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Biologically active sulfonamides moiety: Synthesis, antimicrobial and antimalarial activity

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At present the incident of microbial diseases, especially in immunologically compromised patients is life-long and a growing health challenge. The increasing incidences of drug resistance has become a major concern for physicians. To deal with the problem of these microbial diseases, amalgamation therapy has gained much interest. A new series of sulfonamides hybrids **3a-g** have been synthesized by the reaction of 4-aminoacetophenone with benzensulfonyl chlorides. They have been screened for their antimicrobial and antimalarial activity against four bacteria and against three fugal stains. Compounds **3d**, **3e** and **3c** have excellent antibacterial activities with MIC values of 25, 50 and 62.5 µg/mL respectively. The derivatives **3a**, **3d**, **3e** and **3f** exhibited high anti-antimalarial activity with mean IC_{50} values of 0.70, 0.42, 0.74 and 0.82 µg/mL respectively.

Keywords: Immunological, Multi-drug resistance, Antimicrobial, Antifungal, Antimalarial

Sulfonamides are concert to an imperative group of artificial antimicrobial drugs which are pharmacologically applicable as broad spectrum for the treatment of bacterial infections. Sulfonamides is a characteristic and interesting system that covers a wide range of pharmacopoeias, as well as give information about the nature and condition of the base, describing its features, to do the work. Sulfonamides are such effective scaffolds that cover a comprehensive range of pharmaceuticals activity depending on the nature of substituent's and describe as an antibacterial[1,2], antitumor[3], diuretic[4], anti-malarial activity[5] and anti-carbonic anhydrase[6,7] (Fig. 1). Importantly, all types of invasive Candida species infections are caused by different Candida species. Fungal infections are usually treated with drugs from the classes of antifungal agents; polyarine, echinocandins, azoles and polyenes[8]. In 1958, the chloramidazole sulfa drug became the first clinically available antifungal agent while in 1981, the first orally available antifungal agent, (±)-ketoconazole, received US Food and Drug Administration (FDA) approval from Janssen Pharmaceuticals. There are diverse module of Sulfonamides depending on the structure of substituent's likes: 5-Phenyl-4,5-dihydro-1*H*-pyrazole, 5-phenylisoxazole, 6-phenylpyrimidine-2(1*H*)-thione, 6-phenylpyrimidin-2(1*H*)-one, 2-hydroxy-6-phenyl-4*H*-pyran-3-carbonitrile, *etc*. depending on the pyrazole, isoxazole, thione, pyrimidine, pyran heterocyclic rings. Quinazolinones including a pyrimidine ring were exhibited to act as antimicrobial, antifungal, antitumor and antiviral agents through various mechanisms. Sulfapyrimidine[9], sulfapyridine[10], and sulfathiazole[11] were Some of the best representatives of the group of sulfonamides. The exclusive antimicrobial and antifungal properties of heterocyclic Sulfonamides prompted the additional creation of a bulky number of N-base Sulfonamides, with unexpected activity and low characteristics[12]. After the discovery of pyrazoles, celecoxib and pyrazofurin, pyrazoles, isoxazoles, thiones, pyrimidines and pyrans are demonstrated as antibacterial agents that exhibit a wide range of antimicrobial and antifungal activites[13,14]. Sulfapyrimidine drugs of sulfadimidine are applicable for treatment of urinary infections due to considerable solubility in urine and any kind off side effect[15]. Sulfonamides fused pyrazole moieties are typical molecules and this ring system attempts various relevance in drug detection efforts. Sulfonamides of pyrazole derivatives are demonstrate a wide pharmaceutical activities spectrum such as antibacterial, analgesic, anti-pruritic, anti-inflammatory, antifungal, antiviral and anti-proliferative. Here we illustrate design, synthesized and evaluated of the sulfonamides derivatives of

