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Preparation, Characterization and Study of The Antifungal Activity of some New Thiazolidinones Compounds Derived from Benzilic Acid

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ABSTRACT

In order to study new bioactive compounds, benzilic acid was used as a starting material for some novel derivatives of 2-aryl-1,3-thiazolidin-4-ones, methyl benzilate (R2) was prepared from benzilic acid (R1) and methanol with the presence of sulfuric acid by reflux conditions. Benzilic acid hydrazide (R3) prepared by reflux of methyl benzilate (R2) and hydrazine hydrate in the presence of absolute ethanol, we carried out certain chemical transformations of benzilic acid hydrazide (R3) through reaction with a set of aromatic aldehydes (4-bromo benzaldehyde, 2-nitro benzaldehyde, 3-nitro benzaldehyde, 4-hydroxy benzaldehyde, 2-chloro benzaldehyde, 3-hydroxy benzaldehyde, 3,4-dihydroxy benzaldehyde, 2,6-dichloro benzaldehyde, piperonyl) in absolute ethanol in the presence of three drops glacial acetic acid under reflux conditions to yield the corresponding hydrazone derivatives in moderate to good yields (R4a-i). The corresponding 2-aryl-1,3-thiazolidin-4-one derivatives (R5a-i) were obtained by the reaction of the prepared hydrazone derivatives (R4a-i) with 2-mercapto propionic acid under reflux conditions by using (Dean-stark device) in dry toluene. These derivatives were tested *in vitro* for their antifungal efficiency against *Candida albicans, Rhodotorula sp., and Meyerozyma caribbica*.

Keywords: Thiazolidinone, hydrazones, benzilic acid, antifungal activity.

INTRODUCTION

Hydrazones, related to ketones and aldehydes belong to a class of organic compounds with the structure ($R_1R_2C = NNH_2$), (Uppal *et al.,* 2011). These compounds possess various biological and pharmacological properties such as antimicrobial, anti-tubercular, antioxidant, (Arora *et al*., 2023), anti-inflammatory, analgesic, (Alsaif *et al.,* 2020), antifungal (Zhou *et al.,* 2021), antiviral (Abu-Melha *et al.,* 2020), anticancer, (Han and Imamoglu, 2023), antiplatelet, (Tavili *et al*., 2022), antimalarial, (Taxak *et al*., 2023), anticonvulsant, (Goshain *et al*., 2022), cardio protective, (Ghazouani *et al.,* 2019), anthelmintics, (Anichina *et al.,* 2021), antiprotozoal , (Rollas and Güniz Küçükgüzel, 2007), anti-trypanosome, (Narang *et al.,* 2012), anti-schistosomiasis etc., (Negi, 2012).

These compounds contain C = N bond, which is conjugated with a lone pair of electrons of the functional nitrogen atom (Corey and Enders, 1976), The nitrogen atoms of the hydrazones are nucleophilic and the carbon atom has both electrophilic and nucleophilic nature, (Verma *et al.,* 2014), the α-hydrogen of hydrazones is more potent than that of acidic ketones (Belskaya *et al*., 2010).

The combination of hydrazones with other functional groups leads to compounds with unique physical and chemical characteristics, (Xavier *et al*., 2012), due to their biological and pharmacological properties, they are considered important for the synthesis of heterocyclic compounds, (Banerjee *et al.,* 2009).

Thiazolidinones are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds containing sulfur at position 1, and an atom of nitrogen at position 3, and a carbonyl group at position (2,4, or 5) in a five-member ring, there are numerous biologically active molecules which contain various heteroatoms and always drawn the attention of chemist over the years mainly because of their biological importance (Mehta *et al*., 2014). It belongs to the most frequently studied moieties and its presence in penicillin was the first recognition of its occurrence in nature (Singh *et al*., 1981).

