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Antimicrobial activity of some novel triazolo quinoline derivatives

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ABSTRACT

Some triazolo quinoline derivatives were synthesized and their structures were confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy. Screening of all these synthesized compounds were done *in vitro* against bacteria and three fungal strains in dimethyl sulphoxide and *N, N*-dimethyl formamide. It is observed that *N, N*-dimethyl formamide is good solvent for these compounds in selected strains.

***Keywords*:** Triazolo quinoline derivatives, Dimethyl sulphoxide, *N,N*-dimethyl formamide, Gram positive bacteria, Gram negative bacteria, Fungal strains

1. INTRODUCTION

Bacterial infections are responsible for a vast number of human diseases. Moreover, development of bacterial resistance to common antimicrobial is stimulating intensive research devoted to discovery of new targets in combating the bacteria. The increase in microorganism is serious threat to human health and results in tremendous economy loss annually [1, 2]. These microorganisms are present almost everywhere. Many bacteria and fungi may cause infectious disease or contaminate food negatively influencing on their quality, therefore there is a need to control them. Further, the available antibiotics in market have several draw-backs, including toxicity, low effectiveness and environmental issues [3-5]. It means that it is some time adverse

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effect on the host like hypersensitivity. So, the synthesis of new lead structures and chemical entities for the development of antimicrobial agents in an important task in medical field. The shortage of new antimicrobial drugs and increasing resistance of bacteria to antimicrobial agents are important issues in drug development studies which require some physicochemical properties such as molecular hydrophobicity [6, 7], absorbability [8], surface activity and electron density [9, 10] etc., which control antimicrobial activities.

Incorporation of oxygen, nitrogen, sulfur, or an atom of a related element into an organic ring structure in place of a carbon atom gives rise to a heterocyclic compound. Among heterocycles, nitrogen and sulphur containing heterocyclic compounds benzothiazole, pyridine, quinoline etc. have maintained the interest of researchers through decades of historical development of organic synthesis [11-15]. These compounds have great applicability in pharmaceutics because they have specific chemical reactivity and are of most importance in various pharmaceutical industries [16-19]. Further, these heterocycles have been used as medicinal compounds [20, 21] for centuries.

Triazolo quinoline derivatives are always attraction point for researchers because of its efficiency towards various pharmacological usages. Triazlo quinoline compounds occupy a central position among those molecules that makes life possible. Quinoline moieties are known well effective chemical materials. Triazolo quinoline derivatives are known to process various activities like anti-m1icrobial [22-27], analgesic [28-30], anticonvulsant [31-33], anti-viral [34-36], anti-cancer [37-39], anti-tubercular [40-42], anti-tumour [43-47] etc.

Due to these biological applications, it was of our interest to study the biological activity of triazolo quinoline derivatives in solutions which may be useful for their further applications.

2. EXPERIMENTAL

Synthesis of 2-(benzo[d]thiazol-2-yl) acetonitrile: Equimolar ethanolic solution of 2-amino thiophenol and malano nitrile was cooled at 0-5 ºC and glacial acetic acid was added drop wise to this cooled solution. Ammonia gas was liberated and a cyclized product was formed (Int-I). The completion of reaction was confirmed by analytical thin layer chromatography (TLC) using (0.75:0.25 Hexane:Ethyl acetate) as mobile phase. The resulting product (Int-I) was filtered, washed with hexane and dried under vacuum.

Synthesis of arylidine: Equimolar mixture of 2-(benzo[d]thiazol-2-yl) acetonitrile and different substituted aldehydes in methanol was stirred about 30 minutes at 0-5 ºC using piperidine as a catalyst. The completion of reaction was confirmed by the thin layer chromatography using 9.5:0.5 $CHCl_3$:CH_3OH as mobile phase. After the completion of reaction, the precipitate was filtered, washed with distilled water and dried under vacuum. The dry product (Int-II) was purified by recrystallization using methanol.

Synthesis of oxime: Equimolar mixture of dimedone and isoniazide in methanol was stirred for 30 minutes at room temperature using glacial acetic acid as catalyst. The completion of reaction was confirmed by thin layer chromatography using 9.5:0.5 $CHCl_3$:CH_3OH as a mobile phase. The reaction mass was then filtered, washed with distilled water and dried under vacuum. The dry product (Int-III) was purified by recrystallization from methanol.

Synthesis of pyridine containing trizolo quinoline derivatives: The above synthesized arylidine and oxime were dissolved in ethanol. The solution is then refluxed for 4 hrs at 45-50 ºC using piperidine as catalyst. The completion of reaction can be confirmed by thin layer chromatography using 9.6:0.4 $CHCl_3$:CH_3OH as a mobile phase. The reaction mass was filtered, washed with distilled water and dried under vacuum. This dry product (dihydro pyridine) was refluxed for 1 to 2 hrs in DMF. The completion of reaction can be confirmed by thin layer chromatography using 9.8:0.2 $CHCl_3$:CH_3OH as a mobile phase. The product was recrystallized using methanol.

The reaction scheme for the synthesis of compounds is given in Figure 1.

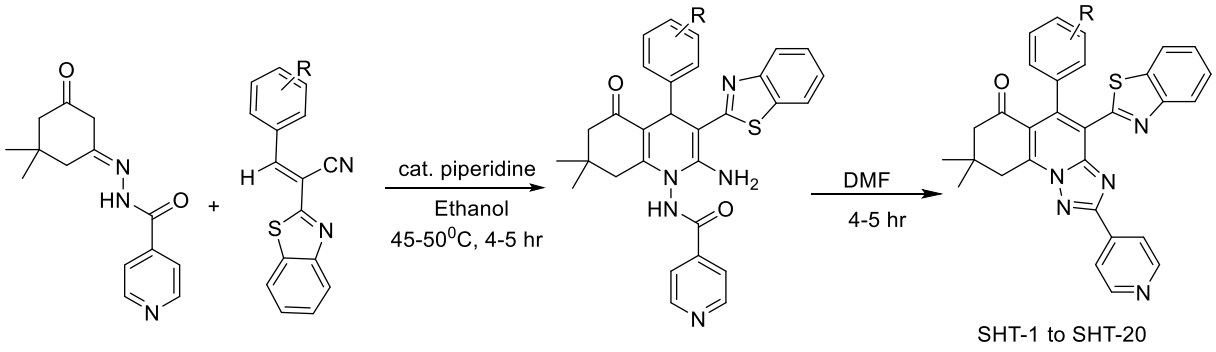

Figure 1. Synthesis of Triazolo quinoline derivatives

2. 1. Structure confirmation

The structures of synthesized crystallized compounds were confirmed by FTIR, ^{1}HNMR, ^{13}C NMR and mass spectral data. IR spectra were recorded on Shimandzu FT-IR-8400 instrument. ^{1}H NMR spectra were taken on a Bruker ADVANCE II 400 using DMSO-d_6 and mass spectra were determined using direct inlet probe on a GCMS-QP-2010 mass spectrometer. (Figure 2 to 4) shows ^{1}H NMR, ^{13}C NMR and mass spectra of SHT-1.