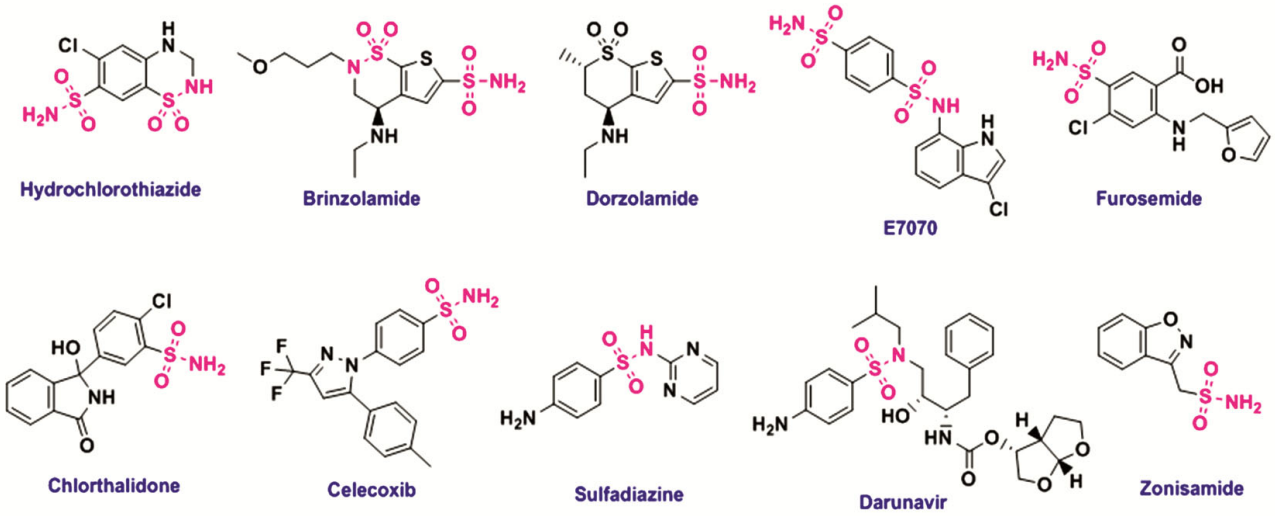


Fig. 1 — Structure of some sulfonamides based drugs

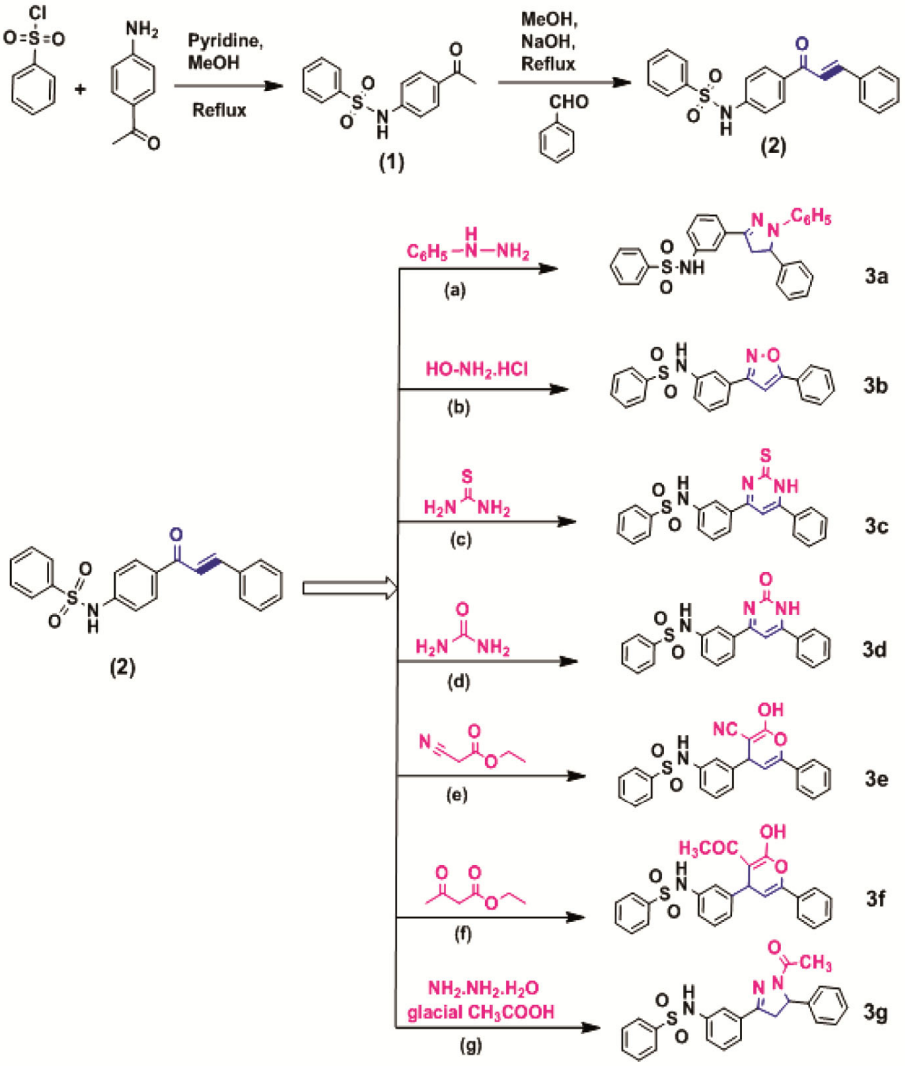
pyrazole moiety (**3a**, **3g**) isoxazole moiety (**3b**) and pyrimidine moiety (**3c**, **5e**) And finally two derivatives of pyran moiety (**3e**) Scheme 1. Here we are comparison between sulfonamides motif of pyrazole, isoxazole, thione, pyrimidine and pyran moieties. In present work, Synthesized sulfonamides introducing substituted N & O-containing ring systems: pyrazole, isoxazole, thione, pyrimidine, pyran moieties. Among the many heterocyclic rings, Sulfonamides constitutes an important framework of antibacterial, antifungal and antimalarial agents.

