Synthesis, antimicrobial and antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

To select a molecule that could become a promising pharmacological agent, chemists use already-known heterocyclic bases by adding pharmacologically active groups. One such heterocyclic system is 1,2,4-triazole base, on the basis of which a huge number of biologically active compounds have already been found. It is known that 1,2,4-triazole derivatives show a fairly high antimicrobial and antifungal effect while remaining low-toxic compounds and 5-alkylthio-1,2,4-triazoles exhibit antimicrobial and antifungal activity. Based on the literature search, it can be concluded that 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles are insufficiently studied.

The aim of the work was to synthesize and investigate antimicrobial and antifungal activity among 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles.

Materials and methods. It was used 5-(2-bromophenyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol as a starting substance, which was synthesized by previously described techniques. 3-(2-Bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles were obtained by alkylation of the starting thiol with halohenalkanes (according to the first method) and the addition of hydrochloric acid in an alcoholic medium, then subsequent heating in microwave synthesis system (by the second method). To study the antimicrobial and antifungal activity of the newly synthesized 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles, the method of serial dilutions was used according to guidelines.

Results. 3-(2-Bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles were obtained by two methods: a) an equivalent amount of halohenalkane was added to 5-(2-bromophenyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (I) (solvent – KOH pre-dissolved in 2-propanol). Boiled to pH = 7; b) 5-(2-bromophenyl)-4-phenyl-4H-1,2,4-triazole-3-thiol (I) (solvent – methyl or 1-propyl alcohol and 10 drops of HCl) was heated in Milestone Flexi Wave microwave synthesis system. Reaction conditions: The mixture was heated for 45 minutes at a temperature of 150 °C, a pressure 14.4 bar, ΔMW ≈ 200 W. The completeness of the reaction was determined using a gas chromatograph Agilent 7890B with a mass spectrometric detector 5977B. Antimicrobial and antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles (6 new compounds) was investigated. The most active compound with antifungal and antimicrobial effect was IIi. Substances IIa–IIe had moderate antimicrobial effect.

Conclusions. New 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles were synthesized by two methods. The antimicrobial and antifungal activity was investigated for the obtained compounds. The most active compound was 3-(2-bromophenyl)-5-(decylthio)-4-phenyl-4H-1,2,4-triazole (IIi). Some conclusions were drawn regarding the dependence of "structure – antimicrobial and antifungal effect": the antimicrobial effect increased with the length of the carbon radical; changing the decyl radical to another one in the molecule 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazole reduced antifungal activity.

Key words: organic synthesis, antimicrobial activity, antifungal activity, 1,2,4-triazole, heterocyclic compounds.

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Синтез, протимікробна та протигрибкова активність 3-(2-бромфеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазолів

А. А. Сафонов, О. І. Панасенко

Для визначення молекули, що могла б стати перспективним фармакологічним агентом, хіміки використовують уже відомі гетероциклічні основи, додаючи до них фармакологічно активні групи. Одна з таких гетероциклічних систем – 1,2,4-тріазолова основа, на базі якої вже одержали величезну кількість біологічно активних сполук. Відомо, що похідні 1,2,4-тріазолу характеризуються доволі сильним протимікробним і протигрибковим ефектами, залишаючись при цьому малотоксичними сполуками. Є дані щодо протимікробної та протигрибкової активності 5-алкілтіо-1,2,4-тріазолів. Ґрунтуючись на результатах літературного пошуку, зробили висновок, що 3-(2-бромфеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазоли вивчено недостатньо.

Мета роботи – синтез і дослідження протимікробної та протигрибкової активності нових 3-(2-бромфеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазолів.

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Key words: organic synthesis, antimicrobial activity, antifungal activity, 1,2,4-triazole, heterocyclic compounds.

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Матеріали та методи. Як вихідну речовину застосували 5-(2-бромфеніл)-4-феніл-4*H*-1,2,4-тріазол-3-тіол, який синтезували за попередньо наведеними методиками. 3-(2-Бромфеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазоли одержали шляхом алкілування вихідного тіолу галогеналканами (за першим методом) і додаванням хлороводневої кислоти в спиртовому середовищі з нагріванням надалі в системі мікрохвильового синтезу (за другим методом). Для вивчення протимікробної та протигрибкової активностей нових синтезованих 3-(2-бромофеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазолів використали метод серійних розведень згідно з рекомендаціями.