Overall, twenty compounds are synthesized and the IUPAC names of these compounds are:

SHT-1:4-(benzo[d]thiazol-2-yl)-5-(4-hydroxy-3-methoxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-2:4-(benzo[d]thiazol-2-yl)-5-(2-chlorophenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-3:4-(benzo[d]thiazol-2-yl)-5-(3-bromophenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-4:4-(benzo[d]thiazol-2-yl)-5-(4-bromophenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-5:4-(benzo[d]thiazol-2-yl)-5-(4-fluorophenyl)-8,8-dimethyl-2-phenyl-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-6:4-(benzo[d]thiazol-2-yl)-5-(3-chlorophenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-7:4-(benzo[d]thiazol-2-yl)-5-(4-chlorophenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-8:4-(benzo[d]thiazol-2-yl)-5-(2-hydroxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-9:4-(benzo[d]thiazol-2-yl)-5-(3-hydroxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-10:4-(benzo[d]thiazol-2-yl)-5-(4-hydroxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-11:4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-5-(2-nitrophenyl)-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-12:4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-5-(3-nitrophenyl)-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-13:4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-5-(4-nitrophenyl)-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-14:4-(benzo[d]thiazol-2-yl)-5-(2,5-dimethoxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-15:4-(benzo[d]thiazol-2-yl)-5-(3,4-dimethoxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

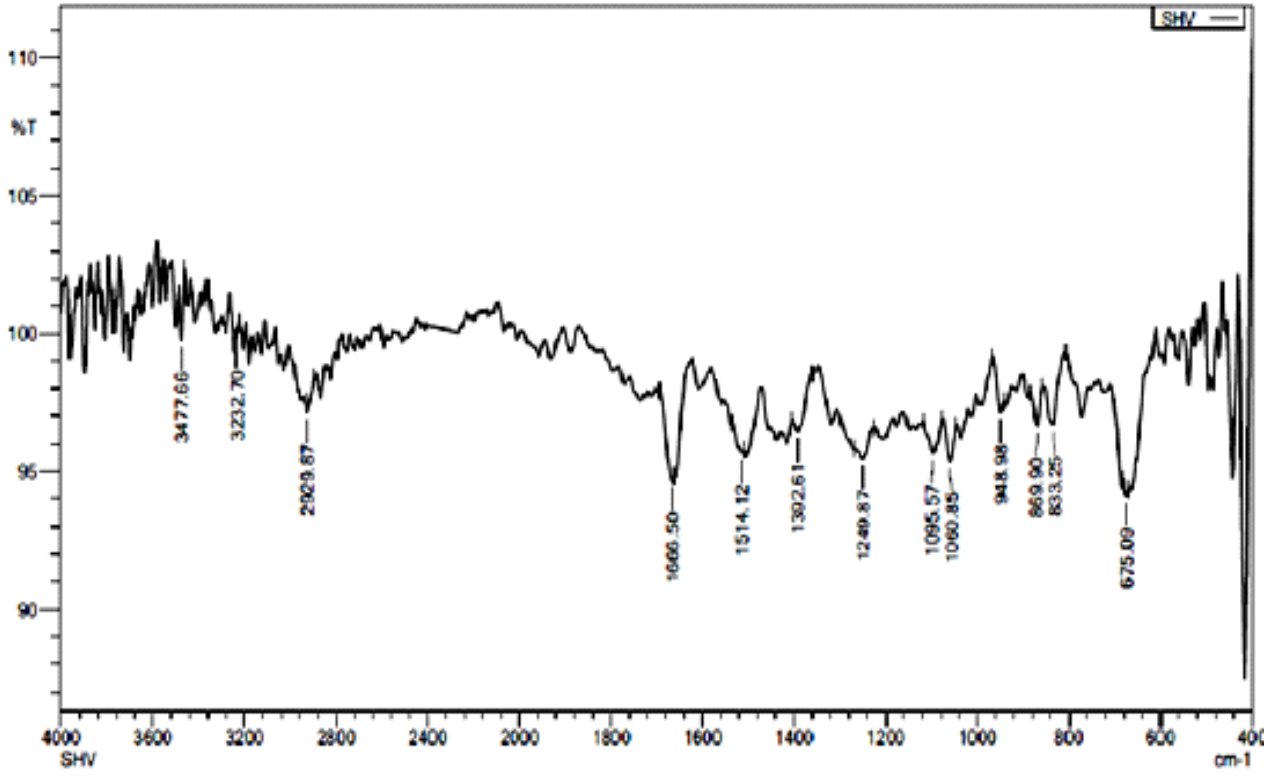

Figure 2. IR spectrum of [A] SHT-1

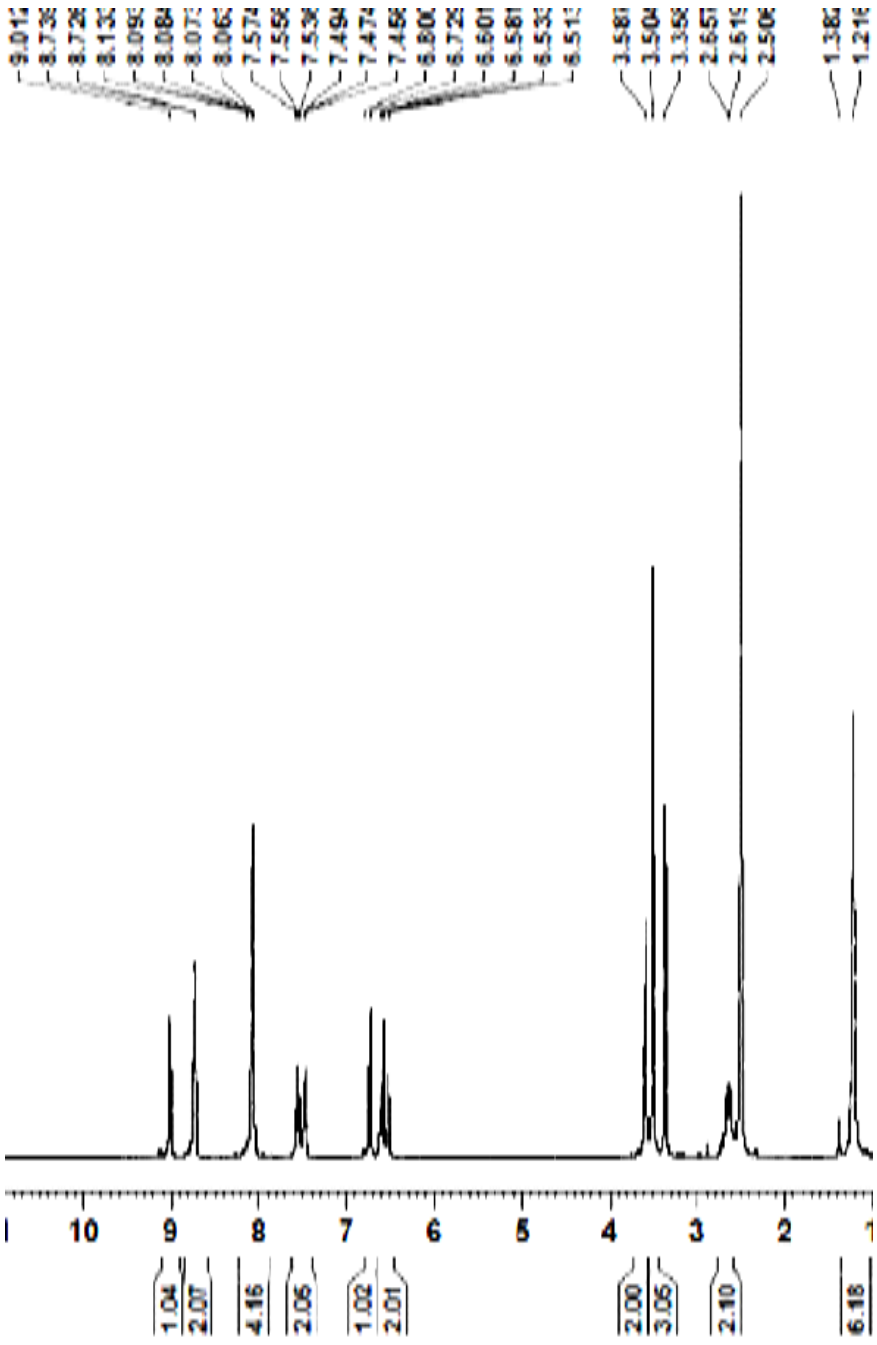

Figure 3. ^{1}H NMR spectrum of SHT-1.

