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Research Article

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Biological studies on derivatives of sulfanilamide and sulfathiazole

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Abstract

Derivatives of sulfanilamide and sulfathiazole were prepared and characterised by analytical data, IR, ^{1}HNMR, ^{13}CNMR and UV-Vis spectra and screened for antibacterial activities against gram - positive bacteria *Staphylococcus aureus* and gram - negative bacteria *Escherichia coli, Klebsiella aerogenes* and *Bacillus subtilis* and antifungal activities against *Aspergillus niger* and *Candida albicans* by disc diffusion method. Ciprofloxacin and Nystatin were used as standard drug for bacteria and fungi.

Keywords: Sulfanilamide and Sulfathiazole, 3,5-diiodosalicylaldehyde, Zone of inhibition, antibacterial activities, antifungal activities, Ciprofloxacin, Nystatin.

Introduction

Sulfa drugs and their derivatives are considered as a very important class of organic compounds, which have wide applications in many biological aspects[1]. These compounds exhibit biological activities such as antibacterial, antifungal, antiviral, antitubercular and antitumor agents because of their specific structure prontosil is the first antibiotic sulfa drug to successfully treat bacterial and fungal infections [2-3]. Sulfonamide have long been used as drugs for diseases, like leprosy, dysentery, gonorrhea, cold and pneumonia. Some of these drugs are showed biological activities when administered in the form of azomethines[4-7]. However azomethine containing derivatives of sulfanilamide and sulfathiazole are limited[8-10]. Therefore 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide may be played a vital role in medicine. This study focuses on the antibacterial and antifungal activities of derivatives of sulfanilamide and sulfathiazole derived from sulfanilamide / sulfathiazole and 3,5-diiodosalicylaldehyde.

Materials and Methods

Materials

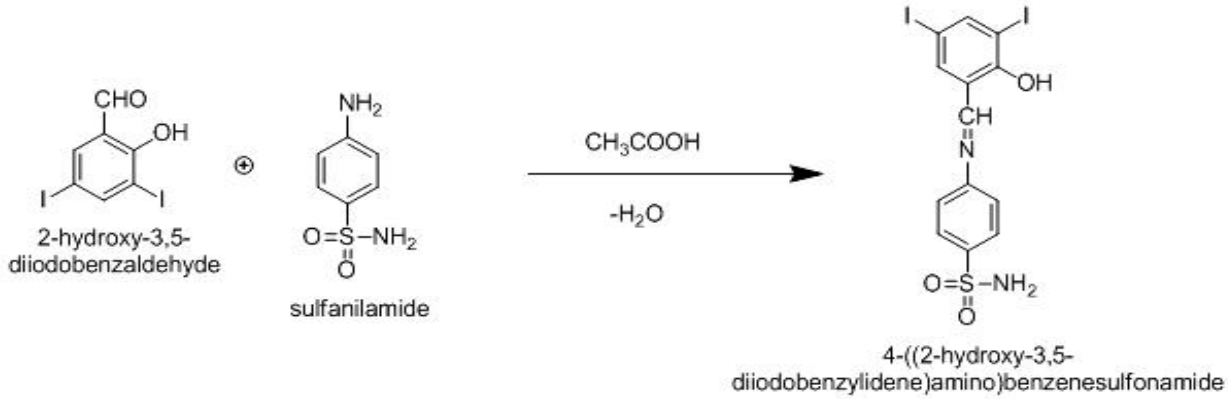
All the reagents used were of AR grade. Commercially available rectified spirit was dried over anhydrous quicklime for 24 hours, filtered and distilled before use (BP 78^{o}C). Dimethylsulphoxide (sigma) and N,N-dimethylformamide (sigma) were used as such. Sulfanilamide, sulfathiazole and 3,5-diiodosalicylaldehyde were purchased from Alfa Aesar.

Instruments

Melting points were determined using Elico melting point apparatus. Elemental analysis (C,H,N,O,S,I) were performed using Elementar Vario EL III. IR spectra of the compounds were recorded in KBr pellets with cary 630 FTIR Spectrometer in the 4000-400 cm^{-1}range. The ^{1}HNMR spectra and ^{13}CNMRwere recorded on a Bruker 400 MHz FT- PMR Spectrometer. The electronic spectra were recorded in Cary Series UV-Vis Spectrophotometer in the 200-800 nm range.