Результати. 3-(2-Бромофеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазоли отримували двома методами: а) еквівалентну кількість галогеналкану додавали до 5-(2-бромофеніл)-4-феніл-4*H*-1,2,4-тріазол-3-тіолу (I) (розчинник – 2-пропанол, у якому попередньо розчинений KOH); кип'ятили до pH = 7; б) 5-(2-бромофеніл)-4-феніл-4*H*-1,2,4-тріазол-3-тіол (I) (розчинник – метанол або 1-пропанол і 10 крапель HCl) нагрівали в системі мікрохвильового синтезу Milestone Flexi Wave; умови реакції: час – 45 хвилин, температура – 150 °C, тиск – 14,4 бар, ΔMW ≈ 200 Вт. Повноту реакції визначали за допомогою газового хроматографа Agilent 7890B з мас-спектрометричним детектором 5977B. Дослідили протимікробну та протигрибкову активності 3-(2-бромофеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазолів. Найактивніша сполука з протигрибковим і протимікробним ефектами – IIi. Речовини IIa–IIe мають помірну протимікробну дію.

Висновки. Нові 3-(2-бромофеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазоли синтезовано двома методами. Оцінювали протимікробну та протигрибкову активності одержаних сполук. Найактивніша – 3-(2-бромофеніл)-5-(децилтіо)-4-феніл-4*H*-1,2,4-тріазол (IIi). Сформулювали висновки щодо залежності «структура – протимікробна та протигрибкова дії»: зміна децильного радикала на пентильний у молекулі 3-(2-бромофеніл)-5-(алкілтіо)-4-феніл-4*H*-1,2,4-тріазолу зменшує протигрибкову активність; антимікробний ефект посилюється зі збільшенням довжини вуглецевого радикала.

Ключові слова: органічний синтез, протимікробна активність, протигрибкова активність, 1,2,4-тріазол, гетероциклічні сполуки.

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Along with the development of new diseases, the search for biologically active substances [1–3] with low toxicity, which in the future could become promising drugs is an urgent task for many scientists. A large number of people take part in the creation of a new drug. These are synthetic chemists, biologists, pharmacologists, and other scientists.

To select a molecule that could become a promising pharmacological agent, chemists use already-known heterocyclic bases by adding pharmacologically active groups [4,5]. One such heterocyclic system is 1,2,4-triazole base, on the basis of which a huge number of biologically active compounds have already been found [6].

It is known that 1,2,4-triazole derivatives show a fairly high antimicrobial and antifungal effect [7,8] while remaining low-toxic compounds [9] and 5-alkylthio-1,2,4-triazoles exhibit antimicrobial and antifungal activity [10].

Based on the literature search, it can be concluded that 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles are insufficiently studied.

Aim

That's why the aim of the work was to synthesize and investigate antimicrobial and antifungal activity among 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles.

Materials and methods

It was used 5-(2-bromophenyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol as a starting substance, which was synthesized by previously described techniques [11].

The chloride acid (35 %), iodomethane (99 %), 1-bromopropane (99 %), 1-bromobutane (99 %), 1-bromopentane (99 %), 1-bromohexane (99 %), 1-bromoheptane (99 %), 1-bromoctane (99 %), 1-bromononane (99 %), 1-bromodecane (99 %), 2-propanol (99,5 %), 1-propanol (anhydrous, 99,7 %) and methanol (99,5 %) were obtained from SIGMA-ALDRICH (Germany).

Milestone Flexi Wave microwave synthesis system (Italy) (technical specifications: rotor SK-15, minimum volume – 10 ml, maximum volume – 100 ml, maximum temperature – 300 °C, maximum working pressure – 100 bar, maximum shutter speed 220 °C – 30 min).

The methods presented in the State Pharmacopoeia of Ukraine (2.2.14) were used to study the physical and chemical properties of the synthesized compounds.

The automatic device to determine the melting point Opti-Melt Stanford Research Systems MPA100 (US production) was used to determine the melting temperature.

The elemental composition of the compounds is installed on the elemental analyzer Elementar Vario L cube (CHNS) (Analysensysteme GmbH, Germany) (standard is sulfanilamide).

