36. M/z=349.

**4c** <sup>1</sup>H NMR (300 MHz, DMSO) δ 13.07 (s, 2H, SH), δ 9.47 (s, 1H, OH), δ 7.60 (t, 2H, Ar), δ 7.45 (m, 9H, Ar), δ 7.17 (s, 2H, Ar). Calculated: C-59.44, H-3.63, N-18.91, S-14.42. Found: C-59.60, H-3.59, N-19.01, S-14.47. M/z=445.

**Compounds 5 a-c** (3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acids). To a solution of 0.2 mol of NaOH in 100 ml of DMF, 0.1 mol of the corresponding 5-(hydroxy(phenyl)methyl)-4-R-4H-1,2,4-triazole-3-thione (**4 a-c**) and 0.25 mol of 2-chloromethylbenzoic acid. The solution is boiled to an acidic medium (5 hours), filtered, 50 ml of water is added and left for a day. Product sediments are filtered and dried.

**Compounds 6 a-c** (2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))diacetate acids). To a solution of 0.2 mol of NaOH in 100 ml of DMF, 0.1 mol of the corresponding 5-(hydroxy(phenyl)methyl)-4-R-4H-1,2,4-triazole-3-thione (**4 a-c**) and 0.25 mol of 1-chloroethane acid. The solution is boiled to an acidic medium (5 hours), filtered, 50 ml of water is added and left for a day. Product sediments are filtered and dried.

**5a** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.80 (s, 2H, OH), δ 9.40 (s, 1H, OH), δ 8.07 (m, 4H, Ar), δ 7.73 (d, 2H, Ar), δ 7.47 (s, 1H, Ar), δ 7.40 (t, 2H, Ar), δ 7.20 (s, 2H, Ar), δ 4.45 (s, 4H, CH<sub>2</sub>) δ 3.60 (s, 6H, N-CH<sub>3</sub>). Calculated: C-57.13, H-4.11, N-14.28, S-10.89. Found: C-57.07, H-4.03, N-13.98, S-11.03. M/z=589.

**5b** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.88 (s, 2H, OH), δ 9.50 (s, 1H, OH), δ 8.10 (m, 4H, Ar), δ 7.83 (d, 2H, Ar), δ 7.66 (s, 1H, Ar), δ 7.52 (m, 2H, Ar), δ 7.22 (s, 2H, Ar), δ 4.51 (s, 4H, CH<sub>2</sub>), δ 4.21 (qu, 4H, CH<sub>2</sub>), 1.53 (t, 6H, CH<sub>3</sub>). Calculated: C-58.43, H-4.58, N-13.63, S-10.40. Found: C-58.50, H-4.51, N-13.50, S-10.55. M/z=617.

**5c** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.70 (s, 1H, OH), δ 9.40 (s, 1H, OH), δ 8.00 (t, 4H, Ar), δ 7.75 (d, 2H, Ar), δ 7.70 (m, 2H, Ar), δ 7.57 (m, 11H, Ar), δ 7.25 (s, 2H, Ar), δ 4.50 (s, 4H, CH<sub>2</sub>) Calculated: C-64.03, H-3.96, N-11.79, S-09.00. Found: C-65.00, H-3.92, N-11.70, S-09.07. M/z=713.

**6a** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.65 (s, 2H, OH), δ 9.40 (s, 1H, OH), δ 7.38 (t, 1H, Ar), δ 7.10 (s, 2H, Ar), δ 4.21 (s, 4H, CH<sub>2</sub>), δ 3.63 (s, 6H, N-CH<sub>3</sub>). Calculated: C-44.03, H-3.70, N-19.26, S-14.69. Found: C-43.97, H-3.59, N-19.44, S-14.73. M/z=437.

**6b** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.85 (s, 2H, OH), δ 9.44 (s, 1H, OH), δ 7.50 (t, 1H, Ar), δ 7.22 (d, 2H, Ar), δ 4.25 (qu, 8H, CH<sub>2</sub>), 1.40 (t, 2H, CH<sub>3</sub>). Calculated: C-48.26, H-4.63, N-24.12, S-18.40. Found: C-48.20, H-4.73, N-24.20, S-18.36. M/z=465.

