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Synthesis and Antimicrobial Activities of Novel Rutin Derivatives Carrying Quinoline Moiety

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Abstract*. Antimicrobial resistance constitutes a topical subject and it is one of the major threats to public health. According to statistics, the incidence of multidrug-resistant microorganisms, such as bacteria, fungi and protozoa has increased in the last decades and it continues to spread. Therefore, the development of novel antimicrobial agents to combat drug-resistant infections is very important, among other research directions in this field. Quinoline ring is a very interesting structure for researchers because of its diverse biological properties (antimicrobial, anticancer, anticonvulsant, antiinflamatory and cardiovascular). On the other hand several studies showed good antibacterial activity (including anti-Pseudomonas effects) and antifungal properties of rutin or vegetal species with a high flavonoids (especially rutin) concentration. Based on the above considerations, eight novel rutin derivatives carrying 4- and 8-aminoquinoline moiety were designed, synthesized and characterized by FTIR, 1H NMR and elemental analysis. All compounds were evaluated for their in vitro antimicrobial activities against representative Gram-positive, Gram-negative and fungal pathogens. The results indicated that all rutin derivatives exhibited good antibacterial activities, similar to ciprofloxacin.*

Keywords*: flavonoids, rutin, quinoline, antimicrobial*

1.Introduction

Antimicrobial resistance constitutes a topical subject and it is one of the major threats to public health. According to statistics, the incidence of multidrug-resistant microorganisms, such as bacteria, fungi and protozoa has increased in the last decades and it continues to spread. One of the most exhaustive official studies of antimicrobial resistance concluded in 2016 that, globally, 700 000 deaths each year can be attributed to antimicrobial resistance [1]. Therefore, the development of novel antimicrobial agents to combat drug-resistant infections is very important, among other research directions in this field.

It is well-known that quinoline ring is an important pharmacophore for many biological effects [2-9]. Among these, perhaps the most important action is antimicrobial. Quinolones like ciprofloxacin and other similar derivatives or chlorquinaldol are very potent antibacterial, but also antifungal and antiprotozoa agents. Other quinoline derivatives like chloroquine or mefloquine have antimalarial action.

On the other hand, there are several significant studies showing a good antibacterial activity (including anti-*Pseudomonas* effects) and antifungal properties of rutin or vegetal species with a high flavonoids (especially rutin) content [10-17]. Based on the above considerations, eight novel rutin derivatives carrying 4- and 8-aminoquinoline moiety were designed, synthesized and characterized by FTIR, 1H NMR and elemental analysis. All compounds were evaluated for their in vitro antimicrobial activities against representative Gram-positive, Gram-negative and fungal pathogens.

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2.Materials and methods

All commercial chemicals and solvents are reagent grade and were used without further purification. Rutin (97-102%) was purchased from Acros Organics, Belgium; 4-aminoquinoline, 8-aminoquinoline and solvents (methanol, isopropanol, ethanol) were purchased from Sigma-Aldrich; halogenated reagents (1, 3-dichloro-2-propanol; 1-brom-3-chloropropane; 1, 2-dibromoethane and dibromomethane) were purchased from Merck-Schuchardt, sodium was delivered by Riedel-de-Haen AG and Silicagel was purchased from Fluka. Melting points are uncorrected and were measured in open capillary tubes on a Electrothermal Mel-Temp device; the elemental analysis were performed on a "Exeter Analytical" CE-440 elemental analyser. The IR spectra were recorded on a FT/IR "Jasco 670 Plus" spectrometer. The H-NMR spectra were recorded on a Bruker Avance DRX-400 spectrometer using tetramethylsilane as internal standard and DMSO-d6 as solvent. The antimicrobial activity was studied using Gram- positive bacteria (*Staphylococcus aureus* ATCC 25923), Gram- negative bacteria (*Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853) and pathogenic yeasts (*Candida albicans* ATCC 90028); all these strains were obtained from the Culture Collection of the Department of Microbiology, Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania.

We intentionally chose 4- and 8-aminoquinoline for their potent antimalarial effects too, and the evaluation of the antiplasmodium activity of the new derivatives is a future goal of our research.