The gas chromatograph Agilent 7890B with a 5977B mass spectrometry detector (US production) was used to control the completeness of the reactions and the individuality of new compounds.

^{1}H NMR spectra were recorded on a spectrometer "Mercury 400" (Umatek International Inc.), as solvent DMSO-D_6 was used, internal standard – tetramethylsilane and deciphered using a computer program ADVASP 143.

To study the antimicrobial and antifungal activity of the newly synthesized 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles, the method of serial dilutions was used according to guidelines [12]. The synthesized compounds were dissolved in dimethylsulfoxide.

Staphylococcus aureus ATCC 25923, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922, *Candida albicans* ATCC 885-653 were used as set of standard test strains. Comparison drugs Chlorhexidine-Zdorovye® (Ukraine) and Fluconazole-Darnitsa® (Ukraine) were used to determine the activity values.

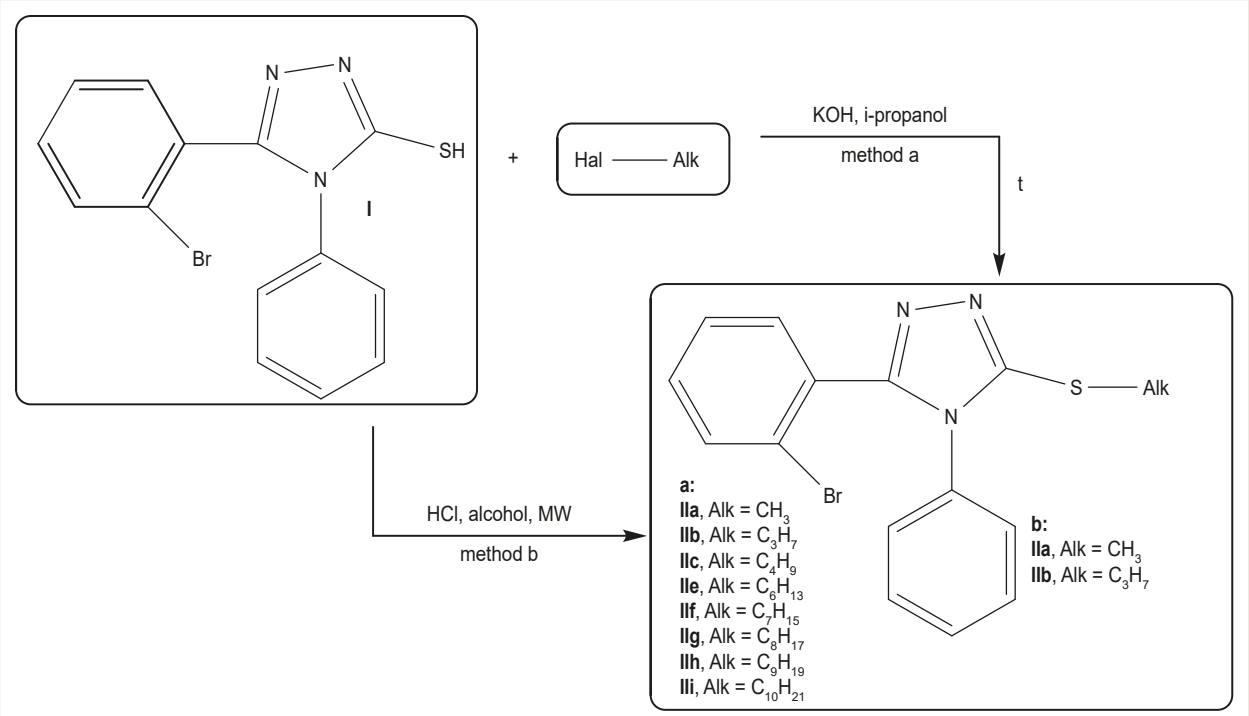


Fig. 1. Synthesis of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles.

