THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023), Issue 3, p.59-65

DOI: https://doi.org/10.56936/18290825-2023.17.3-59

# HYPOTENSIVE AND ANTIOXIDANT PROPERTIES OF GAMMA-HYDROXY ACID HYDRAZIDES

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*Received 15.12.2022; accepted for printing 5.06.2023*

***Abstract***

*A method has been proposed for the preparation of 4-hydroxybutanoic acid hydrazides for the first time. It has been established that the target products are obtained by the interaction of 2-substituted (H, alkyl, aralkyl, allyl, etc.)-4-substituted-4-butanolides with 85% aqueous solution hydrazine hydrate. Testing was carried out on white mongrel mice and reliably shown that the introduction of a hydroxypropyl residue into the composition of the synthesized hydrazides leads to new properties, namely hypotensive activity, not previously observed in compounds class of carboxylic acid hydrazides of various structures. The most active compounds have been selected and tested in rats and cats. It has been established that the lethal dose (lethal doses 50) of the proposed compounds ranges from 550-762 mg/kg and they exhibit superior activity compared to those used in the medical preparation "Dibazol".*

*In order to find new useful properties in a series of gamma-hydroxy acid hydrazides, their antioxidant features were studied by the method of competitive reactions. As a competitive acceptor, 4-nitroso-N,N-dimethylaniline was used.*

*According to the rate of discoloration of the last the reactivity of H radicals with respect to the studied compounds was determined. H radicals were initiated by photolysis of hydrogen peroxide (conc, 10-3 mol/l), under exposure to ultraviolet radiation, at a wavelength of 313 nm. Initiation rate H radicals were measured by the rate of change in the optical density of para-Nitroso-N,N-dimethyl aniline in distilled water and in the presence of the studied compounds.*

*As a result of the research, it was found that all compounds of this series have antioxidant properties, and some of them are comparable with renowned antioxidant vitamin C.*

***Keywords:*** *gamma-hydroxycarboxylic acid hydrazides, cyclic esters, competitive reactions, hypotensive activity, antioxidant activity.*

## Introduction

As is known, derivatives of organic acids, particularly hydrazides, are widely used as starting compounds in fine organic chemistry. The data on the useful properties of the latter are rather scanty. Recently it has been shown that some derivatives of the naproxen series (S) that are acetohydrazides of various structures have antitumor activity against cell lines of human prostate carcinoma [*Han M et al., 2018*]. Some hydrazides of substituted benzoic acids also exhibit a similar property

***Cite This Article as:***

*Ghochikyan T.V., Martiryan A.I., Tadevosyan L.G., Petrosyan I.A., Galstyan A.S., Samvelyan M.A.* (2023). Hypotensive And Antioxidant Properties Of Gamma-Hydroxy Acid Hydrazides; The New Armenian Medical Journal, vol.17(3), p 59-65; https://doi.org/10.56936/18290825-2023.17.3-59

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[*Arjun H et al., 2019*]. It was found that a number of hydrazonohydrazides showed antioxidant and antimicrobial activity [*Afsah E et al., 2019*]. In addition to the aforesaid, hydrazides of carboxylic acids are successfully used for the synthesis of heterocyclic compounds, in particular, oxadiazoles and 1,2,4-triazoles. The role of hydrazides in the synthesis of the latter is especially important, since numerous representatives of 1,2,4-triazoles are widely used in practical medicine – Voriconazole, Triazolam, Fluconazole, Itraconazole, Furaciline, Alprazolam, Estazolame and others.

The uniqueness of these compounds lies in the fact they are not found in natural raw material, easily obtained and have a wide range of application. The development of new methods for producing 1,2,4-triazolesis still under way [*Khan T et al., 2019; Dolzhenko A et al., 2007; Gupta M, 2007; Song Y.-H, Young S, 2010*]. Recent studies show that the biological properties of compounds are increasing from year to year. It was shown that various derivatives of 1,2,4-triazoles possessed antimicrobial [*Koparir M et al., 2013*], antitumor [*Li YH et al., 2017; Zhang G, Hu Y, 2007*], antibacterial [*Gao F et al., 2019; Karnik A et al., 2006; Arafa W, 2010; Puthiyapurayil P et al., 2011; Zeydi M et al., 2017*], fungicidal [*Jian F et al., 2006; Song HX, Shi DQ, 2014*] activities. For the first time it has been found that at a certain set of substituents in a molecule, the triazole derivatives show affinity for the human adenosine A3 receptor [*Federico S et al., 2018*] and exhibit insecticidal properties against T cinnabarinus [*Luo Y et al., 2007*]. As can be seen from the data presented, studies in the field of various derivatives of 1,2,4-triazoles and their starting compounds are relevant and urgent.