Experimental Section

All chemical and starting materials were achieved from sigma-aldrich and the solvents were purified using a purification receptacle suitable for distillation. Melting points, Mass spectra, IR spectra (KBr) and NMR were recorded. Nuclear magnetic resonance are characteristics recorded on 300 MHz spectrometer used in solvent $CDCl_3$ and chemical shifts (δ) are expressed in ppm using TMS. TLC was performed on percolated silica gel GF254 plates and detected with a 254 nm UV lamp.

Chemistry

The compound N-(4-acetylphenyl)benzene sulfonamide (1) was readily obtained from 4-aminoacetophenone (1mol) and benzenesulfonyl chloride (1mol) by boiling in minimum amount of pyridine and methanol. The structure of intermediate compound (1) was supported by mass, IR, NMR of spectroscopic data[16]. Fusion of N-(4-acetylphenyl) benzenesulfonamide derivative (1) with benzaldehyde (1.3 mmol) in solvent methanol and NaOH at 130–140°C afforded to N-(4-cinnamoylphenyl) benzenesulfonamide intermediate (2) was capable for the synthesized of a various sulfonamides[17]. Reaction of compound (2) with a different derivatives like: phenylhydrazine, hydroxylamine, thiourea, urea, ethyl cyanoacetate, ethyl acetoacetate and hydrazine hydrate in various different condition and catalyst to furnished the target compounds (**3a-g**) is shown in Scheme 1. For effective biological applications synthesis of heterocyclic systems is the major objectives of this synthetic approach, therefore N-(4-cinnamoylphenyl)benzenesulfonamide (2) was used as a precursor. Thus, compound (2) condensation reaction with Pheylhydrazide in ethanol and glacial CH_3COOH at refluxed to afforded, N-(3-(1,5-diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl) benzenesulfonamide **3a**. The compound N-(3-(5-phenylisoxazol-3-yl)phenyl)benzenesulfonamide **3b** was created by the reaction of compounds **2** with a solution of hydroxylamine hydrochloride in presence of EtOH and anhydrous CH_3COONa (2 mmol) and refluxed condition. Compound (2) Also, the reaction with thiourea in ethanol and 10% KOH, (1 mmol), yielded N-(3-(6-phenyl-2-thioxo-1,2-dihydropyrimidin-4-yl)phenyl)benzenesulfonamide **3c**. Moreover, N-(3-(2-oxo-6-phenyl-1,2-dihydropyrimidin-4-yl)phenyl) benzenesulfonamide **3d** was also achieved by reaction urea and N-(4-cinnamoylphenyl) benzenesulfonamide in absolute ethanol and KOH at refluxed condition. Same way compound (2) react with ethyl cyanoacetate to gave N-(3-(3-cyano-2-hydroxy-6-phenyl-4*H*-pyran-4-yl)phenyl)benzene



Reagents and Conditions: (a): Phenylhydrazine, EtOH, glacial CH_3COOH, reflux, 8 h; (b): hydroxylamine hydrochloride, EtOH, sodium acetate, acetic acid; (c): Thiourea, ethanol, KOH, refluxed 9h; (d): Urea, EtOH, KOH, reflux, 9h; (e): Ethyl cyanoacetate, EtOH, sodium ethoxide, sodium metal, EtOH, refluxed; (f): Ethyl acetoacetate, ethanol, KOH; (g): Hydrazine hydrate, glacial CH_3COOH, refluxed

Scheme 1 — Synthesis route of sulfonamides compounds **3a-g**

sulfonamide **3e** in ethanol, sodium ethoxide and sodium metal (10mol) at refluxed condition for **4h**. N-(3-(3-acetyl-2-hydroxy-6-phenyl-4*H*-pyran-4-yl) phenyl)benzenesulfonamide **3f** was acquired by condensation reaction of compound **2** with ethyl acetoacetate in the presence of base KOH at refluxed condition for **2h** to achieved good yield 75%. Compound **2** react with hydrazine hydrazine in glacial acetic acid to produced, N-(3-(1-acetyl-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl)benzenesulfonamide **3g**. Analysis of the sulfonamides was conformed on the spectroscopic data of mass, IR and NMR.