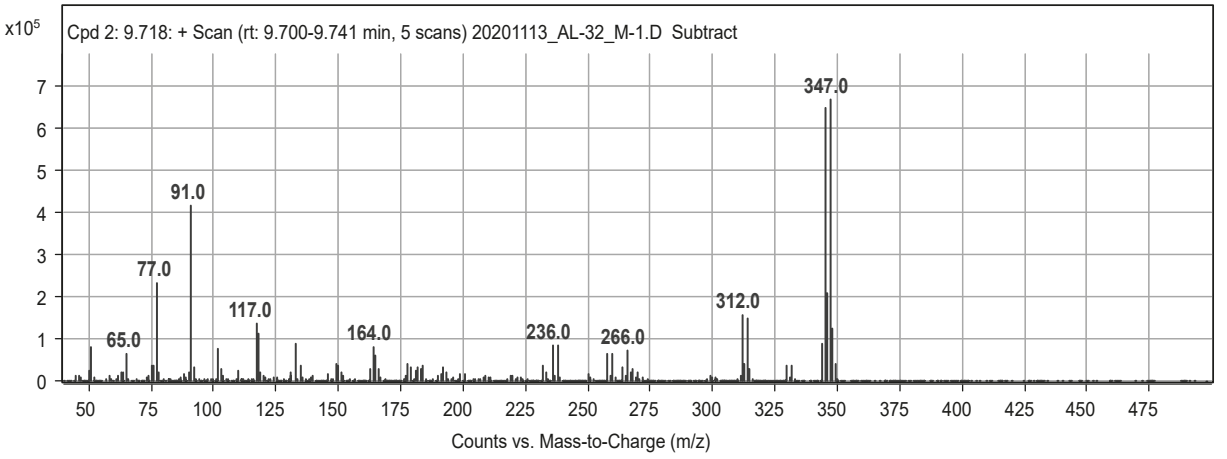


Fig. 2. Mass spectrum of 3-(2-bromophenyl)-5-(methylthio)-4-phenyl-4*H*-1,2,4-triazole (IIa).

Results

Synthesis of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles. 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles were obtained by two methods:

a) In a round bottom flask equipped with a reflux condenser to 5-(2-bromophenyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (I) was added an equivalent amount of KOH pre-dissolved in 2-propanol, heated to dissolving the precipitate and adding an equivalent amount of halohenalkane (iodomethane, 1-bromopropane, 1-bromobutane, 1-bromopentane, 1-bromohexane, 1-bromoheptane, 1-bromoctane, 1-bromononane, 1-bromodecane). Boiled to pH = 7. After cooling, a precipitate formed (*Fig. 1*);

b) In a Teflon vessel for microwave synthesis to 5-(2-bromophenyl)-4-phenyl-4*H*-1,2,4-triazole-3-thiol (I) was added aliphatic alcohol (methanol, 1-propanol) and 10 drops of hydrochloric acid. Reaction conditions in Milestone Flexi Wave microwave synthesis system: The mixture was heated for 45 minutes at a temperature of 150 °C, a pressure 14.4 bar, ΔMW ≈ 200 W (*Fig. 1*).

The completeness of the reaction was determined using a gas chromatograph Agilent 7890B with a mass spectrometric detector 5977B.

Analyzing the GS/MS chromatogram in the MS spectrum there was a molecular peak with a value of 347.0 (m/z) (99.9 %), which corresponds to the calculated theo-

retical value of 3-(2-bromophenyl)-5-(methylthio)-4-phenyl-4*H*-1,2,4-triazole (IIa), and fragment ion peaks 346 (31.1), 344.9 (96.7), 314 (22.4), 312(23.4), 266 (10.5), 260 (9.8), 258 (9.8), 260 (9.8), 258 (9.8), 237.9 (12.5), 236 (12.8), 165 (8.8), 164 (11.8), 132.9 (12.9), 118 (16.6), 117 (20.5), 102 (11.2), 91 (62.2), 77 (34.7), 65 (9.7), 51 (12) (*Fig. 2*).

3-(2-bromophenyl)-5-(methylthio)-4-phenyl-4H-1,2,4-triazole (IIa). Br. yellow residue; yield 81 %; m. p. 218–220 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm): δ 2.75 (3H, CH_3, s), 7.31–7.58 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{15}H_{12}BrN_3S$): found C% 51.86, H% 3.48, N% 12.12, S% 9.24; calculated C% 52.03, H% 3.49, N% 12.14, S% 9.26. MH 346.3. Molecular peak 347.0 (m/z) (99.9 %) and fragment ion peaks 346 (31.1), 344.9 (96.7), 314 (22.4), 312 (23.4), 266 (10.5), 260 (9.8), 258 (9.8), 260 (9.8), 258 (9.8), 237.9 (12.5), 236 (12.8), 165 (8.8), 164 (11.8), 132.9 (12.9), 118 (16.6), 117 (20.5), 102 (11.2), 91 (62.2), 77 (34.7), 65 (9.7), 51 (12).