SHT-16:4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-2-(pyridin-4-yl)-5-(3,4,5-trimethoxyphenyl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-17:4-(4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-6-oxo-2-(pyridin-4-yl)-1,2,6,7,8,9-hexahydro-[1,2,4]triazolo[1,5-a]quinolin-5-yl)benzonitrile

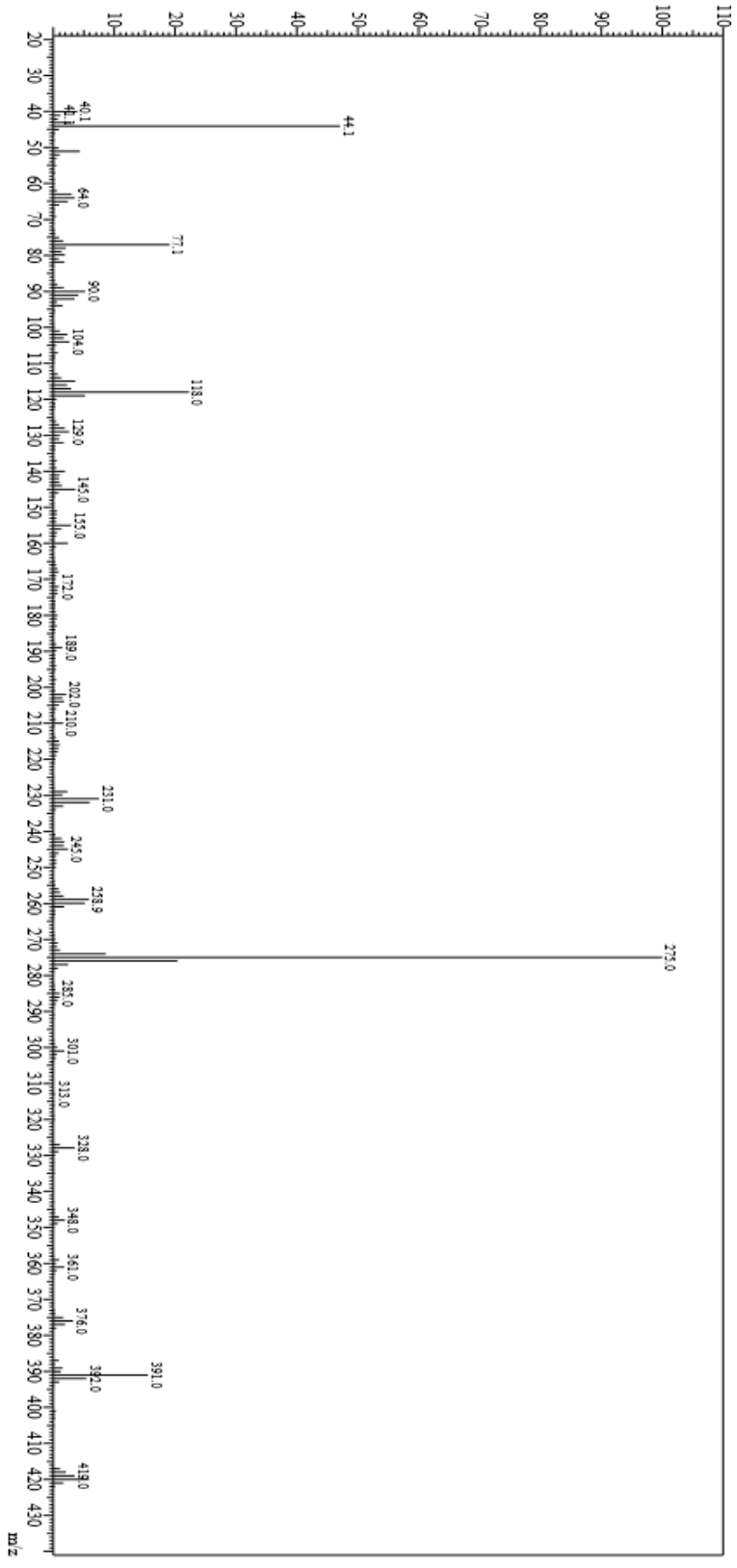

Figure 4. Mass spectrum of [A] SHT-1

SHT-18:4-(benzo[d]thiazol-2-yl)-8,8-dimethyl-2-(pyridin-4-yl)-5-(p-tolyl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-19:4-(benzo[d]thiazol-2-yl)-5-(2-methoxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

SHT-20:4-(benzo[d]thiazol-2-yl)-5-(4-methoxyphenyl)-8,8-dimethyl-2-(pyridin-4-yl)-2,7,8,9-tetrahydro-[1,2,4]triazolo[1,5-a]quinolin-6(1H)-one

2. 2. Preparation of Solutions of compounds

All the synthesized compounds were purified by re crystallization method. The DMF and DMSO were of AR grade supplied by Spectrochem Pvt. Ltd. (Mumbai, India) and were purified according to the standard procedure [45]. The antimicrobial and antifungal activities of all the synthesized compounds were studied in DMF and DMSO by agar well diffusion method.

2. 3. Microorganisms tested

For all the compounds, solution of 20 mg/ml concentration was prepared in DMF and DMSO.

Agar well diffusion method:

In vitro antimicrobial activities of all the triazolo quinoline (SHT series) derivatives were determined by standard agar well diffusion assay [46]. Mueller Hinton agar and Sabouraud dextrose agar media was used for antibacterial and antifungal activity respectively. Molten Mueller Hinton agar/ Sabouraud dextrose agar (40-42 °C) were seeded with 200 µl of inoculum (1×10^8 cfu (colony forming unit) / ml) and poured into Petri dishes. The media were allowed to solidify and wells were prepared in the seeded agar plates with the help of a cup borer (8.5 mm). 100 µl of compound solution in DMSO / DMF was added into the sterile 8.5 mm diameter well. The plates were incubated at 37 °C and 28 °C for 24 and 48 h for bacteria and fungi, respectively. Pure DMSO and DMF solvents were used as a negative control. The antimicrobial activity was assayed by measuring the diameter of the zone of inhibition formed around the well in millimetres. The experiment was done in triplicate and the average values of zone of inhibition were reported.

3. RESULTS AND DISCUSSION

Table1 shows the physical parameters and different substitution groups of the synthesized compounds.

Table 1. Physical constants of pyrazolo chalcone derivatives.

Compound Code	Substitution R	Molecular Formula	Molecular Weight	Yield (%)	R_f * Value
SHT-1	3-OCH_3, 4-OH	$C_{31}H_{25}N_5O_3S$	547.00	80	0.49
SHT-2	2-Cl	$C_{30}H_{22}ClN_5OS$	533.70	89	0.53

SHT-3	3-Br	$C_{30}H_{22}BrN_5OS$	579.07	87	0.51
SHT-4	4-Br	$C_{30}H_{22}BrN_5OS$	579.07	90	0.48
SHT-5	4-F	$C_{31}H_{22}FN_5OS$	519.15	78	0.74
SHT-6	3-Cl	$C_{30}H_{22}ClN_5OS$	535.12	89	0.79
SHT-7	4-Cl	$C_{30}H_{22}ClN_5OS$	535.12	89	0.45
SHT-8	2-OH	$C_{30}H_{23}N_5O_2S$	517.16	78	0.72
SHT-9	3-OH	$C_{30}H_{23}N_5O_2S$	517.16	88	0.73
SHT-10	4-OH	$C_{30}H_{23}N_5O_2S$	517.16	88	0.75
SHT-11	2-NO_2	$C_{30}H_{22}N_6O_3S$	546.15	88	0.94
SHT-12	3-NO_2	$C_{30}H_{22}N_6O_3S$	546.15	89	0.92
SHT-13	4-NO_2	$C_{30}H_{22}N_6O_3S$	548.16	89	0.93
SHT-14	2, 5-di-OCH_3	$C_{32}H_{27}N_5O_3S$	561.18	86	0.82
SHT-15	3, 4-di-OCH_3	$C_{32}H_{27}N_5O_3S$	561.18	86	0.82
SHT-16	3, 4, 5-tri-OCH_3	$C_{33}H_{29}N_5O_4S$	591.19	86	0.81
SHT-17	4-CN	$C_{31}H_{22}N_6OS$	526.16	90	0.89
SHT-18	4-CH_3	$C_{31}H_{25}N_5OS$	515.18	83	0.48
SHT-19	2-OCH_3	$C_{31}H_{25}N_5O_2S$	531.17	84	0.52
SHT-20	4-OCH_3	$C_{31}H_{25}N_5O_2S$	531.17	84.5	0.53