Similarly, 1,3-thiazolidin-4-ones are heterocyclic nucleus that have an atom of sulfur and nitrogen at position 1 and 3, respectively and a carbonyl group at position 4 have been subjected to extensive study in the recent years. The 4-thiazolidinones have attracted considerable attention as they are endowed with a wide range of pharmaceutical activities. The presence of (N-C-S) linkage in the compounds has been shown to have antioxidant (Geronikaki, *et al.,* 2013) ,and antifungal (Molnar *et al*., 2017), and antimicrobial (Kousaxidis, *et al*., 2021), and antitubercular (Subhedar *et al*., 2016), and as antiviral agents, especially as anti-HIVagents (Jain, *ea al*., 2012), (Solankee, *et al*., 2012).

The aim of the research

fungi:*Meyerozyma Caribbica, Rhodotorula Sp.,* and *Candida Albicans* on a number of new hydrazones and thiazolidinones compounds derived from benzilic acid.

Materials and methods

A Stuart SMP30 Melting Point device was used to determine the melting points. Infrared spectra were measured using a Shimadzu FT-IR-8400S, while a Bruker Avance-NEO 400MHz was used to measure 1H and 13C-NMR spectra, which were recorded in ppm (δ). With TMS serving as internal standard and DMSO-d6 as solvent, with normalized chemical shifts of 1H NMR: δ 7.26 (400 MHz) and 13C-NMR: δ 77.16 ppm (100 MHz). While TLC was used to verify the purity of the compounds using 0.5 mm thick silica gel, which was then stained with iodine. The benzylic acid ester (R2) was created using the standard general esterification process. The creation of benzylic acid hydrazide followed the method described in the literature (Mohaimen, 2020).

Preparation of methyl benzilate (R2):

A mixture of (2,28 grams., 0.01 mole) of benzilic acid (R1) and (25 ml) of methanol with (1ml) of sulfuric acid was refluxed for (4) hour and then cooled in crushed ice, (50 ml) of cold water and (20%) sodium carbonate was added, the white solid precipitate was filtered off and

recrystallized from ethanol to afford compound (R2). Yield (93%,71-73) (lit. (mohaymin, 2020) m.p.72-74°C).

Preparation of benzilic acid hydrazide (R3):

A mixture of (2,42 gm., 0.01 mole) of methyl benzilate (R2) and (10 ml, 80%) of hydrazine hydrate in (25 ml) of absolute ethanol was refluxed for (4) hour and after that, solvent was evaporated under vacuum to give a white solid. Yield 95%, m.p 165-167 (lit.(mohaymin, 2020) m.p.167-169°C)

Preparation of benzilic acid hydrazones (R4a-i): (Cacic *et al.*, 2006)

Dissolved benzilic acid hydrazide (R3) (0.242 gm., 0.001mole) and (0.001 mole) of benzaldehyde derivatives in (25 ml) of abs. ethanol then (3) drops of glacial acetic acid was added to the mixture, and the reaction mixture was refluxed for (3) hour, cooled, and added to crushed ice then lifted for (30 min) in refrigerator. The resultant solid was dried, and recrystallized from ethanol. (Table 1).

Table 1: The Physical data for compounds (R4a-i).

Comp. No.	Ar	Melting point °C	Color	Yield %
R4a	4-BrC_6H_4	253-255	White	61%
R4b	2-$NO_2C_6H_4$	179-182	Pale yellow	91%
R4c	3-$NO_2C_6H_4$	208-210	Yellow	80%
R4d	4-OHC_6H_4	262-264	Pale yellow	77%
R4e	2-ClC_6H_4	162-164	Yellow	37%
R4f	3-OHC_6H_4	242-244	Pale yellow	70%
R4g	3,4-diOHC_6H_3	270-273	reddish brown	40%
R4h	2,6-diClC_6H_3	200-202	Pale green	66%
R4i	Piperonyl	201-203	Yellow	61%

Preparation of N-(2-(Substituted Phenyl)-5-Methyl-4-Oxothiazolidin-3-Yl)-2-Hydroxy-2, 2-Diphenylacetamide (R5a-I): (Solankee *et al.*, 2012)

