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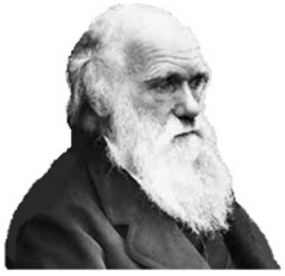

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Synthesis, spectroscopic characterization and antimicrobial evaluation of some (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

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ABSTRACT

In the present study, six numbers of Schiff bases (1-6) have been synthesized by the condensation of 4-fluorobenzenesulfonamide and substituted aromatic aldehyde. The purities of these Schiff bases have been checked by their physical constants, IR, ^{1}H NMR, and ^{13}CNMR spectral data. The antimicrobial activities of these Schiff bases have been evaluated using Bauer-Kirby method.

***Keywords*:** 4-fluorobenzenesulfonamide, IR spectra, NMR spectra, Bauer-Kirby, antimicrobial activities

1. INTRODUCTION

Schiff base, an organic compound having general formula R–C=N–R', where R and R' are aryl, alkyl or cycloalkyl or heterocyclic groups formed by the condensation of an amine and a carbonyl group, is a potential inhibitor. The greatest advantage of many Schiff base compounds is that they can be conveniently and easily synthesized from relatively cheap material. Schiff base compounds, due to the presence of the –C=N– group, electronegative nitrogen, sulfur and/or oxygen atoms in the molecule, have been reported to be effective inhibitors for the corrosion of iron and steel in acidic and alkaline media by several authors [1,12].

Schiff bases exhibit excellent characteristics and structural similarities with natural biological substances, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural scaffolds[13,14].

The Schiff bases are also used as versatile components in nucleophilic addition with organometallic reagents[15] and in cycloaddition reactions[16,17]. Schiff bases have wide applications in food industry, dye industry, analytical chemistry, catalysis, fungicidal, agrochemical and biological activities[18] with the increasing incidence of deep mycosis, there has been increasing emphasis on the screening of new and more effective antimicrobial drugs with low toxicity [19].

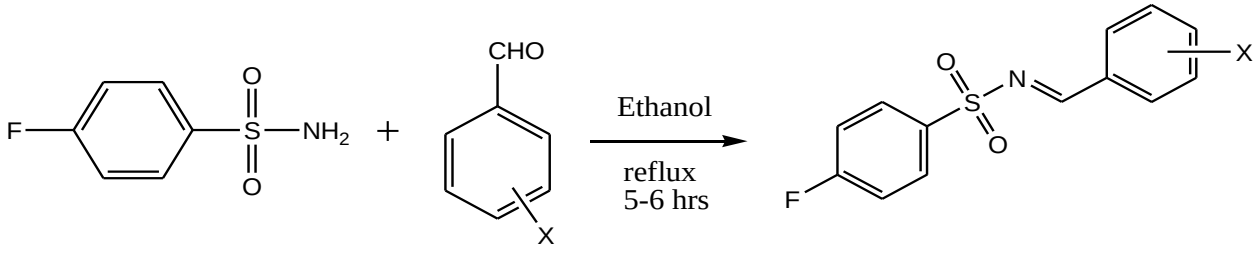
Schiff bases, associated with antibacterial, antifungal, and anti-tubercular activities, have diverse biological activities[20-24]. The Schiff bases engrossed much attention as they demonstrated antimicrobial[25], anticancer[26], anticonvulsant[27], diuretic[28], herbicidal[29], anti-inflammatory[30], antitumor[31], and anti-HIV[32] activities.

In the present work, the syntheses of some new Schiff bases, from 4-fluorobenzenesulfonamide, and substituted aromatic aldehyde, have been investigated. The syntheses of Schiff bases were characterized by IR, 1H NMR, and ^{13}C NMR. The Schiff bases were also screened for their antimicrobial activities of the prepared compounds, assessed against Gram-positive bacteria, Gram–negative bacteria, and fungi.

