ABSTRACT
Schiff bases, such as nitrofurantoin or nifuroxazide, are commonly applied in medicine as antibacterial agents. They are well known for their biological application as antibacterial, antifungal, antiviral, anti-HIV, anti-protozoal, anti-cancer agents. The present paper describes the synthesis of Schiff’s base 3,4,5-trimethoxy-N-[substituted(Aryl/Hetero-Aryl)methylene]benzenamine derivatives 5a-m from commercially available gallic acid. These derivatives were synthesized by condensation with 3,4,5-trimethoxyaniline using various aromatic and hetero-aromatic aldehydes in presence of ZnO Nano particles at room temperature. Furthermore, the present paper describes the green metrics evaluation data for the synthesized Schiff’s base derivatives (5a-m) and its associated intermediates. In addition to the above, these compounds were screened for their anti-bacterial activity.

KEYWORDS: Schiff’s base, Gallic acid, 3,4,5-Trimethoxy aniline, Synthesis, Green metrics
hybridized orbital of the nitrogen atom of the azomethine group, which makes them chemically and biologically important compounds.\textsuperscript{[6]} They are used as intermediates for the formation of various heterocyclic compounds such as oxazoles, thiazolines, thiazolidones.\textsuperscript{[7,8]} Schiff bases, such as nitrofurantoin or nifuroxazide, are commonly applied in medicine as antibacterial agents.\textsuperscript{[9]} They are well known for their biological application as antibacterial\textsuperscript{[10]}, antifungal, antiviral, anti-HIV\textsuperscript{[11]}, anti-protozoal\textsuperscript{[12]}, anti-cancer agents.\textsuperscript{[13]} A large number of different Schiff base derivatives have been used in the field of materials science like solar shell\textsuperscript{[14]}, optical switching\textsuperscript{[15]}, third order non-linear optics (NLO)\textsuperscript{[16]}, electrochemical sensing\textsuperscript{[17]}, Langmuir films and photo-initiated polymerization\textsuperscript{[18]}, Schiff bases have been used as ligands for the formation of metal complexes such as with Cu(II), Ni(II), Co(II), Pd(II), Pt(II).\textsuperscript{[19]} These complexes are relevant for bioinorganic chemistry, biomedical applications, supramolecular chemistry and catalysis.\textsuperscript{[20-23]}

The major problem in the effective antibacterial treatment is increasing resistance of microorganisms to currently available antimicrobial drugs. Therefore, the development of novel antimicrobial drugs is an active area of research.

Gallic acid has been reported to evoke various biological activities such as antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, anticancer, anti-diabetic etc. Gallic acid (GA) is a phenolic compound. It is chemically known as 3, 4, 5-trihydroxybenzoic acid. The structure of gallic acid has phenolic groups that are a source of readily available hydrogen atoms so that radicals produced can be delocalized over the phenolic structure.\textsuperscript{[24]} The interest in these compounds is due to its pharmacological activity as radical scavengers. It has been proved to have potential preventative and therapeutic effects in many diseases, where the oxidative stress has been involved, including cardiovascular diseases, cancer, neurodegenerative disorders and in aging.\textsuperscript{[25,26]} Due to these activities gallic acid could be considered as a promising lead compound for new drug development.

The concept of green chemistry\textsuperscript{[27]} has become a tool for promoting sustainable development in laboratories and industry. The twelve principles of green chemistry\textsuperscript{[28]} are the basis of guidelines addressed to those who want to follow the green chemistry trend. Most efforts in making chemical processes greener emphasize the need for using safer, less toxic, and more benign solvents, or the elimination of solvents, and reduction in the use of reagents and auxiliaries. Other actions include lowering energy consumption through the use of milder reaction conditions\textsuperscript{[29]}, avoiding derivatization and a preference for substrates based on
renewable sources.\cite{30} One of the challenges in green chemistry is the evaluation of the greenness of chemical processes. Control in green chemistry should be understood as a possibility to select the greenest option. The development and application of measurement procedures allows us to compare the greenness of existing solutions with newly developed ones. Control in green chemistry should be understood as a possibility to select the greenest option. The development and application of measurement procedures allows us to compare the greenness of existing solutions with newly developed ones.