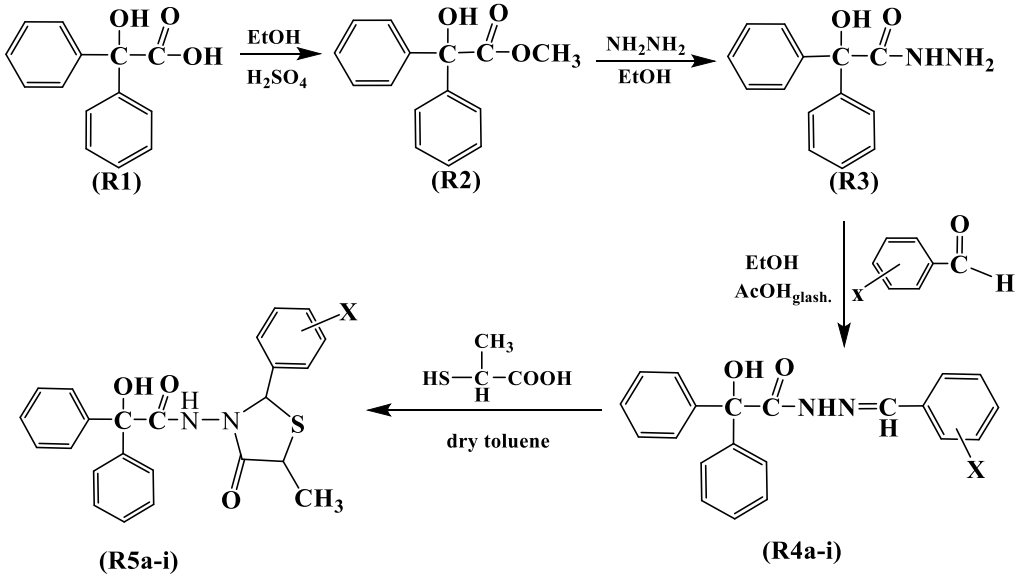
Mix (0.0005 mol) of the prepared hydrazones (R4a-d) with (25 ml) of dry toluene, then add (5 drops) of 2-mercaptopropionic acid, and reflux the mixture using the (Dean-Stark device) for (7 hours), then the excess solvent was evaporated under vacuum, add the mixture to the crushed ice, and neutralize it with a solution of sodium bicarbonate ($NaHCO_3$ 10%) to get rid of the liberated CO_2, then the precipitate is separated by filtration, washed with water, then left to dry, and recrystallized with ethanol. (Table 2).

Table 2: The Physical Data for Compounds (R5a-i).

Comp No.	Ar	Melting point °C	Color	Yield %
R5a	4-BrC_6H_4	240-243	White	55%
R5b	2-$NO_2C_6H_4$	225-230	Pale brown	51%
R5c	3-$NO_2C_6H_4$	233-236	Pink	43%
R5d	4-OHC_6H_4	238-241	Pale brown	62%
R5e	2-ClC_6H_4	134-137	Pale brown	51%
R5f	3-OHC_6H4	223-226	Pale brown	70%
R5g	3,4-diOHC_6H_3	244-247	Gray	53%
R5h	2,6-diClC_6H_3	287-290	White	84%
R5i	Piperonyl	183-186	Pale brown	53%

RESULTS AND DISCUSSION

In the present work, the synthesis of some substituted 4-oxothiazolidin(R5a-i) is achieved by a four-step synthesis using the benzilic acid as the starting material according to (Scheme 1).



X= a: 4-Br, b: 2-NO2, c: 3-NO2, d: 4-OH, e: 2-Cl, f: 3-OH, g: 3,4-diOH, h: 2,6-diCl, i: CH_2O_2 .

Scheme (1) Synthesis of compounds (R5a-i)

We noticed that when heating benzilic acid (R1) with methanol in the presence of sulfuric acid as a catalyst, methyl benzilate (R2) was obtained in very good yield. Which, when treated with hydrazine-hydrate in ethanol as a solvent, produced benzilic acid hydrazide (R3). When this hydrazide reacted with substituted benzaldehydes in the presence of glacial acetic acid and the corresponding hydrazones (R4a-i) were obtained. After that, these hydrazones were reacted with 2-mercaptopropionic acid to prepare 4-thiazolidinone (R5a-i).