2. MATERIALS AND METHODS

All the chemicals involved in the present investigation, have been procured from Sigma-Aldrich and E-Merck chemical companies. Melting points of all Schiff bases have been determined in open glass capillaries on SUNTEX melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000–400 cm^{-1}) have been recorded on Avatar-330 FT-IR spectrophotometer. The NMR spectra of all synthesized compounds have been recorded on Bruker 400 MHz spectrometer operating at 400 MHz for recording ^{1}H spectra and 100 MHz for ^{13}C spectra in $CDCl_3$ solvent using TMS as internal standard.

General procedure for synthesis of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides



X= 4-F, 4-Cl, 4-Br, 4-CH_3, 4-OCH_3, 4-NO_2

Scheme 1. Synthesis of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

The Schiff bases were obtained by 0.1 M solution of 4-fluorobenzenesulfonamide was added to 0.1-M solution of substituted aromatic benzaldehyde in ethanol, the addition reaction mixture is heated under reflux for 5-6 hours at 70 °C. After completion of reaction, the precipitates are formed. The product was filtered after cooling and purified with ethanol. The purity of product was checked by MP and TLC. The synthesized compounds were characterized by their Physical constants, IR, ^{1}H NMR and ^{13}C NMR spectral data. The analytical and spectral data of synthesized Schiff bases are given below.

Spectral data of (E)-N-(4-fluoroobenzylidene)-4-fluorobenzenesulfonamide (1)

IR(ν·cm^{-1}) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H(-NMR(δ ppm) = 8.420 (1H, s, CH=N); 7.090-7.933(12H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 175.767(C=N), 147.825(C_1) 130.745(C_2 & C_6), 116.015.(C_3 & C_5), 161.924 (C_4-F), 158.552(C_{16}-F), 130.774(C_{13}), 132.449(C_{14} & C_{18}), 115.017(C_{15}), 115.869(C_{17}), M.F. $C_{13}H_9F_2NO_2S$, M.W. 281.0; m.p. 61–62 °C.

Spectral data of (E)-N-(4-chlorobenzylidene)-4-fluorobenzenesulfonamide (2)

IR(ν·cm^{-1}) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H(-NMR(δ ppm) = 8.422 (1H, s,CH=N); 7.187-7.975(8H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 175.653(C=N), 162.952.(C-F), 147.842(C1),132.496(C2 & C6), 115.912 (C3), 115.907(C5), 130.762(C13), 130.777(C14&C18), 132.489(C15&C17), 147.818(C16), (M.F.$C_{13}H_9ClFNO_2S$; M.W. 297.73 m.p. 59–60 °C.

Spectral data of (E)-N-(4-bromobenzylidene)-4-fluorobenzenesulfonamide (3)

IR(ν·cm^{-1}) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H(-NMR(δ ppm) = 8.391 (1H, s, CH=N); 7.092-7.780 (8H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 176.178(C=N), 162.100(C-F), 134.0847(C_1), 133.024(C_2 & C_6),119.587(C_3 & C_5), 133.024(C_{15}), & C_{17}, 132.024(C_{13}), 124.33(C_{14}) & C_{18}, 122.508(C_{16}), M.F. $C_{13}H_9BrFNO_2S$; M.W. 342.18; m.p. 57–58 °C.

Spectral data of (E)-N-(4-methylbenzylidene)-4-fluorobenzenesulfonamide (4)

IR(ν·cm^{-1}) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H(-NMR(δ ppm) = 8.421 (1H, S,CH=N); 7.091-7.819 (8H, m, Ar-H); 2.48(3H, s, methyl-H), ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 175.411(C=N), 165.154(C-F), 21.697(CH_3), 148.247(C_1) 133.553 (C_2 & C_6), 128.789(C_3 & C_5), 129.527(C_{13}), 141.967(C_{14}&C_{18}), 128.789(C_{15} & C_{17}), 148.262(C_{16}), M.F. $C_{14}H_{12}FNO_2S$; M.W.277.31; m.p. 55-56 °C.

Spectral data of (E)-N-(4-methoxybenzylidene)-4-fluorobenzenesulfonamide (5)

IR(ν·cm^{-1}) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H(-NMR(δ ppm) = 8.392(1H, S,CH=N); 7.001-7.8274(8H, m, Ar-H); 3.982(3H, s, methoxy H), ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 175.822(C=N), 165.412(C-F), 55.489(OCH_3),148.312 (C_1) 129.149(C_2 & C_6),115.841,.(C_3 & C_5), 122.269(C_{13}), 130.428(C_{14} & C_{18}), 114.217(C_{15} & C_{17}), 161.745 (C_{16}), M.F. $C_{14}H_{12}FNO_3S$, M.W.293.31; m.p. 57-58 °C.

