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Synthesis, Antimicrobial, Antioxidant and Structural Studies of Some New Sulfa Drug Containing an Azo-azomethine Group

Bushra K. Al-Salami[a], Ali J. Hameed[a] and Ali Z. Al-Rubaie[a,b]*

[a]*Department of Chemistry, College of Sciences, University of Basrah, Iraq*

[b]*College of Pharmacy, Al-Ayen University, Nasiriya, Thi-Qar, Iraq*

Abstract

A new series of azo-azomethine compounds derived from sulfadiazine were prepared. The compounds were prepared, starting from the coupling of the sulfadiazine diazonium salt with 2- hydroxy -3- methoxy benzaldehyde, followed by condensation with 4-bromoaniline, 2- chloroaniline, 2- methyl-3-chloroaniline, sulfadiazine, 2,4-dimethylaniline, and 2- hydroxyaniline, respectively. All compounds were characterized by CHN analyses, FT-IR, and NMR spectroscopic data. The antimicrobial activity of all synthesized compounds was studied against gram-positive and gram-negative bacteria and fungi. They were screened for theirantibacterial activities towards the gram-positive *Staphylococcus aureus* and the gram-negative *Escherichia coli*, as well as their antifungal activities against *Aspergillus niger, candidaalbicane,* and *Candida glabrata*, to evaluate their antimicrobial potential. Furthermore, their antioxidant activities were investigated by using the β – Carotene bleaching method. QSAR Properties and Molecular properties of all compounds were obtained by using Hyperchem software.

Keywords: Antibacterial activity; Azo–azomethine; QSAR properties; Sulfadiazine.

1.Introduction

It is well known that azo compounds with one or more azo group (–N=N–) group, separated by two phenyl rings were used in printing systems, biological staining, textile industry, and various photochemical productions [1,2,3,4,5]. Azo compounds were also used in foodstuffs [6] because of their low toxicity, less allergic reactions, and have no hyperactivity effect. In addition, the azo-Schiff bases were reported to display various antimicrobial, anticancer, and antioxidant activities, and several other pharmacological properties [7,8,9,10]. On the other hand, sulfadiazine is an antibacterial prescription medicine for the prevention and treatment of certain types of bacterial infections, including the treatment of cancroids, Toxoplasma gondii encephalitis, urinary tract infections, and other infections [11,12].

It is worth noting that the pyrimidine moiety is one of the most widespread heterocycles in biologically occurring compounds, such as uracil, thymine cytosine, and vitamin B1[13]. Pyrimidine derivatives have a wide spectrum of therapeutic actions such as antimicrobial, anti-HIV, anticancer and other biological activity [14]. Due to the prebiotic nature of pyrimidine to living cells in biodiversity, it is a highly featured idea for the development of molecules of biological and pharmaceutical interest. Several synthetic methods for the pyrimidine heterocyclic synthesis were developed in literature [14-18].

Quantitative structure–activity relationship (QSAR) analysis is an efficient method for building mathematical models, which attempts to find a statistically significant correlation between the chemical structure and the physiochemical properties of drugs, such as toxicity, metabolism, drug and drug interactions, and carcinogenicity [19].

Thus, the present work describes the synthesis of a new series of azo-azomethine compounds based on sulfadiazine to develop new antimicrobial agents and their biological activities will be evaluated. Moreover, the antioxidant activities will be also investigated and the QSAR analysis will be discussed.

*Corresponding author e-mail: alrubaie49@yahoo.com. ORCID ID, https://orcid.org/0000-0002-0569-9039
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2.Experimental

Materials and Reagents

2-chloroaniline, 4-bromoaniline, 2-methyl-3-chloroaniline, 2-hydroxyaniline and 2,4-dimethylaniline were purchased from Fluka and used without further purification. Sodium carbonate, conc. Hydrochloric acid, sodium nitrite, 2-hydroxy-3-methoxy benzaldehyde (ortho-Vanillin), butylated hydroxyl toluene (BHT), and sulfadiazine were obtained from Sigma-Aldrich. All solvents were supplied from the Fluka company.