**6c** <sup>1</sup>H NMR (300 MHz, DMSO) δ 12.65 (s, 2H, OH), δ 9.47 (s, 1H, OH), δ 7.60 (t, 2H, Ar), δ 7.45 (m, 9H, Ar), δ 7.20 (d, 2H, Ar), δ 4.19 (s, H, CH<sub>2</sub>). Calculated: C-46.54, H-4.54, N-18.09, S-13.80. Found: C-47.01, H-4.59, N-17.90, S-13.77. M/z=561.

**Compounds 7, 8 a-c** (alkyl 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))diacetates and alkyl 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene dibenzoates).

A mixture of 0.01 mol of 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))bis(methylene)dibenzoic acid (**5 a-f**) or 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazol-5,3-diyl))bis(sulfandiyl))diacetate acid (**6 a-f**), 50 ml of the appropriate alcohol (ethanol, propanol-1), 1.0 ml of concentrated sulfuric acid, boil for 15 hours, evaporate the solvent, neutralize the mixture with aqueous sodium bicarbonate. The precipitate obtained is filtered, washed on the filter with 50 ml of purified water.

**7a** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.28 (s, 1H, OH), δ 7.92 (d, 2H, Ar), δ 7.77 (s, 2H, Ar), δ 7.66 (d, 2H, Ar), δ 7.58 (s, 1H, Ar), δ 7.41 (t, 2H, Ar), δ 7.11 (s, 2H, Ar), δ 4.35 (m, 8H, CH<sub>2</sub>), δ 3.44 (s, 6H, N-CH<sub>3</sub>), δ 1.28 (t, 6H, CH<sub>3</sub>). Calculated: C-59.61, H-5.00, N-13.03, S-9.94. Found: C-59.47, H-5.07, N-13.18, S-9.90. M/z=645.

**7b** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.44 (s, 1H, OH), δ 7.85 (d, 2H, Ar), δ 7.80 (s, 2H, Ar), δ 7.71 (d, 2H, Ar), δ 7.63 (s, 1H, Ar), δ 7.38 (t, 2H, Ar), δ 7.15 (s, 2H, Ar), δ 4.40 (m, 8H, CH<sub>2</sub>), δ 4.15 (qu, 4H, CH<sub>2</sub>), δ 1.54 (t, 12H, CH<sub>3</sub>). Calculated: C-60.70, H-5.39, N-12.49, S-9.53. Found: C-60.30, H-5.22, N-12.55, S-9.61. M/z=673.

**7c** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.40 (s, 1H, OH), δ 7.93 (d, 2H, Ar), δ 7.90 (s, 2H, Ar), δ 7.60 (t, 4H, Ar), δ 7.44 (m, 11H, Ar), δ 7.22 (s, 2H, Ar), δ 4.35 (m, 8H, CH<sub>2</sub>), δ 1.54 (t, 6H, CH<sub>3</sub>). Calculated: C-65.61, H-4.72, N-10.93, S-8.34. Found: C-60.30, H-5.22, N-12.55, S-9.61. M/z=769.

**7d** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.35 (s, 1H, OH), δ 7.87 (d, 2H, Ar), δ 7.71 (s, 2H, Ar), δ 7.60 (d, 2H, Ar), δ 7.55 (s, 1H, Ar), δ 7.47 (t, 2H, Ar), δ 7.15 (s, 2H, Ar), δ 4.50 (m, 8H, CH<sub>2</sub>), δ 3.67 (s, 6H, N-CH<sub>3</sub>), δ 2.09 (m, 4H, CH<sub>2</sub>), δ 1.28 (t, 6H, CH<sub>3</sub>). Calculated: C-60.70, H-5.39, N-12.49, S-9.53. Found: C-60.67, H-5.19, N-12.21, S-9.77. M/z=673.

**7e** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.49 (s, 1H, OH), δ 7.91 (d, 2H, Ar), δ 7.85 (s, 2H, Ar), δ 7.65 (d, 1H, Ar), δ 7.60 (s, 2H, Ar), δ 7.33 (t, 2H, Ar), δ 7.10 (s, 2H, Ar), δ 4.44 (m, 8H, CH<sub>2</sub>), δ 4.10 (qu, 4H, CH<sub>2</sub>), δ 2.20 (m, 4H, CH<sub>2</sub>), δ 1.52 (t, 6H, CH<sub>3</sub>), δ 1.15 (t, 6H, CH<sub>3</sub>). Calculated: C-61.69, H-5.75, N-11.99, S-9.15. Found: C-61.57, H-5.72, N-11.83, S-9.11. M/z=701.

