Synthesis, Molecular Docking and Pharmacological Investigation of Some 4-Methylphenylsulphamoyl Carboxylic Acid Analogs

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ABSTRACT

Compounds bearing sulphonyl and amino acid moieties are considered the basis for sulfadu drug development. The synthesis of 4-methylphenylsulphamoyl carboxylic acids and the evaluation of their pharmacological activities are reported. The synthesis of these compounds was accomplished by the reaction of various α-amino acids and 4-methyl phenyl sulphonyl chloride in basic aqueous solution. Structures were confirmed by FTIR, 1HNMR, 13CNMR spectra and elemental analytical data. Molecular docking interactions of the analogues were determined using PyRx. In the in vitro antimicrobial activity analysis, compounds 1, 3, 5 and 7 had antimicrobial inhibitory concentration range of 0.5-1.0mg/ml comparable with 0.1-2.0mg/ml of ofloxacin and fluconazole. In the in vitro anti-oxidant activity study compounds 1, 2 and 6 displayed half-maximal inhibitory concentrations (IC50) of 1.104±0.001 μg/ml, 1.159±0.002μg/ml and 1.240±0.001μg/ml respectively comparable with 0.999±0.002μg/ml of ascorbic acid. In the molecular docking study, compound 4 had a strong 2D binding interaction with plasmpsin II amino acid residue and compounds 1, 3, 4, 5, 6 and 7 had in silico antimicrobial, anti-oxidant, antitrypanosomal and antimalarial properties similar to their standard drugs. Considering the outstanding pharmacological properties and their strict compliance with Lipinski’s rule, the synthesized 4-methylphenylsulphamoyl analogues could be considered as antimicrobial, antimalarial, antitrypanosomal and anti-oxidant drug candidates.

INTRODUCTION

The urgent need for the eradication of microbial and oxidative stress-related diseases cannot be ignored; the prevalence and negative effect of these diseases are easily noticed around the world (Jos et al., 2013), (Halliwell, 2007). Oxidative stress and microbial infections are related in their mode of influence on the immune system (Kock et al., 1987). Generally, α-amino acids, when combined with sulphonamides, yield good anti-oxidants and antimicrobials (Egbruor et al., 2019a), (Egbruor and...
Okoro, 2019) they are also known as the most excellent category of pharmacologically active amino acids (Young, 1994). It is expected that the utilization of α-amino acids in this study would achieve improved drug potency. When a compound possessing sulphonyl group is directly bonded to an amino group, sulphonamide formed becomes a central framework for drug structures because of their outstanding stability and considerable tolerance in humans (Rosenthal, 1942), (Shet et al., 2003). The primary sulphonamide groups are often present in various biologically active compounds that are commonly employed as antimicrobial drugs, antithyroid agents, carbonic anhydrase inhibitors and antibiotics (Suparan, 2008), (Remko and von der Lieth, 2004). It is important to note that sulphonamides are generally utilized for the treatment of severe infections of the urinary and intestinal tracts in clinical medicine (Gaded et al., 2003). Sulphonamides are antitumor agents because of their ability to bring about an inhibition of carbonic anhydrase, especially those having aromatic and heteroaromatic structures (El-Sayed et al., 2011), (Garcia-Galan et al., 2008). Additionally, sulphonamides are beneficial pharmaceutical compounds because they possess numerous biological properties. (Egbujor et al., 2019b)

However, the pharmaceutical relevance of sulphonamides has been adversely affected because most of the researches have been confined to the few traditional methods of synthesis and analysis of sulphonamides which have always yielded drugs with drug actions similar to existing ones that have lost efficacy against microbes (Karch, 2011). Moreover, the use of biologically active α-amino acids in sulphonamide synthesis has also been neglected in recent times (Greenfield and Grisanu, 2008), (Fahim and Shalaby, 2019). Biologically, α-amino acids are better than ordinary amines that are conventionally utilized (Nelson and Cox, 2005). The use of amino acids as coupling partners in drug design and synthesis have been found more biologically useful than the use of ordinary amines because of the consideration of their important drug properties and bioavailability (Bandelin and Malesh, 2006), (Remko and von der Lieth, 2004). Consequently, the objective of this study was to synthesize new α-amino acid-based 4-methylbenzenesulphamoyl carboxylic acids and evaluate their antimicrobial and anti-oxidant activities to improve their potency as drug candidates.