Physical measurements

The FT-IR spectra as KBr discs were recorded in the range 4000– 400 cm^{-1}usingShimadzu FT-IR model8400sinstrument. The spectra of ^1H NMR was measured on a Brucker at 400 MHz, with TMS as an internal reference and using DMSO–d_6 as a solvent. Carbon, hydrogen, and nitrogen elemental analysis data are obtained by the Euro vector EA-3000A Elemental analyzer. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected.

Synthesis

4-((3-Formyl-4-hydroxy-5-methoxyphenyl)diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide (**1**)

Compound **1** was prepared according to a literature method [12] by the following method:

A solution of sulfadiazine (1.25g; 0.5 mmol) in 10mL of 2N of hydrochloric acid was added at 0ºC to 5°C. Then, 30 mL of a solution of $NaNO_2$ (0.55 g, 7.5 mmol) was added dropwise to the above solution. The diazonium salt solution thus prepared was added drop by drop to a solution of compound 2-hydroxy-3-methoxy benzaldehyde (0.76g, 0.5 mmol), in methanol (40 mL) with stirring at 0 °C. The reaction mixture was stirred for 2 h at –5ºC. The solid product was washed several times with cold water and crystallized from absolute ethanol. The purity azo compound was checked by TLC (EtOH / $CHCl_3$; 1/9). Rf :0.6, yield: 72%, m.p. 220-221 ºC.

IR (KBr) cm^{-1}: 3441(OH), 3363 (N-H) , 3043(CH_{arom}) , 2963(CH_{aliph}) , 1581($C=N_{sulfa}$), 1430(N=N) , 1334(SO_2) ,1157(SO_2) ,1257(C-O), 945(S-N).

^1H NMR (400 MHz, DMSO-d_6); δ/ppm: 12.56 (s , 1H , O*H*) ; 11.22 (s, 1H , N*H*) ; 10.22 (s , 1H , *H*CO) ; 3.82 (s , 3H , OCH_3) ;7.05(t ,1H, Ar-H) , 7.54(s, 1H, Ar-H) ,7.61 s, 1H, Ar-H),8.03(dd, 2H, Ar-H) , 8.47(dd ,2H, Ar-H), 8.51(d, 2H ,Ar-H).

Anal. Calcd. For C_{18} $H_{15}N_5O_5S$: C, 52.30; H, 3.66; N,16.94. Found C, 52.48; H, 3.60; N, 16.80.

General procedure the Synthesis of Sulfadiazine Azo-azomethines compounds (**2-7**

A mixture of compound **1** (0.41 g; 1mmol) and a1 mmol of substituted aniline (*i.e* 4-bromoaniline, 2-chloroaniline, 2-methyl-3-chloroaniline, sulfadiazine, 4-dimethylaniline and 2-hydroxyanline) was dissolved in methanol (25 mL) with a few drops of glacial acetic acid as a catalyst. The mixture was refluxed for 6 h. The resulting solid product was collected by filtration, washed several times with cold methanol, and recrystallized from a mixture of ethanol/dichloromethane (8/2). The solid product was dried in a vacuum to obtain analytically pure compound. The purity of each compound was checked by TLC. The synthetic procedures for the preparation of compounds **2-7** are presented in Scheme 1.

*4-((3-((4-Bromophenyl)iminomethyl)-4-hydroxy-5-methoxyphenyl)diazenyl)-n-(pyrimidin-2-yl)benzenesulfonamide***(2)**

Yellow long crystals,R_f: 0.9.Yield : 53% , m.p. 109 -110 ºC. IR (KBr) cm^{-1}: 3446(OH),3380(N-H), 3061(CHarmatic), 2930(CHaliphtic), 1612(HC=N), 1570(C=Nsulfa), 1483(N=N) ,1365(SO_2) , 1195(SO_2), 1267(C-O), 963(S-N).^1H NMR (400 MHZ, DMSO-d_6) ;δ /ppm : 12.89 (s , 1H , O*H*) ; 8.95 (s , 1H ,C*H*=N) ; 11.01(s, 1H , N*H*) ; 3.82 (s , 3H , OCH_3) ; 6.93(t , 1H ,Ar-H) , 7.05(dd ,2H ,Ar-H) ,7.27(s , 1H ,Ar-H), 7.77(dd, 2H , Ar-H) , 8.01(dd ,2H ,Ar-H), 8.43(dd ,2H ,Ar-H) ,8.72(s ,1H ,Ar-H) ,8.48(d,2H,ArH)EAnal. Calcd. for $C_{24}H_{19}BrN_6O_4S$: C, 50.80;H,3.88;N, 14.8. Found C, 50.60; H, 3.72; N, 14.59.