**7f** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.51 (s, 1H, OH), δ 8.07 (d, 2H, Ar), δ 7.95 (s, 2H, Ar), δ 7.70 (m, 4H, Ar), δ 7.65 (m, 11H, Ar), δ 7.15 (s, 2H, Ar), δ 4.22 (m, 8H, CH<sub>2</sub>), δ 1.80 (m, 4H, CH<sub>2</sub>), δ 1.50 (t, 6H, CH<sub>3</sub>). Calculated: C-66.31, H-5.06, N-10.55, S-8.05. Found: C-65.99, H-5.20, N-10.55, S-8.58. M/z=797.

**8a** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.50 (s, 1H, OH), δ 7.73 (s, 1H, Ar), δ 7.25 (s, 2H, Ar), δ 4.50 (qu, 8H, CH<sub>2</sub>), δ 3.66 (s, 6H, N-CH<sub>3</sub>), δ 1.20 (s, 6H, CH<sub>3</sub>). Calculated: C-48.77, H-4.91, N-17.06, S-13.02. Found: C-48.60, H-4.79, N-17.19, S-12.97. M/z=493.

**8b** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.43 (s, 1H, OH), δ 7.71 (s, 1H, Ar), δ 7.32 (s, 2H, Ar), δ 4.47 (m, 12H, CH<sub>2</sub>), δ 1.55 (m, 12H, CH<sub>3</sub>). Calculated: C-50.75, H-5.42, N-16.14, S-12.32. Found: C-50.60, H-5.49, N-16.19, S-12.51. M/z=521.

**8c** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.45 (s, 1H, OH), δ 7.58 (t, 2H, Ar), δ 7.47 (t, 5H, Ar), δ 7.32 (s, 2H, Ar), δ 4.50 (qu, 8H, CH<sub>2</sub>), δ 3.66 (s, 6H, N-CH<sub>3</sub>), δ 1.20 (s, 6H, CH<sub>3</sub>). Calculated: C-58.43, H-4.58, N-13.63, S-10.40. Found: C-58.63, H-4.62, N-13.22, S-10.27. M/z=617.

**8d** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.47 (s, 1H, OH), δ 7.40 (s, 1H, Ar), δ 7.00 (s, 2H, Ar), δ 4.15 (t, 8H, CH<sub>2</sub>), δ 3.90 (s, 6H, CH<sub>3</sub>), δ 3.60 (t, 6H, CH<sub>2</sub>), δ 1.50. Calculated: C-50.75, H-5.42, N-16.14, S-12.32. Found: C-50.77, H-5.58, N-16.27, S-12.30. M/z=521.

**8e** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.60 (s, 1H, OH), δ 7.70 (s, 1H, Ar), δ 7.65 (s, 2H, Ar), δ 4.55 (m, 12H, CH<sub>2</sub>), δ 4.55 (m, 12H, CH<sub>2</sub>), δ 1.90 (m, 4H, CH<sub>2</sub>), δ 1.57 (t, 6H, CH<sub>3</sub>), δ 1.10 (t, 6H, CH<sub>3</sub>). Calculated: C-52.54, H-5.88, N-15.32, S-11.69. Found: C-52.65, H-5.93, N-15.67, S-11.44. M/z=549.

**8f** <sup>1</sup>H NMR (300 MHz, DMSO) δ 9.55 (s, 1H, OH), δ 7.63 (t, 2H, Ar), δ 7.55 (t, 5H, Ar), δ 7.32 (s, 2H, Ar), δ 4.37 (t, 8H, CH<sub>2</sub>), δ 1.91 (m, 4H, CH<sub>2</sub>), δ 1.00 (t, 6H, CH<sub>3</sub>). Calculated: C-59.61, H-5.00, N-13.03, S-9.94. Found: C-59.12, H-4.94, N-13.05, S-10.02. M/z=645.

