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Design, Synthesis, and Antibacterial, Antifungal, and Antioxidant Activities of New Four Membered Rings from Derivatives Containing a 4(3*H*)-Quinazolinone Moiety, Activities

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Abstract—Objective: The aim of this study is to produce novel 4(3*H*)-quinazolinone derivatives, analyze their efficacy as antibacterial and antifungal agents, and investigate their antioxidant abilities. **Methods:** New quinazolinone derivatives were synthesized by mixing Schiff bases with three different chemicals: phenyl isocyanate, 4-chlorophenyl isocyanate, and phenyl iso thiocyanate. This resulted in the formation of compounds (**VIa–VIb**), (**VIIa–VIIb**), and (**VIIIa–VIIIb**). The efficacy of these synthesized compounds against bacteria and fungi was evaluated. Subsequently, their antioxidant activity was assessed using the DPPH scavenging method. **Results:** FT-IR, ^{1}H NMR, and ^{13}C NMR spectroscopy were used to investigate all the prepared derivatives. Compounds (**VIIb**), (**VIIIa**), and (**VIIIb**) exhibited good antioxidant activity when compared to ascorbic acid. **Discussion:** The presence of the quinazolinone nucleus in some compounds gives them good biological properties as antimicrobials and antioxidants. **Conclusions:** All the synthesized compounds were highly effective at killing fungi, especially *Rhizopus microrhizosporium*, and *Candida*. Most of them were also very effective at killing bacteria like *E. coli*, *Bacillus cereus*, and *Pseudomonas aeruginosa*. Although most of these compounds have relatively moderate effectiveness against *Staphylococcus aureus*, some of them contain good antioxidants, particularly compound (**VIIIb**).

Keywords: anthranilic acid, Schiff bases, antimicrobial, DPPH, ascorbic acid (Vitamin C)

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INTRODUCTION

Heterocyclic molecules are crucial in medical chemistry due to their nitrogenous bases on heterocyclic rings [1, 2]. Quinazolinone, a heterocyclic molecule, is particularly important due to its structural variety, which is responsible for its broad range of biological activity [3, 4]. Quinazolinone and its analogues, especially 4(3*H*)-quinazolinone, have demonstrated significant biological activity, including, antitumor [5], antiviral [6, 7], antibacterial [8, 9], anticancer [10], anti-inflammatory [11–13], and anti-Alzheimer's disease properties [14]. The name "Schiff's base" comes from the German chemist Hugo Schiff, who established the description of the products arising from the carbonyl compound-primary amine reaction in 1864 [15–17]. Schiff bases are organic molecules that are very important in many areas, like materials science, chemistry, and pharmaceuticals [18, 19]. They have a flexible structure that can be used in many subjects. Schiff bases are widely used in biochemistry and biomedicine due to their unique properties [20]. When a primary amine and an aldehyde or ketone mix, these molecules are formed [21]. The reaction results in an imine group (C=N) [22]. Schiff's bases include interactions within the approved and considered mechanisms. When phenyl isocyanate and phenyl isothiocyanate react with the imine group of Schiff bases, 1,3-diazetidinone is formed [23]. Aza-

beta lactams, which are also known as diazetidine derivatives, are a type of organic compound [24, 25]. Additionally, 1,3-diazetidinone can be produced by the [2 + 2] cycloaddition process through cyclic condensation of Schiff bases with these reagents, resulting in the formation of four organic rings [26]. This article provides comprehensive instructions on how to produce 1,3-diazetidine-2-one of quinazolinone, an antimicrobial and inflammatory compound with potent biological activity.

RESULTS AND DISSCUSION

Chemistry

Benzamidobenzoic acid (**I**) was synthesized in the first step by reacting anthranilic acid with para-methoxybenzoylchloride in the presence of pyridine. The second step involved synthesizing benzoxazinone (**II**) by annular closure and reacting compound (**I**) with acetic anhydride. In the third step, ester (**III**) was synthesized by reacting benzoxazinone with ethyl glycinate hydrochloride in the presence of pyridine. The ester (**III**) was characterized using the hydroxamic acid test (specific ester exam) and gave positive detection in burgundy color. Ester (**III**) was then reacted with an excess of hydrazine hydrate to produce acetohydrazide-4(3*H*)-quinazolinone (**IV**). Schiff base compounds (**Va–Vb**) were formed by reacting compound (**IV**) with *p*-*N*, *N*-dimethylamino benzaldehyde, and *p*-nitro benzaldehyde. Finally, Schiff bases were reacted with various reagents to produce 3-phenyl-1,3-diazetidine-2-one (**VIa–VIb**), 3-(4-chlorophenyl)-1,3-diazetidine-2-one (**VIIa–VIIb**), and 3-phenyl-1,3-diazetidine-2-thione (**VIIIa–VIIIb**) derivatives of 4(3*H*)-quinazolinone in moderate to good yields. Scheme 1 illustrates the structure of all the prepared compounds.