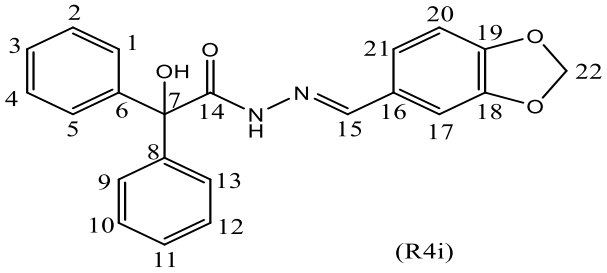
In the FT-IR spectra, some notable stretching bands attributed to (O-H, N-H and C=O) were distinguished at (3303-3564 cm^{-1}, 3200-3236 cm^{-1}, 1606-1661 cm^{-1}) respectively. A new band at (1614-1622 cm^{-1}) in the spectra of (R4a-d) support for imine group of hydrazone derivatives, and a new band at (1651-1683 cm^{-1}) in the spectra of (R5a-d) support for thaione group of lactams as shown in (Table 3).

Table 3: The Infrared data (FT-IR) for compounds (R4a-i) and (R5a-i).

Comp. No.	IR υ ($cm^{-1,}$ KBr)FT-				Others	Comp. No.	IR υ ($cm^{-1,}$ KBr) FT-				Others
	O-H	N-H	C=O	C=N			O-H	N-H	C=O Cyclic	C=O	
R4a	3406	3230	1651	1614	(C-Br)696	R5a	3330	3228	1665	1648	(C-Br)695
R4b	3394	3236	1647	1622	Asym.(C-NO_2)1525 Sym.(C-NO_2)1346	R5b	3346	3236	1668	1647	Asym .(C-NO_2) 1535 Sym.(C-NO_2)1346
R4c	3410	3250	1653	1616	Asym.(C-NO_2)1525 Sym.(C-NO_2)1354	R5c	3564	3250	1672	1651	Asym.(C-NO_2)1525 Sym.(C-NO_2)1352
R4d	3309	3200	1654	1606	(Ar-OH)3275	R5d	3310	3200	1651	1606	(OH)3275
R4e	3336	3236	1647	1600	(C-Cl)758	R5e	3336	3236	1674	1647	(C-Cl)758
R4f	3302	3235	1661	1615	(Ar-OH)3270	R5f	3389	3275	1661	1627	(OH)3302
R4g	3459	3270	1652	1596	(Ar-OH)3280	R5g	3459	3270	1652	1596	(OH)3280
R4h	3371	3265	1660	1599	(C-Cl)777	R5h	3459	3280	1652	1596	(C-Cl)753
R4i	3333	3240	1645	1627	----------	R5i	3303	3237	1683	1645	Asym. (C-O-C)1253 Sym. (C-O-C)1041

In the ^{1}H-NMR spectra of compounds (R4a-e), NH protons showed as a singlet (1H) at 11,324-12,002 ppm, and N=CH protons occurred as a singlet (1H) at 8.533-9.14 ppm.

The ^{13}C-NMR spectra showed peaks for hydrazones (R4a-i), were seen for C=N group identified by the existence of the signals in the range of δ values 147.91-159. 87ppm. The carbon signal of C=O group distinguished at δ values 169.45-171.91ppm, finally the carbon signal of C-OH in the range of δ values 80.58– 81.07ppm. as shown in (Table 4).



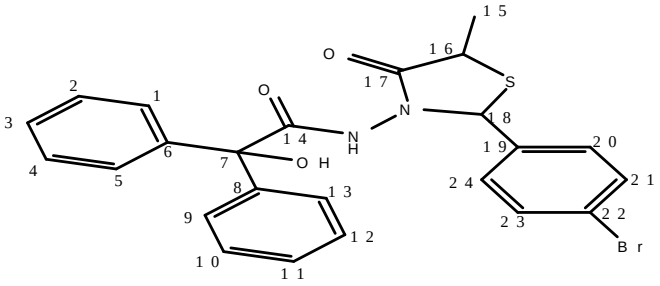
(R4i)

Table 4: The ^{1}H-NMR and ^{13}C –NMR data for compounds (R4a-i).