Synthesis of N-(4-acetylphenyl)benzenesulfonamide, 1

4-Aminoacetophenone (1 mmol) was soluble in a minimal amount of pyridine and 20 mL MeOH was added to it. After them add benzene sulfonychloride (1 mmol) as a drop wise in reaction mixture at 0°C and refluxed it overnight. After the completed of reaction, the reaction mass is put into cold ice water and appeared precipitate was filtered off and treated with 50 mL of dilute hydrochloric acid to give the products directly. The obtained products were recrystallized from methanol (Yield: 80%)[18].

Synthesis of N-(4-cinnamoylphenyl)benzene sulfonamide, 2

The solution of N-(4-acetylphenyl) benzenesulfonamide (1 mmol) suspend in 30 mL of methanol and add freshly prepared 20% NaOH solution (10 mL) and stirred for 5-10 min. After them add benzaldehyde (1.3 mmol) in reaction mixture and refluxed it 8h. After the completed of reaction, the mixture mass was dump in cold ice water and appearing precipitate was separated and wash with 50 mL dilute hydrochloride acid to achieve the crude product. Which was further purify by colum chromatography and recrystallized with methanol (Yield: 67%)[19].

General synthesis of process of compounds, 3a

A mixture of N-(4-cinnamoylphenyl) benzenesulfonamide (2) (1 mmol) in ethanol (20 mL) and phenylhydrazine (1 mmol) in glacial acetic acid (0.5 mL) were refluxed for 6h. After complete of reaction, the mixture mass was dump in ice bath and appearing solid product was filtered, dry and washes with diethyl ether and finally recrystallized from absolute ethanol[20-22,23].

Synthesis of N-(3-(5-phenyl-4,5-dihydroisoxazol-3-yl) phenyl) benzenesulfonamide, 3b

A solution of compounds (2) (1 mmol) in ethanol and anhydrous sodium acetate (2 mmol) dissolved in a minimum amount of glacial acetic acid were stirrer. The solution of hydroxylamine hydrochloride (1 mmol) in ethanol was added in reaction mixture and mixture was refluxed for 8h. After completion of the reaction, the mixture was dump in ice water and obtained solid was removed and dissolved in diethyl ether. Collected the filtrated solution and dry to obtained solid product (Yield: 74%)[21].

Synthesis of N-(3-(6-phenyl-2-thioxo-1,2,3,6-tetra hydropyrimidin-4-yl)phenyl) benzenesulfonamide, 3c

A solution of N-(4-cinnamoylphenyl) benzenesulfonamide (1 mmol) in 20 mL of ethanol, 10% KOH, (1 mmol) and thiourea (1mmol) was mixture was refluxed for 9h. The reaction was monitoring by ethyl acetate: hexane (1:4). After complete of reaction the reaction mixture was dump in an ice bath and obtained solid product was washed with five times of distilled water and finally washed with minimum amount of ethanol to remove extra aldehyde and dry it (Yield: 57%)[22].

Synthesis of N-(3-(2-oxo-6-phenyl-1,2-dihydropyrimidin-4-yl)phenyl) benzenesulfonamide, 3d

Compound **3b** was synthesized by the same process of **3a**.

Synthesis of N-(3-(3-cyano-2-hydroxy-6-phenyl-4*H*-pyran-4-yl)phenyl) benzenesulfonamide, 3e

Prepared a solution of compound (2) (1 mmol) and ethyl cyanoacetate (1 mmol) in 20 mL absolute ethanol. A solution of sodium ethoxide was prepared from 0.23 g Na-metal (10 mmol) and 5 mL ethanol, after it both solution were added and mixture was refluxed for **4h**. After completed the reaction, mixture were cooling in ice bath and papering solid product was collected by filtration and wash with water and diethyl ether. Finally crystallized from ethanol to give brown crystals. (Yield: 71%)[24,25].