***** 9.8:0.2 $CHCl_3$:CH_3OH

3. 1. Spectral Data

SHT-1: IR(cm^{-1}): 3477.66 (free –OH), 3232.70 (alkene CH-str.), 2929.87 (alkane -CH-bending), 1660.50 (-$CONH_2$), 1514.12 (aromatic -C=C- bending), 1392.61 (alkane –CH-str.), 869.90, 833.25, 675.09 (4-OH, 3-OCH_3); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.382-1.216 (s, 6H, CH_3), 2.657-2.507 (s, 2H, -CH_2), 3.358 (s, 3H,CH_3), 3.587-3.544 (d, 2H, -CH_2, *J*=17.2), 6.601-6.503 (m, 2H, Ar-CH), 6.800-6.729 (s, 1H, Ar-CH), 7.574-7.456 (m, 2H, Ar-CH), 8.726-8.063 (m, 4H, Ar-CH, *J*=20.988), 8.739-8.726 (s, 2H, Ar-CH), 9.021 (s, 1H, -OH); **MS: (m/z)**: 549.18

SHT-2: IR(cm^{-1}): 3238.48 (alkene CH-str.), 2958.80 (alkane -CH-bending), 1662.64 (-$CONH_2$), 1504.48, (aromatic -C=C- bending), 1417.68 (alkane -CH-str.), 770 (2-Cl); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.219 (s, 6H, -CH_3), 2.667-2.508 (s, 2H, CH_2), 3.708-3.656 (dd, 2H, CH_2, *J*=20.8), 7.184-7.171 (d, 2H, Ar-CH, *J*=5.2), 7.291-7.268 (m, 1H, Ar-CH_d), 7.459-

7.441 (d, 1H, Ar-CH, *J*=7.2), 7.530-7.441 (m, 2H, Ar-CH_g), 7.918-7.899 (d, 1H, Ar-CH, *J*=20.988), 8.115-8.094 (m, 3H, Ar-CH), 8.92 (d, 2H, Ar-CH); **MS: (m/z):** 537.14

SHT-3: IR(cm^{-1}): 3250.20 (alkene CH-str.), 2962.66 (alkane -CH-bending), 1662.64 (-$CONH_2$), 1502.55, 1504.48 (aromatic -C=C- bending), 1415.75 (alkane –CH-str.), 754.17, 715 (3-Br); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.219 (s, 6H, -CH_3), 2.667-2.508 (s, 2H, CH_2), 3.708-3.666 (dd, 2H, CH_2, *J*=16.8), 7.184-7.171 (d, 2H, Ar-CH, *J*=20.988), 7.291-7.268 (m, 1H, Ar-CH), 7.459-7.441 (d, 1H, Ar-CH, *J*=20.988), 7.530-7.441 (m, 2H, Ar-CH, *J*=20.988), 7.918-7.899 (d, 1H, Ar-CH), 8.115-8.094 (m, 3H, Ar-CH), 8.92 (d, 2H, Ar-CH, *J*=20.988); **MS: (m/z):** 581.09

SHT-4: IR(cm^{-1}): 3280.20 (alkene CH-str.), 2962.66 (alkane -CH-bending), 1664.57 (-$CONH_2$), 1496.76, 1604.77 (aromatic -C=C- bending), 1408.04 (alkane –CH-str.), 835.18 (4-Br); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.301 (s, 6H, -CH_3), 2.767-2.528 (s, 2H, CH_2), 3.789-3.707 (dd, 2H, CH_2, *J*=32.8), 7.374-7.302 (d, 2H, Ar-CH, *J*=28.8), 7.486-7.463 (d, 2H, Ar-CH, *J*=9.2), 7.665-7.635 (d, 2H, Ar-CH, *J*=12), 7.783-7.701 (m, 2H, Ar-CH), 8.311-8.021 (d, 2H, Ar-CH, *J*=20.988), 8.706-8.687 (d, 2H, Ar-CH, *J*=7.6); **MS: (m/z)**: 581.09

SHT-5: IR(cm^{-1}): 3235.70 (alkene CH-str.), 2958.80 (alkane -CH-bending), 1730.15 (-$CONH_2$), 1597.06, 1504.48 (aromatic -C=C- bending), 1390 (alkane –CH-str.), 844.82 (4-F); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.319 (s, 6H, -CH_3), 2.787-2.608 (s, 2H, CH_2), 3.80**1**-3.661 (dd, 2H, CH_2), 7.384-7.272 (d, 2H, Ar-CH), 7.491-7.413 (d, 2H, Ar-CH, *J*=31.2), 7.702-7.641 (d, 2H, Ar-CH, *J*=24.4), 7.793-7.710 (m, 2H, Ar-CH), 8.***318***-8.223 (d, 2H, Ar-CH, *J*=38), 8.712-8.699 (d, 2H, Ar-CH, *J*=5.2); **MS: (m/z)**: 520.17

SHT-6: IR(cm^{-1}): 3238.48 (alkene CH-str.), 2958.80 (alkane -CH-bending), 1662.64 (-$CONH_2$), 1508.33, 1508.33 (aromatic -C=C- bending), 1413.82 (alkane –CH-str.), 752.64, 715 (3-Cl); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.319 (s, 6H, -CH_3), 2.677-2.518 (s, 2H, CH_2), 3.718-3.578 (dd, 2H, CH_2), 7.187-7.175 (d, 2H, Ar-CH), 7.395-7.378 (m, 1H, Ar-CH), 7.468-7.454 (d, 1H, Ar-CH), 7.543-7.451 (m, 2H, Ar-CH), 7.925-7.903 (d, 1H, Ar-CH), 8.125-8.394 (m, 3H, Ar-CH), 8.943 (d, 2H, Ar-CH); **MS: (m/z)**: 537.14

SHT-7: IR(cm^{-1}): 3150.80 (alkene CH-str.), 2935.80 (alkane -CH-bending), 1668.43 (-$CONH_2$), 1504.48 (Ar -C=C- bending), 1415.75 (alkane –CH-str.), 835.18 (4-Cl); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.312 (s, 6H, -CH_3), 2.781-2.60H 1 (s, 2H, CH_2), 3.789-3.757 (dd, 2H, CH_2, *J*=22.8), 7.377-7.369 (d, 2H, Ar-CH, *J*=19.2), 7.488-7.365 (d, 2H, Ar-CH, *J*=33.2), 7.692-7.656 (d, 2, Ar-CH, *J*=14.4), 7.787-7.707 (m, 2H, Ar-CH), 8.***211***-8.181 (d, 2H, Ar-CH, *J*=12), 8.702-8.691 (d, 2H, Ar-CH, *J*=4); **MS: (m/z)**: 537.14

SHT-8: IR(cm^{-1}): 3550.80 (Ar. free -OH), 3248.48 (alkene CH-str.), 2958.80 (alkane -CH-bending), 1662.64 (-$CONH_2$), 1504.48 (aromatic -C=C- bending), 1417.68 (alkane -CH-str.), 770 (2-Cl); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.214 (s, 6H, -CH_3), 2.665-2.506 (s, 2H, CH_2), 3.705-3.662 (dd, 2H, CH_2, *J*=17.2), 7.180-7.169 (d, 2H, Ar-CH, *J*=4.4), 7.289-7.264 (m, 1H, Ar-CH), 7.457-7.438 (d, 1H, Ar-CH, *J*=7.6), 7.528-7.438 (m, 2H, Ar-CH), 7.912-7.888 (d, 1H, Ar-CH, *J*=9.6), 8.110-8.090 (m, 3H, Ar-CH), 8.891 (d, 2H, Ar-CH) 9.625(s, 1H, -OH); **MS: (m/z)**: 519.62

SHT-9: IR(cm^{-1}): 3570.80 (Ar. free -OH), 3258.48 (alkene CH-str.), 2900 (alkane -CH-bending), 1672.43 (-$CONH_2$), 1520.48 (Ar. -C=C- bending), 1425.68 (alkane -CH-str.), 785, 715 (3-OH); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.201 (s, 6H, -CH_3), 2.657-2.5002 (s, 2H, CH_2),