#### 4. 2. 2. Biological part

Free radical scavenging was determined by a free radical assay using 1,1-diphenyl-2-picrylhydrazyl (DPPH) [10]. The exact mass of the substance (0.001 M) was dissolved in 25.00 ml of DMSO in a volumetric flask, then brought up to the mark and mixed. From the resulting solution, 1.00 ml was taken and added to a 10.00 ml volumetric flask (0.0001 M), after which it was again brought up to the mark with DMSO and mixed. Then, 2.00 ml of this solution was transferred to a test tube, and 2.00 ml of a 0.1 mM solution of DPPH in methanol (Sigma-Aldrich, Germany) was added, after which it was tightly closed. The tubes were shaken and left for 30 min in the dark at room temperature, and the absorbance was measured at 516 nm. A solution consisting of 2.00 ml of 0.1 mM DPPH solution and 2.00 ml of methanol was used as a control, and ascorbic acid was used as a standard. The free radical scavenging activity was calculated as a percentage of inhibition using the appropriate formula:

$$\% \text{ of antioxidant activity} = \frac{(A_0 - A_1)}{A_0} \cdot 100,$$

where  $A_0$  – value of the absorption coefficient of the control sample;  $A_1$  – absorption coefficient of the sample under study. The absorption of the investigated solutions is measured in aqueous-organic solutions, and the absorption maximum at 516 nm is recorded on a Lambda 365 spectrophotometer.

#### 5. Discussion of research results

Based on the data of the conducted experiments, it is worth noting that 6 compounds (4b, 4c, 5a, 6b, 7c, 7d) have a higher level of antioxidant activity than the comparison drug – the natural antioxidant ascorbic acid. High activity can be associated with the presence of electron-donating groups [10–13] (because they are able to donate electrons and can reduce the activity of free radi-

cals, contributing to their stabilization. This can be done by hydrogen atoms or by  $\pi$ -electron delocalization) and the Sulfur atom [14–17] associated with 1,2,4 triazole.

Considering the antioxidant activity demonstrated by 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol derivatives (Table 2), these compounds have the potential for possible use in the fight against diseases associated with oxidative stress. Further studies may examine their effectiveness in protecting cells from oxidative damage and their potential as therapeutic agents in conditions such as neurodegenerative diseases and cardiovascular diseases [18–20].

**Practical significance.** The practical significance of this research lies in the possibility of using synthesized derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenol as promising antioxidants. This opens new opportunities for the creation of pharmacological preparations with low toxicity for the correction of pathological conditions associated with oxidative stress. In addition, these compounds can be used in the production of biologically active additives and materials that improve the preservation of food products and reduce the risks of oxidation in the food industry.

**Study limitations.** The study was focused on a specific set of derivative compounds, which naturally limits the total number of variants investigated.

The study of antioxidant activity was carried out *in vitro*, which is standard practice at the initial stages, with the prospect of further studies *in vivo*.

The antioxidant activity was evaluated by the DPPH method, which is widely accepted, but can be supplemented by other approaches in subsequent steps.

The synthesis process has certain variations inherent in laboratory conditions, which may affect the obtained results, but creates a basis for optimization in future studies.

**Prospects for further research.** The conducted studies of antioxidant action are the basis for the search for new highly effective antihypoxic drugs based on derivatives of 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols.

## 6. Conclusions

1. 21 new compounds were synthesized, in particular 3,5-bis(5-mercapto-4-R-4H-1,2,4-triazol-3-yl)phenols, 2,2'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-

triazole-5,3-diyl))bis(sulfandiyl))diacetate acids, 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4H-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene))dibenzoic acids and their esters.

2. The synthesized structures were confirmed by a complex of physicochemical methods of analysis, in particular  $^1\text{H-NMR}$  spectroscopy, elemental analysis, ultra-high-performance liquid chromatography with mass detection.

3. For all compounds, indicators of antioxidant action using the free radical test method (DPPH) have been established.

4. Substances with a high level of antioxidant activity were found among the synthesized structures.

5. The best antioxidant effect was demonstrated by ethyl 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4-phenyl-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene))dibenzoate (compound 7c) and propyl 3,3'-(((5-hydroxy-1,3-phenylene)bis(4-R-4-methyl-1,2,4-triazole-5,3-diyl))bis(sulfandiyl))bis(methylene))dibenzoate (compound 7d).