Spectral Analysis

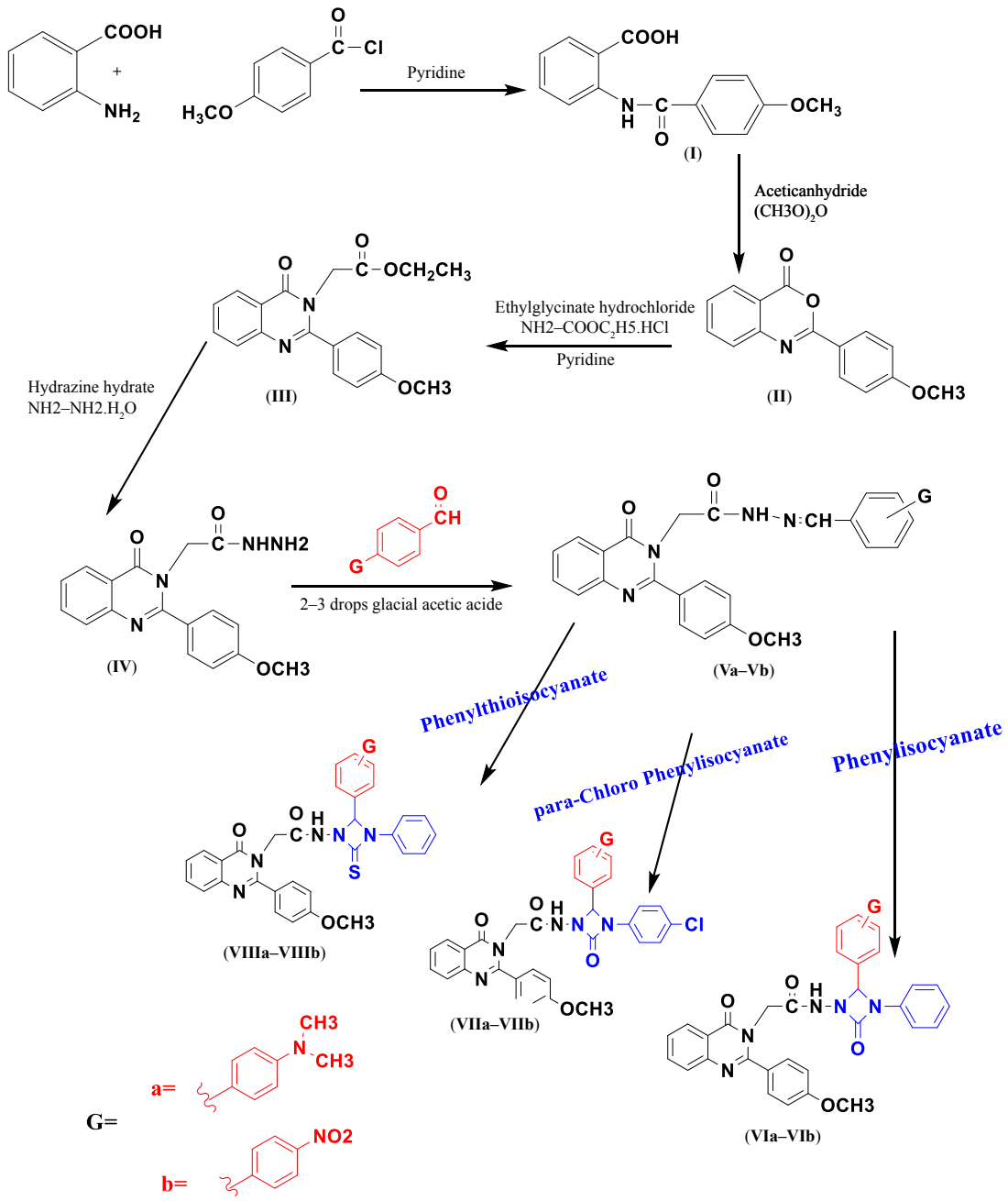
Silverstein's spectrometric identification of organic compounds, 7th edition was used to analyze all spectra. The FT-IR spectrum showed a significant N–H absorption band around 3407 and 3209 cm^{-1}, indicating the presence of the acetohydrazid group and the absence of an ester absorption band. The azomethine group of the Schiff bases was clearly visible in absorption measurements at 1639–1633 cm^{-1}. The ^{13}C NMR spectra for the diazetidine-2-one ring revealed signals at 164.45–162.71 ppm for C=O. They also exhibited signals at 191.43 and 180.08 ppm for C=S in diazetidine-2-thione. The ^{1}H NMR spectra showed signals at 6.76–5.72 ppm for C–H in the diazetidine ring [27].