*4-((3-((2-Chlorophenyl)iminomethyl)-4-hydroxy-5-methoxyphenyl)diazenyl)-n-(pyrimidin-2-yl)benzenesulfonamide***(3)**

Yellow solid, Rf :0.9, yield: 57%, m.p. 115 -117 ºC. IR (KBr) cm^{-1}: 3450(OH), 3440(N-H), 3070 (CH-arom)2962 (CH-aliph), 1616(HC=N), 1570(C=Nsulfa), 1465(N=N),1366(SO_2), 1203(SO_2), 1253(C-O), 912 (S-N).

^1H NMR(400 MH_Z, DMSO-d_6) ; δ /ppm: 12.87 (s , 1H, O*H*) ; 8.92 (s , 1H ,C*H*=N) ; 11.20 (s, 1H, N*H*) ; 3.80 (s ,3H, OCH_3) ; 6.92(t ,1H ,Ar-H) ,7.25(t, 1H ,Ar-H), 7.27(s, 1H ,ArH) ,7.32(t, 1H, Ar-H), 7.57(d,1H, Ar-H), 8.03(dd,2H,Ar-H), 8.47(dd, 2H, Ar-H), 8.51(d, 2H, Ar-H), 8.56(s, 1H,ArH)

Anal. Calcd. for $C_{24}H_{19}ClN_6O_4S$: C, 55.12; H, 3.66: N, 16.07. Found: C, 54.98; H ,3.53; N, 16.20.

*4-((3-((3-Chloro-2-methylphenyl)iminomethyl)–4–hydroxy-5-methoxyphenyl)diazenyl)–N-(pyrimidin-2-yl)benzenesulfonamide***(4)**

Orange crystals, Rf :0.8, yield: 67%, m.p. 110 -112 ºC. IR (KBr)cm $^{-1}$: 3448(OH), 3441 (N-H), 3063(CH-arom) , 2966(CH-aliph), 1612(HC=N) , 1562(C=N-

sulfa),1465(N=N),1365(SO_2), 1180(SO_2), 1263(C-O), 968(S-N).
^{1}H NMR(400 MH_Z, DMSO-d_6) ; δ /ppm: 12.87 (s,1H, O*H*) ; 8.83(s, 1H,C*H*=N) ; 11.19 (s, 1H , N*H*) ; 3.81 (s, 3H, OCH_3) ; 2.36 (s,3H, CH_3) ; 6.93(d, 1H, Ar-H), 7.02(t, 1H, Ar-H), 7.27(s, 1H, Ar-H), 7.39(t, 1H, Ar-H), 7.55(d, 1H, Ar-H), 8.03(dd, 2H ,Ar-H), 8.46(dd, 2H, Ar-H), 8.53(d, 2H ,Ar-H) ,8.56(s, 1H, Ar-H).
Anal.Calcd. For: $C_{25}H_{21}ClN_6O_4S$: C, 55.92; H, 3.81; N,15.41. Found: C, 55.73; H,3.81; N, 15.41.

4-((4-Hydroxy-3-methoxy-5-(-((4-(N-(pyrimidin-2-yl)sulfamoyl) phenyl)imino)- methyl)phenyl) -diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide **(5)**
Pale brown powder, Rf :0.5, yield: 44% , m.p. 217 - 218 ^{o}C.
IR(KBr) cm^{-1}: 3479(OH), 3363(N-H), 3043(CH-arom), 2943(CH-aliph), 1616(HC=N), 1577(C=Nsulfa), 1438(N=N),1338(SO_2), 1157(SO_2), 1267(C-O), 945(S-N).
^{1}H NMR (400 MH_Z, DMSO-d_6):δ /ppm: 12.57 (s, 1H, OH); 8.96 (s, 1H,CH=N); 11.84 (s, 2H, NH) ; 3.82 (s, 3H, OCH_3); 6.91(d, 1H, Ar-H), 7.05(t, 2H, Ar-H) ,7.15(s, 1H, Ar-H), 7.25(dd, 2H ,Ar-H), 7.27(s, 1H, Ar-H), 7.53(dd, 2H, Ar-H), 8.02(dd, 2H, Ar-H), 8.47(d, 4H, Ar-H), 8.56(s, 1H, Ar-H), .
Anal. Calcd. For $C_{28}H_{23}N_9O_6S_2$: C, 52.09; H, 3.59; N,19.52. Found: C, 52.00; H,3.51; N, 19.42.

