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Microwave-assisted synthesis of new pyrazole derivatives bearing 1,2,3-triazole scaffold as potential antimicrobial agents

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Abstract: A new series of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-((1-aryl-1*H*-1-2,3-triazol-4-yl)methoxy)phenyl)-prop-2-en-1-one derivatives was synthesized. The synthesis of the title compounds involved the 1,3-dipolar Cu(I)-catalyzed alkyne–azide cycloaddition (CuAAC) reaction of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4--yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-ones with aromatic azides. The structures were confirmed by NMR, FT-IR, mass and elemental analysis. All the synthesized compounds (**6a**–**j**) were evaluated for their antimicrobial activity. Compounds **6a**, **6d** and **6e** demonstrated promising inhibitory effects on both bacterial and fungal strains.

Keywords: pyrazole; chalcone; 1,2,3-triazole; microwave irradiation; antimicrobial activity.

INTRODUCTION

Infectious diseases caused by microbes, such as bacteria and fungi, are one of the leading causes of morbidity and mortality. The major reason for the increase in microbial infections is the resistance developed by these microbial organisms.[1] Thus, the development of new antimicrobial or antipathogenic agents that act upon new microbial targets is a necessity.[2]

Pyrazole scaffolds possess a wide range of bioactivities, including antiviral,[3] anti-inflammatory,[4] anticonvulsant,[5] anticancer,[6] insecticidal,[7] and antifungal.[8,9] In recent years, several drugs developed from pyrazole derivatives, such as celecoxib that demonstrates anti-inflammation effects and inhibits COX-2, rimonabant that functions as a cannabinoid receptor inverse agonist and is utilized in obesity treatment, fomepizole that inhibits alcohol dehydrogenase and sildenafil that inhibits phosphodiesterase (Fig. 1).

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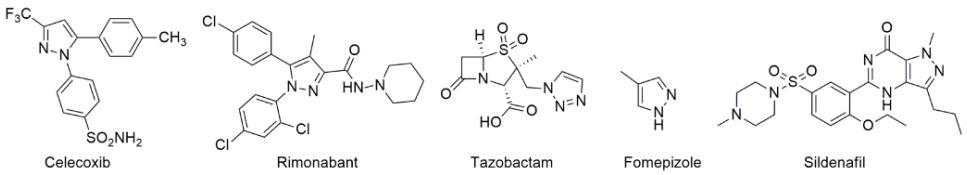


Fig. 1. Commercially available bioactive pyrazole and triazole drugs.

On the other hand, 1,2,3-triazoles have received attention due to their ease of synthesis by click chemistry bearing attractive features as well as their numerous biological activities.[10–14] 1,2,3-Triazole derivatives have gained interest for their various biological activities, such as chemotherapeutic agents,[15,16] and potent antimicrobial,[17] anti-inflammatory,[18,19] local anaesthetic,[20] anticonvulsant,[21] antineoplastic,[22] antimalarial[23] and antiviral activity.[24] Among the best known examples of triazole-containing drugs, tazobactam, a commercially available *β*-lactamase inhibitor, plays an eminent role in combination with broad-spectrum antibiotics (Fig. 1).

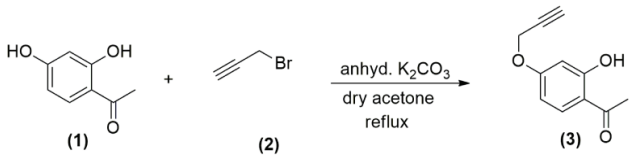
Considering the above facts, it seemed worthwhile to integrate both pyrazole and 1,2,3-triazole pharmacophore units in one molecular platform to generate a newer scaffold for biological evaluation. Pharmacophore hybridization is believed to be analogous to conventional combination therapy wherein the two drugs are covalently linked and available as a single entity.[4] In continuation to ongoing research activities[25–27] to discover and develop potential new antimicrobial agents, an efficient method for the synthesis of (*E*)-3-(3-(4-substituted-phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-((1-aryl-1*H*-1,2,3-triazol-4--yl)methoxy) phenyl)prop-2-en-1-one derivatives in excellent yields is reported herein.