One of the most important tool which can be considered as a fundamental green chemistry metric that forms the basis for all of the other metrics is Atom Economy. This measure was introduced in 1991 by Trost and it is the simplest, fundamental and the most popular parameter used in drug synthesis. Atom Economy calculation (Equation (1)) estimates the amount of reagents (substrates, solvents, catalysts) that will be incorporated into the final desired product.\cite{31,32} One of the tools for measuring the greenness of synthesis is reaction mass efficiency (RME, Equation-2). It is a comprehensive tool in terms of mass balance of a chemical process.\cite{33} Reaction yield, atom economy and stoichiometric factor taking into account the excess of reagents, are included in calculation of RME. Amounts of auxiliary compounds, solvents, catalysts, as well as a recovery of these compounds after reaction are also considered. The results of analysis can be visualized to facilitate the actions to improve the greenness of chemical process.\cite{34}

\[
AE = \frac{\text{Molecular weight of product}}{\text{Sum of all molecular weight of reactants}} \times 100 \quad (1)
\]

\[
RME = \frac{\text{mass of product (g)}}{\text{sum of mass of reactants (g)}} \times 100 \quad (2)
\]

These observations have led to the conception that a series of some novel Schiff bases derived from gallic acid were synthesized using different aromatic and hetero-aromatic aldehydes by condensation with 3,4,5-trimethoxyanline and their structural elucidation were confirmed by IR, \(^1\)H-NMR and Mass spectroscopy. These compounds were screened for their antibacterial activity properties. The results of such studies along with the green metrics calculation for individual steps are discussed in this article.
2.0 MATERIALS AND METHODS
Chemicals and solvents were purchased from Sigma-Aldrich and Merck. All the reagents were of analytical grade. Thin-layer chromatography (TLC) was performed on E. Merck AL silica gel 60 F254 plates and visualized under UV light. IR spectra were recorded as KBr pellets with Perkin-Elmer Spectrum GX FTIR instrument and only diagnostic and/or intense peaks were reported. $^1$H NMR spectra were recorded in DMSO-$d_6$ with Varian Mercury plus 400 MHz instrument. Signals due to the residual protonated solvent ($^1$H NMR) served as the internal standard. All the chemical shifts were reported in $\delta$ (ppm) using TMS as internal standard. The $^1$H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity was indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); the list of coupling constants ($J$) correspond to the order of multiplicity assignment. Mass spectra were recorded with a PE Sciex model API 3000 instrument. All the reactions were carried out under nitrogen atmosphere.

2.1 EXPERIMENTAL
2.1.1 Preparation of 3,4,5-Trimethoxy benzoic acid (2)
A mixture of Gallic acid 1 (1g, 5.88 mmol), dimethyl carbonate (2.86g, 18.78 mmol), Boron trifluoride etherate (2.67 g, 18.81 mmol) in sealed tube (screw cap) was to 120°C for 24h. The temperature of the reaction contents was brought to room temperature and extracted with dichlormethane (30 ml) and washed with water followed by brine solution. The organic layer was dried over sodium sulphate (6.5g), filtered and evaporated under reduced pressure to obtain the crude compound. The crude compound was recrystallized from 50% methanol: water to obtain the pure compound 2. White solid; Yiled: 1.16g (96%).

2.1.2 Preparation of 3,4,5-Trimethoxybenzamide (3)
To a stirred solution of 3,4,5-trimethoxybenzoic acid 2 (1g, 4.71 mmol) in THF (15 mL) and triethylamine (0.71g, 7.01 mmol), cooled to 5°C, was slowly added iso-butylchloroformate (0.77g, 5.64 mmol) followed by Ammonium carbonate (1.58g, 16.44 mmol) in portions. The reaction contents were stirred at room temperature for 14h. After completion of the reaction (checked by T.L.C), the reaction contents were dilulted with water (25 mL) and stirred for 1 h at 5-10°C and the precipitated solid was filtered and recrystallized from water to obtain compound 3. White solid; Yield: 0.97g, 98%; M.p 173-175°C (Lit., 174–176°C). $^{[35,36]}$ $^1$H NMR: $\delta$ 7.06 (s, 2H), 3.92 (s, 6H), 3.91(s, 3H); ESI MS: m/z, 211.0 (M+1)$^+$;
2.1.3 Preparation of 3,4,5-Trimethoxyaniline (4)