Searches of literature data have shown that there are no data on *gamma*-hydroxy acid hydrazides. The interest in these compounds can be explained by the fact that the first representative of the homologous series – *gamma*-hydroxybutyric acid plays a crucial role in the human central nervous system, and the sodium salt of this acid is widely used in anesthesiology and ophthalmology. Based on the foregoing, it can be assumed that the introduction of the gamma-hydroxybutyric acid residue into the molecules of the biologically active substance can lead to manifestation of new useful properties in this class of compounds.

The lack of data on the hydrazides mentioned can most likely be explained by the absence of a raw material base since γ-hydroxy acids and their esters are unstable and gamma-hydroxybutyric acid even in aqueous solution is in equilibrium with a cyclic form.

### *RESULTS AND DISCUSSION*

Dihydrofuran-2(3H)-one (butyrolactone or butan-4-olide) is a cyclic ester of *gamma*-hydroxybutyric acid. Similarly, but under harsher conditions, other representatives of *gamma*-hydroxycarboxylic acids undergo cyclization to form dihydrofuran-2(3H)-ones of various structures. We previously synthesized a series of 2,4,4-trisubstituted-4-butanolides (**1a-k**) (fig.1) [*Kochikyan T et al., 2003; Haroutunyan V et al., 2000*].

Compounds **2a-k** [*Ghochikyan T et al., 2023*] were subjected to preliminary biological screening and it was established that some of those hydrazides showed hypotensive and antioxidant activities. The most promising compounds were studied in rats and cats. Specifically, the effect of com-

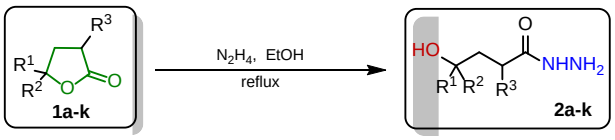


***FIGURE 1.*** *Schem synthesis of compaunds 2a-k radicals of compaunds is show in table 1*

***TABLE 1***

Yields of compaunds 2a-k

| Comp. # | $R^1$ | $R^2$ | $R^3$ | Yield, (%) |
|---|---|---|---|---|
| **2a** | $PrOCH_2$ | H | Et | 93 |
| **2b** | $^iBuOCH_2$ | H | H | 90 |
| **2c** | $^iBuOCH_2$ | H | Bu | 85 |
| **2d** | $AmOCH_2$ | H | H | 89 |
| **2e** | Am | H | H | 85 |
| **2f** | $PrOCH_2$ | H | Bu | 83 |
| **2g** | $^iBuOCH_2$ | H | Bn | 87 |
| **2h** | $^iAmOCH_2$ | H | Bn | 91 |
| **2i** | Am | H | All | 94 |
| **2j** | Me | Me | Bu | 86 |
| **2k** | Me | H | $^i$Am | 80 |

pounds **2b** and **2d** on the level of systemic blood pressure (SBP) was studied in the usual way in experiments on anesthetized (Nembutal 50 *mg/kg*) animals. In a separate series of experiments on the anesthetized cats, the effect of substances on the central hemodynamics was studied; SBP was recorded in the common carotid artery. Minute blood volume was studied by thermodelation. The heart rate (HR) was calculated by the electrocardiogram recorded in the 2nd standard lead. The total peripheral resistance (TPR), stroke volume (SV) and the left ventricle (LVF) work were determined by calculation.

Acute toxicity was studied in experiments on white mice with intraperitoneal administration according to the method of Miller and Teitner. Acute toxicity of **4b** was 762 *mg/kg*, and that of **2d** – 550 *mg/kg*.

The test substances were administered intravenously in an aqueous solution at doses of 10, 20, 50 and 100 *mg/kg*.