4-((3-((2,4-Dimethylphenyl)iminomethyl)-4-hydroxy-5-methoxyphenyl)diazenyl)-n-(pyrimidin-2-yl)benzenesulfonamide **(6)**
Orange crystal, Rf :0.9, yield: 68%, m.p. 98-100 ^{o}C.
IR (KBr) cm^{-1}: 3425(OH), 3356(N-H), 3039(CH-arom)2939(CH-aliph), 1651(HC=N),1566(C=Nsulfa), 1469(N=N),1327(SO_2), 1157(SO_2), 1253(C-O), 941(S-N).
^{1}H NMR(400 MH_Z, DMSO-d_6); δ /ppm: 13.70 (s, 1H, O*H*); 8.88 (s, 1H,C*H*=N); 11.81 (s, 1H, N*H*); 3.81 (s, 3H, OCH_3); 3.31(s,3H, CH_3) ; 2.30 (s,3H, CH_3); 6.93(d, 1H, Ar-H), 7.00(d, 1H, Ar-H),7.03(t, 1H, Ar-H), 7.06(s, 1H, Ar-H), 7.27(s, 1H, Ar-H), 8.01(dd, 2H, Ar-H), 8.40(dd, 2H, Ar-H), 8.48(d, 2H, Ar-H), 8.51(s, 1H, Ar-H).
Anal. Calcd. for $C_{26}H_{24}N_6O_4S$: C, 60.45; H, 4.68; N,16.27. Found: C,60.22; H, 4.53; N, 16.01.

4-((4-Hydroxy-3-(-((2-hydroxyphenyl)imino)methyl)-5-methoxyphenyl)diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide **(7)**
Orange crystal, Rf :0.24, yield: 59%, m.p. 188-190 ^{o}C.
IR (KBr) cm $^{-1}$: 3435(OH), 3350(N-H), 3059(CH-arom), 2938(CH-aliph), 1631(HC=N), 1500(C=Nsulfa)), 1454(N=N),1365(SO_2), 1168(SO_2), 1226(C-O), 900(S-N).
^{1}H NMR (400 MH_Z, DMSO-d_6); δ /ppm : 12.71 (s, 1H, O*H*) ; 8.95 (s, 1H,C*H*=N); 9.75 (s, 1H, O*H*);11.80 (s, 1H, N*H*); 3.83 (s, 3H , OCH_3) ; 6.83(d, 1H, Ar-H), 6.95(t, 1H, Ar-H), 6.97(d, 1H, Ar-H), 7.02(t, 1H, Ar-H), 7.11(t, 1H, Ar-H), 7.27(s, 1H, Ar-H), 7.99(dd, 2H, Ar-H), 8.45(dd, 2H, Ar-H), 8.48(d, 2H, Ar-H), 8.57(s, 1H, Ar-H).
Anal. Calcd. for $C_{24}H_{20}N_6O_5S$: C, 57.14; H, 4.00; N, 16.66. Found: C,57.65; H,4.10; N, 16.89.

Antimicrobial activity
The antimicrobial activity of all synthesized compounds (*i.e*. compounds **1** – **7**) was tested against Gram-positive *Staphylococcus aureus* (ATCC 25923) and Gram-negative *Escherichia coli* (ATTC 25922). The antifungal activity for all compounds was tested against *candida albicans, Aspergillus niger,* and *candida glabrata.* by the hole diffusion method, grown on nutrient agar [20]. The solutions of compounds **1**-**7** were prepared by dissolving them in dimethylsulfoxide (DMSO) as a solvent. A series of different concentrations were prepared to determine the lowest concentration that could affect the pathogen. All bacterial plates were incubated at 37^{o}C for 24 hours, and the fungal plates were incubated at 25^{o}C for 24 hours also. The inhibition zone of each tested compound was measured in mm unit.