Comps. No.	^{1}H-NMR δ(ppm) DMSO-6	Comps. No.	^{13}C –NMR δ(ppm)
R4a	3.379(s,H,OH),7.049-7.848(m,14H,ArH), 8.533,(s,1H,N=CH), 11,627(s,1H,NH)	R4a	81.0(C_7),123.7(C_{19}),127.9(C_3, C_{11}), 128.0(C_1, C_5, C_9, C_{13}),129.4(C_2, C_4, C_{10}, C_{12}), 130.7(C_{17}, C_{21}),132.3(C_{18}, C_{20}),134.1(C_6, C_8), 144.2(C_{16}),147.9(C_{15}),169.9(C_{14})
R4b	3.353(s,H,OH),7.049-8,243(m,14H,ArH), 8.947,(s,1H,N=CH), 12,002(s,1H,NH)	R4b	81.0(C_7),125.0(C_{18}),127.9(C_3, C_{11}), 128.2(C_1, C_5, C_9, C_{13}),128.4(C_2, C_4, C_{10}, C_{12}), 129.1(C_{16}),131.1(C_{21}),134.1(C_{19}),144.0(C_{20}), 144.1(C_{15}),148.9(C_{17}),170.4(C_{14})
R4c	3.725(s,H,OH),7.080-8,322(m,14H,ArH), 8.867, (s,1H, N=CH), 11,799(s,1H, NH)	R4c	81.1(C_7),121.3(C_{17}),124.7(C_3, C_{11}), 127.5(C_1, C_5, C_9, C_{13}),128.2(C_2, C_4, C_{10}, C_{12}), 130.9(C_{20}),133.8(C_{21}),36.7(C_{16}),144.1(C_6, C_8), 146.8(C_{15}),148,7(C_{18}),170.3 (C_{14})
R4d	3.439(s,H,OH),4.407(s,1H,ArOH)6.612-8,636 (m,14H, ArH), 9.949, (s,1H, N=CH), 11,324(s,1H, NH)	R4d	80.9(C_7),116.2(C_{18}, C_{20}),125.8(C_3, C_{11}),127.5(C_{16}), 127.8(C_1, C_5, C_9, C_{13}),127.9(C_2, C_4, C_{10}, C_{12}), 129.3(C_{17}, C_{21}),144.4(C_6, C_8),149.4(C_{15}), 159.9(C_{19}),169.5(C_{14})
R4e	3.711(s,H,OH),6.578-8.012(m,14H,ArH), 9.14 (s,1H,N=CH), 11,924(s,1H,NH)	R4e	81.0(C_7),127.4(C_3, C_{11}),128.2(C_{20}), 128.3(C_1, C_5, C_9, C_{13}),128.9(C_{21}), 130.4(C_2, C_4, $C_{10,}$ C_{12}),131.9(C_{18}),132.3(C_{19}), 133.8(C_{17}),144.2(C_{16}),144.7(C_{15}),145.1(C_6, C_8), 171.9(C_{14})
R4g	3.39 (s,1H, OH),6.758-7.644 (m,13H, ArH) , 8.333 (s,1H, N=CH),9.346 (s,1H, ArOH), 11.266(s,1H, NH)	R4g	80.9(C_7),113.2(C_{17}),116.0(C_{20}),120.9(C_{21}), 126.2(C_3, C_{11}),127.8(C_1, C_5, C_9, C_{13}), 128.1(C_2, C_4, C_{10}, C_{12}),144.4(C_{16}),146.1(C_6, C_8), 146.9(C_{18}),148.4(C_{15}),149.6(C_{19}), 169.3(C_{14})
R4i	2.508(s,H,OH),6.086(s,2H,O-CH_2-O),6.969-7.849 (m,13H,ArH), 8.446(s,H,N=CH),11.432(s,H,NH)	R4i	80.9(C_7),102.0(C_{22}),105.4(C_{17}),108.9(C_{20}), 123.8(C_{21}),127.8(C_3, C_{11}),127.9(C_1, C_5, C_9, C_{13}), 128.1(C_2, C_4, C_{10}, C_{12}),129.2(C_{16}),144.3(C_6, C_8), 148.4(C_{15}),148.9(C_{18}),149.5(C_{19}),169.6(C_{14})