Spectral data of (E)-N-(4-nitrobenzylidene)-4-fluorobenzenesulfonamide (6)

IR($\nu \cdot cm^{-1}$) = 1589.34 (C=N); ^{1}H-NMR (400 MHz, DMSO-d_6), ^{1}H-NMR(δ ppm) = 8.399 (1H, S, CH=N); 7.101-7.8271(8H, m, Ar-H); ^{13}C-NMR (100 MHz, DMSO-d_6), ^{13}C-NMR(δ ppm) = 175.706(C=N), 165.359(C-F), 150.400(C-NO_2), 145.663(C_1), 132.315(C_2 & C_6), 121.246 (C_3 & C_5), 134.242(C_{13}), 130.588(C_{14}& C_{18}), 127.170(C_{15}&C_{17}), M.F.$C_{13}H_9FN_2O_4S$, M.W. 308.28; m.p. 109–110 °C.

3. ANTIMICROBIAL ACTIVITIES

Antibacterial activity

(*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides(1-6) were tested for their antibacterial activity against two gram positive pathogenic strains *Bacillus substilis*, *Staphylococcus aureu s*and two gram negative strains *Escherichia coli* and *Pseudomonas aerogenosa*. The disc diffusion technique was followed using the Kirby–Bauer [33] method, at a concentration of 250 mg/mL with ciprofloxacin taken as the standard drug. The antibacterial screening effect of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides is shown in **Fig. 1** (Plates1–4). The measured zone of inhibitions is shown in **Table 1** and the clustered column chart in **Fig. 2**.

Results showed that most of the compounds possess potent to moderate activity as compared to the reference drug *ciprofloxacin*. Schiff base analogues (1-6) showed potent activity against gram positive and significant activity against gram negative bacterial strains. Compounds (2) and (3), having 4-chloro and 4-bromo phenyl group in Schiff base, exhibited potent activity against *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*, while a significant activity against *Bacillus subtilis*.

Plate – 1

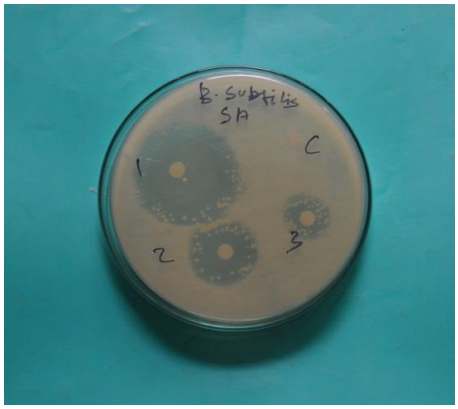


Plate – 2

Plate – 3

Plate – 4

Fig. 1. Petri-plates (1-4) for antibacterial activities of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

When bromo or chloro group was replaced by fluoro or nitro group (1) and (6), the activity was enhanced for *Bacillus subtilis*, while it was diminished for *E. coli* and *Staphylococcus aureus*. Compound (5) showed significant activity against only *Pseudomonas aeruginosa* with 25 mm, and also, moderate activity was noticed against other strains. Compounds (2), (3), and (4) revealed better activity in comparison to other compounds used in the study, indicating that methyl and halogen substitution at 4-position of Schiff base nucleus showed better activity as compared to standard.