Antibacterial and Antifungal Activity

The synthesized compounds demonstrated strong antifungal activity [28, 29], particularly against *Rhizopus microrhizosporium* and *Candida* [30], with most of them exhibiting similar efficacy against the bacteria *E. coli*, *Bacillus cereus*, and *Pseudomonas aeruginosa* [31]. Seemingly these compounds were relatively less effective against *Staphylococcus aureus* [23, 33], all the results are presented in Table 1 and Fig. 1.

Antioxidant Activity

The radical-scavenging activity of DPPH is a widely used technique to test antioxidant activity. The approach is favored due to its low cost, speed, and high sensitivity [34]. When a purple DPPH solution is mixed with any other substance that can give up a hydrogen atom, the reduced form of the molecule 2,2-diphenyl-1-picrylhydrazyl DPPH is created. As a result, the DPPH loses its violet color and becomes pale yellow due to the presence of the picryl group [35]. Ascorbic acid was utilized as a standard to assess the antioxidant capacity of these compounds using the DPPH technique. The compounds were tested by mixing 1 mL of reagent with different concentrations of 50, 100, 150, and 200 mg/mL. The mixture was kept in the dark for 30 min to avoid exposing the DPPH-free radicals to light. The absorption of substances was measured using UV-VIS spectroscopy at 517 nm with ascorbic acid as a reference [36]. Table 2 and Fig. 2 show the recently synthesized compounds (**VIa–VIb**), (**VIIa–VIIb**), and (**VIIIa–VIIIb**). Antioxidant activity is highest in compounds (**VIIIa**) and (**VIIIb**), while the activity of the others is limited.



Scheme 1. Preparation of new quinazolinone derivative (**I–VIII**).

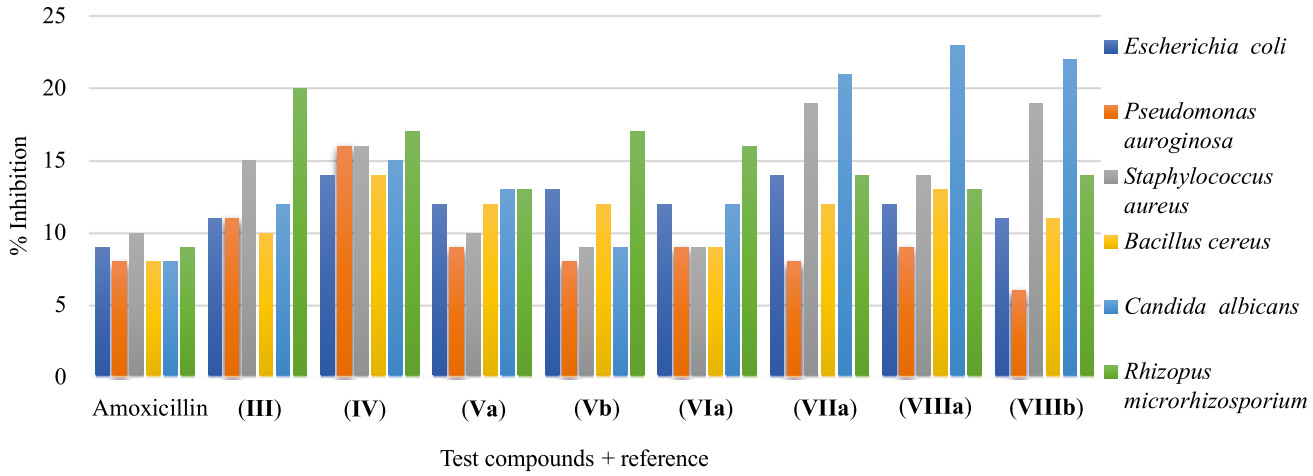


Fig. 1. Inhibition of the test compounds compared with drug.

Table 1. Presents the antibacterial and antifungal effects of the compounds testing (**III–VIII**)

Compound	The diameter of the inhibiting zone (mm)					
	E. coli (G–)	*P. auroginosa* (G–)	*S. aureus* (G+)	*B. cereus* (G+)	*C. albicans*	*Rhizopus microrhizosporium*
Control\DMSO	–	–	–	–	–	–
Amoxicillin	9	8	10	8	8	9
(III)	11	11	15	10	12	20
(IV)	14	16	16	14	15	17
(Va)	12	9	10	12	13	13
(Vb)	13	8	9	12	9	17
(VIa)	12	9	9	9	12	16
(VIIa)	14	8	19	12	21	14
(VIIIa)	12	9	14	13	23	13
(VIIIb)	11	6	19	11	22	14

Concentration, 0.08 mg/mL; –, no inhibition; *, not tested; weak, 1–8; moderate, 9–14; strong, 15–19; very strong, 20–24.