RESULTS AND DISCUSSION

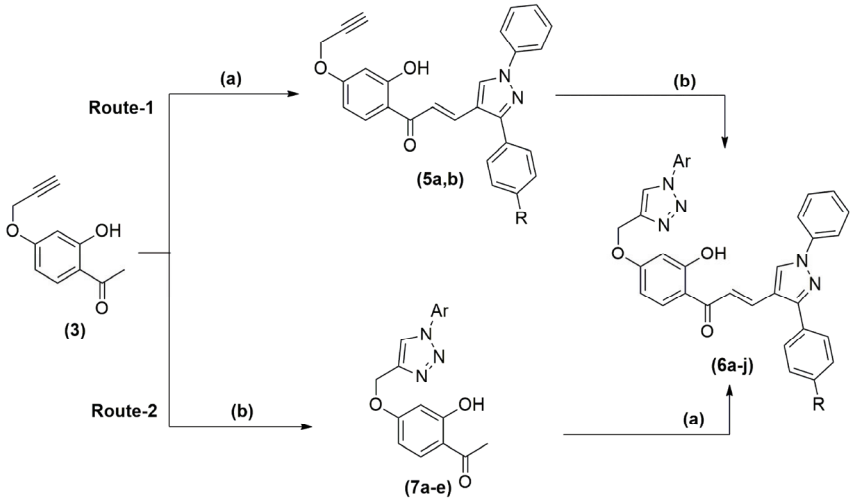
The synthetic approach adapted to obtain the target compounds is depicted in Schemes 1 and 2. The selective preparation of the starting material 1-(2-hydroxy--4-(prop-2-yn-1-yloxy)phenyl)ethanone[28] (**3**) was realized by the nucleophilic substitution reaction of 1-(2,4-dihydroxyphenyl)ethanone (**1**) with propargyl bromide (**2**) in the presence of K_2CO_3 (Scheme 1). The selective mono-propargylation of the hydroxy group without altering the *o*-hydroxy acetyl functionality was performed in high yields when starting from compound **1** rather than the other positional isomers. The synthesis of the title compounds **6a**–**j** was accomplished by two synthetic strategies as shown in Scheme 2.

In order to develop a high yield protocol for the synthesis of the title compounds by click chemistry, the yields of compound **6g** were investigated using $CuSO_4 \cdot 5H_2O$/sodium ascorbate and CuI in different solvents, such as THF/H_2O, *t*-BuOH/H_2O and DMF/H_2O, under both conventional conditions and MWI. In

the above optimization study, higher yields using CuI in DMF/H_2O (1:3) under MWI were attained (Table I).



Scheme 1. Synthesis of 1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)ethanone (**3**).



Reaction conditions: (a) 3-(4-chlorophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **(4a)** or 1-phenyl-3-(*p*-tolyl)-1*H*-pyrazole-4-carbaldehyde **(4b)**, KOH, r.t. or MWI
(b) Ar-N_3, CuI or $CuSO_4.5H_2O$/sodium ascorbate, DMF/H_2O, r.t. or MWI

6a: R = Cl, Ar = 2-chlorophenyl
6b: R = Cl, Ar = 2-methoxyphenyl
6c: R = Cl, Ar = 4-methylphenyl
6d: R = Cl, Ar = 3-(trifluoromethyl)phenyl
6e: R = Cl, Ar = benzyl
6f: R = CH_3, Ar = 2-chlorophenyl
6g: R = CH_3, Ar = 2-methoxyphenyl
6h: R = CH_3, Ar = 4-methylphenyl
6i: R = CH_3, Ar = 3-(trifluoromethyl)phenyl
6j: R = CH_3, Ar = benzyl
7a: Ar = 2-chlorophenyl
7b: Ar = 2-methoxyphenyl
7c: Ar = 4-methylphenyl
7d: Ar = 3-(trifluoromethyl)phenyl
7e: Ar = benzyl
5a: R = Cl
5b: R = CH_3

Scheme 2. Synthetic route for the preparation of pyrazole-based 1,2,3-triazole hybrids (**6a**–**j**).

In route-1 (Scheme 2), the (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivatives (**5a** and **b**) were synthesized by Claisen–Schmidt condensation of compound **3** with substituted 1H-pyrazole-4-carboxaldehydes (**4a** and **b**) in presence of KOH under conventional conditions and microwave irradiation. These compounds (**5a** and **b**) *via* a Huisgen 1,3-dipolar cycloaddition reaction with aromatic

azides using CuI in DMF under MWI gave compounds **6a**–**j**. In route-2 (Scheme 2), compound **3** in a click reaction with aromatic azides using CuI in DMF under MWI followed by reaction with substituted 1H-pyrazole-4-carboxaldehydes (**4a** and **b**) in the presence of KOH under conventional conditions and microwave irradiation gave compounds **6a–j**.