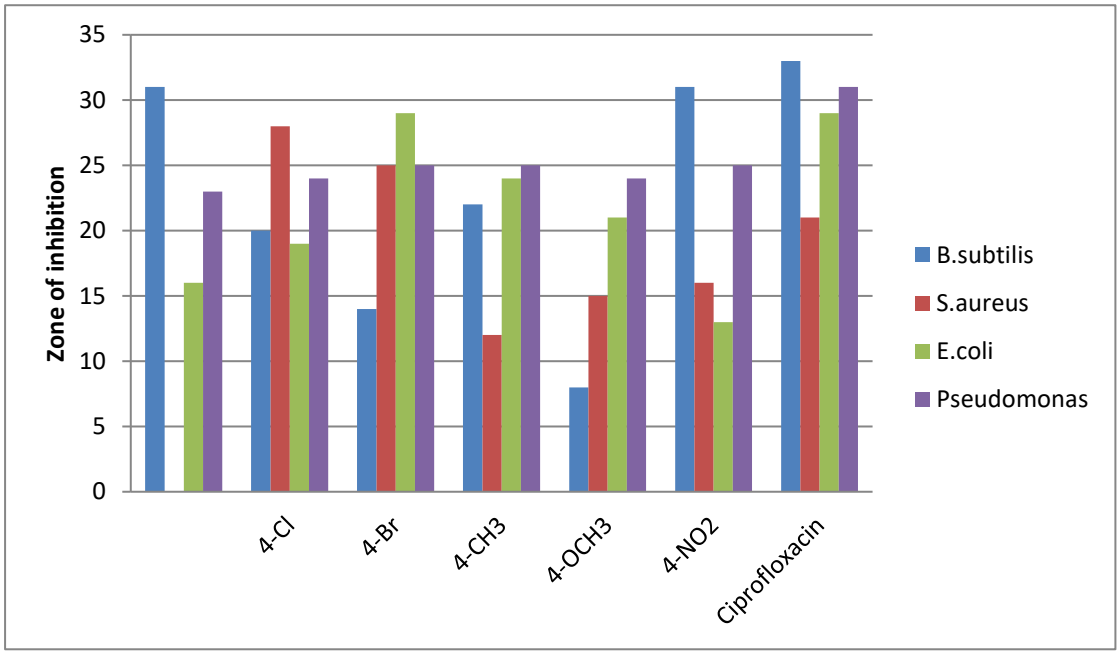


Fig. 2. Cluster Column for Antibacterial activity of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

Table 1. Zone of Inhibition (mm) values of antibacterial activities of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

S. No.	Substituents	Zone of Inhibition (mm)			
		Gram positive Bacteria		Gram negative Bacteria	
		B. subtilis	*S. aureus*	*E. coli*	*Pseudomonas*
1	4-F	31	-	16	23
2	4-Cl	20	28	19	24
3	4-Br	14	25	29	25

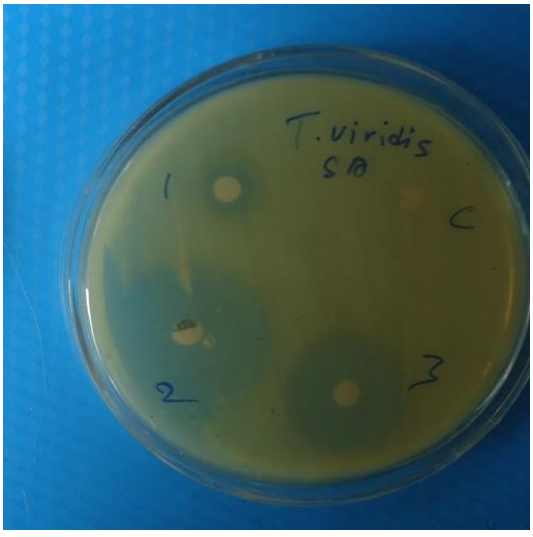
4	4-CH_3	22	12	24	25
5	4-OCH_3	8	15	21	24
6	4-NO_2	31	16	13	25
Standard	Ciprofloxacin	33	21	29	31
Control		-	-	-	-

Antifungal activity

The antifungal activities of all the synthesized compounds have been studied against *Tricodermaviridi*, *Aspergillusniger*, *Muccor species*, and *Candida albicans.* The disc diffusion technique was followed using the Kirby–Bauer[33] method, at a concentration of 250 mg/mL, with Miconazole taken as the standard drug. The antifungal activities of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides have been studied, and are shown in **Fig. 3**. Plates (5-8) and the zone of inhibition values are given in **Table 2** and the Clustered column Chart, given in **Fig. 4**.