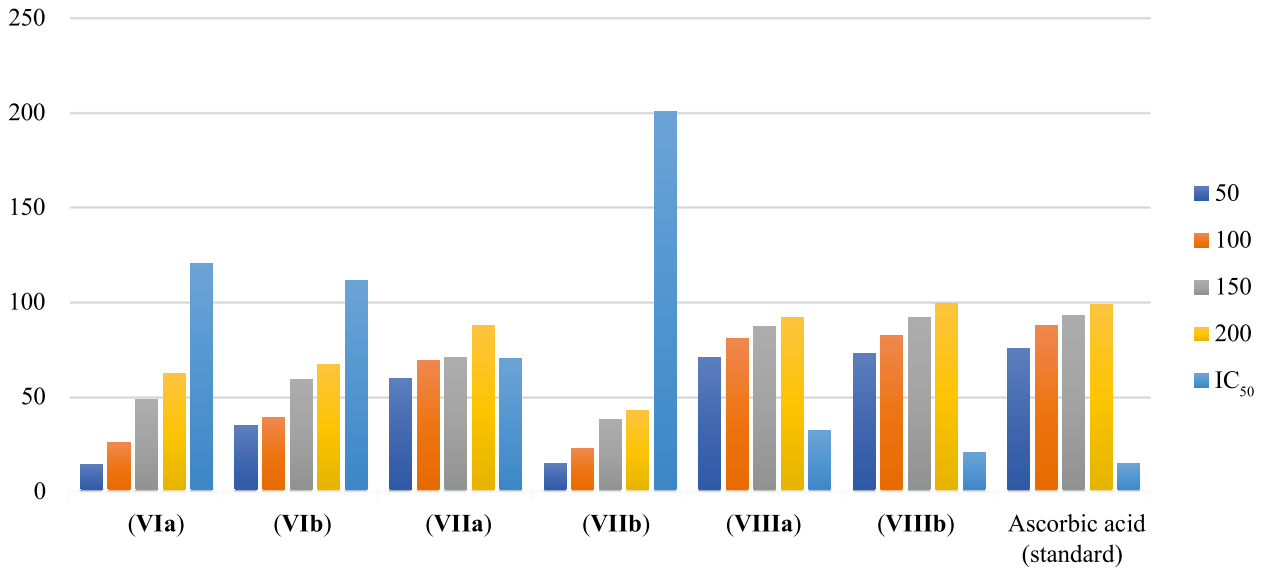


Fig. 2. Scavenging percentage of the test compound against standard.

Table 2. Description This study compares the molecules' radical scavenging % and IC_{50} concentrations against ascorbic acid

Concentration (µg/mL)	(VIa)	(VIb)	(VIIa)	(VIIb)	(VIIIa)	(VIIIb)	Ascorbic acid (standard)
	scavenging RSA%						
50	14.64	34.87	59.94	15.07	70.94	73.06	75.92
100	25.97	39.17	69.32	23.12	80.76	82.80	87.97
150	48.62	59.10	70.82	38.40	87.31	92.01	93.03
200	62.68	67.43	88.08	42.74	92.32	99.45	98.88
IC_{50}	120.51	111.76	70.54	200.67	32.28	20.76	15.05

EXPERIMENTAL

The solvents and starting substances for the synthesized compounds were provided by Sigma-Aldrich and Fluka and were employed without further purification. The uncorrected Gallen Kamp capillary melting point instrument was used to measure the melting points of the synthesized compounds. FT-IR measurements were done using a SHIMADZU FT-IR-8400S with a KBr disc; in addition, ^{1}H NMR and ^{13}C NMR spectra were collected at 400 and 100.64 MHz, respectively, on a Bruker spectrophotometer type ultra-shield with TMS as an internal standard.

Synthesis 2-(4-methoxybenzamido)-benzoic acid (I). Anthranilic acid (0.0073 mol, 1 g), *p*-methoxybenzoyl-chloride (0.0073 mol, 0.98 mL), and pyridine (0.5 mL) were combined with 15 mL of dry acetone in a round-bottomed flask. The mixture was then heated in a water bath at 50–60°C for 3 h. After the reaction, the solution was cooled down and filtered. The resulting products could be recrystallized from ethanol [37].

Synthesis 2-(4-methoxyphenyl)-quinazolin-4(3*H*)-one (II). Acetic anhydride (0.008 mol, 2 mL), was combined with compound (**I**) (0.008 mol, 1 g) and refluxed for 4 h under dry conditions. After the solution reached a suitable temperature, the resulting crystals were put into a 250 mL beaker containing cold petroleum ether. The solution was cooled and filtered following to the reaction. From ethanol, the resulting products could be recrystallized. [38].