Rutin derivatives (I-VIII) were synthesized according to the procedure described in a previous paper [18]; rutin (IX) was dissolved in sodium methoxide, under reflux heating for 30 minutes, subsequently treating with 1,3-dichloro-2-propanol; 1-brom-3-chloropropane; 1,2-dibromoethane and dibromomethane, respectively (X - XIII) and finally, reflux heating for twelve hours with 4-, and 8-aminoquinoline, respectively, in the presence of pyridine, afforded the corresponding compounds I - VIII. (Figure 1, Table 1). From reaction mixtures, which are yellow-orange solutions, we obtained the crude derivatives through isopropanol precipitation, filtration and ambient temperature drying.

The crude compounds were purified by column chromatography (0.5 cm x 25 cm; Silicagel H (10-40 μm), elution with hexane-ethyl acetate (1:1) (0,8-1 mL/min.).

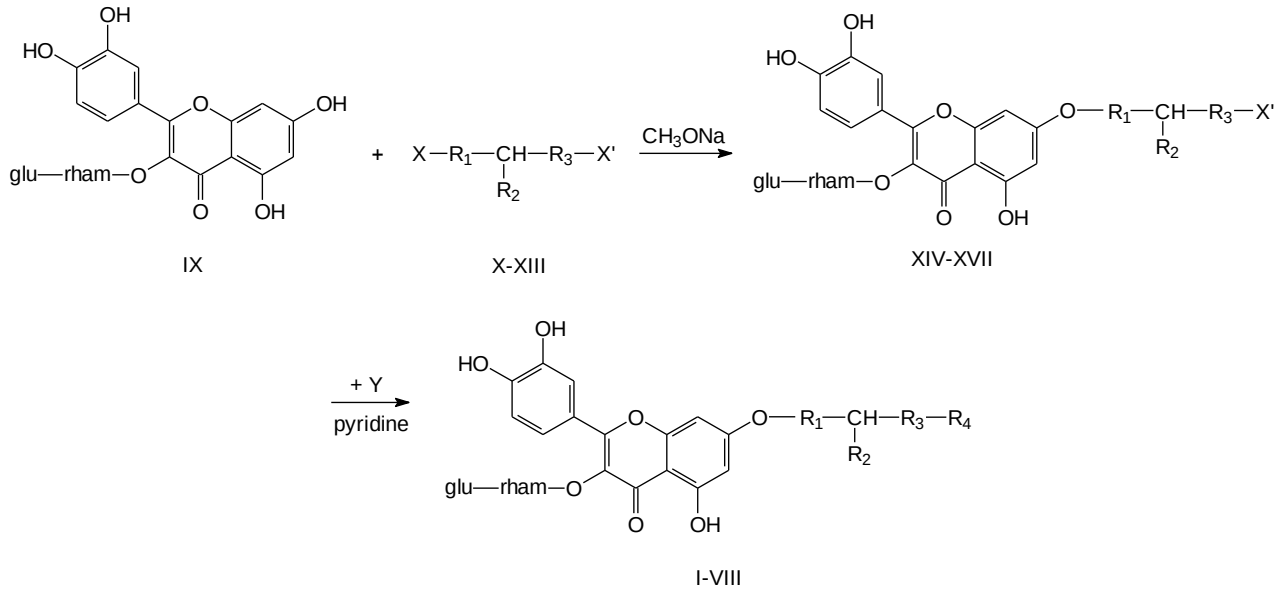
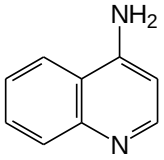
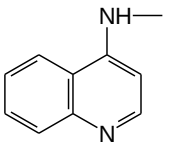
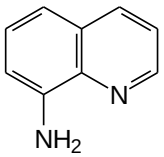
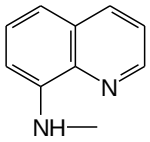


Figure 1. The synthesis of rutin derivatives I-VIII

Table 1. Assignment of functional groups in chemical synthesis of rutin derivatives I-VIII