MATERIALS AND METHODS

Reagents and Instrumentation

Reagents were supplied by Sigma Aldrich Corporation, United States of America. The melting point ranges of 4-methylphenylsulphamoyl compounds were ascertained using melting point equipment, IA9200 model of Cole-Parmer Ltd, Staffordshire, UK and were uncorrected. FT-IR spectroscopy of the synthesized compounds was determined with Shimadzu 8400s FT-IR of Shimadzu Corporation, Kyoto, Japan. Proton and Carbon Nuclear Magnetic Resonance (NMR), were ascertained with Bruker Avance III 400MHz NMR spectrophotometer of Bruker Corporation, Massachusetts, USA, and results were recorded. Nitrogen gas was utilized for all inert reaction conditions. Compounds were obtained in analytical grade, so chromatographic purification was not needed.

Chemistry

Procedure for 4-methylbenzenesulphamoyl carboxylic acids synthesis

Inside a 100ml beaker, α-amino acid (2.2g, 25mmol) was dissolved in water (30ml) and sodium carbonate (5.58g, 52.50mmol) was added. It was stirred thoroughly and cooled to -5°C and 4-methyl sulphonyl chloride (5.12g, 30mmol) was intermittently added in four parts within 1 hour. This was followed by 4 hours of stirring at normal room temperature. On addition of 2M HCl, crystallization occurred. Reaction steps were monitored strictly using TLC (MeOH/DCM, 1:8). It was kept untouched for at least 12 hours and filtered by suction, and the solid product was washed with tartaric acid (pH2.2) and dried to afford 4-methylbenzenesulphonamoyl carboxylic acids (1-7) as represented in Scheme 1. The title compounds were represented in Scheme 2.

Mechanism of reaction

Amino acids form zwitterions in a basic aqueous medium as a result of hydrogen ion transfer to another end (Levesque et al., 2010). This enables the nucleophilic attack of the amino group that results in the breaking of the S=O bond. It is followed by the formation and elimination of HCl thereby generating...
Table 1: Results of Antimicrobial activities

| Compounds | E. coli | S. typhi | S. aureus | B. subtilis | P. aeruginosa | C. albicans | A. niger |
|-----------|---------|----------|-----------|-------------|---------------|-------------|---------|
| 1         | 0.9     | 0.8      | -         | 0.8         | 0.6           | 0.7         | -       |
| 2         | 0.8     | 0.7      | 0.9       | 0.8         | 0.8           | -           | 0.9     |
| 3         | 0.9     | -        | 0.9       | 0.8         | -             | -           | -       |
| 4         | 0.8     | 0.6      | 0.7       | 0.6         | 0.7           | -           | 1.0     |
| 5         | 0.9     | -        | 0.9       | 0.8         | 0.9           | -           | -       |
| 6         | 0.7     | 0.7      | 0.9       | 0.5         | 0.9           | -           | 0.9     |
| 7         | 0.9     | 0.9      | 0.8       | 0.8         | -             | -           | -       |
| Ofloxacin | 0.05    | 0.01     | 0.01      | 0.020       | 0.025         | -           | -       |
| Fluconazole | -      | -        | -         | -           | 0.020         | 0.005       |         |

Key: - = nosensitivity

*p*-toluene sulphonamide as shown in Scheme 3

Biological studies

Antimicrobial evaluation

Some pathogenic bacteria and fungi were obtained as clinical isolates and standardized with 0.5 McFarland turbid equivalents, and these pathogenic microorganisms were standardized. Ofloxacin and fluconazole were used as antibacterial and antifungal drugs, respectively. Using agar dilution method (Wiegand et al., 2008), the antimicrobial properties of the 4-methylphenylsulphamoyl analogues were investigated using the procedures outlined by CLSI (Sader et al., 2013), (Lamie et al., 2015).

Anti-oxidant Evaluation Procedure

The anti-oxidative properties of 4-
Scheme 3: Mechanism of reaction for 4-methylbenzenesulphonamides synthesis.