Synthesis ethyl 2-(2-(4-methoxyphenyl)-4-oxo-quinazolin-3(4*H*)-yl) acetate (III). Compound (**II**) (0.004 mol, 1 g) was mixed in 3 mL of anhydrous dimethyl formamide. Dry pyridine (0.5 mL) was added to 3 mL of anhydrous DMF dissolved ethyl glycinate (0.004 mol, 0.5 g). The reaction mixture was refluxed for 4 h and put into ice-cold (0.05% HCl) to form solid crystals [39]. Filtering, washing with distilled water, and recrystallizing from ethanol yielded solid precipitate.

Synthesis 2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetohydrazide (IV). To synthesize the compound (**IV**), hydrazine hydrate (80%) (0.002 mol, 0.15 mL) was added to (0.0015 mol, 0.5 g) of compound (**III**) that was dissolved in (15 mL) absolute ethanol. The reaction mixture was refluxed for 8 h and then left overnight to cool. The resulting mixture was poured into ice-cold water, which produced a solid crystalline precipitate. The precipitate was filtered, washed with distilled water, and recrystallized from acetone [40].

General synthesis of *N*-[(4-substituted benzylidene)-acetohydrazone]-2-(4-methoxyphenyl)-quinazoline-3(4*H*)-one (Va–Vb). A solution of compound (**IV**) (0.001 mol, 0.5g) dissolved in 12 mL of absolute ethanol was gradually added to a solution of various substituted aromatic aldehydes (0.001 mol) dissolved in 5 mL of absolute ethanol with a few drops of glacial acetic acid to synthesize the compound. The mixture was stirred constantly for 15 min in a 50–60°C water bath. The reaction mixture was heated for 1 h, and then the water bath was removed with continuous reflux for 8–10 h. A solid precipitate was filtered and recrystallized in a suitable solvent after the mixture was placed into ice-crushing [41, 42].

General procedure for the synthesis 3-phenyl-1,3-diazetidine-2-one (VIa–VIb), 3-(4-chlorophenyl)-1,3-diazetidine-2-one (VIIa–VIIb), and 3-phenyl-1,3-diazetidine-2-thione (VIIIa–VIIIb). The compounds (**VIa–VIb**, **VIIa–VIIb**, and **VIIIa–VIIIb**) were synthesized by mixing 0.015 mol of phenyl isocyanate, *p*-chlorophenyl isocyanate, and phenyl isothiocyanate with 0.015 mol of Schiff bases (**Va–Vb**) in 15 mL of dimethylformamide. The mixture was heated at 65–70°C for 14–16 h, and the residue was recrystallized from ethanol after the mixture was chilled [43].

2-(4-Methoxybenzamido)-benzoic acid (I). Pale yellow solid; Yield: 90%; mp: 212–214°C, FT-IR (ν_{max}, cm^{-1}): 3436–2700 (O–H), 3257 (N–H), 3068 (Ar–H), 2974–2929 (C–H) aliphatic, 1710 (C=O) acid, 1672 (C=O) amide, 1602 (C=C); ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.85 (s, 3H, $–CH_3$), 7.06–8.13 (m, 8H, H aromatic), 11.60 (s, 1H, NH), 12.30 (s, 1H, OH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 55.80, 114.47, 140.07, 147.43, 164.67 (C=O) amide, 169.98 (C=O) acid; $C_{15}H_{19}NO4$; Calculated, %: C, 66.41; H, 4.83; N, 5.16; O, 23.59; Found, %: C, 66.44; H, 4.85; N, 5.19; O, 23.62.

2-(4-Methoxyphenyl)-quinazolin-4(3*H*)-one (II). White solid; Yield: 90%; mp: 158–160°C, FT-IR (ν_{max}, cm^{-1}): 3037 (Ar–CH), 2977, 2941 (alipha–CH), 1758 (C=O) lactone, 1645 (C=N) cyclic, 1600 (C=C); ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.82 (s, 3H, CH_3), 7.06–8.32 (m, 8H, H aromatic); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 55.50, 114.31–148.28, 158.23, 164.26 (C=O); $C_{15}H_{11}NO_3$; Calculated, %: C, 71.14; H, 4.38; N, 5.53; O, 18.95; Found, %: C, 71.18; H, 4.42; N, 5.57; O, 18.99.

Ethyl 2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetate (III). Pale orang solid; Yield: 80%; mp: 98–100°C, FT-IR (ν_{max}, cm^{-1}): 3068 (Ar–CH), 2977, 2904 (alipha–CH), 1749 (C=O) ester, 1681 (C=O) amide, 1641 (C=N), 1602 (C=C), 1186 (C–O–C); ^{1}H NMR (400 MHZ, DMSO-d_6), ppm: 1.32 (t, 3H, $–CH_3$), 3.85 (s, 3H, $–OCH_3$), 4.35 (q, 2H, $–OCH_2$), 5.08 (s, 2H, $–NCH_2$), 7.09, 8.66 (m, 8H, H aromatic); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 14.52, 41.48, 55.95, 61.87, 114.6, 147.07, 156.44, 164.55 (C=O) cyclic amide, 170.63 (C=O) ester;

$C_{19}H_{18}N_2O_4$; Calculated, %: C, 74.49; H, 5.92; N, 9.14; O, 10.44; Found, %: C, 74.53; H, 5.95; N, 9.17; O, 10.47.