3.703-3.659 (dd, 2H, CH_2, *J*=17.6), 7.180-7.168 (d, 2H, Ar-CH, *J*=4.8), 7.288-7.263 (m, 1H, Ar-CH), 7.454-7.437 (d, 1H, Ar-CH, *J*=6.8), 7.527-7.433 (m, 2H, Ar-CH), 7.908-7.887 (d, 1H, Ar-CH, *J*=8.4), 8.103-8.091 (m, 3H, Ar-CH), 8.87 (d, 2H, Ar-CH),9.203 (s, 1H, -OH); **MS: (m/z)**: 519.17

SHT-10: IR(cm^{-1}): 3575.80 (Ar. free -OH), 3262.48 (alkene CH-str.), 2905 (alkane -CH-bending), 1682.43 (-$CONH_2$), 1522.48 (Ar. -C=C- bending), 1428.60 (alkane -CH-str.), 850 (4-OH); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.298 (s, 6H, -CH_3), 2.764-2.525 (s, 2H, CH_2), 3.787-3.640 (dd, 2H, CH_2, *J*=20.988), 7.368-7.258 (d, 2H, Ar-CH, *J*=20.988), 7.481-7.360 (d, 2H, Ar-CH, *J*=20.988), 7.661-7.631 (d, 2H, Ar-CH, *J*=20.988), 7.780-7.698 (m, 2H, Ar-CH), 8.***308***-8.215 (d, 2H, Ar-CH, *J*=20.988), 8.687-8.285 (d, 2H, Ar-CH, *J*=20.988),9.403(s, 1H, -OH); **MS: (m/z)**: 519.17

SHT-11: IR(cm^{-1}): 3258.48 (alkene CH-str.), 2960.80 (alkane -CH-bending), 1665.35 (-$CONH_2$), 1512.68, (Ar. -C=C- bending), 1427.15 (alkane -CH-str.), 770 (2-nitro); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.415 (s, 6H, -CH_3), 2.701-2.608 (s, 2H, CH_2), 3.725-3.672 (dd, 2H, CH_2, *J*=21.2), 7.373-7.282 (d, 2H, Ar-CH, *J*=36.4), 7.491-7.378 (m, 1H, Ar-CH), 7.501-7.461 (d, 1H, Ar-CH, *J*=16), 7.540-7.485 (m, 2H, Ar-CH), 8.638-8.632 (d, 1H, Ar-CH, *J*=2.4), 8.706-8.642 (m, 3H, Ar-CH), 8.954 (d, 2H, Ar-CH); **MS: (m/z)**: 548.16

SHT-12: IR(cm^{-1}): 3260.48 (alkene CH-str.), 2962.80 (alkane -CH-bending), 1667.35 (-$CONH_2$), 1514.88, (Ar. -C=C- bending), 1435.18 (alkane -CH-str.), 760 (3-nitro); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.358 (s, 6H, -CH_3), 2.682-2.525 (s, 2H, CH_2), 3.728-3.582 (dd, 2H, CH_2, *J*=20.988), 7.197-7.178 (d, 2H, Ar-CH, *J*=7.6), 7.401-7.408 (m, 1H, Ar-CH), 7.478-7.398 (d, 1H, Ar-CH, *J*=32), 7.553-7.462 (m, 2H, Ar-CH), 7.955-7.915 (d, 1H, Ar-CH), 8.168-8.409 (m, 3H, Ar-CH), 8.956 (d, 2H, Ar-CH); **MS: (m/z)**: 548.16

SHT-13: IR(cm^{-1}): 3300 (alkene CH-str.), 2964.59 (alkane -CH-bending), 1660.71 (-$CONH_2$), 1508.33, (Ar. -C=C- bending), 1415.75 (alkane -CH-str.), 835 (4-nitro); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.412 (s, 6H, -CH_3), 2.887-2.778 (s, 2H, CH_2), 3.878-3.670 (dd, 2H, CH_2, *J*=83.2), 7.454-7.382 (d, 2H, Ar-CH, *J*=28.2), 7.541-7.468 (d, 2H, Ar-CH, *J*=29.2), 7.792-7.685 (d, 2H, Ar-CH, *J*=42.8), 7.828-7.765 (m, 2H, Ar-CH), 8.***618***-8.423 (d, 2H, Ar-CH, *J*=78), 8.942-8.719 (d, 2H, Ar-CH, *J*=89.2); **MS: (m/z)**: 548.16

SHT-14: IR(cm^{-1}): 3250 (alkene CH-str.), 2920 (alkane -CH-bending), 1695.43 (-$CONH_2$), 1606.70 (Ar. -C=C- bending), 1417.68, 1375.25 (alkane -CH-str.), 837.11, 752.24 (o, m-dimethoxy); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.402-1.328 (d, 6H, CH_3), 2.529 (s, 1H, -CH_2), 3.345 (s, 1H, CH_2), 3.652-3.483 (s, 6H, -OCH_3), 3.587 (s, 2H, CH_2), 6.584-6.564 (d, 1H, Ar-CH, *J*=8.0), 7.589-7.478 (d, 2H, Ar-CH, *J*=44.4), 8.735-8.058 (m, 4H, Ar-CH), 8.787-8.748 (m, 2H, Ar-CH), 8.878-8.952 (m, 2H, Ar-CH); **MS: (m/z)**: 563.20

SHT-15: IR(cm^{-1}): 3245 (alkene CH-str.), 2968.48 (alkane -CH-bending), 1660.71 (-$CONH_2$), 1660.71 (Ar. -C=C- bending), 1415.75, 1309.67 (alkane -CH-str.), 839.09, 669.30 (o, m-dimethoxy); **^{1}H NMR (DMSO-d_6) δ(ppm):** 1.399-1.228 (d, 6H, CH_3), 2.505 (s, 1H, -CH_2), 3.339 (s, 1H, CH_2), 3.592-3.543 (s, 6H, -OCH_3), 3.601 (s, 2H, CH_2), 6.575-6.559 (d, 1H, Ar-CH, *J*=6.4), 7.581-7.480 (d, 2H, Ar-CH, *J*=40.4), 8.729-8.041 (m, 4H, Ar-CH), 8.762-8.744 (m, 2H, Ar-CH), 8.868-8.948 (m, 2H, Ar-CH). **MS: (m/z)**: 563.20

SHT-16: IR(cm^{-1}): 3155.54 (alkene CH-str.), 2939.52 (alkane -CH-bending), 1662.64 (-$CONH_2$), 1500.62 (Ar. -C=C- bending), 1411.89, 1309.67 (alkane -CH-str.), 842.89, 756.10

(O,m, p-triOCH$_3$); **^{1}H NMR (DMSO-d$_6$) δ(ppm):** 1.400-1.345 (d, 6H, CH$_3$, *J*=22), 2.527 (s, 1H, -CH$_2$),), 3.342 (s, 1H, CH$_2$), 3.648-3.480 (s, 9H, -OCH$_3$), 3.587 (s, 2H, CH$_2$), 6.552-6.571(s, 1H, Ar-CH), 7.578-7.465 (s, 1H, Ar-CH), 8.728-8.048 (m, 4H, Ar-CH), 8.775-8.740 (m, 2H, Ar-CH), 8.870-8.942 (m, 2H, Ar-CH); **MS: (m/z)**: 593.21

SHT-17: IR(cm^{-1}): 3300 (alkene CH-str.), 2964.59 (alkane -CH-bending), 2231.64 (-C≡N), 1660.71 (-CONH$_2$), 1660.91 (Ar. -C=C- bending), 1415.75 (alkane -CH-str.), 835.18 (4-CN); **^{1}H NMR (DMSO-d$_6$) δ(ppm):** 1.455 (s, 6H, -CH$_3$), 2.897-2.788 (s, 2H, CH$_2$), 3.892-3.678 (dd, 2H, CH$_2$, *J*=85.6), 7.460-7.390 (d, 2H, Ar-CH, *J*=28), 7.550-7.460 (d, 2H, Ar-CH, *J*=36), 7.805-7.778 (d, 2H, Ar-CH, *J*=10.8), 7.858-7.760 (m, 2H, Ar-CH), 8.***630***-8.488 (d, 2H, Ar-CH, *J*=56.8), 8.958-8.905 (d, 2H, Ar-CH, *J*=21.2); **MS: (m/z)**: 528.17