In the ^{1}H-NMR spectra of 4-thiazolidinone compounds (R5a-e), NH protons showed as a singlet (1H) at 8,561-9,946 ppm, and C_{16}-H protons appeared as a multiple (1H) at 2.798-3.521 ppm, C_{18}-H protons showed as a singlet at 3.480-6.074 ppm, CH_3 protons occurred as a doublet (3H) at 2.301-2.851 ppm.

The ^{13}C-NMR spectra showed peaks for 4-thiazolidinone compounds (R5a-i), were seen for C_{17}=O group identified by the existence of the signals in the range of δ values 169.92-175.46 ppm. The carbon signal of C_{14}=O group distinguished at δ values 169.85- 170.72ppm, finally the carbon signal of C_7-OH in the range of δ values 80.81– 81.03 ppm. as shown in (Table 5).



(R5a)

Table 5: The ^{1}H-NMR and ^{13}C –NMR Data for Compounds (R5a-i)

Comp. No.	^{1}H-NMR δ(ppm)	^{13}C-(NMR) δ(ppm)
R5a	2.351(d,3H, C_5-CH_3),2.550(s,1H, C-OH) ,2.965 (m,1H, thiazolidine-C_{16}-H), 5.95(s,1H, thiazolidine-C_{18}-H),7.152-7.878(m,14H, ArH), 8.561(s,1H, CONH)	36.6(C_{15}),40.6(C_{16}),65.2(C_{18}),80.9(C_7),123.6(C_{22}), 127.6(C_3, C_{11}),127.8(C_1, C_5, C_9, C_{13}),129.3(C_2, C_4, C_{10}, C_{12}), 131.4(C_{20}, C_{24}),132.3(C_{21}, C_{23}),134.2(C_{19}), 144.3(C_6, C_8), 170.1(C_{14}),171.7(C_{17})
R5b	2.851(d,3H, C_5-CH_3),2.557(s,1H, C-OH), 2.798 (m,1H, thiazolidine-C_{16}-H), 3.684(s,1H, thiazolidine-C_{18}-H),7.149-7.800(m,14H, ArH), 8.922(s,1H, CONH)	36.6(C_{15}), 38.2(C_{16}), 40.6(C_{18}),80.9(C_7), 124.9(C_{21}), 127.7(C_3, C_{11}), 127.9 (C_1, C_5, C_9, C_{13}),128.1(C_{22}), 128.4(C_2, C_4, C_{10}, C_{12}), 129.3(C_{24}),130.9(C_{19}),134.0(C_{23}), 144.4(C_6, C_8), 148.8(C_{20}), 170.8(C_{14}),175.3(C_{17})
R5c	2.301(d,3H, C_5-CH_3),2.508(s,1H, C-OH) ,2.842 (m,1H, thiazolidine-C_{16}-H), 6.074(s,1H, thiazolidine-C_{18}-H),7.094-7.750(m,14H, ArH), 8.659(s,1H, CONH)	36.7(C_{15}),38.3(C_{16}),40.5(C_{18}), 81.0(C_7),121.2(C_{22}),124.6(C_{20}), 127.6(C_3, C_{11}),127.9(C_1, C_5, C_9, C_{13}),128.1(C_2, C_4, C_{10}, C_{12}), 130.9(C_{23}),133.9(C_{24}),136.9(C_{19}),144.4(C_6, C_8),148.7(C_{21}), 170.7(C_{14}), 175.5(C_{17})
R5d	2.321(d,3H, C_5-CH_3),2.509(s,1H, C-OH) ,2.852 (m,1H, thiazolidine-C_{16}-H), 3.480(s,1H, thiazolidine-C_{18}-H),6.823-7.734(m,14H, ArH), 8.569(s,1H, CONH)	19.1(C_{15}),40.6(C_{16}),56.6(C_{18}),80.9(C_7),116.3(C_{21}, C_{23}), 125.3(C_3, C_{11}),127.8(C_1, C_5, C_9, C_{13}),129.3(C_2, C_4, C_{10}, C_{12}), 130.5(C_{20}, C_{24}),134.8(C_{19}),144.3(C_6, C_8),160.5(C_{22}), 169.5(C_{14}), 169.9(C_{17})
R5e	1.247(d,3H, C_5-CH_3),2.509(s,1H, C-OH) ,3.521 (m,1H, thiazolidine-C_{16}-H), 3.727(s,1H, thiazolidine-C_{18}-H),7.219-7.982(m,14H, ArH), 8.561(s,1H, CONH)	33.6(C_{15}),40.6(C_{16}), 79.7(C_{18}), 81.0(C_7), 127.4(C_{19}), 127.5(C_3, C_{11}), 127.6(C_{23}), 127.8(C_1, C_5, C_9, C_{13}),128.7(C_{22}), 129.3(C_{21}), 130.4(C_2, C_4, C_{10}, C_{12}),131.9(C_{24}),133.8(C_{20}),144.2(C_6, C_8), 169.9(C_{14}), 171.9(C_{17})
R5g	2.351(d,3H, C_5-CH_3),2.550(s,1H, C-OH) ,2.965 (m,1H, thiazolidine-C_{16}-H), 5.95(s,1H, thiazolidine-C_{18}-H),7.152-7.878(m,14H, ArH), 8.565(s,1H, CONH)	----------
R5i	2.508(d,3H, C_5-CH_3),2.899(s,1H, C-OH) ,3.386 (m,1H, thiazolidine-C_{16}-H), 5.855(s,1H, thiazolidine-C_{18}-H),6.0768(s,2H-O-CH_2-O)6.088-7.450 (m,13H, ArH),9.946(s,1H, CONH)	24.1(C_{15}),36.7(C_{16}),65.8(C_{18}),80.9(C_7),101.6(C_{25}),109.1(C_{23}), 121.8(C_{20}),123.9(C_{24}),127.5(C_3, C_{11}),127.9(C_1, C_5, C_9, C_{13}), 129.4(C_2, C_4, C_{10}, C_{12}), 131.9(C_{19}), 144.0(C_6, C_8), 147.4(C_{22}), 148.9(C_{21}), 169.9(C_{14}), 171.6(C_{17})