2-(2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-acetohydrazide (IV). White solid; Yield: 75%; mp: 180–182°C; FT-IR (ν_{max}, cm^{-1}): 3436, 3290 (NH_2), 3182 (N–H), 3002 (Ar-CH), 2977, 2939 (alipha–CH), 1668 (C=O) amide, 1602 (C=C); ^1H NMR (400 MHz, DMSO-d_6), ppm: 3.85 (s, 3H, –OCH_3), 4.15 (s, 2H, –NCH_2), 4.67 (s, 2H, NH_2), 7.09, 8.13 (m, 8H, H aromatic); 8.67 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 41.8, 113.21, 148.46, 165.45 (C=O) cyclic, 169.82 (C=O) amide; $C_{17}H_{16}N_4O_3$; Calculated, %: C, 62.95; H, 4.97; N, 17.27; O, 14.80; Found, %: C, 62.99; H, 5.03; N, 17.31; O, 14.84.

***N′*-(4-(Dimethylamino)-benzylidene)-2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-acetohydrazide (Va).** Dark yellow solid; Yield: 92%; mp: 238–240°C; FT-IR (ν_{max}, cm^{-1}): 3419 (N–H), 3070 (Ar-CH), 2960, 2910 (alipha–CH), 1679 (C=O) amide, 1639 (C=N) imine; ^1H NMR (400 MHz, DMSO-d_6), ppm: 3.04 (s, 6H, –CH_3), 3.85 (s, 3H, –OCH_3), 4.35 (s, 2H, –NCH_2), 7.12, 8.01 (m, 12H aromatic), 8.67 (s, 1H, N=CH), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 55.08, 61.87, 112.64, 147.07, 162.80, 164.67 (C=O) cyclic, 168.20 (C=O) amid; $C_{26}H_{25}N_5O_3$; Calculated, %: C, 68.56; H, 5.53; N, 15.37; O, 10.54; Found, %: C, 68.59; H, 5.56; N, 15.41; O, 10.57.

2-(2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-*N′*-(4-nitrobenzylidene) acetohydrazide (Vb). Yellow solid; Yield: 70%; mp: 215–217°C; FT-IR (ν_{max}, cm^{-1}): 3296 (N–H), 3072 (Ar-CH), 2987, 2912 (alipha–CH), 1681 (C=O) amide, 1633 (C=N) imine, 1558, 1389 (NO_2); ^1H NMR (400 MHz, DMSO-d_6), ppm: 3.85 (s, 3H, OCH_3), 4.15 (s, 2H, –NCH_2), 7.13, 7.58 (m, 12H, H aromatic), 8.63 (s, 1H, N=CH), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 41.48, 55.08, 114.64, 148.46, 162.46, 165.82 (C=O) cyclic, 170.63 (C=O) amide; $C_{24}H_{19}N_5O_5$; Calculated, %: C, 63.02; H, 4.19; N, 15.31; O, 17.49; Found, %: C, 63.05; H, 4.24; N, 15.35; O, 17.53.

***N*-(2-(4-(Dimethylamino)-phenyl)-4-oxo-3-phenylazetidin-1-yl)-2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetamide (VIa).** Pale brown solid; Yield: 75%; mp: 140–142°C; FT-IR (ν_{max}, cm^{-1}): 3406 (N–H), 3060 (Ar-CH), 2977, 2935 (alipha–CH), 1728 (C=O) diazetidine ring, 1706 (C=O) cyclic, 1602 (C=C), 1649 (C=O) amide; ^1H NMR (400 MHz, DMSO-d_6), ppm: 2.98 (s, 6H, –NCH_3), 3.85 (s, 3H, –OCH_3), 4.69 (s, 2H, –NCH_2), 6.76 (s, 1H, –NCH cyclic), 6.98, 7.58 (m, 17H, H aromatic), 9.68 (s, 1H, –NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 41.48 (N$\underline{C}H_3$), 55.92 (O$\underline{C}H_3$), 61.87 (NCH_2), 73.01 (NCH) diazetidine ring, 112.64, 139.45 (Ar-C), 162.68 (C=O) diazetidine ring, 165.85 (C=O) cyclic, 170.63 (C=O) amide; $C_{33}H_{30}N_6O_4$; Calculated, %: C, 68.98; H, 5.26; N, 14.63; O, 11.14; Found, % : C, 69.03; H, 5.30; N, 14.67; O, 11.17.