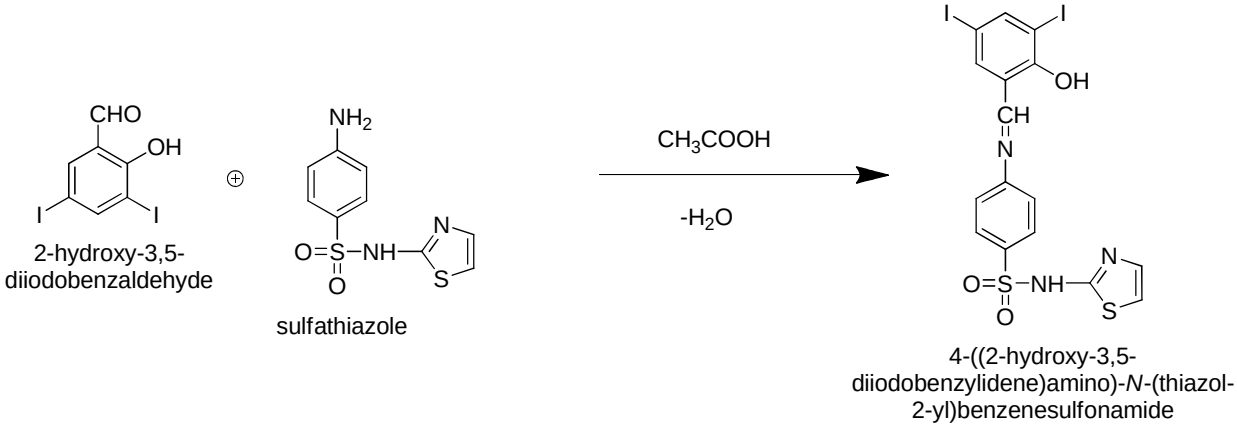
Preparation of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide.

One grams of sulfanilamide (0.005mm) was mixed with 2.17 gram of 3,5-diiodosalicylaldehyde (0.005mm) and was grained well in acidic medium at room temperature. The mixture was transferred into hundred milliliter Round Bottom flask and was reflexed for four hours in oil bath. The solid of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide was filtered and washed with ethanol and recrystallized from acetone and then dried over vacuum desiccator.



Preparation of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-) benzenesulfonamide

Two grams of sulfathiazole (0.007mm) was mixed with 2.93 gram of 3,5-diiodosalicylaldehyde (0.007mm) and was grained well in acidic medium at room temperature. The mixture was transferred into hundred milliliter Round Bottom flask and was reflexed for five hours in oil bath. The solid of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzene sulfonamide was filtered and washed with ethanol and recrystallized from THF and then dried over vacuum desiccator.



Antimicrobial susceptibility test by Disc diffusion Technique

Principle

Disc impregnated with known concentration of antibiotics are placed on an agar plate that has been inoculated uniformly over the entire plate with a culture of the bacterium to be tested. The plate is incubated for 18 to 24 hours at 37^{o}C. During this period, the antimicrobial agent diffuses through the agar and may prevent the growth of the organism. Effectiveness of susceptibility is proportional to the diameter of the inhibition zone around the disc. Organisms which grow up to the edge of the disc are resistant.

Procedure

The plate was labeled with the name of the culture, sample and standard at the bottom of the plate. Then sterile cotton swab on a wooden applicator stick was dipped into the bacterial suspension. Excess fluid was removed by rotating the swab and rubbed gently over the plate to obtain uniform distribution of the inoculums. The sterile disc was held on the inoculated plate with the help of micropipette. The sample was leveled in the sterile disc and incubated at 37^{o}C in an incubator. After incubation, the diameter of the zone of inhibition of growth was measured.

Table.1

Observation	Report
Inhibition zone > 15mm	Highly active
Inhibition zone > 10mm	Moderately active
Inhibition zone > 5mm	Slightly active
Inhibition zone ≤ 5mm	Inactive

Results and Discussion

The physical character and analytical data of the derivatives of sulfa drugs 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide are shown in table. 2.

Table. 2 The physical and analytical data of the derivatives of4-((2-hydroxy-3,5-diiodobenzylidene) amino) benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino) -N-(thiazole-2-yl-)benzenesulfonamide.

S.No	Derivatives of Sulfa Drugs	M.Weight	Colour	M.P	Yield	Elemental analysis						
						C	H	O	N	S	I	M/Z
1	**$C_{13}H_{10}I_2N_2O_3S$** 4-((2-hydroxy-3,5-diiodobenzylidene) amino) benzenesulfonamide	528.10	Pale red	197	88%	29.57	1.91	9.09	5.30	6.07	48.06	100
2	**$C_{16}H_{11}O_3N_3S_2I_2$** 4-((2-hydroxy-3,5-diiodobenzylidene) amino) -N-(thiazole-2-yl-) benzenesulfonamide	611.22	Red	239	85%	31.44	1.81	7.85	6.87	10.49	41.53	99.99

4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide.

FTIR (cm^{-1})=1617 (-CH=N-), 3328 (-OH), 1151 (O=S=O).

^{1}H NMR δ(ppm) =(-CH=N)8.20,(-OH)5.81, ($-NH_2$)2.09.

^{13}C NMR δ (ppm) = (-CH=N) 160.0, (-C-CH) 121.7, (-C-OH) 159.1, (-C-SO2) 142.2

UV-Vis (λ_{max}) =258 nm (n - π*), 348 nm (n - π*), 433 nm (π - π*)

Fluorescence Spectra(λ_{max}) = 491 nm

4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide.

FTIR (cm^{-1}) =1576 (-CH=N-), 3142 (-OH), 1148 (O=S=O).

^{1}H NMR δ (ppm) =(-CH=N)8.92,(-OH)5.41,(-NH)2.01.

^{13}C NMR δ (ppm) = (-CH=N) 160.0, (-C-CH) 121.7, (-C-OH) 159.1, (-C-SO2) 138.2, (-C-NH) 171.7, (-C-N) 155.2.