Synthesis of N-(3-(3-acetyl-2-hydroxy-6-phenyl-4*H*-pyran-4-yl)phenyl) benzenesulfonamide, 3f

Prepared a solution of N-(4-cinnamoylphenyl) benzenesulfonamide (1 mmol) and ethyl acetoacetate (1 mmol) in absolute ethanol (10 mL) and add aqueous potassium hydroxide solution (1 mL, 10%). The reaction mixture was refluxed for 1.5–2 hours and then left at RT overnight. The residual solid was collected by filtration, washed with ethanol and diethyl ether and finally recrystallized from ethanol. (Yield: 81%).

Synthesis of N-(3-(1-acetyl-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl)benzene sulfonamide, 3g

Prepared a mixture of N-(4-cinnamoylphenyl) benzenesulfonamide (1 mmol) and hydrazine hydrate (1 mmol) in glacial acetic acid and refluxed it for **5h**. After the completed of reaction, the mixture was dump in ice water and collected the papering predicated which was further purifying by recrystallized (Yield: 61%).

Spectral analysis

N-(4-Acetylphenyl)benzenesulfonamide, 1

Physical appearance: Brown powder. Mol. Wt. 275.32. IR (KBr): 3488.1 (N-H), 1611.21(C=O), 1258.7 (S=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, NH), 7.97 (d, 2H, J = 8.7 Hz), 7.99 (d, 2H, J = 8.7 Hz), 7.67 (d, 2H, J = 8.7 Hz), 7.46 (d, 2H, J = 8.7 Hz), 2.61 cm^{-1} (s, H_{methyl}); UV-Vis (EtOH) λmax (nm): 274 and 333; ^{13}C NMR(100 MHz,

$CDCl_3$): δ 171.50 (C=O), 131.84, 131.50, 132.41 (Ar-C, First aromatic ring), 122.12, 130.24, 132.23, 142.45 (Ar-C, Second aromatic ring).

N-(4-Cinnamoylphenyl)benzenesulfonamide, 2

Physical appearance: Colourless crystals. Mol. Wt. 363.43. IR (KBr): 3425.9 (NH), 1609.1(amide C=O) , 1598.2 (C=C), 1158.2 cm^{-1} (S=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (s, 1H, SO_2NH), 9.13 (S, 1H, CO-NH), 7.84 (d, 1H, CH=HC), 7.76 (d, 1H, CH=HC), 7.55-7.58 (d, 4H, Ar-H), 7.43-7.23 (s, 4H, Ar-H), 7.50-7.10 (d, 10H, Ar-H), 4.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.51 (amide C=O), 156.89 (C=C), 135.83, 133.91, 132.51 (Ar-C, First aromatic ring), 132.40, 120.5, 126.92 (Ar-C, Second aromatic ring).

N-(3-(1,5-Diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl)benzenesulfonamide, 3a

Physical appearance: White crystals. Mol. Wt. 453.56. IR (KBr): 3235(NH), 1316 cm^{-1} (S=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d,2H,HC, HArs), 7.88(d,2H,HC, HArs), 7.99 (s,1H,HC, HArs), 11.01(s,1H,HN), 5.15(s, 1H, HC, prazole ring), 7.56-7.85(m, 4H, HArs), 8.28(d,2H,HC, HArs), 7.66(d,2H,HC, HArs), 8.56(s,1H,HC, HArs), 8.22(d,2H,HC, HArs), 8.22(d,2H,HC, HArs), 8.33(s,1H,HC, HArs) ; ^{13}C NMR ($CDCl_3$): δ 126.2,127.0, 128.12,130.5, 131.6(CH, First aromatic ring), 116.1,121.8,128.7,134.1 (CH, Second aromatic ring), 124.0,125.9,129.1,133.1,146.7 (CH, Third aromatic ring),126.2,128.3,135,147.5(CH, Fourth aromatic ring).

N-(3-(5-Phenyl-4,5-dihydroisoxazol-3-yl)phenyl)benzenesulfonamide, 3b

Physical appearance: Yelow crystals. Mol. Wt. 378.45. IR (KBr): 3322(NH), 1401 cm^{-1} (S=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65 (d,2H,HC, HArs), 7.99 (d,2H,HC, HArs), 8.14 (s,1H,HC, HArs), 10.68 (s,1H,HN), 7.56-7.85 (m, 4H, HArs), 6.10 (s, 1H, HC, oxazole ring), 8.11 (d,2H,HC, HArs), 9.23 (d,2H,HC, HArs), 8.68 (s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 125.2,126.7, 128.4, 130.1, 133.6(CH, First aromatic ring), 118.129.8, 130.7, 134.5 (CH, Second aromatic ring), 124.4, 126.9, 131.0, 133.1, 140.7 (CH, Third aromatic ring).