SHT-18: IR(cm^{-1}) :3150 (alkene CH-str.), 2956.87 (alkane -CH-bending), 1697.36 (-CONH$_2$), 1664.97 (Ar. -C=C- bending), 1400.0 (alkane -CH-str.), 837.11 (4-CH$_3$); **^{1}H NMR (DMSO-d$_6$) δ(ppm):** 1.391-1.225 (d, 6H, CH$_3$, *J*=20.988), 2.500 (s, 1H, -CH$_2$),), 3.332 (s, 1H, CH$_2$), 3.582-3.523 (s, 3H, -CH$_3$), 3.586 (s, 2H, CH$_2$), 6.568-6.551 (d, 2H, Ar-CH, *J*=6.8), 7.577-7.483 (d, 2H, Ar-CH, *J*=37.2), 8.725-8.032 (m, 4H, Ar-CH), 8.752-8.741 (m, 2H, Ar-CH), 8.860-8.942 (m, 2H, Ar-CH); **MS: (m/z)**: 517.19

SHT-19: IR(cm^{-1}): 3235.22 (alkene CH-str.), 2952.22 (alkane -CH-bending), 1660.00 (-CONH$_2$), 1500.48, (Ar. -C=C- bending), 1416.50 (alkane -CH-str.), 745.50 (2-OCH$_3$); **^{1}H NMR (DMSO-d$_6$) δ(ppm):** 1.188 (s, 6H, -CH$_3$), 2.642-2.456 (s, 2H, CH$_2$), 3.688-3.658 (dd, 2H, CH$_2$, *J*=12), 7.176-7.162 (d, 2H, Ar-CH, *J*=5.6), 7.281-7.261 (m, 1H, Ar-CH), 7.453-7.430 (d, 1H, Ar-CH, *J*=9.2), 7.526-7.432 (m, 2H, Ar-CH), 7.906-7.880 (d, 1H, Ar-CH, *J*=10.4), 8.106-8.099 (m, 3H, Ar-CH), 8.886 (d, 2H, Ar-CH); **MS: (m/z)**: 533.19

SHT-20: IR(cm^{-1}): 3280.00 (alkene CH-str.), 2962.06 (alkane -CH-bending), 1664.07 (-CONH$_2$), 1495.71, 1604.71 (Ar. -C=C- bending), 1402.04 (alkane –CH-str.), 832.12 (4-Br); **^{1}H NMR (DMSO-d$_6$) δ(ppm):** 1.402-1.335 (d, 6H, CH$_3$, *J*=26.8), 2.508 (s, 1H, -CH$_2$), 3.342 (s, 1H, CH$_2$), 3.589-3.528 (s, 3H, -CH$_3$), 3.597 (s, 2H, CH$_2$), 6.562-6.563 (d, 2H, Ar-CH, *J*=39.2), 7.570-7.478 (d, 2H, Ar-CH, *J*=36.8), 8.705-8.025 (m, 4H, Ar-CH), 8.742-8.730 (m, 2H, Ar-CH), 8.852-8.930 (m, 2H, Ar-CH); **MS: (m/z)**: 533.19

3. 2. Antimicrobial activity:

Figure 5 [A] shows zone of inhibition against Gram positive bacteria in DMSO solution of all compounds. It is observed that against *Bacillus cereus* (BC), only SHT-18 and SHT-19 exhibited inhibition and inhibition of SHT-19 is greater than that of SHT-18. Rest of the compounds had no effect on this bacterial strain. For *Bacillus subtilis* (BS), many compounds such as SHT-3, SHT-4, SHT-5, SHT-6, SHT-8, SHT-9, SHT-12, SHT-13, SHT-14, SHT-15, SHT-19 and SHT-20 showed inhibition. Among these compounds, SHT-15 caused maximum inhibition and SHT-3 had minimum inhibition. Against *Staphylococcus aureus* (SA), compounds SHT-14, SHT-15, SHT-16, SHT-17, SHT-18, SHT-19 and SHT-20 showed inhibition. Rest of the compounds had no effect on this bacterial strain. None of the twenty compounds could inhibit *Corynebacterium rubrum* (CR).

As mentioned above, zone of inhibition depends on solvent, bacterial strain and structure of compounds. All the studied compounds have the same central moiety but different substitution groups. Thus, in a particular solvent, substitution groups affect different strains. Thus, for BC, 2-OCH$_3$ (in SHT-19) is more effective than 4-CH$_3$ (in SHT-19). Other

substitution groups had no effect at all. For BS, 3,4-diOCH_3 (in SHT-15) is more effective whereas 3-Br (in SHT-13) is least effective. Against SA, only few substitution groups such as 2,5-di-OCH_3, 3,4-di-OCH_3, 3,4,5-tri-OCH_3, 4-CN, 4-CH_3, 2-OCH_3, 4-OCH_3 are found to be effective. Other groups had no effect at all. None of the substitution group could inhibit CR.

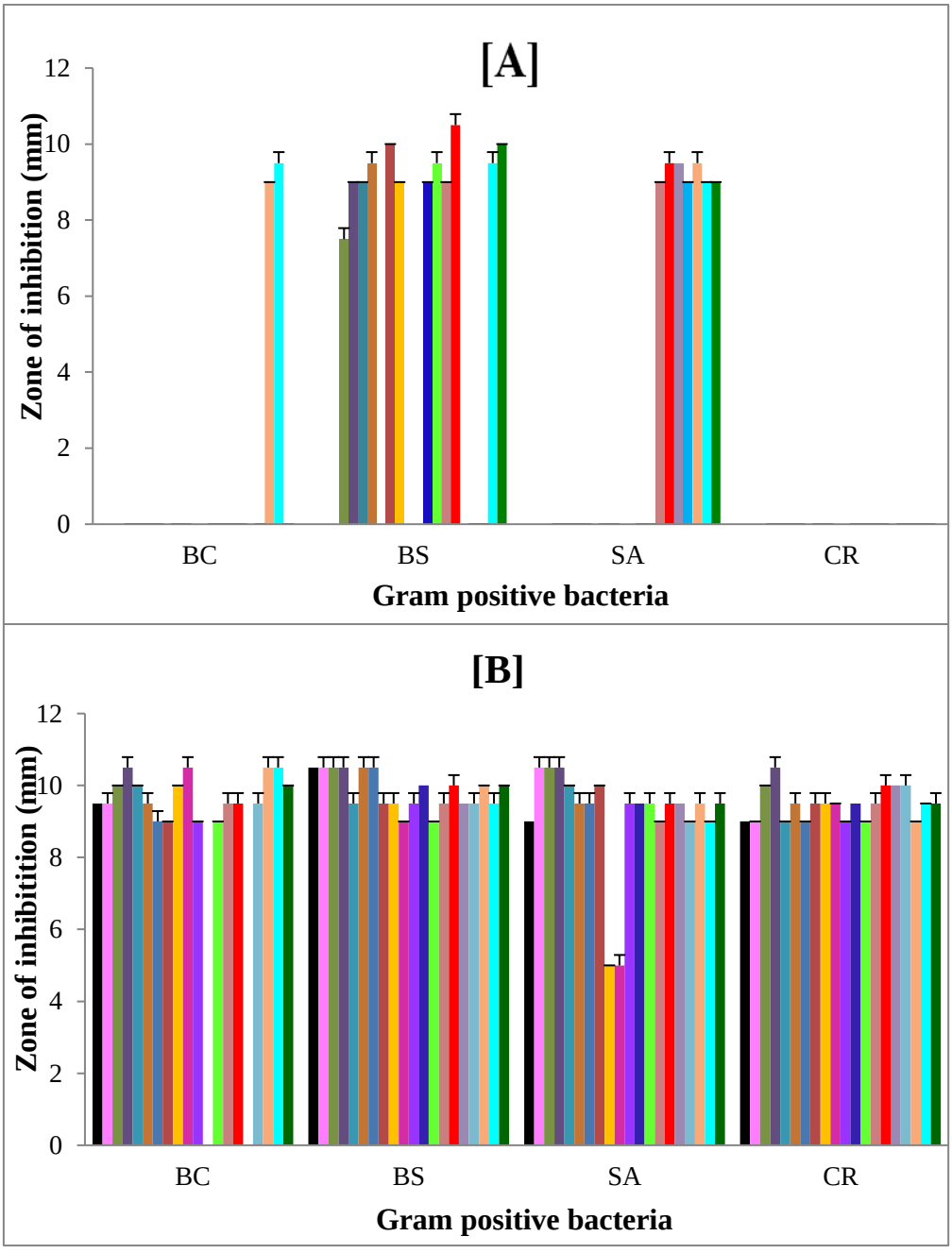

Figure 5. Zone of inhibition of triazoloquinoline derivatives against Gram positive bacteria in [A] DMSO and [B] DMF.