Compound **2b** at doses of 20 and 50 mg/kg reduced SBP moderately and briefly, at a dose of 100 *mg/kg* more pronounced hypotension was observed (Table 2). Compound **2d** significantly exceeded compound **2b** in hypotensive activity. So already a dose of 10 *mg/kg* caused a distinct decrease in SBP. Increase of the dose to 20 and 50 *mg/kg* led to a significant strengthening of the hypotensive effect (Table 2).

In experiments on anesthetized cats, compound **2d** caused a less hypotensive effect than in experiments on rats. This can probably be explained by unequal species sensitivity to this substance. The decrease in SBP after administration of **2d** in experiments on cats is due to a decrease in TPR, while multivesicular body (MVB) increased slightly (Table 3). Heart rate and LVF after administration of **2d** at doses of 25 and 50 *mg/kg* were practically unchanged.

Thus, compounds **2b** and **2d** have pronounced hypotensive activity being low toxic at that (Table 4).

In order to find new useful properties in a series of *gamma*-hydroxy acid hydrazides, their antioxi-

***Table 2***

The effect of compounds **2b** and **2d** on the level of SBP (experiments on rats)

| Comp. # | Dose *mg/kg* | Number of experiences | Changes in SBP* after administration of the substance (in% to the initial) after a time (*min*) | | | | |
|---|---|---|---|---|---|---|---|
| | | | 5 | 15 | 30 | 45 | 60 |
| **2b** | 20 | 5 | -21±6** | -13±5 | -8±5 | -3±4 | -1±4 |
| | 50 | 5 | -18±5** | -9±3 | -8±4 | -7±2 | -5±2 |
| | 100 | 5 | -26±6** | -16±7 | -14±5 | -13±5 | -11±5 |
| **2d** | 20 | 5 | -17±4** | -13±6 | -9±3 | -3±3 | -3±3 |
| | 50 | 5 | -25±7** | -14±4** | -12±4 | -10±4 | -6±2 |
| | 100 | 5 | -35±8** | -27±8** | -19±6** | -18±6** | -11±5 |

***Notes:*** ** – "-" decrease, "+" increase SBP, ** – changes SBP statistically reliable*

***Table 3***

The effect of compound **2d** on the level of SBP (experiments on cats)

| Dose *(mg/kg)* Time from start (*min*) | Changes in SBP* after administration of the substance (in % to the initial) after a time (*min*) | | | | | |
|---|---|---|---|---|---|---|
| | SBP | HR | MVB | TPR | SV | LVF |
| 25 ID | 170±20.2 | 148±12.2 | 686±42.6 | 15156±139.8 | 12.3±2.3 | 14103±96.2 |
| 5 | -1.2±0.4 | -1.9±3.9 | -38.7±6.4 | +63.3±6.4 | +38.4±4.3 | -39.0±9.2 |
| 15 | -1.2±0.4 | -1.9±4.2 | -29.9±6.8 | +40.65±5.8 | -29.5±4.8 | -39.0±9.2 |
| 30 | -1.8±0.6 | -3.6±3.8 | -17.6±8.9 | +31.9±12.4 | -16.2±3.6 | -17.3±6.4 |
| 45 | -1.9±0.6 | -4.6±3.6 | -15.8±7.4 | +19.6±7.9 | -10.1±4.2 | -12.2±6.9 |
| 60 | -2.0±0.5 | -4.6±3.4 | +24.8±12.6 | -16.4±9.6 | +12.8±6.4 | +11.8±6.2 |
| 50 ID | 140±20.6 | 140±25.3 | 292±42.6 | 31169±83.4 | 2.3±2.3 | 3577±64.3 |
| 5 | -6.4±3.6 | -0.8±1.2 | +4.1±3.8 | -9.7±4.3 | +15.3±6.2 | +3.7±3.5 |
| 15 | -14.6±4.9 | -0.8±1.2 | +0.5±3.2 | -16.8±3.7 | +6.9±2.4 | -18.3±6.8 |
| 30 | -14.6±4.9 | -0.4±0.2 | +6.3±2.4 | -21.4±6.2 | +3.4±1.8 | -1.5±0.9 |
| 45 | -17.5±5.3 | 0 | +16.2±4.6 | -29.5±4.3 | +13.9±3.3 | -0.9±0.2 |
| 60 | -17.6±5.4 | 0 | +12.4±6.2 | -38.0±5.5 | +12.5±3.8 | +6.9±4.3 |