Table 2: Antioxidant activities of compounds 1-7

| compounds   | % inhibition at 200µg/ml | % inhibition at 100µg/ml | % inhibition at 50µg/ml | IC50 Values (µg/ml) |
|-------------|--------------------------|--------------------------|--------------------------|---------------------|
| Ascorbic acid | 96.83±0.001              | 97.68±0.001              | 97.31±0.001              | 0.999±0.002         |
| 1           | 95.67±0.002              | 92.39±0.001              | 81.09±0.000             | 1.104±0.001         |
| 2           | 91.64±0.000              | 84.26±0.001              | 80.55±0.001             | 1.159±0.002         |
| 3           | 78.09±0.001              | 77.47±0.001              | 71.86±0.001             | 1.311±0.003         |
| 4           | 94.36±0.001              | 82.30±0.001              | 37.91±0.001             | 1.407±0.001         |
| 5           | 93.54±0.001              | 82.78±0.003              | 72.83±0.003             | 1.201±0.002         |
| 6           | 96.73±0.002              | 73.08±0.001              | 71.79±0.004             | 1.240±0.001         |
| 7           | 87.32±0.001              | 86.33±0.002              | 79.55±0.001             | 1.172±0.002         |

Key: The standard antioxidant drug is ascorbic acid. The results are expressed at ±S.D.
Methylphenylsulphamoylanalogues were evaluated via the DPPH free radical scavenging method using Blois Procedure (Blois, 1958). Then 50 μg/ml, 100 μg/ml and 200 μg/ml of the DPPH solution were obtained, vortexed and kept in the darkroom for 30 minutes at room temperature. The result of absorbance was recorded in triplicate with the help of spectrophotometer at 517 nm against the appropriate blank solution. The percentage scavenging DPPH radical inhibitions were calculated by using the formula given below

\[
\text{DPPH radical scavenging activity (\%) = } \left( \frac{\text{Abs}_{\text{control}} - \text{Abs}_{\text{sample}}}{\text{Abs}_{\text{control}}} \right) \times 100
\]

Where, \(\text{Abs}_{\text{control}}\) was the absorbance of DPPH radical and n-hexane/methanol, \(\text{Abs}_{\text{sample}}\) was the absorbance of DPPH radical and sample/standard. The graph of percentage inhibition determined half-maximal inhibitory concentration (IC\(_{50}\)) was plotted against the concentration of the 4-methylphenylsulphamoylanalogues.

In silico Procedure

Physicochemical properties

The physicochemical parameters were obtained in silico. These are the molecular weight (MW), number of hydrogen bond acceptor (HBA), number of hydrogen bond donor (HBD), number of rotatable bond (NRB), octanol/water partition coefficient logP(o/w), aqueous solubility (SlogP) and topological polar surface area (TPSA). The descriptors calculator in Swiss dock online servers was used in the computation of these parameters. Lipinski’s rule of five was the basis for the drug-likeness evaluation.

Molecular docking Assessments

Microbial infections and oxidative stress were the two disease conditions studied. Drug targets were selected accordingly for molecular assessment. The drug targets for antibacterial: E. coli DNA gyrase in complex with 1-ethyl-3-[8-methyl-5-(2-methyl-pyridine-4-yl)-isoquinolin-3-yl]urea (PDB code: 5MMN); antifungal: urate oxidase from Aspergillus flavus complexed with uracil (PDB code: 1WS3), and antioxidant: human peroxiredoxin 5 (PDB code: 1HD2). From the Protein Data Bank (PDB), database, the 3-Dimensional structures of these drug targets were downloaded. Molecular docking via PyRx the 4-methylphenylsulphamoyl analogues interacted with the receptors accordingly. This protocol enabled flexible docking for several compound conformers, and most excellent conformation was taken for each compound. The observed interactions were visualized in Discovery studio.

RESULTS AND DISCUSSION

Spectra data

2-[(4-methylphenylsulphonyl)amino]propanoic acid (1) yields 3.50g (81.9%), mp 117-119°C.

IR(KBr)cm\(^{-1}\): 3250(N-H), 3060(O-H), 1927(C-H), 1722(C=O of COOH), 1587(C=C aromatic), 1367, 1170(SO\(_2\) twobands),741(Ar-H).

\(^1\)H-NMR(DMSO, 400 MHz): 8.16-8.14(d,J=8.3Hz,IH,NH), 7.79-7.76 (d,J=8.1Hz,2H,Ar-H), 7.48-7.46 (d,J=8.2Hz,2H,CH\(_3\)-CH).