Antifungal activity

The disc diffusion method was used to conduct antifungal activity (Baron, 1994). Twenty milliliters of sterile Sabouraud Glucose Agar (SGA) were prepared for use in petri dishes. The test culture was swabbed onto the surface of the solidified media and given an hour to dry (1ml of a dilution solution of fresh fungus). A sterile disc was loaded with three different concentrations of the prepared compounds (1.66, 5, and 8.33 mg/ml/disc), and it was placed on the medium's surface at room temperature, for compound diffusion at 37 °C, these plates were incubated for 48 hours. The millimeters of the zone of inhibition were recorded.

The compounds (R4a-i and R5a, R5c) were screened for their *in vitro* antifungal activity against three pathogenic fungi: *Meyerozyma Caribbica, Rhodotorula Sp.*, and *Candida Albicans.* (Suspension of fresh colony, 24hours age using phosphate buffer solution, McFarland tube approved). Nistatin was used as a reference drugs-positive control. The results of antifungal activities are listed in (Table 6).

Table 6: Inhibition zones of compounds (R4a-i and R5a-d, f, h).

Comp. No.	*Meyerozyma Caribbica*			*Rhodotorula Sp.*			*Candida albicans*		
	A	**B**	**C**	**A**	**B**	**C**	**A**	**B**	**C**
R4a	6	8	10	17	20	20	7	8	8
R4b	10	12	12	15	18	20	6	8	8
R4c	10	10	10	7	10	13	7	8	8
R4d	11	10	10	15	16	17	10	10	12
R4e	10	12	25	14	18	20	9	12	12
R5a	8	7	8	8	8	10	14	14	23
R5b	7	10	10	Ø	8	8	12	12	12
R5c	7	8	9	21	20	22	13	14	17
R5d	9	13	14	20	21	22	11	15	12
R5f	8	10	11	19	21	25	13	13	20
R5h	10	10	10	19	19	20	12	20	25