Comp.no.	X	X'	R_1	R_2	R_3	Y	R_4
I	Cl	Cl	CH_2	OH	CH_2		
II	Br	Cl	CH_2	H	CH_2		
III	Br	Br	CH_2	H	-		
IV	Br	Br	-	H	-		
V	Cl	Cl	CH_2	OH	CH_2		
VI	Br	Cl	CH_2	H	CH_2		
VII	Br	Br	CH_2	H	-		
VIII	Br	Br	-	H	-		

The antimicrobial activity was evaluated using the disk diffusion methods [19, 20]. Mueller Hinton agar (Oxoid) and Mueller-Hinton agar Fungi (Biolab) were inoculated with the suspensions of the tested microorganisms: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Candida albicans* ATCC 90028. Sterile stainless steel cylinders (5 mm internal diameter; 10 mm height) were applied on the agar surface in Petri plates. Then, 100 µL of the tested compounds (I-VIII), with a concentration of 1 mg/mL each were added into cylinders. The plates were left 10 minutes at room temperature to ensure the equal diffusion of the compound in the medium and then incubated at 35ºC for 24 hrs. As reference antimicrobial drugs there were used commercial available discs containing Ciprofloxacin (5 µg/disk), Fluconazole (25 µg/disk) and Voriconazole (1 µg/disk). After incubation, the diameters of inhibition zones were measured in mm, including disc size.

3.Results and discussions

Eight novel derivatives of rutin were synthesised and purified by column chromatography in acceptable yield (77,2-82,5%); all these compounds are crystalline, hygroscopic, yellow powders, with no odour and having a slightly bitter taste, soluble in water, alcohol, dimethylsulfoxide and dimethylformamide and insoluble in 2-propanol, dioxane, acetone, ether, benzene and chloroform. The chemical structure have been proven by C,H,N elemental analysis and by IR and ^{1}H NMR spectroscopy.

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl]- oxy] – 2 - (3, 4 –dihydroxy-phenyl) - 5-hydroxy- 7 -(oxy-1-(β-hydroxy-propyl)-3-(aminoquinolin-4-yl))-4H-1-benzopyran-4-one (I): yield 77,8%; mp 198-201 °C; IR (KBr) (cm^{-1}): 3440 (OH), 3192 (NH), 2920 (CH arom.), 1670 (C=O on aromatic ring), 1610 (C=N), 1511 (aromatic C=C), 1364, 1300, 1210, 1041 (C-O-C), 800 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.57 (dd, 1H, H-2 quinoline ring), 8.03 (m, 1H, H-5 quinoline ring), 7.84 (m, 1H, H-8 quinoline ring), 7.73 (dd, 1H, H-6'), 7.61 (m, 1H, H-7 quinoline ring), 7.55 (m, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 6.74 (dd, 1H,H-5'), 6.71 (dd, 1H, H-3 quinoline ring), 6.46 (d, 1H, H-8), 6,31 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.41 (d, 1H, H1-rhamnosyl), 4.27 (d, 2H, O7-CH2), 4.13 (d, 2H, CH_2 between glu-rha), 3.96 (m, 1H, CH alkyl chain), 3.89 (m, CH rha), 3.58 (m, 1H, CH glu), 3.42 (d, 2H, CH_2-N), 3.40 (dd, 3H, CH glu) 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{39}H_{42}N_2O_{17}$; Molecular weight = 810.76; Calculated = C (57.77%) H (5.22%) N (3.45%); Found = C (57.65%) H (5.20%) N (3.40%).

3-[[6-O-(6-deoxy-α-L- manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 - dihydroxyphenyl)-5-hydroxy-7-(oxy-1-propyl-3-(aminoquinolin-4-yl))-4H-1-benzopyran-4-one (II): yield 78.3%; mp 207-210 °C; IR (KBr) (cm-1): 3412 (OH), 3185 (NH), 2911 (CH arom.), 1668 (C=O