\(^13\)CNMR (CD\(_3\)N, 400MHz): 170.584,(C=O), 148.927, 140.120, 131.603, 128.464, 126.345, 117.346 (aromatic carbons), 60.342, 45.231, 25.905(aliphatic carbons). Anal.calcd. for C\(_{10}\)H\(_{12}\)NO\(_4\)S (243.08): C, 49.48, H, 5.49, N, 5.87, S, 13.26. Found: C,49.45,H,5.51,N,5.80,S,13.31.

1-[(4-methylphenyl)sulphonyl]pyrrolidine-2-carboxylic acid (2) yields 3.25g (96.1%), mp 40-42°C. IR(KBr)cm\(^{-1}\) : 2967(O-H), 2881(C-H), 1724(C=O of COOH), 1636(C=C aro-
Table 3: Physicochemical parameters of 4-methylphenylsulphamoyl analogs (1-7)

| mol | HBA | HBD | NRB | logP(o/w) | SlogP | TPSA | Weight | lip-violation |
|-----|-----|-----|-----|----------|-------|------|--------|--------------|
| 1   | 4   | 3   | 4   | 1.27     | 0.75  | 83.47| 243.28 | 0            |
| 2   | 4   | 2   | 3   | 1.11     | 1.23  | 74.68| 269.32 | 0            |
| 3   | 4   | 3   | 5   | 1.38     | 0.66  | 122.27| 275.35 | 0            |
| 4   | 4   | 3   | 7   | 1.92     | 1.48  | 83.47| 303.40 | 0            |
| 5   | 5   | 4   | 5   | 0.23     | -0.28| 103.70| 259.28 | 0            |
| 6   | 5   | 4   | 5   | 0.69     | 0.11  | 103.70| 273.31 | 0            |
| 7   | 4   | 3   | 6   | 2.68     | 1.77  | 83.47| 285.36 | 0            |

Table 4: Antibacterial, Antifungal and Anti-oxidative Properties of compounds 1-7

| Compounds | Antibacterial (5MMN) | Antifungal (1WS3) | Antioxidant (1HD2) |
|-----------|----------------------|-------------------|-------------------|
| 1         | -10.26               | -11.11            | -12.05            |
| 2         | -9.82                | -10.03            | -12.55            |
| 3         | -10.95               | -10.07            | -12.55            |
| 4         | -10.25               | -10.53            | -14.90            |
| 5         | -10.82               | -10.97            | -12.39            |
| 6         | -14.16               | -10.28            | -13.13            |
| 7         | -13.65               | -11.09            | -13.20            |
| Standard drugs | -19.36        | -10.85            | -14.82            |

Standard drugs for antibacterial=Penicillin; antifungal=Ketoconazole; antioxidant= α-Tocopherol

2-{{4-methylphenyl} sulphonyl}amino}-3-sulphanylpropanoic acid (3) yields

2-{{4-methylphenyl} sulphonyl}amino}-4-(methylthiol) butanoic acid(4) yields

Figure 3: The binding pose of compound 4 in the binding cavity of 1HD2
127.778 (aromatic carbons), 50.669, 47.448, 46.213, 45.036, 36.847 (aliphatic carbons). Anal. calcd. for C_{12}H_{17}NO_2S_2 (303.138): C, 47.52, H, 5.67, N, 4.64, S, 21.08. Found: C, 47.49, H, 5.71, N, 4.60, S, 21.12.

3-hydroxy-2-{{(4-methylphenyl)sulphonamino} propanoic acid (5) yields}

2.85 (72.6%), mp, IR(KBr) cm^{-1}: 3405 (N-H), 3282 (O-H of COOH), 2957 (CH aromatic), 1735 (C=O of COOH), 1589 (C=C aromatic), 1373, 1172 (S=O two bands), 809 (Ar-H). ^1^H-NMR (DMSO, 400 MHz) δ: 7.795 - 7.773 (m, 2H, ArH), 7.699 - 7.520 (m, 2H, ArH), 4.755 (s, IH, OH), 3.5565 - 3.520 (m, IH, CH). Anal. calcd. for C_{14}H_{15}NO_2S_2 (287.096): C, 56.10, H, 7.61, N, 5.03, S, 11.21. Found: C, 56.34, H, 5.40, N, 5.11, S, 11.18.

Antimicrobial activities

Table 1 showed that compounds 2, 4 and 6 inhibited the growth and replication of all the bacteria used while compounds 2, 4 and 6 inhibited the growth of Aspergillus niger. Candida Albicans displayed the highest antifungal resistance although susceptible to only compound 1.