N-(3-(6-Phenyl-2-thioxo-1,2,3,6-tetrahydropyrimidin-4-yl)phenyl) benzenesulfonamide, 3c

Physical appearance: colourless crystals. Mol. Wt. 421.53. IR (KBr): 3400(NH), 1363 (S=O) , 1677 cm^{-1} (C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.67(d,2H,HC, HArs), 7.91(d,2H,HC, HArs), 8.99(s,1H,HC, HArs), 10.09(s,1H,HN), 6.46-7.28 (m, 4H, HArs), 6.88 (s, 1H, HC, pyrimidine ring), 10.1,13.62 (s, 1H, HN, pyrimidine ring), 9.21 (d,2H,HC, HArs), 9.13 (d,2H,HC, HArs), 9.86 (s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 127.2,128.1, 129.12,131.1, 132.6(CH, First aromatic ring), 117.1,129.1,129.7,135.1 (CH, Second aromatic ring), 126.0,126.9,129.7,134.2,144.7 (CH, Third aromatic ring).

N-(3-(2-Oxo-6-phenyl-1,2-dihydropyrimidin-4-yl)phenyl) benzenesulfonamide, 3d

Physical appearance: Orange crystals. Mol. Wt. 403.46. IR (KBr): 3389(NH), 1532.21(C=O), 1386 (S=O) 1668 cm^{-1} (Amide C=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89(d,2H,HC, HArs), 8.51(d,2H,HC, HArs), 8.92(s,1H,HC, HArs), 10.78(s,1H,HN), 7.61-8.22(m, 4H, HArs), 5.87(s, 1H, HC, pyrimidine ring),11.64(s, 1H, HN, pyrimidine ring), 7.21(d,2H,HC, HArs), 8.13(d,2H,HC, HArs), 8.71(s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 128.2, 128.9, 130.12, 133.1, 134.5(CH, First aromatic ring), 116.1, 121.1, 128.5, 134.2 (CH, Second aromatic ring), 126.8,128.9,132.7,134.8,142.1 (CH, Third aromatic ring).

N-(3-(3-Cyano-2-hydroxy-6-phenyl-4*H*-pyran-4-yl)phenyl) benzenesulfonamide, 3e

Physical appearance: Reddish colour. Mol. Wt. 430.48. IR (KBr): 3441(NH), 1461 (S=O), 3512(OH), 1319 cm^{-1} (CN); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87(d,2H,HC, HArs), 7.77(d,2H,HC, HArs), 8.71 (s,1H,HC, HArs), 11.78(s,1H,HN), 6.67-7.74(m, 4H, HArs), 5.44(s, 1H, HC, pyran ring), 8.22(d,2H,HC, HArs), 8.79(d,2H,HC, HArs), 9.74(s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 129.2, 130.0, 132.1, 133.1, 134.7(CH, First aromatic ring), 118.1, 123.1, 128.4, 135.1 (CH, Second aromatic ring), 127.8, 127.9, 131.7, 136.8, 144.4 (CH, Third aromatic ring).

N-(3-(3-Acetyl-2-hydroxy-6-phenyl-4*H*-pyran-4-yl)phenyl) benzenesulfonamide, 3f

Physical appearance: Yellow crystals. Mol. Wt. 447.51. IR (KBr): 3311(NH), 1251 (S=O), 1308(C=O), 3563(OH), 1661 cm^{-1} (C=C); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.07(d,2H,HC, HArs), 8.74(d,2H,HC, HArs), 8.97 (s,1H,HC, HArs), 10.18(s,1H,HN), 7.42-8.69(m, 4H, HArs), 6.21(s, 1H, HC, pyran ring), 31.2 (s, 3H, CH_3), 7.12(d,2H,HC, HArs), 7.49(d,2H,HC, HArs), 8.56(s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 128.4, 128.9, 133.14, 135.1, 136.7(CH, First aromatic

ring), 117.2, 123.7, 128.9, 137.69 (CH, Second aromatic ring), 129.8,130.4, 131.6,138.8,142.9 (CH, Third aromatic ring).