(■): SHT-1; (■): SHT-2; (■): SHT-3; (■): SHT-4; (■): SHT-5; (■): SHT-6; (■): SHT-7; (■): SHT-8; (■): SHT-9; (■): SHT-10; (■): SHT-11; (■): SHT-12; (■): SHT-13; (■): SHT-14; (■): SHT-15; (■): SHT-16; (■): SHT-17; (■): SHT-18; (■): SHT-19; (■): SHT-20

In DMSO, out of the four bacterial strains selected, CR is most resistant bacteria whereas BS is most susceptible bacteria.

Figure 5 [B] shows zone of inhibition for compounds against gram positive bacterial strains in DMF where all the compounds could inhibit these bacteria. For BC, maximum inhibition is observed SHT-4 (containing 4-Br), SHT-10 (containing 4-OH), SHT-18 (containing 4-CH_3) and SHT-19 (containing 2-OCH_3). The compounds SHT-7 (containing 4-Cl), SHT-8 (containing 2-OH) and SHT-9 (containing 3-OH) exhibited minimum inhibition. Other compounds showed intermediate inhibition. For BS, maximum inhibition is observed by SHT-1, SHT-2, SHT-3, SHT-4, SHT-6 and SHT-7. Thus, 3-OCH_3, 4-OH, 2-Cl, 3-Br, 4-Br, 3-Cl and 4-Cl are most effective. SHT-10 containing 4-OH is least effective. For SA, maximum and equal inhibition exhibit by SHT-2, SHT-3 and SHT-4 which contain 2-Cl, 3-Br and 4-Br respectively. SHT-9 and SHT-10 showed minimum inhibition. These compounds contain OH group at 3rd and 4th position respectively. The compound SHT-8 also contains hydroxyl group but at 2nd position but it showed almost double inhibition than those of SHT-9 and SHT-10. This again proves that position of group is also important for inhibition. Against CR, SHT-4 containing 4-Br showed maximum inhibition. Other compounds also exhibited significant inhibition. Overall, all the four selected bacterial strains are susceptible in DMF. So, DMF is good solvent for the selected Gram positive bacteria.

Figure 6 [A] shows zone of inhibition for compounds against gram negative bacterial strains in DMSO. Against EC, SHT-20 which contains 4-OCH_3 showed maximum inhibition. This is followed by SHT-19 containing 2-OCH_3. The compounds SHT-5, SHT-8 and SHT-12 having 4-F, 2-OH and 3-NO_2 respectively could also affect EC. Other compounds had no effect at all. Only SHT-9, SHT-14, SHT-17 and SHT-18 showed inhibition against KP. These compounds contain 3-OH, 2,5-diOCH_3, 4-CN and 4-CH_3 respectively. Out of these four compounds, SHT-17 containing 4-CN had maximum effect. Other compounds had no effect. Against PA, only 3 compounds had inhibition and the order is SHT-12 (containing 3-NO_2) > SHT-13 (containing 4-NO_2) > SHT-14 (containing 2,5-diOCH_3). For ST also only for compounds, SHT-12, SHT-13, SHT-14 and SHT-18 exhibited inhibition and maximum inhibition is for compounds SHT-13 and SHT-14 containing 4-NO_2 and 2,5-diOCH_3 respectively. Among the all strains, EC is more susceptible and PA is resistant bacteria in DMSO.

Figure 6 [B] shows zone of inhibition against gram negative bacteria for SHT series in DMF. Except SHT-5, SHT-18 and SHT-19, all the compounds could affect EC and maximum inhibition was shown by SHT-12 (containing 3-NO_2) and SHT-17 (containing 4-CN). For KP, all the compounds were effective and SHT-3 and SHT-16 containing 3-Br and 3,4,5-triOCH_3 groups respectively had maximum and equal inhibition. The compounds from SHT-1 to SHT-9 and SHT-12 showed inhibition against PA. Other compounds had no effect. SHT-3 and SHT-4 containing 3-Br and 4-Br groups respectively had maximum inhibition. All the compounds could inhibit ST and 4-Br group present in SHT-4 and 3,4,5-triOCH_3 present in SHT-16 exhibited maximum and equal inhibition. Overall, all the four selected bacterial strains are susceptible in DMF.

Comparison of inhibition of compounds in both the solvents shows that in DMF, most of the compounds could inhibit gram negative bacterial strains. So, for the studied compounds, DMF is better solvent for the selected gram negative bacterial strains.

Figure 7 [A] shows the inhibition against some fungal strains for the synthesized compounds in DMSO. CA is not affected by any of the synthesized compounds. For CG, only

six compounds were effective and maximum inhibition was exhibited by SHT-18 containing 4-CH_3 group.