3-(2-bromophenyl)-5-(prophylthio)-4-phenyl-4H-1,2,4-triazole (IIb). Br. yellow residue; yield 68 %; m. p. 98–100 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm): δ 0.96 (3H, CH_3, t), 1.62 (2H, CH_2, m), 3.32 (2H, CH_2, t), 7.31–7.58 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{17}H_{16}BrN_3S$): found C% 54.38, H% 4.32, N% 11.27, S% 8.59; calculated C% 54.55, H% 4.31, N% 11.23, S% 8.57. MH 374.3. Molecular peaks 374.0 (13.1), 373 (63.0), 372 (26.3), 371 (60.23), 359 (18.55), 357.9 (99.9), 357 (20.5), 356 (98.7), 190 (24.9), 189 (22), 157 (56.5), 156 (15.6), 136 (13.6), 135 (21.2), 77 (31.9).

3-(2-bromophenyl)-5-(butylthio)-4-phenyl-4H-1,2,4-triazole (IIc). White residue; yield 63 %; m.p. 180–182 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm): δ 0.92 (3H, CH_3, t), 1.29–1.43 (4H, $2CH_2$, m), 3.45 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{18}H_{18}BrN_3S$): found C% 56.01, H% 4.68, N% 10.84, S% 8.28; calculated C% 55.67, H% 4.67, N% 10.82, S% 8.26. MH 388.3. Molecular peaks 389 (15.4), 388 (14.6), 359 (16.9), 358 (17.8), 341 (99.9), 340 (98.4), 331.9 (86.3), 330.9 (62.4), 252 (24.6), 194 (22.1), 149 (26.8), 91 (29.1), 77 (39.4).

3-(2-bromophenyl)-5-(pentylthio)-4-phenyl-4H-1,2,4-triazole (IId). White residue; yield 64 %; m. p. 102–104 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm): δ 0.89 (3H, CH_3, t), 1.25–1.36 (4H, $2CH_2$, m), 1.40 (2H, CH_2, t), 3.46 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{19}H_{20}BrN_3S$): found C% 56.86, H% 5.03, N% 10.46, S% 8.01; calculated C% 56.72, H% 5.01, N% 10.44, S% 7.97. MH 402,3. Molecular peaks 402 (25.6), 401 (19.3), 326.9 (7.0), 282 (9.5), 281 (25.1), 223 (19.8), 177 (99.9), 131 (25.7), 130 (41.7), 113 (20.7), 105 (38.3), 103 (26.4), 85 (30.4), 77 (27.2).

3-(2-bromophenyl)-5-(hexylthio)-4-phenyl-4H-1,2,4-triazole (IIe). Br. yellow residue; yield 64 %; m.p. 94–96 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm): δ 0.87 (3H, CH_3, t), 1.20–1.32 (6H, $3CH_2$, m), 1.40 (2H, CH_2, t), 3.46 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{20}H_{22}BrN_3S$): found C% 57.58, H% 5.36, N% 10.07, S% 7.78; calculated C% 57.69, H% 5.33, N% 10.09, S% 7.70. MH 416,3. Molecular peaks 416.4 (99.9), 414 (34.8) 396.4 (62.5), 381.3 (38.2), 329.3 (28.4), 303.3 (54.6), 255 (47.4), 204.0 (51.3), 161 (35.7), 159.1 (33.8), 145 (39.4), 105 (32.9).

3-(2-bromophenyl)-5-(heptylthio)-4-phenyl-4H-1,2,4-triazole (IIf). Yellow residue; yield 71 %; m. p. 68–70 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm; δ 0.87 (3H, CH_3, t), 1.19–1.32 (8H, $4CH_2$, m), 1.40 (2H, CH_2, t), 3.46 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{21}H_{24}BrN_3S$): found C% 58.74, H% 5.64, N% 9.79, S% 7.41; calculated C% 58.60, H% 5.62, N% 9.76, S% 7.45. MH 430,4. Molecular peaks 431.0 (27.5), 430 (22.7), 347 (47.1), 346 (66.3), 345 (50.9), 343.9 (65.5), 333 (23.7), 331.9 (25.1), 312 (29.9), 285.9 (22.4), 285 (60.2), 284 (34.2), 283 (50.8), 204 (99.9), 183.9 (36.3), 181.9 (27.5), 102 (23.6), 91 (39), 77 (40.7).