## Conflict of interests

The authors declare that they have no conflict of interest in relation to this study, including financial, personal, authorship, or any other, that could affect the study and its results presented in this article.

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## Data availability

The manuscript has no associated data.

## Use of artificial intelligence

The authors confirm that they did not use artificial intelligence technologies when creating the presented work.

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## References

1. Demchenko, N., Suvorova, Z., Fedchenkova, Y., Shpychak, T., Shpychak, O., Bobkova, L., Demchenko, S. (2021). Synthesis and antibacterial activity of 3-arylaminoethyl-1-(2-oxo-2-arylethyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a] azepin-1-ium bromides and aryl-(4-R1-phenyl-5,6,7,8-tetrahydro-2,2a,8a-triazacyclopenta[cd]azulen-1-ylmethyl)-amines. *ScienceRise: Pharmaceutical Science*, 6 (34), 51–57. <https://doi.org/10.15587/2519-4852.2021.249480>
2. Koval, A., Lozynskyi, A., Shtrygol', S., Lesyk, R. (2022). An overview on 1,2,4-triazole and 1,3,4-thiadiazole derivatives as potential anesthetic and anti-inflammatory agents. *ScienceRise: Pharmaceutical Science*, 2 (36), 10–17. <https://doi.org/10.15587/2519-4852.2022.255276>
3. Shcherbyna, R., Kalchenko, V., Kulish, S., Salionov, V., Morozova, L., Nedorezaniuk, N., Mazur, O. (2023). Synthesis, characterization, molecular docking studies of new alkyl derivatives of 5-(2-bromo-4-fluorophenyl)-4-ethyl-4H-1,2,4-triazole-3-thiol. *Ceska a Slovenska Farmacie*, 72 (4), 190–200. Available at: <https://csfarmacie.cz/pdfs/csf/2023/04/05.pdf>
4. Shcherbyna, R. (2020). An investigation of the pharmacokinetics and potential metabolites of potassium 2-((4-amino-5-(morfolinometyl)-4H-1,2,4-triazol-3-yl)thio) acetate on rats. *Journal of Faculty of Pharmacy of Ankara University*, 44 (2), 233–241. <https://doi.org/10.33483/jfpau.681611>