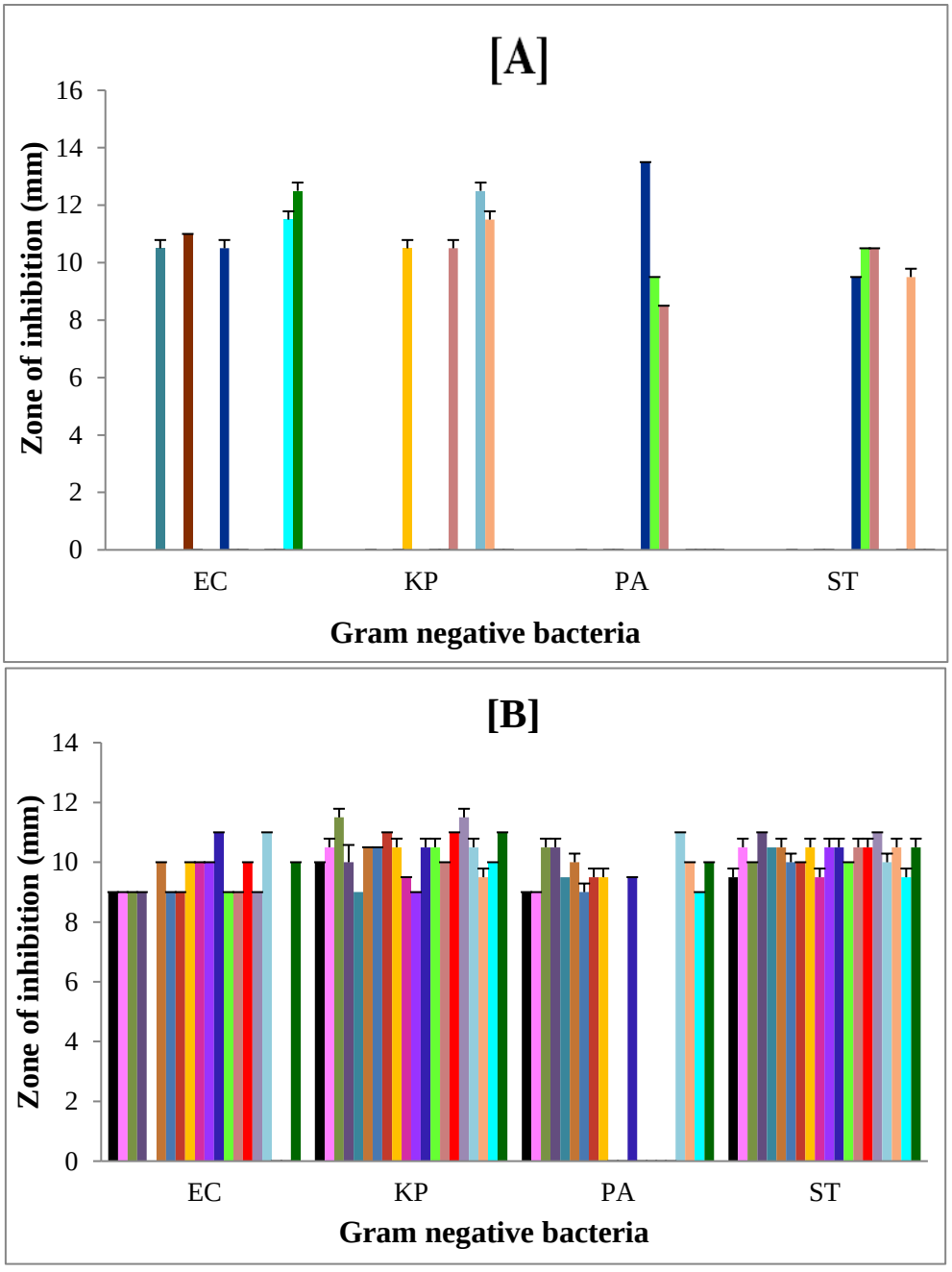

Figure 6. Zone of inhibition of triazoloquinoline derivatives against Gram negative bacteria in [A] DMSO and [B] DMF.

(■): SHT-1; (■): SHT-2; (■): SHT-3; (■): SHT-4; (■): SHT-5; (■): SHT-6; (■): SHT-7; (■): SHT-8; (■): SHT-9; (■): SHT-10; (■): SHT-11; (■): SHT-12; (■): SHT-13; (■): SHT-14; (■): SHT-15; (■): SHT-16; (■): SHT-17; (■): SHT-18; (■): SHT-19; (■): SHT-20

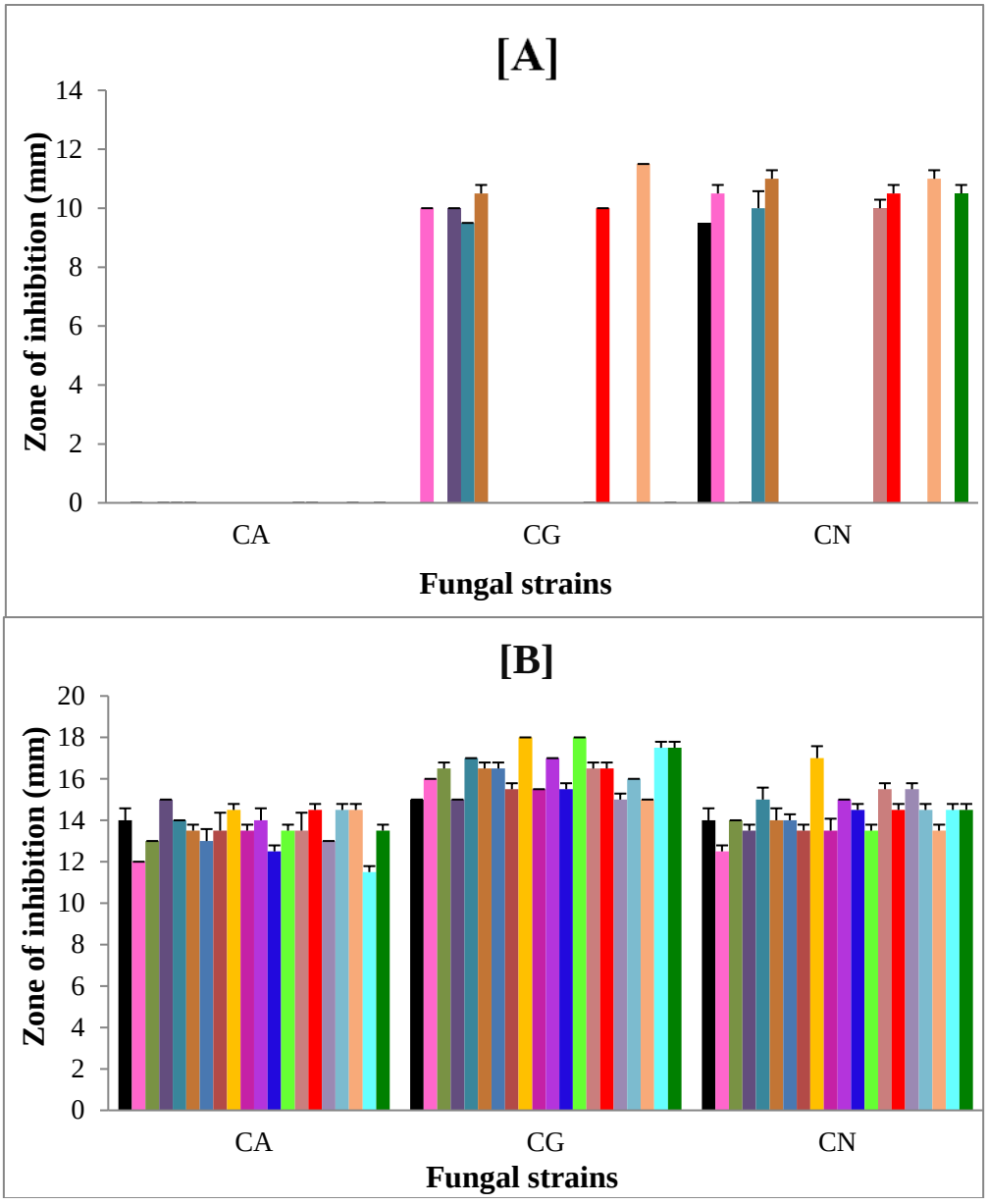

Figure 7: Zone of inhibition of triazoloquinoline derivatives against anti fungai bacteria in [A] DMSO and [B] DMF.

(■): SHT-1; (■): SHT-2; (■): SHT-3; (■): SHT-4; (■): SHT-5; (■): SHT-6; (■): SHT-7; (■): SHT-8; (■): SHT-9; (■): SHT-10; (■): SHT-11; (■): SHT-12; (■): SHT-13; (■): SHT-14; (■): SHT-15; (■): SHT-16; (■): SHT-17; (■): SHT-18; (■): SHT-19; (■): SHT-20

The order of inhibition by other compounds was: SHT-6 > SHT-2 ≈ SHT-4 ≈ SHT-15 > SHT-5 and these compounds have 3-Cl, 2-Cl, 4-Br, 3,4-diOCH_3 and 4-F groups respectively. For CN, SHT-6 and SHT-18 exhibited maximum inhibition which is followed by SHT-20. SHT-1, SHT-2, SHT-5, SHT-14, SHT-15 and SHT-20 also had effect on CN. Remaining

compounds had no effect. Thus, out of these three selected strains, CA is more resistant bacteria and CN is more susceptible bacteria in DMSO.

Figure 7 [B] shows zone of inhibition against fungal strains in DMF. All compounds could inhibit all the three strains i.e., CA, CG and CN. CA was highly affected by SHT-4 which has 4-Br group whereas SHT-19 containing 2-OCH_3 group exhibited minimum inhibition. In CG, SHT-9 and SHT-13 containing 3-OH and 4-NO_2 groups respectively exhibit maximum inhibition. For CN, again SHT-9 containing 3-OH exhibited maximum inhibition.

Comparison of inhibition of compounds between both the solvents shows that in DMF, all the compounds could inhibit selected fungal strains in comparison to DMSO. Thus, DMF is better solvent for the studied compounds.

4. CONCLUSIONS

The present work contains quinolone, benzothiazole, triazolo and pyridine all are active heterocycles. The reaction rout is well designated in such a way that reaction required a minimum time for completion of reaction. The percentage of yield is good with maximum purity. In antimicrobial activity, Comparison of inhibition of compounds between both the solvents shows that in DMF, all the compounds could inhibit selected all three strains in comparison to DMSO. Thus, DMF is better solvent for the studied compounds.

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