on aromatic ring), 1628 (C=N), 1514 (aromatic C=C), 1361, 1312, 1212, 1055 (C-O-C), 803 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.57 (dd, 1H, H-2 quinoline ring), 8.03 (m, 1H, H-5 quinoline ring), 7.84 (m, 1H, H-8 quinoline ring), 7.73 (dd, 1H, H-6'), 7.60 (m, 1H, H-7 quinoline ring), 7.55 (m, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 6.74 (dd, 1H, H-5'), 6.71 (dd, 1H, H-3 quinoline ring), 6.45 (d, 1H, H-8), 6,30 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.41 (d, 1H, H1-rhamnosyl), 4.21 (t, 2H, O7-CH_2), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, 1H, CH rha), 3.58 (m, 1H, CH glu), 3.41 (d, 2H, CH_2-N), 3.36 (dd, 3H, CH glu) 3.28 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 2.05 (m, 2H, CH_2 propyl chain), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{39}H_{42}N_2O_{16}$; Molecular weight = 794.76; Calculated = C (58.93%) H (5.32%) N (3.52%); Found = C (58.89%) H (5.28%) N (3.50%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy-7-(oxy-1-ethyl-2-(aminoquinolin - 4 - yl)) - 4H - 1 -benzopyran-4-one (III): yield 80%; mp 193-196 °C; IR (KBr) (cm^{-1}): 3403 (OH), 3207 (NH), 2904 (CH arom.), 1664 (C=O on aromatic ring), 1618 (C=N), 1510 (aromatic C=C), 1360, 1308, 1213, 1061 (C-O-C), 807 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.57 (dd, 1H, H-2 quinoline ring), 8.03 (m, 1H, H-5 quinoline ring), 7.84 (m, 1H, H-8 quinoline ring), 7.73 (dd, 1H, H-6'), 7.61 (m, 1H, H-7 quinoline ring), 7.55 (m, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 6.74 (dd, 1H, H-5'), 6.71 (dd, 1H, H-3 quinoline ring), 6.46 (d, 1H, H-8), 6,31 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.42 (t, 2H, O7-CH_2), 4.38 (d, 1H, H1-rhamnosyl), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, 1H, CH rha), 3.64 (t, 2H, CH_2-N), 3.58 (m, 1H, CH glu), 3.41 (d, 2H, CH_2-N), 3.40 (dd, 1H, CH glu) 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{38}H_40N_2O_{16}$; Molecular weight = 780.73; Calculated = C (58.46%) H (5.16%) N (3.58%); Found = C (58.40%) H (5.18%) N (3.52%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy-7 - (oxy - methyl - aminoquinolin - 4 - yl)) - 4H - 1 -benzopyran-4-one (IV): yield 79,7%; mp 212-214°C; IR (KBr) (cm^{-1}): 3400 (OH), 3200 (NH), 2907 (CH arom.), 1670 (C=O on aromatic ring), 1622 (C=N), 1513 (aromatic C=C), 1356, 1300, 1217, 1058 (C-O-C), 811 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.59 (dd, 1H, H-2 quinoline ring), 8.03 (m, 1H, H-5 quinoline ring), 7.86 (m, 1H, H-8 quinoline ring), 7.73 (dd, 1H, H-6'), 7.61 (m, 1H, H-7 quinoline ring), 7.57 (m, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 6.80 (dd, 1H, H-3 quinoline ring), 6.74 (dd, 1H, H-5'), 6.45 (d, 1H, H-8), 6,42 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 5.11 (s, 2H, O7-CH_2), 4.41 (d, 1H, H1-rhamnosyl), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, 1H, CH rha), 3.58 (m, 1H, CH glu), 3.39 (dd, 1H, CH glu), 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{37}H_{38}N_2O_{16}$; Molecular weight = 766.71; Calculated = C (57.96%) H (4.99%) N (3.65%); Found = C (58.00%) H (5.02%) N (3.61%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] – 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy- 7 -(oxy-1-(β-hydroxy-propyl)-3-(aminoquinolin-8-yl))-4H-1-benzopyran-4-one (V): yield 78.1%; mp 200-203 °C; IR (KBr) (cm^{-1}): 3439 (OH), 3189 (NH), 2918 (CH arom.), 1666 (C=O on aromatic ring), 1608 (C=N), 1508 (aromatic C=C), 1362, 1304, 1208, 1053 (C-O-C), 803 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.76 (dd, 1H, H-2 quinoline ring), 8.12 (m, 1H, H-4 quinoline ring), 7.87 (m, 1H, H-5 quinoline ring), 7.73 (dd, 1H, H-6'), 7.62 (m, 1H, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 7.39 (m, 1H, H-3 quinoline ring), 7.33 (dd, 1H, H-7 quinoline ring), 6.74 (dd, 1H, H-5'), 6.46 (d, 1H, H-8), 6,31 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.41 (d, 1H, H1-rhamnosyl), 4.29 (d, 2H, O7-CH_2), 4.13 (d, 2H, CH_2 between glu-rha), 3.96 (m, 1H, CH alkyl chain), 3.89 (m, CH rha), 3.58 (m, 1H, CH glu), 3.40 (dd, 3H, CH glu), 3.38 (d, 2H, CH_2-N), 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{39}H_{42}N_2O_{17}$; Molecular weight = 810.76; Calculated = C (57.77%) H (5.22%) N (3.45%); Found = C (57.71%) H (5.24%) N (3.48%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy-7-(oxy-1-propyl-3 - (aminoquinolin-8-yl)) - 4H - 1 -benzopyran-4-one (VI): yield