*Notes: * – "-" decrease, "+" increase, SBP – systemic blood pressure, HR - Heart rate, MVB – multivesicular body, TPR – total peripheral resistance, SV – stroke volume, LVF – left ventricle, ID - Initial data*

***TABLE 4***

Comparative effect of compound **2b** (experiments on cats) (in comparable doses of 1/10 of $LD_{50}$)

| Dose *(mg/kg)* | Time from start(*min*) | Changes in SBP* after administration of the substance (in % to the initial) after a time (*min*) | | | | | |
|---|---|---|---|---|---|---|---|
| | | SBP | HR | MVB | TPR | SV | LVF |
| Compound **2b** | | | | | | | |
| 60 | ID | 125±15.3 | 200±13.3 | 184±58 | 50497±320 | 1.2±0.3 | 2931±305 |
| | 5 | -4.4±1.3 | -1.2±4.3 | -6.7±7.3 | +30.5±12.3 | -7.2±5.8 | -9.5±1.5 |
| | 15 | -4.4±1.3 | -5.5±6.1 | -8.5±3.5 | +40.2±8.7 | -12.6±3.4 | -10.5±4.2 |
| | 30 | -8.7±2.9 | -9.9±9.0 | -22.0±9.8 | +55.8±14.6 | -18.7±9.8 | -18.7±9.8 |
| | 45 | -8.7±2.9 | -9.9±9.0 | -22.0±9.8 | +55.8±14.6 | -18.7±9.8 | -18.7±9.8 |
| | 60 | -12.0±4.0 | -9.9±9.0 | -30.6±12.4 | +50.3±6.7 | -18.7±6.4 | -20.5±7.5 |
| *Dibazole* | | | | | | | |
| 60 | ID | 140±4.6 | 200±18.5 | 328±12.6 | 32012±159.8 | 2.4±0.7 | 0.7±0.1 |
| | 5 | -21.4±6.8 | -10.6±8.3 | -15.2±3.8 | -27.3±6.2 | -21.9±3.6 | -30.9±5.6 |
| | 15 | -7.8±2.4 | -7.1±8.1 | -23.8±1.6 | -13.8±3.2 | -29.8±5.4 | -10.4±8.7 |
| | 30 | -4.2±3.8 | -1.3±0.9 | -34.3±6.5 | -1.9±1.8 | -59.6±8.7 | -12.1±8.7 |
| | 45 | -1.5±2.2 | +0.7±1.2 | -19.4±5.4 | 36.7±6.4 | -27.6±10. | -4.3±3.2 |
| | 60 | +5.1±4.3 | +2.4±1.3 | -17.4±3.6 | -63.5±9.8 | +21.3±9.7 | +9.9±7.8 |

***NOTES:*** ** – "-" decrease, "+" increase, SBP – systemic blood pressure, HR - Heart rate, MVB –* multivesicular body, *TPR – total peripheral resistance, SV – stroke volume, LVF – left ventricle, ID* - Initial data

dant features were studied by the method of competitive reactions. As a competitive acceptor, 4-nitroso-N,N-dimethylaniline (PNDMA) was used, by the rate of discoloration of which the reactivity of H radicals in relation to compounds **2a-k** was determined. H was initiated by the photolysis of $H_2O_2$($10^{-3}$*mol/l*) under the influence of UV radiation at λ = 313 *nm*. The rate of H initiation was measured by the rate of change in the optical density of PNDMA in distilled water (**2a-k**).

The kinetic data of the effect of compounds of various concentrations on the optical density of PNDMA depending on the irradiation time are given below (Fig. 2).

Based on experimental data (Fig. 2,3) according to [*Bielski B et al., 1985; Ernestova L, 1988; Simonsen M et al., 2010; Galstyan A et al., 2018*] the rate constants were calculated by equation (1):

$$k_{OH+P} = 1.25\times10^{10}\times \frac{[PNDMA]}{[P]}\times[\frac{W_1}{W_2}-1] \quad (\frac{l}{mol\times sec})$$

where $1.25\times10^{10}$ is the rate constant of the interaction of H radicals with PNDMA, [P] is the concentration of compounds **2a-k**, $W_1$ and $W_2$ are the rates of PNDMA discoloration in distilled water and in the presence of the studied compounds, respectively.