To a stirred solution of 12% sodium hypochlorite (0.45g, 3.75 ml, 5.81 mmol) and 2M NaOH (0.3g, 3.75 mL, 7.5 mmol) was added compound 3 (1g, 4.73 mmol) in portions over 30 minutes. The reaction mixture was stirred at 10-15°C for 5h. After completion of the reaction (monitored by TLC), the reaction mixture was then heated to 90°C for 1h under stirring. The reaction contents were cooled to 10°C, and the obtained solids was filtered and dried (1st lot). The filtrate was extracted with dichloromethane (2 X 15 ml), washed with water (2 X 20 mL) followed by brine solution. The organic layer was separated, dried over sodium sulphate (8g), filtered and evaporated under reduce pressure to give the solids (2nd lot). The combined solids were recrystallized from water to obtain compound 4. Off white solid; Yield: 0.71g, 82%; M.p 111-113°C, (Lit., 110–110.5°C).[36] ¹HNMR: δ 5.95(s, 2H), 3.82(s, 6H), 3.77(s, 3H); ESI MS: m/z, 183.0 (M+1)+;

2.1.4 General procedure for the preparation of 5(a-l) using ZnO NPs: To a stirred mixture of compound 4 (0.273 mmol), ZnO Nano Particles (0.02 mmol) in ethanol (5 mL) was added appropriate aromatic aldehyde/Hetero-aromatic aldehyde a-m (0.273 mmol) and stirred at room temperature for 5 min to 120 min. After completion of reaction (checked TLC), the reaction mixture was filtered through a nanofiltration membrane. The filtrate was evaporated under reduced pressure and dried to obtain pure products 5a-m. The analytical data of compounds 5i, 5j, 5k, 5l and 5m is in agreement with the reported literature data.[35,36]

3,4,5-trimethoxy-N-((5-nitrothiophen-3-yl)methylene)benzenamine (5a)

Yellow solid; Yield: 95%; M.p: 94-95°C; IR (KBr): ν max 1620, cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): 8.68 (s, 1H), 8.50 (d, J = 1.5 Hz, 1H), 8.38 (d, J = 1.5 Hz, 1H), 6.65 (s, 2H), 3.82 (s, 6H), 3.67 (s, 3H); ESI MS: m/z, 323.1 (M+1)+;

3,4,5-trimethoxy-N-((5-nitrothiophen-2-yl)methylene)benzenamine (5b)

Yellow solid; Yield: 92%; M.p: 104-105°C; IR (KBr): ν max 1620, cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): 8.94 (s, 1H), 8.19 (d, J = 4.5 Hz, 1H), 7.67 (d, J = 4.2 Hz, 1H), 6.75 (s, 2H), 3.83 (s, 6H), 3.67 (s, 3H); ESI MS: m/z, 323.1 (M+1)+;

3,4,5-trimethoxy-N-((quinoxalin-2-yl)methylene)benzenamine (5c)

Yellow solid; Yield: 96%; M.p: 124-125°C; IR (KBr): ν max 1582, cm⁻¹; ¹H NMR (300 MHz, DMSO-d₆): 9.64 (s, 1H), 8.98 (s, 1H), 8.19 (s, 1H), 7.97 (s, 2H), 6.90 (s, 2H), 3.87 (s, 6H), 3.71 (s, 3H); ESI MS: m/z, 324.1 (M+1)+;
3,4,5-trimethoxy-N-((quinolin-4-yl)methylene)benzenamine (5d)
Pale yellow solid; Yield: 88%; M.p: 88-89°C; IR (KBr): \(\nu_{\text{max}}\) 1585 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): 10.56 (s, 1H), 9.09 (t, J = 7.5 Hz, 2H), 8.13 (t, J = 8.1 Hz, 1H), 8.07 (d, J = 4.5 Hz, 1H), 7.87 (t, J = 6.9 Hz, 1H), 7.77 (t, J = 8.1 Hz, 1H), 6.85 (s, 2H), 3.87 (s, 6H), 3.70 (s, 3H); ESI MS: m/z, 323.3 (M+1)\(^+\);

N-((1H-indol-3-yl)methylene)-3,4,5-trimethoxybenzenamine (5e)
Off-white solid; Yield: 88%; M.p: 114-115°C; IR (KBr): \(\nu_{\text{max}}\) 1620 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): 12.10 (s, 1H), 8.28 (s, 1H), 8.09 (dd, J = 1.5, 8.4 Hz, 1H), 7.51 (dd, J = 1.1, 6.6 Hz, 1H), 7.28-7.18 (m, 2H), 6.55 (s, 2H), 3.82 (s, 6H), 3.76 (s, 3H); ESI MS: m/z, 311.3 (M+1)\(^+\);