77.2%; mp 217-220 °C; IR (KBr) (cm^{-1}): 3422 (OH), 3200 (NH), 2910 (CH arom.), 1655 (C=O on aromatic ring), 1631 (C=N), 1511 (aromatic C=C), 1360, 1307, 1212, 1052 (C-O-C), 808 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.76 (dd, 1H, H-2 quinoline ring), 8.12 (m, 1H, H-4 quinoline ring), 7.87 (m, 1H, H-5 quinoline ring), 7.73 (dd, 1H, H-6'), 7.62 (m, 1H, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 7.39 (m, 1H, H-3 quinoline ring), 7.28 (dd, 1H, H-7 quinoline ring), 6.74 (dd, 1H, H-5'), 6.45 (d, 1H, H-8), 6,30 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.41 (d, 1H, H1-rhamnosyl), 4.22 (t, 2H, O7-CH_2), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, CH rha), 3.58 (m, 1H, CH glu), 3.40 (dd, 3H, CH glu), 3.35 (t, 2H, CH_2-N), 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 2.05 (m, 2H, CH_2 propyl chain), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{39}H_{42}N_2O_{16}$; Molecular weight = 794.76; Calculated = C (58.93%) H (5.32%) N (3.52%); Found = C (58.97%) H (5.30%) N (3.48%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy-7-(oxy-1- ethyl - 2 - (aminoquinolin-8-yl)) - 4H - 1 -benzopyran-4-one (VII): yield 78,6%; mp 187-190 °C; IR (KBr) (cm^{-1}): 3398 (OH), 3200 (NH), 2906 (CH arom.), 1669 (C=O on aromatic ring), 1621 (C=N), 1511 (aromatic C=C), 1361, 1311, 1216, 1064 (C-O-C), 810 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.76 (dd, 1H, H-2 quinoline ring), 8.12 (m, 1H, H-4 quinoline ring), 7.87 (m, 1H, H-5 quinoline ring), 7.73 (dd, 1H, H-6'), 7.62 (m, 1H, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 7.39 (m, 1H, H-3 quinoline ring), 7.33 (dd, 1H, H-7 quinoline ring), 6.74 (dd, 1H,H-5'), 6.46 (d, 1H, H-8), 6,31 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 4.42 (t, 2H, O7-CH_2), 4.38 (d, 1H, H1-rhamnosyl), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, CH rha), 3.58 (m, 1H, CH glu), 3.50 (t, 2H, CH_2-N), 3.40 (dd, 3H, CH glu), 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{38}H_{40}N_2O_{16}$; Molecular weight = 780.73; Calculated = C (58.46%) H (5.16%) N (3.58%); Found = C (58.50%) H (5.21%) N (3.61%).