All Prepared compounds showed a significant activity against *Rhodotorula Sp.*, which was comparable with the standard drug Nistatin which has zone of inhibition value of 19- 20mm. The outcomes showed that different substitutions had a significant impact on the activity. Compound R4a and R5c showed good activity against *Meyerozyma Caribbica.*

Compound R5a, on the other hand, was the most potent antifungal activity against *Rhodotorula Sp*. compound R4d, R5a, R5d, and R5c were found to be more potent antifungal activity against *Candida Albicans.* in comparison to Nistatin, 14, 19 and 20 mm., the reference drug.

CONCLUSION

The synthesized 2-aryl-1,3-thiazolidin-4-ones were obtained in the cyclization reaction of appropriate hydrazone derivatives with 2-mercapto propionic acid under reflux conditions by using (Dean-stark device) in dry toluene medium. The structures of obtained compounds were confirmed by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectroscopic methods and support for thaione group of lactams confirmed the synthesis pathway, the assumed molecular structures of the analyzed 2-aryl-1,3-thiazolidin 4-one's derivatives, and showed that all the final investigated compounds exist in thiazolidinones system.

Among the synthesized compound, mainly R4a, R5c, R5d, R5f, and R5h were found to be most active as antifungal agents *Rhodotorula Sp.*, and the zone of inhibition was in between 17 and 25 mm., compounds R4b, R4c, R4d, R4e and R5h were active as antifungal agents against *Meyerozyma Caribbica*, and the zone of inhibition was in between 10 and 12 mm., it was concluded

the compounds having thiazolidinones system enhanced the activity of hydrazone system as antifungal agents. And exhibited promising antimicrobial activities.

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تحضير، تشخيص ودراسة الفعالية المضادة للفطريات لبعض مركبات الثايازولدينون الجديدة المشتقة من حامض البنزيليك

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الملخص

من أجل دراسة المركبات الجديدة النشطة بيولوجيا، تم استخدام حامض البنزيليك كمادة أساس لتحضير بعض المشتقات الجديدة من 2-أريل-1،3-ثيازوليدين-4-ون، حيث تم تحضير بنزيلات الميثيل (R2) من حامض البنزيليك (R1) والميثانول بوجود حامض الكبريتيك بالتصعيد. وهيدرازيد حامض البنزيليك (R3) المحضر بالتصعيد من بنزيلات الميثيل (R2) و الهيدرازين المائي بوجود الإيثانول المطلق، أجريت بعض التفاعلات الكيميائية لهيدرازيد حامض البنزيليك (R3) من خلال التفاعل مع مجموعة من الألدهايدات الاروماتية (4-برومو بنزلديهايد، 2-نيترو بنزلديهايد، 3-نيترو بنزلديهايد، 4-هيدروكسي بنزلديهايد، 2-كلورو بنزلديهايد، 3-هيدروكسي بنزلديهايد، 3،4-ثنائي هيدروكسي بنزلديهايد، 2،6-ثنائي كلورو بنزلديهايد، بيبيرونال) في الإيثانول المطلق بوجود ثلاثة قطرات من حامض الخليك الثلجي وذلك من خلال التصعيد لإنتاج مشتقات الهيدرازونات المقابلة (R4a-i) حيث اعطى ناتج بنسبة جيدة الى معتدلة. كما تم الحصول على مشتقات 2-أريل-1،3-ثيازوليدين-4-ون (R5a-i) من تفاعل مشتقات الهيدرازونات المحضرة (R4a-i) مع 2- مركابتو حامض البروبانويك وذلك بعملية التصعيد وباستخدام جهاز (Dean-Stark) في التلوين الجاف. تم اختبار هذه المشتقات في المختبر كعوامل مضادة للفطريات ضد *Candida albicans* و*Rhodotorula sp.* و*Meyerozyma caribbica*.

الكلمات الدالة: ثايازولدينون، هيدرازونات، حامض البنزيليك، فعالية كمضاد للفطريات.