5. Shcherbina, R., Pruhlo, Y., Duchenko, M., Kulagina, M., Kudria, V., Valentyna, V. (2022). Evaluation of Antioxidant Activity of 1, 2, 4-Triazole Derivatives With Morpholine Moiety. Hacettepe University Journal of the Faculty of Pharmacy, 42 (2), 73–82. <https://doi.org/10.52794/hujpharm.1033112>
6. Safonov, A., Demianenko, D., Vashchik, Y., Larianovska, Y., Lytkin, D., Shcherbina, R. et al. (2022). Histological study of a corrective influence of sodium 2-((4-amino-5-(thiophen-2-ylmethyl)-4H-1,2,4-triazol-3-yl)thio)acetate on the state of rats liver under conditions of acute immobilization stress. Journal of Faculty of Pharmacy of Ankara University, 46 (2), 330–341. <https://doi.org/10.33483/jfpau.1012893>
7. Safonov, A. (2020). Method of synthesis novel N-substituted 2-((5-(thiophen-2-ylmethyl)-4H-1, 2, 4-triazol-3-yl) thio) acetohydrazides. Journal of Faculty of Pharmacy of Ankara University, 44 (2), 242–252. <https://doi.org/10.33483/jfpau.580011>
8. Safonov, A. (2020). Microwave synthesis of new 3-(alkylthio)-5-(thiophen-2-ylmethyl)-1,2,4-triazol-4-amines. Journal of Faculty of Pharmacy of Ankara University, 44 (1), 89–98. <https://doi.org/10.33483/jfpau.620599>
9. Varynskyi, B. A., Scherback, M. A., Kaplaushenko, A. G., Yurchenko, I. A. (2014). The study of thione-thiol tautomerism of 4-amino-5-(4-nitrophenyl)-2, 4-dihydro-3H-1, 2, 4-triazole-3-thione by HPLC-MS method. Journal of Chemical and Pharmaceutical Research, 6 (5), 1342–1350.
10. Hamid, K., Saha, M. R., Urmi, K. F., Habib, M. R., Rahman, M. M. (2010). Screening of different parts of the plant Pandanus odoratus for its antioxidant activity. International Journal of Applied Biology and Pharmaceutical Technology, 1 (3), 1364–1368.
11. Beyzaei, H., Ghanbari Kudeyani, M., Samareh Delarami, H., Aryan, R. (2020). Synthesis, antimicrobial and antioxidant evaluation, and molecular docking study of 4,5-disubstituted 1,2,4-triazole-3-thiones. Journal of Molecular Structure, 1215, 128273. <https://doi.org/10.1016/j.molstruc.2020.128273>
12. Taieb Brahimi, F., Belkhadem, F., Trari, B., Othman, A. A. (2020). Diazole and triazole derivatives of castor oil extract: synthesis, hypoglycemic effect, antioxidant potential and antimicrobial activity. Grasas y Aceites, 71 (4), 378. <https://doi.org/10.3989/gya.0342191>
13. Yildirim, N. (2020). Synthesis of Novel 3-(4-tert-Butylphenyl)-5-Cylopropyl-4H-1,2,4-Triazole Derivatives with Antioxidative and Antimicrobial Activities. Letters in Drug Design & Discovery, 17 (8), 954–964. <https://doi.org/10.2174/1570180817999200424073524>
14. Khokhar, D., Jadoun, S., Arif, R., Jabin, S., Budhiraja, V. (2021). Copolymerization of o-phenylenediamine and 3-Amino-5-methylthio-1H-1,2,4-triazole for tuned optoelectronic properties and its antioxidant studies. Journal of Molecular Structure, 1228, 129738. <https://doi.org/10.1016/j.molstruc.2020.129738>
15. Geetha, B. M., Brinda, K. N., Achar, G., Małecki, J. G., Alwarsamy, M., Betageri, V. S., Budagumpi, S. (2020). Coumarin incorporated 1,2,4-triazole derived silver(I) N-heterocyclic carbene complexes as efficient antioxidant and antihemolytic agents. Journal of Molecular Liquids, 301, 112352. <https://doi.org/10.1016/j.molliq.2019.112352>
16. Dovbnya, D. V., Kaplaushenko, A. H., Frolova, Y. S., Pruglo, E. S. (2022). Synthesis and antioxidant properties of new (2, 4-and 3, 4-dimethoxyphenyl)-1, 2, 4-triazoles. Pharmacia, 69 (1), 135–142.
17. Bulut, N., Kocyigit, U. M., Gecibesler, I. H., Dastan, T., Karci, H., Taslimi, P. et al. (2017). Synthesis of some novel pyridine compounds containing bis-1,2,4-triazole/thiosemicarbazide moiety and investigation of their antioxidant properties, carbonic anhydrase, and acetylcholinesterase enzymes inhibition profiles. Journal of Biochemical and Molecular Toxicology, 32 (1). <https://doi.org/10.1002/jbt.22006>
18. Pachuta-Stec, A. (2022). Antioxidant Activity of 1,2,4-Triazole and its Derivatives: A Mini-Review. Mini-Reviews in Medicinal Chemistry, 22 (7), 1081–1094. <https://doi.org/10.2174/1389557521666210401091802>
19. Barbuceanu, S.-F., Ilies, D., Saramet, G., Uivarosi, V., Draghici, C., Radulescu, V. (2014). Synthesis and Antioxidant Activity Evaluation of New Compounds from Hydrazinecarbothioamide and 1,2,4-Triazole Class Containing Diarylsulfone and 2,4-Difluorophenyl Moieties. International Journal of Molecular Sciences, 15 (6), 10908–10925. <https://doi.org/10.3390/ijms150610908>
20. Khan, I., Ali, S., Hameed, S., Rama, N. H., Hussain, M. T., Wadood, A. et al. (2010). Synthesis, antioxidant activities and urease inhibition of some new 1,2,4-triazole and 1,3,4-thiadiazole derivatives. European Journal of Medicinal Chemistry, 45 (11), 5200–5207. <https://doi.org/10.1016/j.ejmech.2010.08.034>

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