Antioxidant Activity
The β-carotene bleaching method is based on the loss of the yellow color of β-carotene because of its reaction with radicals formed by linoleic acid oxidation in an emulsion and according to previous methods[21-23]. β-Carotene (0.2 mL/mg was dissolved in chloroform and linoleic acid (0.02 mL) and Tween 20 (0.2 mL) were added to 1 mL of this solution. Chloroform was evaporated under vacuum at and 50 mL of distilled water was added; then the emulsion was vigorously shaken for two minutes. The emulsion (3.8 mL) was added to a tube containing 0.2 mL of solutions of 0.1 mg/mL of reference compound butylated hydroxyl toluene (BHT), and a synthesized compound. The reaction was followed by spectrophotometry at λ = 470 nm and the test emulsion was incubated in a water bath at 45°C for 2 h when the absorbance was measured again. The absorbance was measured at 15 min. interval to observe the rate of bleaching of β– Carotene [24]. The results obtained were compared with the reference antioxidant BHT and expressed as a percentage of antioxidant activity (%A) using the following formula:

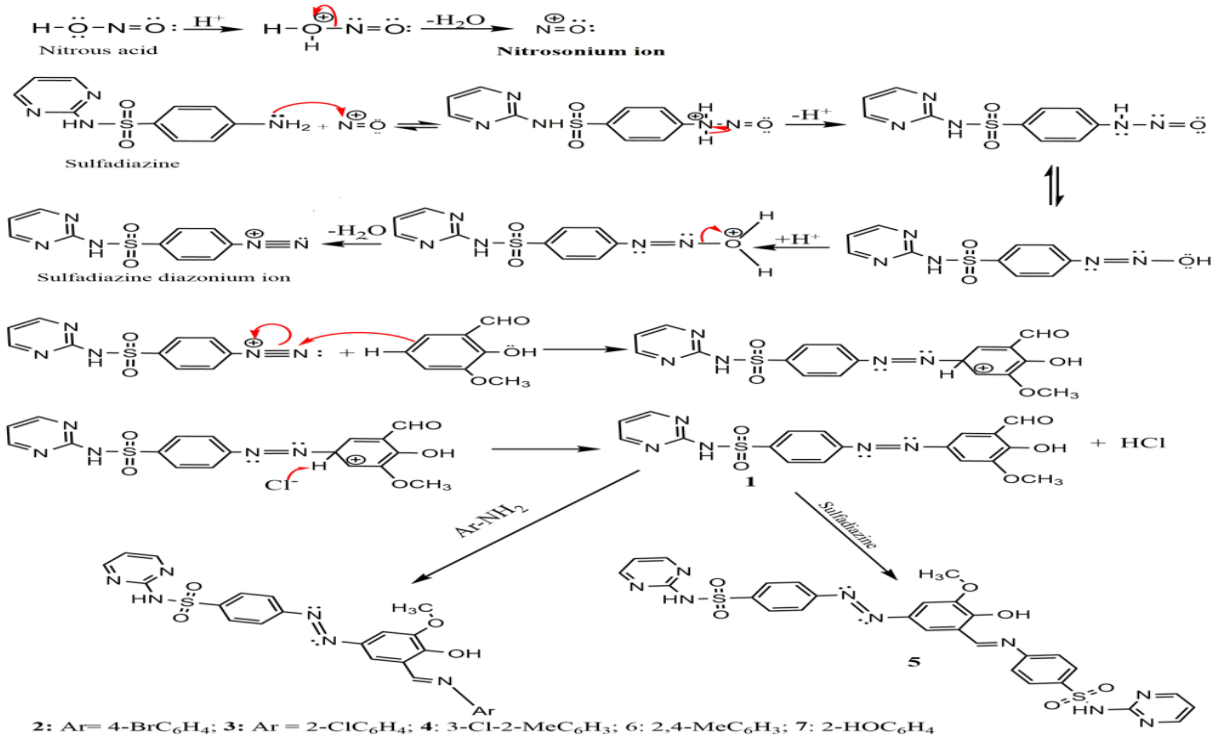
$$\%A = 1- [(Ao – A_f) / (*Ao - *A_f)] \times 100$$

where A_0 is the initial absorbance and A_f is the final absorbance measured for the test sample and $*A_0$ is the initial absorbance and $*A_f$ is the final absorbance measured for the control.