TABLE I. Optimization study for the synthesis of compound **6g** under different catalyst and solvent conditions

Entry	Catalyst	Solvent	Conventional		Microwave irradiation	
			Time, h	Yield, %[a]	Time, min	Yield, %[a]
1	$CuSO_4$/sod. ascorbate	THF/H_2O (1:2)	72	21	20	25
2	$CuSO_4$/sod. ascorbate	THF/H_2O (1:3)	72	27	20	32
3	$CuSO_4$/sod. ascorbate	DMF/H_2O (1:2)	24	35	15	40
4	$CuSO_4$/sod. ascorbate	DMF/H_2O (1:3)	24	54	14	61
5	$CuSO_4$/sod. ascorbate	*t*-BuOH/H_2O (1:2)	24	40	16	46
6	$CuSO_4$/sod. ascorbate	*t*-BuOH/H_2O (1:3)	24	44	16	49
7	CuI	THF/H_2O (1:2)	72	30	20	42
8	CuI	THF/H_2O (1:3)	72	34	20	44
9	CuI	DMF/H_2O (1:2)	14	47	10	69
10	CuI	DMF/H_2O (1:3)	12.5	67	8.5	91
11	CuI	*t*-BuOH/H_2O (1:2)	24	41	16	52
12	CuI	*t*-BuOH/H_2O (1:3)	24	50	16	63

[a]Isolated yields

By comparing the above routes, the target compounds were synthesized in excellent yields in route-1 (Table II) to give overall yields of 81–92 % in shorter reaction time, while in route-2, the overall yields were much lower in the range of 34–48 % and a longer time (24–48 h)was necessary to complete the reaction.

TABLE II. Comparison of the yields of compounds **5a,b** and **6a–j** under different synthetic conditions

Compound	M.p., °C	Conventional		MWI	
		Time, h	Yield, %[a]	Time, min	Yield, %[a]
5a	150–152	12	49	8	89
5b	128–130	10	51	7	90
6a	142–144	14	54	10	87
6b	101–103	12.5	48	8	81
6c	171–173	12	50	9	84
6d	162–164	13	49	9.5	87
6e	184–186	12	53	8	90
6f	133–135	13	52	9	89
6g	147–149	12.5	54	8.5	91
6h	197–199	13	57	10	92
6i	142–144	12.5	46	10	91
6j	134–136	12	52	10	92

[a]Isolated yields

The formation of pyrazole derivatives containing 1,2,3-triazoles **6a–j** was confirmed by IR, NMR and mass analysis (the spectral data are given in Supplementary material to this paper). The IR spectrum of compound **6g** showed absorption bands at 3111 and 1631 cm^{-1} due to OH and C=O groups, respectively. The ^{1}H-NMR spectrum of **6g** showed three singlets at δ 2.40, 3.86 and 5.35 ppm corresponding to CH_3, OCH_3 and OCH_2 protons. The appearance of a doublet at δ 7.78 ppm (J = 15.29 Hz) was due to the β-proton of the α,β-unsaturated carbonyl group. Two singlets at δ 8.65 and 9.46 ppm correspond to triazole and pyrazole protons, respectively. A broad singlet due to the OH protons was observed at δ 13.52 ppm.[29] In the ^{13}C-NMR spectrum of **6g**, the CH_3, OCH_3 and OCH_2 carbons resonated at δ 20.2, 55.4 and 60.7 ppm, respectively. The carbonyl carbon appeared at δ 190.8 ppm. The mass spectra of **6g** showed the molecular ion peak at m/z = 584 $[M+H]^+$.