2-(2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-*N*-(2-(4-nitrophenyl)-4-oxo-3-phenyl-1,3-diazetidin-1-yl) acetamide (VIb). Orange solid; Yield: 75%; mp: 213–215°C; FT-IR (ν_{max}, cm^{-1}): 3209 (N–H), 3055 (Ar-CH), 2904, 2842 (alipha–CH), 1704 (C=O) diazetidine ring, 1666 (C=O) amide, 1602 (C=C), 1527, 1344 (NO_2); ^1H NMR (400 MHz, DMSO-d_6), ppm: 3.85 (s, 3H, OCH_3), 4.69 (s, 2H, –NCH_2), 6.98 (s, 1H, –NCH), 7.13, 7.58 (m, 17H, H aromatic), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 55.92, 61.87, 73.53, 112.64, 139.45, 164.74(C=O) diazetidine ring 165.28 (C=O) cyclic, 170.34(C=O) amide; $C_{31}H_{24}N_6O_6$; Calculated, %: C, 64.58; H, 4.20; N, 14.58; O, 16.65; Found, % : C, 64.62; H, 4.24; N, 14.62; O, 16.69.

***N*-(3-(4-Chlorophenyl)-2-(4-(dimethylamino)-phenyl)-4-oxo-1,3-diazetidin-1-yl)-2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetamide (VIIa).** Orang solid; Yield: 75%; mp: 239–241°C; FT-IR (ν_{max}, cm^{-1}): 3298 (N–H), 3076 (Ar-CH), 2977, 2916 (alipha–CH), 1706 (C=O) diazetidine ring, 1668 (C=O) amide, 1602 (C=C), 1089 (Ar-Cl); ^1H NMR (400 MHz, DMSO-d_6), ppm: 3.82 (s, 3H, –OCH_3), 4.50 (s, 2H, –NCH_2), 6.76 (s, 1H, NCH), 7.13, 8.62 (m, 16H, H aromatic), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 41.48 (NCH_3), 55.02 (OCH_3), 61.12 (–NCH_2), 73.35 (–NCH) diazetidine ring, 114.64, 146.17 (Ar-C), 164.45 (C=O diazetidine), 165.83 (C=O) cyclic, 169 (C=O) amide; $C_{33}H_{29}ClN_6O_4$; Calculated, %: C, 65.08;

H, 4.80; Cl, 5.82; N, 13.80; O, 10.51; Found, %: C, 65.11; H, 4.84; Cl, 5.85; N, 13.84; O, 10.55.

***N*-(3-(4-Chlorophenyl)-2-(4-nitrophenyl)-4-oxo-1,3-diazetidin-1-yl)-2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetamide (VIIb).** Red solid; Yield: 85%; mp: 283–285°C; FT-IR (ν_{max} cm^{-1}): 3290 (N–H), 3056 (Ar-CH), 2909, 2983 (alipha–CH), 1708 (C=O) diazetidine ring, 1645 (C=O) amide, 15371346 (NO_2), 1027 (Ar-Cl); ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.82 (s, 3H, OCH_3), 4.50 (s, 2H, NCH_2), 6.76 (s, 1H, NCH), 7.13, 8.62 (m, 16H, H aromatic), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 55.87 (OCH_3), 61.12 (NCH_2), 73.53 (NCH), 110.66, 140.34, 162.71 (C=O) diazetidine ring, 165.66 (C=O) cyclic, 170.23 (C=O) amide; $C_{31}H_{23}ClN_6O_6$; Calculated, %: C, 60.94; H, 3.79; Cl, 5.80; N, 13.75; O, 15.71; Found, %: C, 60.98; H, 3.82 ; Cl, 5.83; N, 16.75; O, 15.74.

***N*-(2-(4-(Dimethylamino)-phenyl)-3-phenyl-4-thioxo-1,3-diazetidin-1-yl)-2-(2-(4-methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl) acetamide (VIIIa).** Yellow solid; Yield: 70%; mp: 110–112°C; FT-IR (ν_{max}, cm^{-1}): 3257 (N–H), 2904, 2989 (alipa–CH), 1672 (C=O) cyclic, 1647 (C=O) amide, 1386 (C=S); ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 1.78 (s, 6H, NCH_3), 3.85 (s, 3H, –OCH_3), 4.15 (s, 2H, –NCH_2), 5.72 (s, 1H, –NCH), 6.76, 8.63 (m, 12H, H aromatic), 9.86 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 41.42 (NCH_3), 55.88 (OCH_3), 61.12 (NCH_2), 73.53 (NCH), 114.23–140.35, 165.27 (C=O) cyclic, 169.86 (C=O) amide, 211.43 (C=S); $C_{33}H_{30}N_6O_3S$; Calculated, %: C, 67.10; H, 5.12; N, 14.23; O, 8.13; S, 5.43; Found, %: C, 67.13; H, 5.16; N, 14.26; O, 8.16; S, 5.47.