3-(2-bromophenyl)-5-(octylthio)-4-phenyl-4H-1,2,4-triazole (IIg). Yellow residue; yield 72 %; m. p. 72–74 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm; δ 0.91 (3H, CH_3, t), 1.19–1.32 (10H, $5CH_2$, m), 1.40 (2H, CH_2, t), 3.46 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{22}H_{26}BrN_3S$): found C% 59.32, H% 5.92, N% 9.48, S% 7.24; calculated C% 59.45, H% 5.90, N% 9.45, S% 7.21. MH 444,4. Molecular peaks 444.9 (99.9), 443 (61.2), 384 (32.5), 383 (45.1), 348 (21.8), 347 (23.7), 314 (45.3), 312 (32.4), 235.9 (15.7), 118 (18.3), 117 (9.6), 77 (18.2).

3-(2-bromophenyl)-5-(nonylthio)-4-phenyl-4H-1,2,4-triazole (IIh). Yellow residue; yield 65 %; m. p. 85–87 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm: δ 0.89 (3H, CH_3, t), 1.19–1.32 (12H, $6CH_2$, m), 1.40 (2H, CH_2, t), 3.46 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{23}H_{28}BrN_3S$): found C% 60.20, H% 6.12, N% 9.11, S% 6.97; calculated C% 60.26, H% 6.16, N% 9.17, S% 6.99. MH 458.4. Molecular peaks 458.0 (99.9), 457 (68.3), 431 (39.4), 386 (14.7), 331.9 (12.7), 302.0 (9.8), 276 (11.4), 184 (15.3), 183 (29.9), 174 (20.2), 91 (17).

3-(2-bromophenyl)-5-(decylthio)-4-phenyl-4H-1,2,4-triazole (IIi). White residue; yield 73 %; m. p. 65–67 °C; ^{1}HNMR (400 MHz, DMSO-d6, δ = ppm; δ 0.87 (3H, CH_3, t), 1.19–1.32 (14H, $7CH_2$,m), 1.42 (2H, CH_2, t), 3.49 (2H, CH_2, t), 7.29–7.56 (5H, Ar-H, m), 7.74–7.88 (4H, Ar-H, m); CHNS elemental analysis Calcd. for ($C_{24}H_{30}BrN_3S$): found C% 60.84, H% 6.43, N% 8.84, S% 6.75; calculated C% 61.01, H% 6.40, N% 8.89, S% 6.79. MH 472,4. Molecular peaks 472.0 (46.1), 470 (32.5), 433 (55.7), 432 (41.8), 370 (48.2), 368 (25.7), 331.9 (99.9), 330.9 (86.4), 328 (48.2), 252 (14.6), 149 (18.5), 91 (9.6), 77 (26.9).

Antimicrobial and antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles (6 new compounds) was investigated.

The most active compound with antifungal and antimicrobial effect was IIi. Substances IIa–IIe had moderate antimicrobial effect.

Discussion

The antifungal (*Candida albicans)* and antimicrobial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*) activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles was moderate. The most active compound was 3-(2-bromophenyl)-5-(decylthio)-4-phenyl-4*H*-1,2,4-triazole (IIi) (*Table 1, 2*).

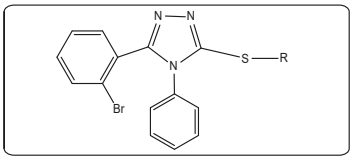
Considering the antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles, the substances IIi, IId exhibited antifungal effect. MIC and MFcC for substance IIi are 15.6 μg/ml and 31.25 μg/ml respectively (*Fig. 3*).

Changing the decyl radical to pentyl reduced antifungal activity. Other compounds have moderate effect.

Also, the antimicrobial activity of compound IIi to *S. aureus* was the biggest among investigated substances (MIC 7.8 μg/ml, MBcC 15.6 μg/ml).

It was possible to note growth of antimicrobial effect with increase in a carbon radical.