Antibacterial activity

The synthesized compounds **5a** and **b** and **6a**–**j** were screened *in vitro* for their antibacterial activity against *Bacillus subtilis* (ATCC 6633) and *Staphylococcus aureus* (ATCC 6538), as examples of Gram-positive bacteria, and *Escherichia coli* (ATCC 11229) and *Proteus vulgaris* (ATCC 13315), as examples of Gram-negative bacteria. The agar well-diffusion method was used to assay the antibacterial activity against the test strains on Mueller–Hinton agar plates. Gentamicin was employed as the standard antibacterial drug. The results obtained as zone of inhibition in mm and minimum inhibitory concentration (*MIC*) in μg mL^{-1} are presented in Table III. Investigation of the antibacterial efficiency of the synthesized compounds involved varying the substitution with electronegative chloro- and electron-donating methyl group on phenyl ring of the pyrazole nucleus and variable substitutions on phenyl ring of triazole nucleus. It is evident from Table III that compound **6a** with chloro substitutions on both the pyrazole and triazole nucleus exhibited the highest antibacterial inhibitory efficacy with inhibition zones of 28, 27 and 31 mm and an *MIC* of 3.125 μg mL^{-1} against *B. subtilis*, *S. aureus* and *E. coli*, respectively, and 26 mm with an *MIC* 6.25 μg mL^{-1} against *P. vulgaris* compared to standard drug gentamicin. After **6a**, came compound **6d**, with zones of inhibition in range of 24–28 mm (*MIC* 6.25–12.5 μg mL^{-1}), with chloro substitution on the pyrazole scaffold and trifluoromethyl group on the triazole nucleus, and **6e**, with inhibition zones in range of 22–24 mm (*MIC* 12.25 μg mL^{-1}) with chloro substitution on the pyrazole scaffold and a benzyl group on triazole nucleus. This indicates that electron withdrawing groups and an electronegative chlorine atom on the phenyl ring strongly affect the antibacterial activity. The remaining compounds displayed moderate antibacterial potency with inhibition zones in the range 15–21 mm and with *MIC* values of 25–50 μg mL^{-1}.

TABLE III. Antimicrobial activity of the synthesized compounds

Compound	Gram positive bacteria		Gram negative bacteria		Fungal strains	
	B. subtilis	*S. aureus*	*E. coli*	*P. vulgaris*	*A. niger*	*C. albicans*
5a	19[a] (25)[b]	15 (50)	21 (25)	17 (25)	15(25)	16(50)
5b	23 (12.5)	18 (25)	19 (25)	16 (50)	12(50)	18(50)
6a	28 (3.125)	27 (3.125)	31 (3.125)	26 (6.25)	24(6.25)	25(6.25)
6b	20 (25)	17 (25)	17 (50)	21 (25)	16(50)	18(25)
6c	19 (12.5)	19 (25)	21 (25)	24 (12.5)	21(25)	19(12.5)
6d	26 (6.25)	24 (12.5)	27 (12.5)	28 (6.25)	21(12.5)	18(12.5)
6e	24 (12.5)	22 (12.5)	23 (25)	23 (12.5)	19(12.5)	21(12.5)
6f	21 (12.5)	21 (25)	23 (12.5)	19 (25)	13(50)	19(25)
6g	16 (50)	16 (50)	21 (25)	18 (50)	15(50)	14(50)
6h	18 (25)	21 (12.5)	23 (25)	23 (50)	18(25)	13(50)
6i	15 (50)	18 (25)	16 (50)	20 (50)	18(50)	16(25)
6j	21 (25)	15 (50)	18 (25)	15 (50)	12(50)	16(50)
Gentamicin	32 (1.56)	29 (1.56)	34 (1.56)	30 (3.125)	–	–
Fluconazole	–	–	–	–	34(3.125)	31(1.56)

[a]Zone of inhibition in mm; [b]*MIC* in μg mL^{-1}

Antifungal activity

The compounds were evaluated for their *in vitro* antifungal activity against *Aspergillus niger* (ATCC 9029) and *Candida albicans* (ATCC 10231) fungal strains. The agar well diffusion method was used to evaluate the antifungal activity against test strains on PDA plates. Fluconazole was used as the standard antifungal drug. The results are given in Table III, from which it is evident that compound **6a** displayed the best antifungal activity with zones of inhibition of 24 and 25 mm, and an *MIC* of 6.25 μg mL^{-1} against *A. niger* and *C. albicans*, respectively. Compounds **6d** (21 and 18 mm) and **6e** (19 and 21 mm) were able to induce appreciable promising growth inhibitory activity with an *MIC* 12.5 μg mL^{-1} against *A. niger* and *C. albicans*. Thus, it was hypothesized that compounds with a chlorine atom and electron withdrawing groups on the phenyl ring of pyrazole and the triazole moieties would exhibit the highest antimicrobial inhibitory potency.