2-(2-(4-Methoxyphenyl)-4-oxoquinazolin-3(4*H*)-yl)-*N*-(2-(4-nitrophenyl)-3-phenyl-4-thioxo-1,3-diazetidin-1-yl) acetamide (VIIIb). Yellow solid; Yield: 80%; mp: 77–°C; FT-IR (ν_{max}, cm^{-1}): 3271 (N–H), 3055 (Ar–CH), 2941, 2908 (alipha–CH), 1666 (C=O) cyclic, 1641 (C=O) amide, 1558, 1344 (NO_2), 1413 (C=S); ^{1}H NMR (400 MHz, DMSO-d_6), ppm: 3.85 (s, 3H, OCH_3) 4.35 (s, 2H, NCH_2), 7.13, 8.74 (m, 12H, H aromatic), 6.98 (s, 1H, NCH), 9.68 (s, 1H, NH); ^{13}C NMR (100.64 MHz, DMSO-d_6), ppm: 45.55 (NCH_2), 55.90 (OCH_3), 73.53 (NCH), 114.62, 146.61, 165.82 (C=O) cyclic, 170.63 (C=O) amide, 180.08 (C=S); $C_{31}H_{24}N_6O_5S$; Calculated, %: C, 62.83; H, 4.08; N, 14.18; O, 13.50; S, 5.41; Found, %: C, 62.87; H, 4.12; N, 14.22; O, 13.54; S, 5.44.

Biological testing. Initially, all test substances were dissolved in dimethyl sulphoxide (DMSO) at a concentration of 0.08 mg/mL. The solution was then diluted in steps to create a growth medium, which was used to investigate the effects of four different types of bacteria and two types of fungi. The bacteria included two Gram-negative strains [44, 45], *Escherichia coli* and *Pseudomonas aeruginosa*, and two Gram-positive strains, *Bacillus subtilis* and *Staphylococcus aureus*. The fungi used were *Candida albicans* and *Rhizopus microrhizosporium* [46]. The investigations were conducted at the B.P.C. analysis laboratory.

Antibacterial and antifungal. To test compounds (**III**), (**VIIIa–VIIIb**) a solution was prepared using the organic solvent dimethyl sulphoxide DMSO [47]. A test solution of 0.08 mg/mL was made for each compound, which was then used to investigate the effects on four bacteria and two fungi. The agar-well diffusion method was used to distribute the concentration on plates, and a 5 mm diameter hole was made in the middle of the agar at the plate's edge. The fluid was then pumped into the hole using a micropipette, and the results were recorded at 37°C after 18–24 h. To test the antifungal properties of the compounds, they were grown in potato dextrose agar (PDA), a medium for fungi, at a temperature of 28°C for 3–5 days [48]. The chemicals that were tested were used to measure the areas where microbial organisms were destroyed, as shown in Table 1 and Fig. 1.

Antioxidant activity. 0.002 g of (1,1-diphenyl-2-picryl-hydroxyl) (DPPH) was dissolved in 50 mL of methanol in a volumetric flask coated in aluminum foil and insulated from light. In 5 mL of dimethyl sulfoxide, 0.0015 g of each compound was dissolved to create a 200 ppm stock solution. This stock solution was used to create 150, 100, and 50 ppm solutions [49]. Vitamin C (L-ascorbic acid) was also produced in equal quantities. After filling test tubes with 1 mL of each concentration (200, 150, 100, and 50 ppm), mixing them with 1 mL

of newly prepared DPPH solution, and keeping them at room temperature for 30 min in a dark place, a UV-Vis spectrophotometer examined each solution at 517 nm after incubation [50]. The substances examined measured microbial destruction (Table 2, Fig. 2).

$$\text{DPPH Inhibition \%} = \frac{ABSn + ABSc}{ABSn} \times 100\%, \quad (1)$$

where *ABSn* = mixed (sample) absorbance, *ABSc* = blank absorbance.

CONCLUSIONS

The purpose of this study was to produce a series of novel quinazolinone 4(3*H*) derivatives (**VIa–VIb**, **VIIIa–VIIIb**) and to investigate their antimicrobial properties. The results demonstrated significant effectiveness against both Gram-negative and Gram-positive bacteria, with a focus on *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus*, and *Bacillus cereus*. Additionally, noteworthy activity was observed for *Rhizopus microrhizosporium* and *Candida albicans*.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article does not contain any studies involving patients or animals as test objects.

Informed consent was not required for this article.

CONFLICT OF INTEREST

No conflicts of interest was declared by the authors.

AUTHOR CONTRIBUTION

The author SMH selected literature data relevant to the subject of the review, while author NNS assisted in producing the manuscript.

All authors were present during the discussions.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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