The following data for the reaction rate constant of interaction of H radicals and the test substance were obtained (Table 5).

## *CONCLUSION*

For the first time, a method for producing 4-hydroxybutanoic acid hydrazides is proposed. It was found that the target products are obtained on the basis of 2-substituted (H, alkyl, aralkyl, allyl, etc.) – 4,4-disubstituted-4-butanolides, which undergo hy-

***TABLE 5***

The reaction rate constant of the interaction of H radicals and the test compounds were obtained

| Compound # | Reaction rate constant for interaction of H radicals + test compound |
|---|---|
| **2a** | $3.92\times10^8$ |
| **2b** | $4.82\times10^8$ |
| **2c** | $4.86\times10^8$ |
| **2d** | $4.95\times10^8$ |
| **2e** | $1.75\times10^8$ |
| **2f** | $5.25\times10^8$ |
| **2g** | $6.2\times10^8$ |
| **2h** | $2.7\times10^8$ |
| **2i** | $4.0\times10^8$ |
| **2j** | $1.71\times10^8$ |
| **2k** | $0.965\times10^8$ |
| Ascorbic acid (control) | $9.45\times10^9$ |

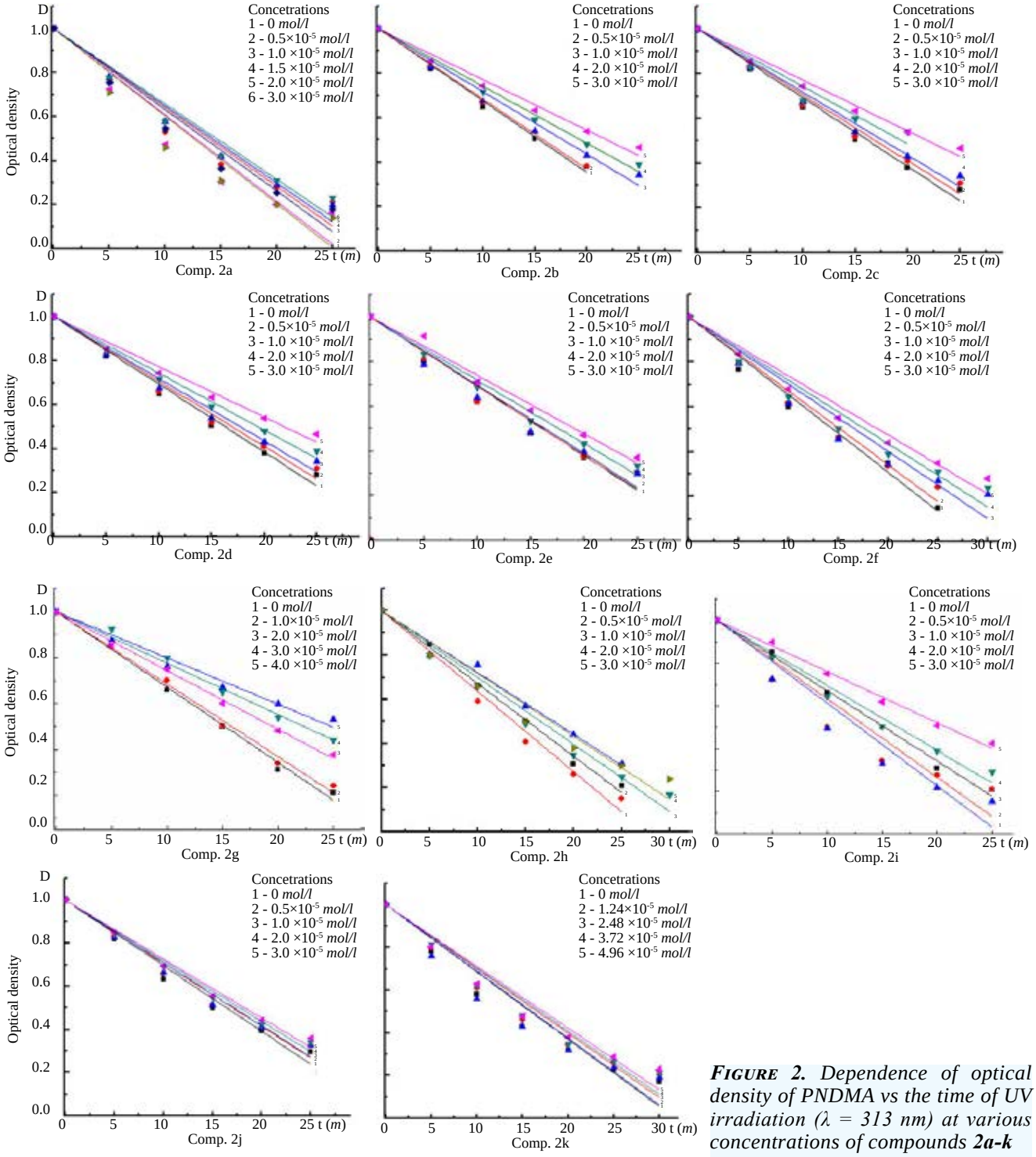


***Figure 2.*** *Dependence of optical density of PNDMA vs the time of UV irradiation (λ = 313 nm) at various concentrations of compounds* ***2a-k***

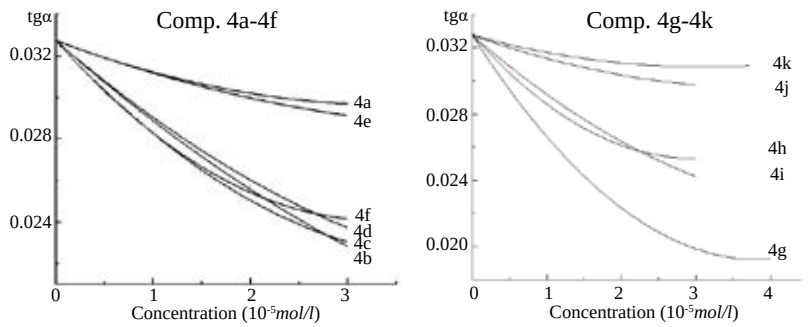


***Figure 3.*** *The dependence of the rate of PNDMA decolouration (in relative units) on concentration*

drazinolysis with 85% solution of hydrazine hydrate.