Thus, the substituents place a vital role in imparting enhanced antifungal activity to the compounds. Compounds (1), (2), and (3) were found to have better antifungal activities than those of other compounds. The higher activity of (1), (2), and (3) were influenced by the presence of electron with drawing such as halogen on phenyl ring. Compound (4), having methyl group on para-position of phenyl ring showed increased activity (19 mm) against *Candida albicans*, and similarly the compound (5) having methoxy group, on para-position of phenyl ring showed (19 mm) against *Aspergillus niger.* Among these compounds, compound (3) has strong selectivity towards all the fungal strains, but compound (2) has strong activity (26 mm) against *Tricoderma viridi.*

Plate – 5



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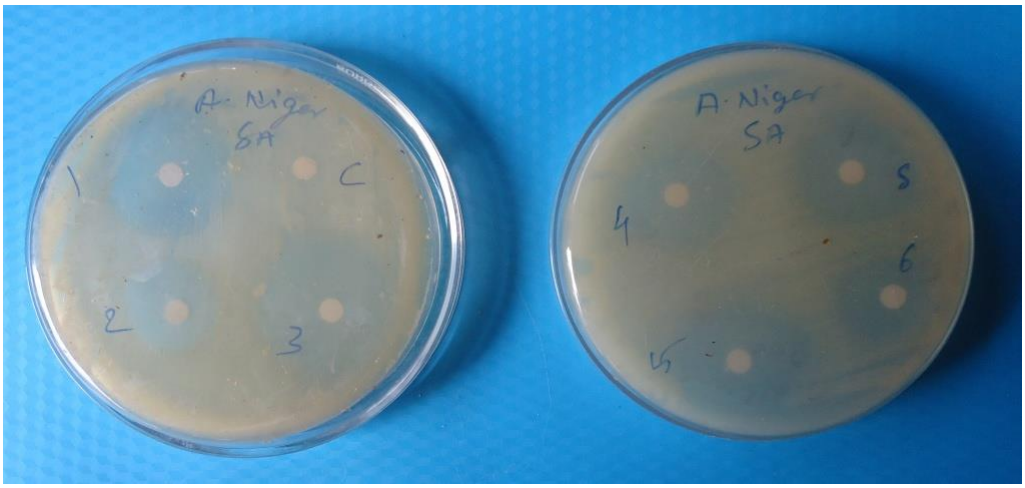

Plate – 7

Plate – 8

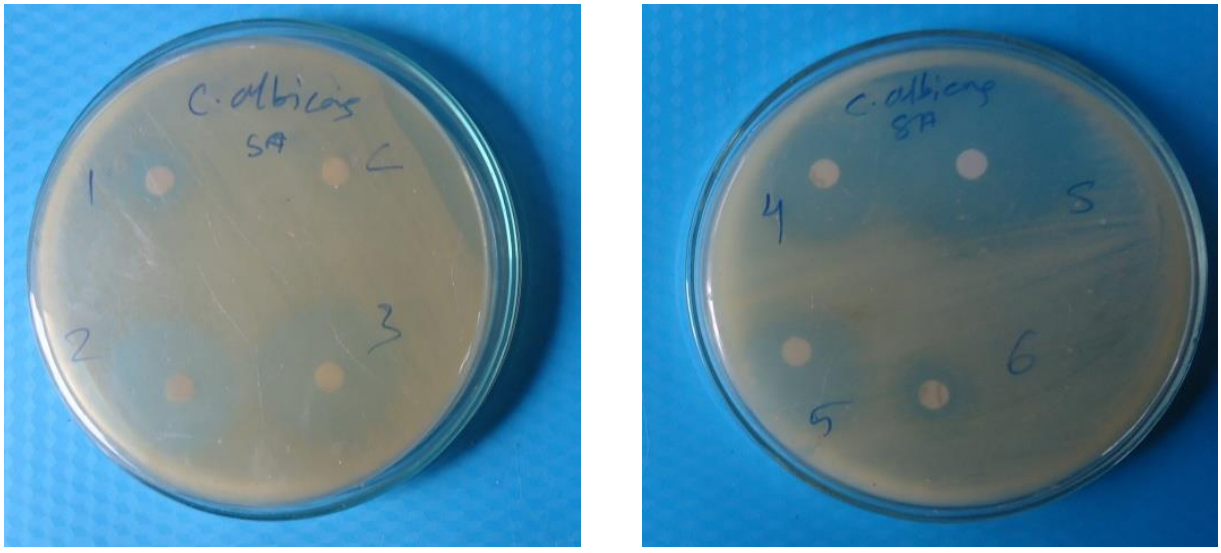

Fig. 3. Petri-plates for antifungal activities of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