Table 1. "Structure – effect" dependence between 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles



Substance	R	Antimicrobial effect	Antifungal effect
IIa	CH_3	↑	↔
IIb	C_3H_7	↔	↔
IIc	C_4H_9	↔	↔
IId	C_5H_{11}	↑	↑
IIe	C_6H_{13}	↑	↔
IIi	$C_{10}H_{21}$	↑↑	↑↑

↑: insignificant effect; ↑↑: significant effect; ↔: no effect.

Table 2. The antimicrobial and antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles

	Antimicrobial activity						Antifungal activity	
	E. coli ATCC 25922		*S. aureus* ATCC 25923		*P. aeruginosa* ATCC 27853		*C. albicans*	
	MIC, μg/ml	MBcC, μg/ml	MIC, μg/ml	MBcC, μg/ml	MIC, μg/ml	MBcC, μg/ml	MIC, μg/ml	MFcC, μg/ml
Chlorhexidine	–	25.0	–	18.8	–	200	–	–
Fluconazole							15.6	31.25
IIa	31.25	62.5	62.5	125	31.25	62.5	62.5	62.5
IIb	31.25	62.5	62.5	125	62.5	125	62.5	62.5
IIc	62.5	125	62.5	125	31.25	62.5	62.5	62.5
IId	62.5	125	31.25	62.5	31.25	62.5	31.25	62.5
IIe	62.5	125	15.6	31.25	31.25	62.5	62.5	125
IIi	31.25	62.5	7.8	15.6	15.6	31.25	15.6	31.25

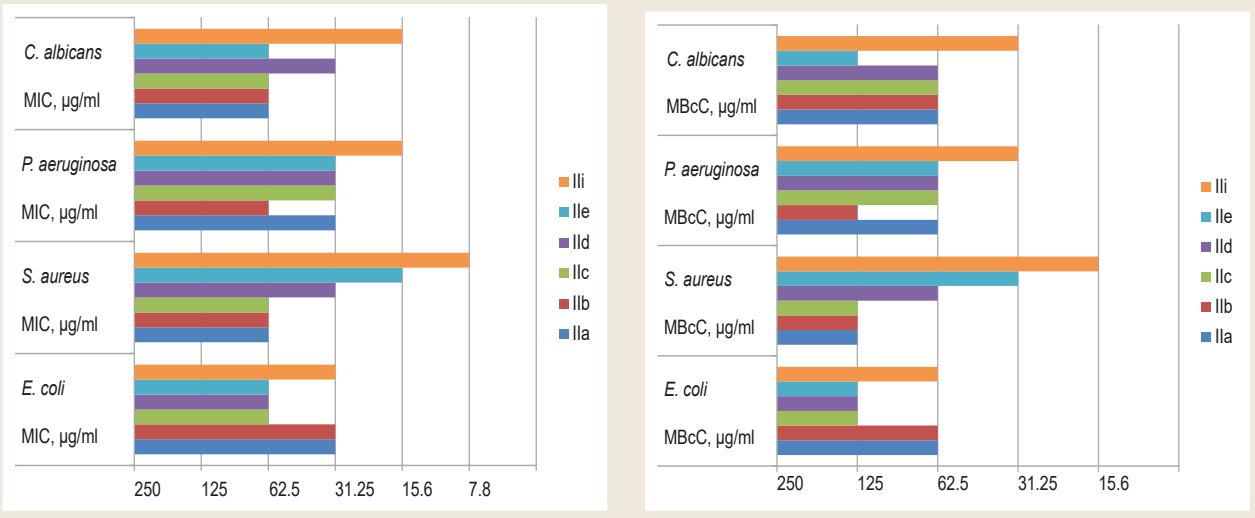


Fig. 3. The antimicrobial and antifungal activity of 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles.

Conclusions

1. New 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazoles were synthesized by two methods. The antimicrobial and antifungal activity was investigated for the obtained compounds. The most active compound was 3-(2-bromophenyl)-5-(decylthio)-4-phenyl-4*H*-1,2,4-triazole (IIi).

2. Some conclusions were drawn regarding the dependence of "structure – antimicrobial and antifungal effect": the antimicrobial effect increased with the length of the carbon radical; changing the decyl radical to another one in the molecule 3-(2-bromophenyl)-5-(alkylthio)-4-phenyl-4*H*-1,2,4-triazole reduced antifungal activity.

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