N-(3-(1-Acetyl-5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)phenyl) benzenesulfonamide, 3g

Physical appearance: Light yellow crystals. Mol. Wt. 419.50 . IR (KBr): 3319(NH), 1357 (S=O),1670 cm^{-1} (C=O); ^1H NMR (500 MHz, $CDCl_3$): δ 7.37(d,2H,HC, HArs), 8.23(d,2H,HC, HArs), 8.15(s,1H,HC, HArs), 11.32(s,1H,HN), 7.02-8.22(m, 4H, HArs), 4.66,7.69(s, 2H, HC, pyrazole ring), 7.32(d,2H,HC, HArs), 8.01(d,2H,HC, HArs), 8.96(s,1H,HC, HArs); ^{13}C NMR ($CDCl_3$): δ 126.4, 127.8, 130.74, 133.15, 136.7(CH, First aromatic ring), 117.2, 118.4, 121.6, 133.7 (CH, Second aromatic ring), 123.1,129.6,130.6,132.8,140.9 (CH, Third aromatic ring).

Results and Discussion

Antibacterial activity (*in vitro*)

The antimicrobial assay of achieved sulfonamides were evaluated *in vitro* using hole plate and agar plate diffusion technique[26]. In addition to some fungal plant pathogens, various types of gram-positive and gram-negative bacteria were used and comparison between achieved sulfonamides with Chloramphenicol, Ciprofloxacin, Norfloxacin, Ampicillin and Gentamycin as standard drug was discussed. Test organisms were *E. coli* (MTCC-443), S. *aureous* (MTCC-96) and *S. pyogenes* (MTCC-442) as gram-positive bacteria while *P. aerugnosa* (MTCC-1688) as gram-negative bacteria. For evaluated of antimicrobial assay different concentrations have been preferred *i.e*. (125, 250, 500 mg/mL) and appeared data listed in Table 1. Antimicrobial activity of the achieved compounds **3c**, **3d**, **3e**, **3f** were found be highly active against gram-positive and gram-negative bacteria. The higher assay of tested compounds due to the inclusive properties of pyrimidine, pyran and pyrazole moieties, while compounds **3a**, **3b**, **3c** and **3g** are moderate active towards antimicrobial as compared with standard drug of Chloramphenicol, Ampicillin, Ciprofloxacin, Norfloxacin and Gentamycin (Fig. 2).

Antifungal activity (*in vitro*)

Antifungal assay of achieved compounds **3a-g** were evaluated against three fungal medium of C. Albicans, A. Niger and A. Clavatus which MIC value are MTCC-227, MTCC-282 and MTCC-1323 respectively, according to the literature approach[27]. The results of activity were record and compare with standard drugs of Nystain and Greseofulvin. The fungus was reported to be minimum fungicidal concentration (MFC). The result was evacuated that compounds **3d**, **3e**, **3f** and **3g** exhibited potential antifungal assay against A.N., C.N. and A.N., A.N. and A.C. respectively which MIC Value is 250 µg/mL. While Compounds **3a**, **3b** and **3f** exhibited moderated antifungal activity which MIC Value is 500 µg/mL (Fig. 2).

Table 1 — Biological activity of sulfonamides derivatives **3a-g**

Compd	Anti-bacterial assay MIC (µg/mL)				Anti-fungal assay MIC (µg/mL)			Anti-malarial assay Mean IC_{50} (µg/mL)
	E.C.	P.A.	S.A.	S.P.	C.A.	A.N.	A.C.	P.F.
3a	250	100	125	100	1000	500	1000	0.70
3b	500	62.5	100	125	500	>1000	500	1.15
3c	62.5	250	250	250	1000	500	>1000	2.64
3d	250	100	25	62.5	500	250	500	0.42
3e	250	50	150	100	250	250	500	0.74
3f	250	250	62.5	125	500	250	>1000	0.82
3g	500	250	100	250	>1000	500	250	2.20
CHL	50	50	50	50	–	–	–	–
AMP	100	-	250	100	–	–	–	–
CIP	25	25	50	50	–	–	–	–
NOR	10	10	10	10	–	–	–	–
GEN	0.05	1	0.25	0.5	–	–	–	–
NYS	–	–	–	–	100	100	100	–
GRE	–	–	–	–	500	100	100	–
QUI	–	–	–	–	–	–	–	0.268
CHL	–	–	–	–	–	–	–	0.020

E.C.: *E. coli* (MTCC-443), S.A.: *S. aureus* (MTCC-96), P.A.: *P. aeruginosa* (MTCC-1688), S.P.: S. pyogenus (MTCC 442), C.A.: C. albicans (MTCC-227), A.N.: A. niger (MTCC-282), A.C.: *A. clavatus* (MTCC-1323). P. F.: *Plasmodium falciparum*.