EXPERIMENTAL

Materials

All the used materials were obtained commercially, mostly from Sigma–Aldrich, and used without further purification.

Equipment

Melting points were determined in open capillaries and are uncorrected. The purity of the compounds was checked by TLC on silica gel 60 F_{254} (Merck). The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker Avance II 400 spectrometer using TMS as an internal standard. The IR spectra were recorded in KBr on a Shimadzu FTIR 8400S spectrophotometer. The mass spectra were recorded on Shimadzu LCMS-2020 mass spectrometer. Ele-

mental microanalysis was performed on a Perkin Elmer CHN-2400 analyzer. All the microwave irradiation experiments were realized in a CEM Discover microwave system and reaction temperatures were monitored by an equipped IR sensor.

Analytical and spectral data are presented in Supplementary material to this paper.

*General procedure for the synthesis of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivatives (**5a** and **b**)*

Conventional heating method. To a mixture of 1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)ethanone (**3**, 1 mmol) and powdered KOH (2 mmol), substituted 1H-pyrazole-4-carboxaldehydes (**4a** and **b**, 1 mmol) was added and the reaction mixture was heated at 80 °C for 10–12 h. After completion of the reaction (as indicated by TLC), the reaction mixture was poured into ice-cold water and neutralized with 10 % HCl solution. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (9:1 volume ratio) as eluent to afford compound **5**.

Microwave irradiation method. To a mixture of 1-(2-hydroxy-4-(prop-2-yn-1-yloxy)-phenyl)ethanone (**3**, 1 mmol) and powdered KOH (2 mmol) in a glass vial, a substituted 1H-pyrazole-4-carboxaldehydes (**4a** and **b**, 1 mmol) was added and the vial was tightly sealed. The mixture was then irradiated for 7–8 min at 90 °C, at an irradiation power of 180 W. After completion of the reaction (as indicated by TLC), the vial was cooled, the reaction mixture was poured into ice-cold water and neutralized with 10 % HCl solution. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (9:1) as eluent to afford compound **5**.

*General procedure for the synthesis of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-((1-aryl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)prop-2-en-1-one derivatives (**6a–j**) using CuI catalyst*

Conventional method. To a well stirred mixture of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivatives (**5a** and **b**, 1 mmol) and CuI (0.05 equiv.) in H_2O/DMF (3:1) (6 mL), an aromatic azide was added and the reaction mixture was stirred at room temperature for 12–14 h. After completion of the reaction (as indicated by TLC), the reaction mixture was poured into ice-cold water. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (7:3, v/v) as eluent to afford compound **6**.

Microwave irradiation method. A mixture of a (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivative (**5a** and **b**, 1 mmol) and CuI (0.05 equiv.) was suspended in H_2O/DMF (3:1 volume ratio, 2 mL) in a glass vial equipped with a small magnetic stirring bar. To this, an aromatic azide was added and the vial was tightly sealed. The mixture was then irradiated for 8–10 min at 60 °C, at an irradiation power of 100 W. After completion of the reaction (as indicated by TLC), the vial was cooled, and the reaction mixture poured into ice-cold water. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (7:3, v/v) as eluent to afford compound **6**.

*General procedure for the synthesis of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-((1-aryl-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)prop-2-en-1-one derivatives (**6a–j**) using $CuSO_4$/sodium ascorbate catalyst*

Conventional method. To a well stirred mixture of (*E*)-3-(3-(4-substituted phenyl)-1-phenyl-1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivative (**5a** and **b**, 1 mmol), $CuSO_4 \cdot 5H_2O$ (0.05 equiv.) and sodium ascorbate (0.05 equiv.) in

H_2O/DMF (2:1 volume ratio, 10 mL), an aromatic azide was added and the reaction mixture was stirred at room temperature for 24 h. After completion of the reaction (as indicated by TLC) the reaction mixture was poured into ice-cold water. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as eluent to afford compound **6**.