Results and discussion

4-((3-Formyl-4-hydroxy-5-methoxyphenyl)diazenyl)-N-(pyrimidin-2-yl)benzenesulfonamide(**1**) was prepared from sulfadiazine, which was diazotized with $NaNO_2$ and HCl to form the corresponding diazonium salt, and then treated with 2-hydroxy-3-methoxy benzaldehyde at 0°C, Scheme 1. Compound 1 was reacted with 4-bromoaniline, 2-chloroaniline, 2-methyl-3-chloroaniline, sulfadiazine, 4-dimethylaniline, and 2-hydroxyanline, to afford compounds **2**, **3**, **4**, **5**, **6**, and **7**, respectively in good yield, Scheme 1. All compounds (**1-7**) gave satisfactory elemental analyses (see, Experimental Section). They are stable solids and non-hygroscopic. All compounds were confirmed by FT-IR spectroscopy. The infrared spectra of studied compounds displayed strong bands between 3435 – 3479 cm^{-1}, which can be attributed to the stretching vibration of OH. Furthermore, the IR spectra of all compounds showed absorption bands due to the stretching vibrations of C-O between 1257 - 1226 cm^{-1}, and C=N sulfa between 1581- 1500 cm^{-1}, SO_2 at the range 1368 – 1327 $cm^{-1}$and 1203 – 1153 cm^{-1} for asymmetric and symmetric vibration. The formation of azo-azomethine compounds was confirmed by the presence of two characteristic bands namely N=N together with C=N groups at the rang 1430-1469 cm^{-1} and 1612-1651 cm^{-1} respectively [25].

Structures of all new compounds (**1-7**) were confirmed by ^{1}H NMR spectra. Compound 1 showed a signal at 10.22 ppm attributed to CH=O group which disappeared in compounds 2-7. This indicates the formation of the Schiff-bases (2-7). Compounds **2** – **7** show a signal at range 8.83-8.96 ppm for the proton of the CH=N group [24]. The phenolic hydrogen of all compounds appeared as a singlet at 12.56 – 13.70 ppm and the NH signal appears as a broad signal in the region 11.01-11.84 ppm [25]. The signals around3.8 ppm are assigned to the CH_3O group for all compounds, see Experimental Section. Signals of protons of the aromatic rings appeared within the expected range. In general, the ^{1}H NMR spectra of all compounds show all the expected peaks in the proper intensity ratio, Experimental section.



Scheme 1.

Antioxidant Activity

The antioxidant can be defined as a substance that reduces damage due to free radicals. Phenol compounds which owned OH act as reducing agent by donating a hydrogen atom to free radical, so that it leads to the elimination of oxygen species (ROS) which create during biochemical operation in the body system [26,27]

The antioxidant activity of compounds **1**–**7** have been compared with BHT. These compounds (*i.e.* **1-7**) containing hydroxyl groups that are very useful for scavenging free radicals and prevent damaging cells [28]. The ability of the compounds to inhibit *β*-carotene was evaluated using BHT as the reference, as seen in Figures 1 and 2. As shown in Table 1, the

significant antioxidant properties were observed for the synthetic compounds **3** and **2**, while compounds such as **5** and **6** possess less effectiveness. The antioxidant activity of these compounds changed with the change of substructures [22]. Therefore, the antioxidant activity of these new compounds is as follows:

3 > 2 > 1 > 7 = 4 > 6 > 5

As it is well known that highly antioxidant materials should be associated with high antibacterial activities. No clear relations between the antioxidant and antibacterial behaviours of these investigated compounds were observed, as illustrated, for example, compound **1** showed the highest antibacterial activity, but moderate activity as an antioxidant, Tables 1 and 2.