Antioxidant activities

Table 2 showed that compound 6 displayed the highest percentage inhibition of 96.73 ± 0.002 µg/m at the highest concentration (200 µg/ml) while compound 1 displayed the best IC_{50} value of 1.104 ± 0.001 µg/ml. For comparison, ascorbic acid had percentage inhibition of 98.83 ± 0.001 µg/m and an IC_{50} of 0.999 ± 0.002 µg/ml under the same conditions.

Results of Molecular Docking Studies

Table 3 showed that the hydrogen bond acceptor (HBA) ≤ 5, hydrogen bond donor (HBD) ≤ 4, number of rotatable bond (NRB) ≤ 7, octanol/water partition co efficientlogP(o/w) ≤ 2.68, aqueous solubility (Slog P) ≤ 1.77, topological polar surface area (TPSA) ≤ 122.27 and molecular weight (MW) ≤ 303.40. For comparison, the Lpinski’s rule of 5 recommended that LogP ≤ 5, MW ≤ 500, HBA ≤ 10, HBD ≤ 5 for a drug molecule.

The In silico Studies of Antibacterial, Antifungal and Anti-oxidative Properties

Table 4 showed compound 6, 1 and 4 had the highest antibacterial, antifungal and antioxidant binding energies of -14.16, -11.11 and -14.90 kcal/mol respectively.

Table 4 displayed the free binding energy of the compounds assessed. All the 4-methylphenylsulphamoyl analogs had an outstanding binding interaction with the receptors employed in these docking studies. Compounds with the lowest binding energies have the highest binding affinities and vice versa. For clarity, the molecular docking interaction of compound 4 with the receptors was examined as shown in Figures 1, 2 and 3.

Chemistry

4-methylphenylsulphonamoyl carboxylic acids (1-7) were obtained in excellent yields (70.1-96.1%) by the reaction of 4-methylsulphonylchloride and amino acids in a basic solution (Price et al., 1997) at temperature of -5°C.
The general diagnostic peaks of C=O, N-H and C=C bonds were observed in the FT-IR, 1H-NMR, 13C-NMR and elemental analytical data.

**Antimicrobial activities**

The antimicrobial studies (Table 1) revealed that compounds 1-7 have outstanding antimicrobial properties when compared to standard reference drugs. It was discovered that compounds 1, 3, 5 and 7, possess significant antibacterial and antifungal properties similar to ofloxacin and fluconazole. The antifungal resistance of *Candida, Albicans* could be because the amino acid intracellular pools in *candida albican* can reduce the antimicrobial potential of some of these amino acid-based carboxylic acids (Choudary and Rao, 1983). However, many sulphonamide derivatives exhibit good antimicrobial activities (Egbujor et al., 2020a).

**Anti-oxidant activities**

The *in vitro* Anti-oxidative results given in (Table 2) showed that all the 4-methylphenylsulphamoyl analogues had anti-oxidative properties. Compounds 1, 3, and 4 showed impressive anti-oxidant activities. Compound 1 displayed the best IC50 value of 1.104±0.001μg/ml comparable to 0.999±0.001μg/ml of ascorbic acid. Amino acids potentiated the anti-oxidant activities of sulphonamide derivatives (Egbujor et al., 2020b). This suggests that further structural modification of these potent compounds is required to improve their anti-oxidant activities.

**Assessment of the drug-likeness and oral bioavailability**

The physicochemical parameters are given in Table 3 above. Lipinski's rule of five is often required as the assessment reference point in the determination of the drug-likeness of a molecule (Lipinski et al., 2001). According to this rule, a molecule must have a molecular weight value of ≤ 500, hydrogen bond donor ≤ 5, hydrogen bond acceptor ≤ 10, and partition coefficient (Log P) value ≤ 5. When more than one parameter is violated, there could be bio availability problems of the molecule in case of the oral formulation. From Table 3, the 4-methylphenylsulphamoyl analogues synthesized are in perfect agreement with Lipinski’s rule of five and are therefore druggable. Physicochemical parameters have long been used as a reference point for the prediction and estimation of drug pharmacokinetic properties and drug-likeness (Karlgren and Bergstrom, 2015). (Petit et al., 2012). It implies that essential factors such as the absorption, distribution, metabolism, and excretion of drugs in humans could be maximized using the physicochemical properties (Almi et al., 2014). A molecule with TPSA 140 Å2 can permeate the cell. All the compounds synthesized had TPSA < 140 and therefore can permeate the cell membranes while compounds 1, 2, 4 and 7 can permeate the blood-brain barrier having TPSA less than 90 Å2.