Microwave irradiation method. A mixture of a (*E*)-3-(3-(4-substituted phenyl)-1-phenyl--1*H*-pyrazol-4-yl)-1-(2-hydroxy-4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one derivative (**5a** and **b**, mmol) $CuSO_4 \cdot 5H_2O$ (0.05 equiv.) and sodium ascorbate (0.05 equiv.) were suspended in H_2O/DMF (2:1 volume ratio, 2 mL) in a glass vial equipped with a small magnetic stirring bar. To this, an aromatic azide was added and the vial was tightly sealed. The mixture was then irradiated for 15 min at 60 °C, at an irradiation power of 100 W. After completion of the reaction (as indicated by TLC), the vial was cooled and the reaction mixture poured into ice-cold water. The thus-obtained solid was filtered and purified by column chromatography on silica gel using hexane/ethyl acetate (7:3) as eluent to afford compound **6**.

Biological assay

Antimicrobial activity. The *in vitro* antimicrobial studies were performed by the agar well diffusion method against test organisms.[30,31] Nutrient broth (NB) plates were swabbed with 24 h-old broth culture (100 mL) of the test bacteria. Using a sterile cork borer, wells (6 mm) were made into each Petri plate. Different concentrations of test samples dissolved in DMSO were added into the wells using sterile pipettes. Simultaneously, the standard antibiotics, gentamicin for antibacterial activity, fluconazole for antifungal activity were tested against the pathogens. The plates were incubated at 37 °C for 24 h for the bacteria and at 28 °C for 48 h for the fungi. After appropriate incubation, the diameter of zone of inhibition of each well was measured. The broth dilution test was used to determine the minimum inhibitory concentration (*MIC*) of the samples.[32,33] Freshly prepared nutrient broth was used as the diluent. The 24 h-old culture of the test bacteria *B. subtilis*, *S. aureus*, *E. coli* and *P. vulgaris* and the test fungi *A. niger* and *C. albicans* were diluted 100-fold in nutrient broth (100 μL bacterial cultures in 10 mL NB). Increasing concentrations of the test samples were added to the test tubes containing the bacterial and fungal cultures. All the tubes were incubated at 37 °C for 24 h for the bacteria and at 28 °C for 48 h for the fungi. The tubes were examined for visible turbidity using NB as the control. The lowest concentration that inhibited visible growth of the tested organisms was recorded as the *MIC*.

CONCLUSION

In summary, a new series of compounds **6a**–**j** was synthesized by conventional and microwave irradiation methods. In the microwave irradiation method, reactions were completed in a short reaction time under mild reaction conditions and convenient operation in high yields. All the titled compounds were screened for their *in vitro* antimicrobial activity. Compound **6a** was found to be the most potent and compounds **6d** and **6e** were found to be moderately potent compared to the standard drug gentamicin against the pathogenic bacteria, while compounds **6a**, **6d** and **6e** exhibited potent activity against the pathogenic fungi compared to the standard drug fluconazole with their respective concentrations. Antimicrobial screening results revealed that, compound **6a** of the synthetic library could be considered as a promising antimicrobial drug candidate.

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SUPPLEMENTARY MATERIAL

Spectral and analytical data of the synthesized compounds are available electronically at the pages of journal website: http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

ИЗВОД

СИНТЕЗА НОВИХ 1,2,3-ТРИАЗОЛСКИХ ДЕРИВАТА ПИРАЗОЛА, ПОД УСЛОВИМА МИКРОТАЛАСНОГ ЗРАЧЕЊА, КАО ПОТЕНЦИЈАЛНИХ АНТИМИКРОБНИХ ЈЕДИЊЕЊА

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Синтетисана је серија нових деривата (*E*)-3-(3-(4-супституисани фенил)-1-фенил--1*H*-пиразол-4-ил)-1-(2-хидрокси-4-((1-арил-1*H*-1,2,3-триазол-4-ил)метокси)фенил)-проп-2-ен-1-она. Синтеза деривата укључује Cu(I)-катализовану 1,3-диполарну алкин––азид циклоадицију (CuAAC) реакцијом (*E*)-3-(3-(4-супституисани фенил)-1-фенил-1*H*--пиразол-4-ил)-1-(2-хидрокси-4-(проп-2-ин-1-илокси)фенил)проп-2-ен-1-она и ароматичних азида. Структуре производа су потврђене NMR и FTIR спектроскопијом, масеном спектрометријом и микроанализом. Испитана је антимикробна активност свих синтетисаних деривата **6a**–**j.** Једињења **6a**, **6d** и **6e** показују интересантне инхибиторне активности према бактеријама и гљивама.

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