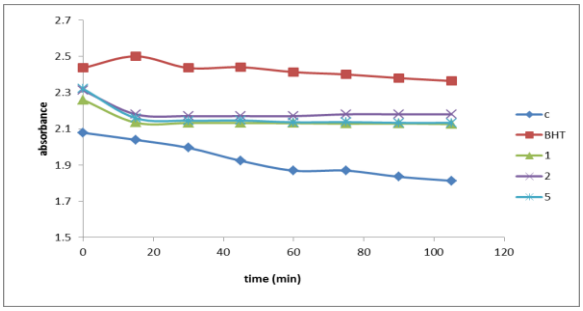


Figure 1. Antioxidant activity of compounds 1, 2, and 5 (c, control)

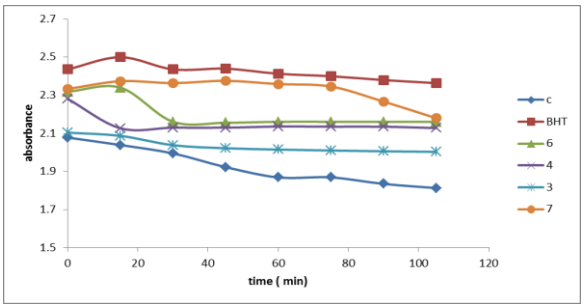


Figure 2. Antioxidant activity of compounds **4**, **3,** and 7 (c, control)

Antimicrobial activity

Compounds **1** –**7** were tested for their antimicrobial activity in vitro against

human pathogens. These tests were carried against are gram-positive *Staphylococcus aureus* (*S. aureus*) and gram-negative *Escherichia coli* (*E coli*). Furthermore, compounds **1-7** were screened for antifungal activity against *Candida albicanse*, *Candidae glabrata*, and *Aspergillus nigere* by agar well diffusion method. The results of the antimicrobial testing data are presented in Table 2 and Figures 3and 4. The investigation of antimicrobial testing data shown that the studied compounds displayed a good to moderate activity against the selected microorganism at a concentration of 30 mg/mL. Thus, in comparison with amoxicillin, compound **1**showed a good activity, while compounds **2**, **3**, **4**, **5**, **6** and **7** show moderate activity against *E. Coli* and *S. aurous*, Table 2.

In comparison with standard amoxicillin, compounds (**1**, **3**, **4**, and **5**) were showed moderate activity against *S. aurous* while the same compounds showed low effectiveness towards *E. Coli* expect compound **1** which showed a moderate activity toward *E. Coli.* Compound **1** – **7** display an excellent to moderate antifungal activity against *C. albicons* and *Aspergillus niger* except compound **4** which showed a moderate activity towards them. On the other hand, all the synthesized compounds were displayed moderate activity toward *C. glabrata* except compound **2**, which shows no effectiveness, Table 1. The inhibition zone of all compounds against bacteria and fungi at a concentration of 30mg/mL is represented in Figs. 3 and 4.

One of the main components of our synthesized compounds was sulfadiazine, it is an antibiotic that is a member of sulfa drugs. Many types of research have given clear, detailed information on the biological activity of Schiff bases which have proven efficacy and effectiveness as strong bactericidal factors [29].

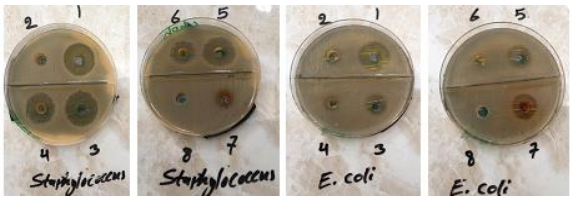


Figure 3. Inhibition Zone of all compounds against bacteria at a concentration of 30 mg/ml.

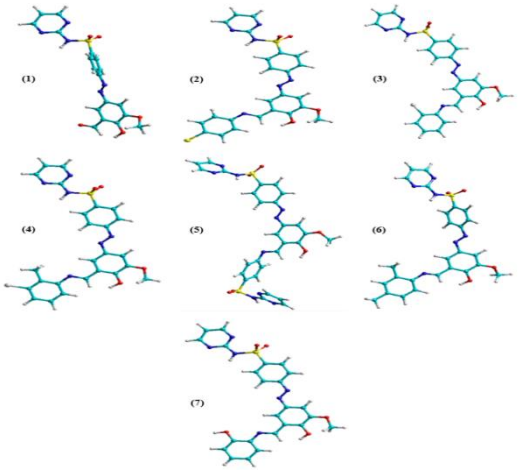
Figure 4. Inhibition Zone of all compounds against fungi at a concentration of 30mg/mL.