Preliminary screening established that newly synthesized compounds exhibited hypotensive activity. The selected, most active compounds were tested on rats and cats. It has been reliably established that the proposed compounds exceed in activity the drug *Dibazole* used in medical practice.

By the method of competitive reactions, it has been found that the proposed compounds also exhibit significant antioxidant activity.

**Experimental Section**

The most promising compounds were studied in rats and cats. Specifically, the effect of compounds **4b** and **4d** (fig.4) on the level of systemic blood pressure was studied in the usual way in experiments on anesthetized (Nembutal 50 *mg/kg*) animals. Ina separate series of experiments on the anesthetized cats, the effect of substances on the central hemodynamics was studied; SBP was recorded in the common carotid artery. Minute blood volume was studied by thermodelation. The heart rate was calculated by the electrocardiogram recorded in the 2nd standard lead. The total peripheral resistance, stroke volume and the left ventricle work were determined by calculation.

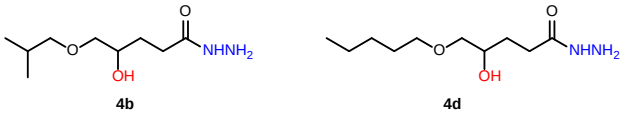


***FIGURE 4.*** *Strakcher of compaunds 4b and 4d*

Acute toxicity was studied in experiments on white mice with intraperitoneal administration according to the method of Miller and Teitner. Acute toxicity of **2b** was 762 *mg/kg*, and that of **2d** – 550 *mg/kg*.

The test substances were administered intravenously in an aqueous solution at doses of 10, 20, 50 and 100 *mg/kg*.