Table 2. Zone of Inhibition (mm) values of antifungal activities of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

S. NO.	Substituents	Zone of Inhibition (mm)			
		Tricoderma viridi	*Aspergillus niger*	*Mucor species*	*Candida albicans*
1	4-F	10	23	18	11
2	4-Cl	26	20	18	20
3	4-Br	21	22	22	21
4	4-CH_3	14	18	11	19
5	4-OCH_3	16	19	14	15
6	4-NO_2	18	18	14	15
Standard	Miconazole	28	24	22	29
Control	DMSO	-	-	-	-

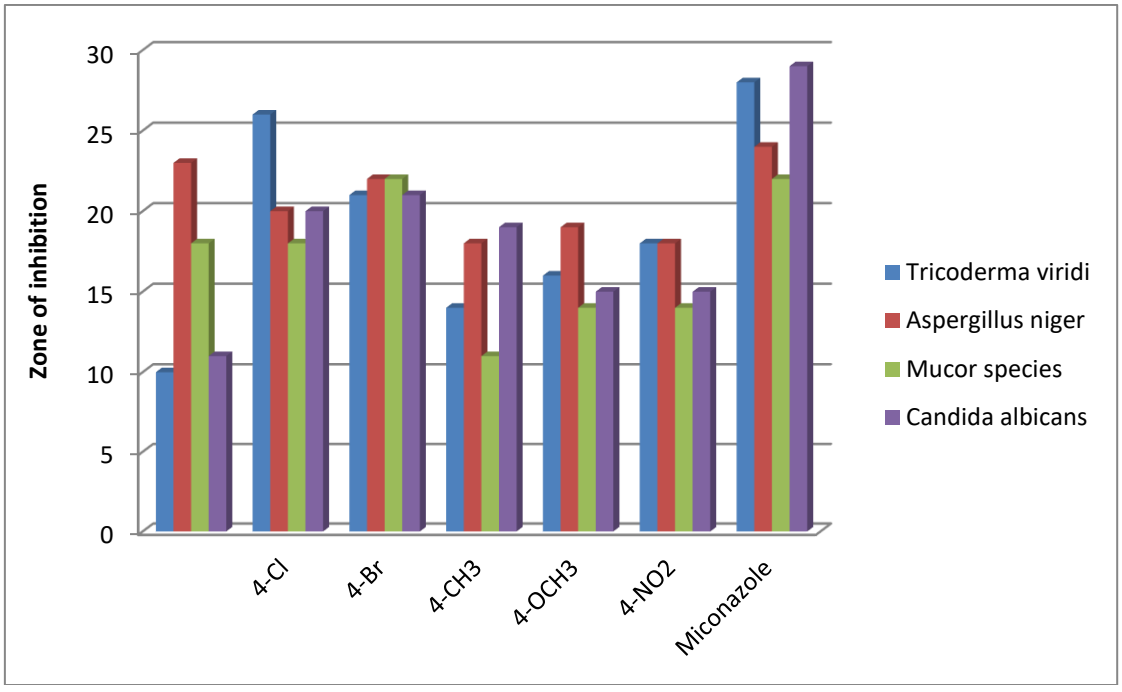

Fig. 4. Cluster Column for Antifungal activity of (*E*)-N-(4-substitutedbenzylidene)-4-fluorobenzenesulfonamides

4. CONCLUSION

Six new Schiff bases have been synthesized by condensation method. These Schiff bases have been characterized by their physical constants, IR, ^{1}H NMR, and ^{13}C NMR spectral data. The antibacterial activity of all synthesized schiff bases has been studied using Bauer-Kirby method. Most of the synthesized Schiff bases have shown better activity against Gram positive, Gram negative bacterial, and Fungal Species compared to the standard drugs Ciprofloxacin and Miconazole.

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