Computational study

Scheme 2 shows a graphical representation of the Sulfadiazine Azo-azomethine compounds described in this work the optimized geometrical structures of the systems calculated performing semi-empirical methods. Semi-empirical self-consistent field molecular orbital (SCF-MO) the method at the AM1 level of theory. These optimized structures are essential to study the geometrical parameters of compounds and give information about their point groups.

The optimization of structures is an essential step to proceed with other meaningful calculations.

Table 3 shows some of the selected QSAR properties of the investigated compounds. The trends of surface area and volume values are quite clear since it is obvious that the compounds which have bulky chemical group have larger values of surface and volume. In the present calculations, the total volume of the studied series varied from 1087.56 to 1607.46 $Å^3$. The calculated log p values of the studied compounds vary from 3.89 to 6.97, this indicates that the studied molecules are lipophilic.



The calculated refractivity and polarizability of the studied compounds have indicated different values for each one of them. This means that the structural change of molecules has an observant effect on the theoretical refractivity and polarizability values for the two series, (Table 3).

Scheme 2. The optimized structures of Sulfadiazine Azo-azomethine compounds

4. Conclusion

A new series of azo-azomethine compounds derived from sulfadiazine was prepared. Antimicrobial and antioxidant activity was evaluated for these compounds. The compounds show moderate antimicrobials activities against *Staphylocuses aureas* and Escherichia *coli*, and good to moderate activities against three types of pathogenic fungi. The most elegant result as antimicrobial activity was obtained for compounds **3**,**5**, and **7** while the synthesized compounds **2**, **3** showed high activities as an antioxidant agent.

Conflict of interest

The author declares that he has no conflict of interest.

Table 1: Effectiveness of synthesized compounds (azo – azomethine) as an antioxidant

Comp. symbol	A_0	A_f	$^*A_0$	$^*A_f$	A%
BHT	2.436	2.364	2.057	1.803	73
1	2.266	2.126	2.057	1.803	45
2	2.312	2.184	2.057	1.803	50
3	2.104	2.003	2.057	1.803	61
4	2.281	2.128	2.057	1.803	40
5	2.321	2.133	2.057	1.803	26
6	2.319	2.161	2.057	1.803	38
7	2.333	2.18	2.057	1.803	40

Table 2. The inhibition zones of the synthesized compounds against selected microbes.

	Bacteria		**Fungal**		
Compound	**Escherichia coli**	**Staphylocuses aureas**	**Candida glabrata**	**Candida albicane**	**Aspergillus niger**
1	45	49	30	35	40
2	25	22	0	22	40
3	21	25	30	32	40
4	22	30	25	25	25

5	20	20	30	32	40
6	30	23	20	15	40
7	22	25	20	40	40
8(DMSO)	0	0	0	0	0
Sulfadiazin	20	18	20	0	0
Amoxicillin	38	40	----	-----	----
Nystatin	---	----	0	35	30

Table 3. Selected QSAR properties of compounds **1-7** for the AM1 optimized structures.

Compounds	**Surface area (approx) ($Å^2$)**	**Surface area (grid) ($Å^2$)**	**Volume ($Å^3$)**	**Hydration energy (kcal/mol)**	**Log P**	**Refractivity ($Å^3$)**	**Polarizability ($Å^3$)**
1	571.74	657.15	1087.56	-10.08	3.89	110.29	37.92
2	721.63	808.59	1376.18	-23.78	6.78	144.64	51.05
3	703.96	792.87	1352.61	-23.47	6.51	141.82	50.35
4	736.05	812.56	1398.15	-22.40	6.97	146.86	52.19
5	769.33	930.59	1607.46	-22.97	6.39	172.18	59.15
6	742.36	839.78	1427.50	-22.40	6.92	147.10	52.09
7	680.59	782.53	1332.01	-28.84	5.70	138.71	49.06

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