## *REFERENCES*


1. *Afsah EM, Abdel-Galil E, Youssef I, Elsaedy YH (2019).* Synthesis and Biological Activity of Novel Hydrazide-Hydrazones Incorporating Piperidine and Piperazine Moieties and Related Mannich Bases. American Journal of Chemistry and Materials Science. 6: 58-65
2. *Arafa WAA (2010).* Preparation and evaluation of antibacterial activity of some new 1,2,4-triazole derivatives. J. Heter. Chem. 47: 1109-1115 https://doi.org/10.1002/jhet.431.
3. *Arjun HA, Elancheran R, Manikandan N, Lakshmithendral K, Ramanathan M., et al (2019).* Front. Chem. 7: 474 https://doi.org/10.3389/fchem.2019.00474
4. *Bielski BHJ, Cabelli DE, Arudi RL, Ross AB (1985).* Reactivity of HO2/O−2 Radicals in Aqueous Solution. J. Phys. Chem. Ref. Data. 14: 1041-1100 https://doi.org/10.1063/1.555739.
5. *Dolzhenko AV, Dolzhenko AV, Chui WK (2007).* Practical synthesis of regioisomeric 5(7)-amino-6,7(4,5)-dihydro[1,2,4]triazolo[1,5-a][1,3,5]triazines. Tetrahedron. 63: 12888-12895 https://doi.org/10.1016/j.tet.2007.10.046
6. *Ernestova LS (1988).* Water Quality Indicators. In book "Ecological chemistry of the aquatic environment", M. 256-277
7. *Federico S, Margiotta E, Salmaso V, Pastorin G, Kachler S., et al (2018).* [1,2,4]Triazolo[1,5-c]pyrimidines as adenosine receptor antagonists: Modifications at the 8 position to reach selectivity towards A3 adenosine receptor subtype. Eur. J. Med. Chem. 157: 837-851 https://doi.org/10.1016/j.ejmech.2018.08.042
8. *Galstyan AS, Martiryan AI, Grigoryan KR, Ghazaryan AG, Samvelyan MA., et al (2018).* Synthesis of Carvone-Derived 1,2,3-Triazoles Study of Their Antioxidant Properties and Interaction with Bovine Serum Albumin. Molecules. 23: 2991 https://doi.org/10.3390/molecules23112991
9. *Gao F, Wang T, Xiao J, Huang G (2019).* Antibacterial activity study of 1,2,4-triazole derivatives. Eur. J. Med. Chem. 173: 274-281 https://doi.org/10.1016/j.ejmech.2019.04.043
10. *Ghochikyan TV, Galstyan AS, Samvelyan MA (2003).* A new method for the preparation of hydrazides of substituted gamma-hydroxybutanoic acids. Proc. YSU B: Chem. Biol. Sci. 57: 68-76 https://doi.org/10.46991/PYSU:B/2023.57.2.068
11. *Gupta M (2007).* Synthesis and antifungal activity of novel 3,6-diaryl-5H-[1,2,4]triazolo[4,3-b][1,2,4]triazepines. J. Het. Chem. 44: 1023-1027 https://doi.org/10.1002/jhet.5570440508.

12. *Han MI, Cumaoglu A, Kügükgüzel SG (2018).* Synthesis and characterization of 1,2,4-triazole containing hydrazide-hydrazones derived from (S)-Naproxen as anticancer agents. Marmara Pharm. J. 22: 559-569 http://dx.doi.org/10.12991/jrp.2018.98

13. *Haroutunyan VS, Kochikyan TV, Haroutunyan EV, Avetisyan AA (2000).* [One-stage method for obtaining 2-carbethoxy-2,4-disubstituted-4-pentanolids] [Published in Russian]. Chemical Journal of Armenia.53: 121-122.

14. *Jian F, Xiao H, Zhu Ch, Xu L (2006).* Synthesis, structure and biological activities of [α-(alkylcarbonyl)-2-(1,2,4-triazol-1-yl)] ethyl-N,N-dialkydithiocarbamate derivatives. J. Heter. Chem. 43: 925-929 https://doi.org/10.1002/jhet.5570430417.

15. *Karnik AV, Malviya NJ, Kulkarni AM, Jaimini D, Jadhav BL (2006).* Synthesis and antibacterial studies of 6-aryl-2,2a-dihydronaphtho-[2′,1′-5,6]pyrano[4,3-e][1,2,4] triazolo[3,4-b][1,3,4]thiadiazine and its derivatives. J. Heter. Chem. 43: 489-493 https://doi.org/10.1002/jhet.5570430236.