**In silico Antibacterial, Antifungal and Antioxidant studies**

**In silico Antibacterial Activities**

Table 4 showed that compound 3 and 6 had a better binding affinity of -10.95 and -11.51Kcal/mol, respectively than penicillin(-10.89 kcal/mol). This implies that compounds 3 and 6 are more potent than penicillin as antibacterial agents.

**In silico Antifungal Activities**

From Table 4, 1WS3 had a higher binding affinity with compounds 1, 5 and 7 of -11.11, -10.97 and -11.09 Kcal/mol respectively which were more excellent than ketoconazole (-10.38 kcal/mol). Compound 1 is the most potent antifungal agent, and this is supported by the *in vitro* antimicrobial analysis in which it was the only compound that could inhibit the growth of *candida albican*.

**In silico Anti-oxidant Activities**

From Table 4, compound 4 was better than α-tocopherol in its interaction with 1HD2. Compound 4 had a binding affinity of -14.90kcal/mol, which is similar to that of the standard drug α-tocopherol(-14.82 kcal/mol). Compound 4 is the most promising and could serve as anti-oxidant agents if further developed. For clarity, the binding poses of compound 4 in the binding cavities of the drug receptors were represented in Figures 1, 2 and 3.

Figures 1 and 2 showed how compound 4 occupied the binding sites of 1SME and its interactions with the amino residues of the receptor. There were distinct H-bond interactions. Firstly, the O-atom of compound 4 formed H-bonds with VAL 78 and SER79 through intermolecular distances of 3.61 and 3.57 Å respectively. Also, SER 218 interacted with another O-atom of 4 to form H-bond (4.37Å). Other forms of interactions include π-sulphur interaction between the π electrons of PHE 111 and S-atom of 4 (6.84 Å); 7 π-alkyl interactions involving ILE 123, ILE 32, VAL 78, PHE 294, ILE 300, ILE 212 and TYR 193. They interacted with the alkyl groups of 4, and their intermolecular distance of interactions are given in Figure 2. Van der Waals interaction was observed between THR 217 and compound 4 (4.04 Å). The π electrons of the 6-membered aromatic ring of 4, through π-anion interaction, interacted with the ASP 214 (5.77Å).
Figure 3 gives the picture of the binding interaction compound 4 with 1HD2. Compound 4 was found to interact with 1HD2 amino acid residues, resulting in the observed anti-oxidative properties in the biological studies. There was H-acceptor interaction between O-17 of 4 and the N GLY 46. The distance of 3.28 Å and energy (-0.5 kcal/mol) of this interaction was recorded. Likewise, O-17 of 4 through H-acceptor interaction, interacted with the NH2 of ARG 127 (3.41Å and -0.6 kcal/mol). The S-18 of 4 formed three H-acceptor bonds with CD1 LEU 116, CD2 LEU 116 and CD1 ILE 119 respectively.

CONCLUSIONS

In this research, a convenient, eco-friendly, and efficient approach to the synthesis of 4-methylphenylsulphonamoyl carboxylic acid analogues (1-7) of medicinal importance has been described. The structures were in agreement with the spectral analysis. In the in vitro antimicrobial activity analysis, compounds 1, 3, 5 and 7 had antimicrobial inhibitory concentration range of 0.5-1.0mg/ml comparable with 0.1-2.0mg/ml of ofloxacin and fluconazole. In the in vitro antioxidant activity study compounds 1, 2 and 6 displayed half-maximal inhibitory concentrations (IC50) of 1.104±0.001 µg/ml, 1.159±0.002 µg/ml and 1.240±0.001 µg/ml respectively comparable with 0.999±0.002 µg/ml of ascorbic acid. It was observed that the 4-methylphenylsulphonamoyl analogues possessed good antibacterial, antifungal and anti-oxidant properties similar to their reference drugs like penicillin, ketocanazole and α-tocopherol respectively. The 4-methylphenylsulphonamoyl analogues were observed to possess antibacterial, antifungal and anti-oxidative properties and therefore could be considered as potential drug candidates.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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