CHL: Chloramphenicol, AMP: Ampicillin, CIP: Ciprofloxacin, NOR: Norfloxacin, GEN: Gentamycin, NYS: Nystain, GRE: Greseofulvin, QUI: Quinine, CHL: Chlroquinine

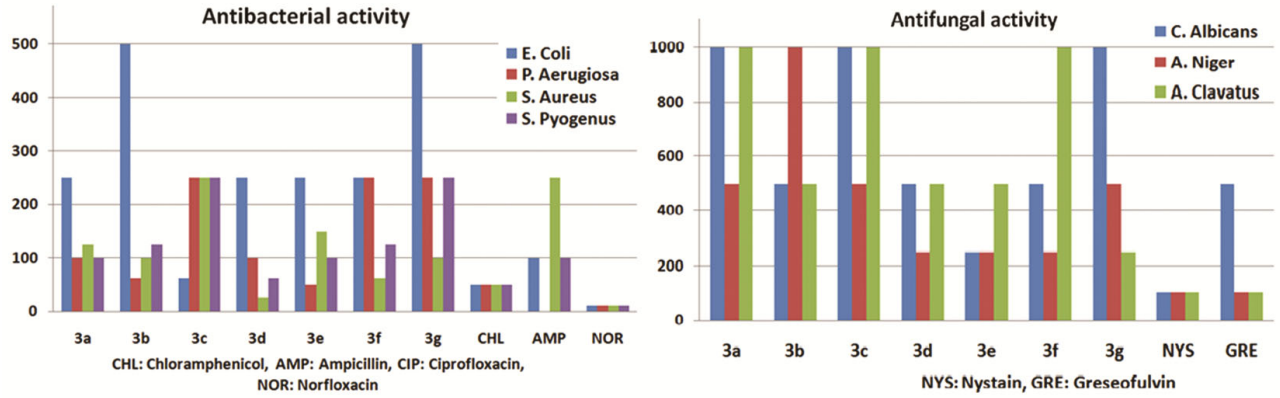


Fig. 2 — Representation of Antimicrobial and antifungal activity of compounds **3a-g**

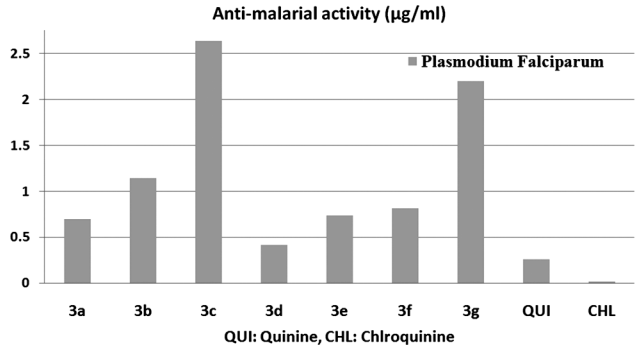


Fig. 3 — Representation of antimalarial activity against *P. Falciparum*

Anti-malarial activity

Seven motiff of sulfonamides have been obtained using the most general description which was very useful as they allowed us to obtain moderate to potential of our synthetic strategies. There is evidence that mortality caused by P. Vivax is underestimated[28,29]. The *in vivo* antimalarial activity of achieved compounds **3a**, **3d**, **3e** and **3f** exhibited higher anti-antimalarial activity which Mean IC_{50} value are 0.70, 0.42, 0.74 and 0.82 respectively (Fig. 3).

Conclusions

The sulfonamides are group of synthetic antimicrobial agent's which are exhibited broad pharmaceuticals activity and inhibit the growth of bacterial and fungal. In present article we are synthesized a series of novel sulfonamides and were evaluated other antibacterial, antifungal and antimalarial activities. Synthesized compounds **3c**, **3d** and **3e** are illustrated potential antibacterial activities. The most excellent antibacterial activities were obsessed of compounds **3d** and **3e**. The results were compared with the standard drugs Nystain and Greseofulvin. These results illustrated that compounds **3d**, **3e** and **3g** display a significant activity against A. Niger and C. Albicans, while compound **3g** also exhibited a significant activity against A. Clavatus while compound **3b** and **3f** showed moderate activity. In conclusion, the activities of novel fused sulfonamides derivatives anticipated anti-malarial activity. The Quinine and Chloroquinane were used as standard drugs. It was observed that most active compound was different fused heterocyclic with sulfonamides with Mean IC_{50} = 0.42, 0.70, 0.74, and 0.82 µg/mL for compounds **3d**, **3a**, **3e** and **3f** respectively.

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