16. *Khan T, Yadav R, Gound SS (2018).* An Efficient Synthesis and Antibacterial Activity of Some Novel 2-Azetidinone Derivatives of 4H-1,2,4-Triazoles Under Mild Conditions. J. Het. Chem. 55: 1042-1047 https://doi.org/10.1002/jhet.3136

17. *Kochikyan TV, Samvelyan MA, Arutyunyan VS, Avetisyan AA (2003).* Synthesis and Some Transformations of Ethyl 5-Alkoxymethyl-3-(2-methyl-3-oxobutyl)-2-oxotetrahydrofuran-3-carboxylates. Russ. J. Org. Chem. 39: 1329-1333 https://doi.org/10.1023/B:RUJO.0000010223.97769.33

18. *Koparir M, Orek C, Parlak AE, Söylemez A, Koparir P., et al (2013).* Synthesis and biological activities of some novel aminomethyl derivatives of 4-substituted-5-(2-thienyl)-2,4-dihydro-3H-1,2,4-triazole-3-thiones. Eur. J. Med. Chem. 63: 340-346 https://doi.org/10.1016/j.ejmech.2013.02.025

19. *Li YH, Zhang B, Yang HK, Li Q, Diao PCh., et al (2017).* Eur. J. Med. Chem. 125: 1098-1106 https://doi.org/10.1016/j.ejmech.2016.10.051

20. *Luo YP, Lin L, Yang GF (2007).* Design and synthesis of diheterocyclic compounds containing tetrazolinone and 1,2,4-triazole. J. Heter. Chem. 44: 937-943 https://doi.org/10.1002/jhet.5570440433

21. *Puthiyapurayil P, Poojary B, Kumar S, Hunnur R (2011).* Synthesis and biological activities of a novel series of 3,6-disubstituted-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles containing gem-dimethylbenzyl moiety. J. Heter. Chem. 48: 998-1005 https://doi.org/10.1002/jhet.674.

22. *Simonsen ME, Muff J, Bennedsen LR, Kowalski KP, Søgaard EG (2010).* Photocatalytic bleaching of p-nitrosodimethylaniline and a comparison to the performance of other AOP technologies. Journal of Photochemistry and Photobiology A: Chemistry. 216: 244-249 https://doi.org/10.1016/j.jphotochem.2010.07.008

23. *Song HX, Shi DQ (2014).* Synthesis and Fungicidal Activity of (E)-α-(Methoxyimino)benzene-acetate Derivatives Containing 1,2,4-Triazole Schiff Base Side Chain. J. Heter. Chem. 51: 1345-1348 https://doi.org/10.1002/jhet.1795.

24. *Song YH, Young SH (2010).* Synthesis of new sulfur-linked 1,2,4-triazolothienopyrimidine and 1,2,4-triazolopyrazolopyrimidine derivatives containing fused heterocyclic pyrimidines. J. Het. Chem. 47: 1183-1187 https://doi.org/10.1002/jhet.461.

25. *Zeydi MM, Montazeri N, Fouladi M (2017).* Synthesis and Evaluation of Novel [1,2,4]Triazolo-[1,5-c]quinazoline Derivatives as Antibacterial Agents. J. Heter. Chem. 54: 3549-3553 https://doi.org/10.1002/jhet.2979.

26. *Zhang G, Hu Y (2007).* Synthesis and antitumor activities of 2-(substituted)phenyl-1,2,4-triazolo[1,5-a]pyridines. J Heter Chem. 44: 919-922 https://doi.org/10.1002/jhet.5570440428

THE NEW ARMENIAN MEDICAL JOURNAL
Volume17 (2023). Issue 3

## CONTENTS

# THE NEW ARMENIAN MEDICAL JOURNAL

Volume17 (2023). Issue 3



The Journal is founded by
Yerevan State Medical
University after M. Heratsi.

**Rector of YSMU**

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**Copy editor: Tatevik R. Movsisyan**

Printed in "LAS Print" LLC
Director: Suren A. Simonyan
Armenia, 0023,Yerevan,
Acharyan St. 44 Bulding,
Phone: (+374 10) 62 76 12,
E-mail: las.print@yahoo.com