3-[[6-O-(6-deoxy-α-L-manopyranosyl) - β - D - glucopyranosyl] - oxy] - 2 - (3, 4 –dihydroxy-phenyl)-5-hydroxy-7-(oxy - methyl - aminoquinolin - 8 - yl)) - 4H - 1 -benzopyran-4-one (VIII): yield 82,5%; mp 184-186°C; IR (KBr) (cm^{-1}): 3396 (OH), 3189 (NH), 2914 (CH arom.), 1662 (C=O on aromatic ring), 1623 (C=N), 1510 (aromatic C=C), 1352, 1298, 1215, 1051 (C-O-C), 808 (aromatic substituents); ^{1}H NMR (DMSO-d6): δ ppm: 8.77 (dd, 1H, H-2 quinoline ring), 8.14 (m, 1H, H-4 quinoline ring), 7.88 (m, 1H, H-5 quinoline ring), 7.73 (dd, 1H, H-6'), 7.70 (m, 1H, H-6 quinoline ring), 7.44 (dd, 1H, H-2'), 7.39 (m, 1H, H-3 quinoline ring), 7.36 (dd, 1H, H-7 quinoline ring), 6.74 (dd, 1H, H-5'), 6.45 (d, 1H, H-8), 6,42 (d, 1H, H-6), 5.53 (d,1H, H1-glucosyl), 5.12 (s, 2H, O7-CH_2), 4.41 (d, 1H, H1-rhamnosyl), 4.13 (d, 2H, CH_2 between glu-rha), 3.99 (m, CH rha), 3.58 (m, 1H, CH glu), 3.39 (dd, 3H, CH glu), 3.29 (dd, 1H, CH glu), 3.24, 3.20, 3.16 (dd, CH rha), 1.27 (s, 3H, CH_3 rha); Molecular formula: $C_{37}H_{38}N_2O_{16}$; Molecular weight = 766.71; Calculated = C (57.96%) H (4.99%) N (3.65%); Found = C (57.91%) H (5.03%) N (3.64%).

The diameters of the inhibition zones (in mm) corresponding to the tested compounds are shown in Table 2. All tests were performed in triplicate and the results are expressed as mean diameter ± standard deviation (SD).

Table 2. Antibacterial and Antifungal Activities of the Tested Compounds (I-VIII)

Compounds	Diameter of inhibition zones (mm)			
	Staphylococcus aureus ATCC 25923	*Escherichia coli* ATCC 25922	*Pseudomonas aeruginosa* ATCC 27853	*Candida albicans* ATCC 90028
I	33.0±0.00	30.0±0.00	19.0±0.00	0
II	31.3±0.57	31.0±0.00	18.3±0.57	0
III	34.0±0.00	32.0±0.00	16.3±0.57	0
IV	34.1±0.05	30.1±0.17	16.0±0.00	0
V	31.5±0.50	28.3±0.57	14.3±0.57	0
VI	32.3±0.57	31.3±0.57	18.1±0.05	0
VII	33.3±0.57	31.3±0.57	16.0±0.00	0

VIII	31.1±0.17	30.0±0.00	17.1±0.17	0
Ciprofloxacin (5 µg/disc)	25.7±0.06	30.5±0.50	30.0±0.00	*NT
Fluconazole (25 µg/disc)	NT*	NT*	NT*	34.0±0.00
Voriconazole (1 µg/disc)	NT*	NT*	NT*	33.5±0.50

*NT-not tested

The tested compounds showed a better antibacterial activity than ciprofloxacin against Gram-positive tested species (*Staphylococcus aureus*) and a similar activity against *Escherichia coli*. They also have some anti-Pseudomonas activity (Table 2). We have not registered any antifungal action.

5.Conclusions

Eight new water-soluble rutin derivatives carrying quinoline moiety in their structures were synthesised; molecular formula, weight, yield, melting points and solubility have characterized the new derivatives. Elemental analysis and spectral analysis in IR and H-NMR have confirmed the structure of new compounds. The tested compounds have shown a good activity against Gram-positive and Gram-negative bacterial strains (including *Pseudomonas aeruginosa*), similar to ciprofloxacin and no activity against *Candida albicans*.

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