UV-Vis (λ_{max}) =262 nm (n - π*), 294 nm (n - π*), 422 nm (π - π*).

Fluorescence Spectra (λ_{max}) = 485 nm.

Antibacterial bioassay

Antibacterial activities of derivatives of sulfa drugs were screened against bacterial gram positive bacteria *Staphylococcus aureus,* and gram negative bacteria *Escherichia coli, Klebsiella aerogenes* and *Bacillus subtilis* by disc diffusion method and the results obtained were formulated in Table.3 and Fig. 3-6 and 9-12. The experiments were carried out in DMSO solution at a concentration of 100ppm using Muller Hinton agar media. Ciprofloxacin was used as a standard drug.

Antifungal bioassay

Antifungal screening of derivatives of sulfa drugs were carried out against *Aspergillus niger* [11-12] and *Candida albicans* by disc diffusion method and the results obtained were formulated in Table.3 and Fig.1, 2, 7 and 8. The test was carried out in DMSO solution at a concentration of 100 ppm. Results were compared with standard drug Nystatin at the same concentration.

Table. 3 Antibacterial and antifungal activity of derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino) benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide.

Name of the Organisms	Zone of Inhibition in mm		
	4-((2-hydroxy-3,5-diiodobenzylidene) amino)benzenesulfonamide	**4-((2-hydroxy-3,5-diiodobenzylidene) amino)-N-(thiazole-2-yl-) benzenesulfonamide**	**Standard**
Staphylococcus aureus	21	21	35
Bacillus subtilis	20	30	40
Klebsiella aerogenes	20	20	30
Escherichia coli	15	18	38
Aspergillus niger	22	27	35
Candida albicans	25	20	32

Antifungal activities of derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide.(Fig. 1 & 2)

Fig. 1
Aspergillus niger

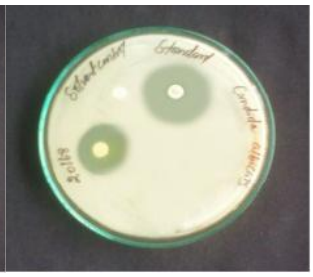


Fig. 2
Candida albicans

Antibacterial activities of derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide.(Fig. 3 - 6)

Fig. 3
Staphylococcus aureus

Fig. 4
Klebsiella aerogenes

Fig. 5
Bacillus subtilis

Fig. 6
Escherichia coli

Antifungal activities of derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl) benzenesulfonamide. (Fig. 7 & 8)

Fig. 7
Candida albicans

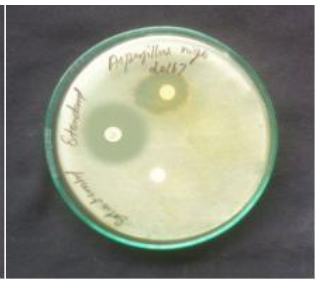


Fig. 8
Aspergillus niger

Antibacterial activities of derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl) benzenesulfonamide. (Fig. 9 - 12)

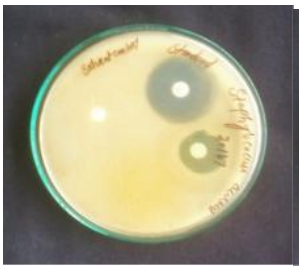


Fig. 9
Staphylococcus aureus

Fig. 10
Escherichia coli

Fig. 11
Bacillus subtilis

Fig. 12
Klebsiella aerogenes

The nature of bonding and structure of azomethine organic compounds were elucidated by the elemental analysis, UV-Vis, FTIR, Melting Point, NMR, Chromatography and Molar ratio methods Gomathi et.al were prepared 4-(3-ethoxy-2-hydroxybenxzelideneaminno-N-(thiazole-2-yl-) benzenesulfonamide, Mohamed et.al and were prepared 4-(-phenyl-propylideneamino)-benzenesulfonamide. In accordance with the data obtained from antibacterial activities of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide, were moderately inhibited the growth of tested bacteria but our derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene) amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-) benzenesulfonamide were highly inhibited the growth of tested bacteria.

In accordance with the data obtained from antifungal activities of 4-(3-ethoxy-2-hydroxybenxzelideneamino-N-(thiazole-2-yl-)benzenesulfonamide (Gomathi et.al) were moderately inhibited the growth of tested fungi but our derivatives of 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide were highly inhibited the growth of tested fungi.

From the results and previous work, antibacterial and antifungal activity studies were indicated that iodine substituted derivatives of sulfonamides were more active against bacteria and fungi than other derivatives of sulfonamide.

Conclusion

The derivatives of sulfa drugs 4-((2-hydroxy-3,5-diiodobenzylidene)amino)benzenesulfonamide and 4-((2-hydroxy-3,5-diiodobenzylidene)amino)-N-(thiazole-2-yl-)benzenesulfonamide were prepared by the condensation of sulfanilamide, sulfathiazole and 3,5-diiodosalicylaldehyde and bio-assay were tested against important bacteria and fungi and these derivatives were found to show significant anti-microbial properties.

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