3,4,5-trimethoxy-N-((5-phenyl-1H-imidazol-2-yl)methylene)benzenamine (5f)
Pale yellow solid; Yield: 90%; M.p: 94-95°C; IR (KBr): \(\nu_{\text{max}}\) 1582 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): 8.72 (s, 1H), 8.41 (s, 1H), 8.05 (d, J = 8.5 Hz, 2H), 7.86 (t, J = 5.4 Hz, 3H), 7.15 (s, 1H), 6.67 (s, 2H), 3.83 (s, 6H), 3.67 (s, 3H); ESI MS: m/z, 338.1 (M+1)\(^+\);

N-(4-ethoxy-3-methoxybenzylidene)-3,4,5-trimethoxybenzenamine (5g)
White solid; Yield: 88%; M.p: 128-129°C; IR (KBr): \(\nu_{\text{max}}\) 1578 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): 8.54 (s, 1H), 7.53 (d, J = 1.8 Hz, 2H), 7.41 (dd, J = 1.8, 8.1 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 6.59 (s, 2H), 4.09 (q, J = 6.9 Hz, 2H), 3.84 (s, 6H), 3.82 (s, 3H), 3.66 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H); ESI MS: m/z, 346.1 (M+1)\(^+\);

N-(3-methoxy-4-propoxybenzylidene)-3,4,5-trimethoxybenzenamine (5h)
Off-white solid; Yield: 90%; M.p: 118-119 °C; IR (KBr): \(\nu_{\text{max}}\) 1577 cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): 8.54 (s, 1H), 7.53 (d, J = 1.8 Hz, 2H), 7.42 (t, J = 1.8 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 6.59 (s, 2H), 3.99 (q, J = 6.6 Hz, 2H), 3.84 (s, 6H), 3.82 (s, 3H), 3.66 (s, 3H), 1.75 (q, J = 6.9 Hz, 2H), 1.02 (t, J = 7.5 Hz, 3H); ESI MS: m/z, 360.1 (M+1)\(^+\);

(4-Methoxybenzylidene)-(3,4,5-trimethoxyphenyl)amine (5i)
White solid; Yield: 88%; M.p: 59-60°C; IR (KBr): \(\nu_{\text{max}}\) 1624 (-C=N) cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d\(_6\)): \(\delta\) 3.88 (s, 3H), 3.90 (s, 6H), 3.92 (s, 3H), 6.51 (s, 2H), 7.32-7.52 (m, 4H), 8.46 (s, 1H); ESI MS: m/z, 302.1 (M+1)\(^+\);
(4-Nitrobenzylidene)-(3,4,5-trimethoxyphenyl)amine (5j)
Yellow solid; Yield: 82%; M.p: 158°C; IR (KBr): \( \nu_{\text{max}} \) 1587 (-C=N) cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d6): \( \delta \) 3.90 (s, 3H), 3.94 (s, 6H), 6.57 (s, 2H), 8.09 (d, \( J=8.0 \) Hz, 2H), 8.34 (d, \( J = 8.0 \) Hz, 2H), 8.59 (s, 1H). ESI MS: m/z, 317.1 (M+1)+;

4-[(3,4,5-Trimethoxyphenylimino)methyl]benzonitrile (5k)
Pale yellow solid; Yield: 92%; M.p: 134 °C; IR (KBr): \( \nu_{\text{max}} \) 1580 (-C=N), 2223 (C≡N) cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d6): \( \delta \) 3.88 (s, 3H), 3.92 (s, 6H), 6.55-8.02 (m, 6H), 8.53 (s, 1H); ESI MS: m/z, 297.3 (M+1)+;

(4-Bromobenzylidene)-3,4,5-trimethoxyphenylamine (5l)
Pale yellow solid; yield 70%; M.p: 110-112°C; IR (KBr): \( \nu_{\text{max}} \) 1624 (-C=N) cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d6): \( \delta \) 3.89 (s, 3H), 3.92 (s, 6H), 6.51 (s, 2H), 7.63 (d, \( J = 8.5 \) Hz, 2H), 7.79 (d, \( J = 8.5 \) Hz, 2H), 8.45 (s, 1H); ESI MS: m/z, 351.3 (M+1)+;

(4-Methylsulfanylbenzylidene)-(3,4,5-trimethoxyphenyl)amine (5m)
Yellow solid; Yield: 88%; M.p: 96-97°C; IR (KBr): \( \nu_{\text{max}} \) 1628 (-C=N) cm\(^{-1}\); \(^1\)H NMR (300 MHz, DMSO-d6): \( \delta \) 2.52 (s, 3H), 3.87 (s, 3H), 3.89 (s, 6H), 6.48-7.80 (m, 6H), 8.41 (s, 1H); ESI MS: m/z, 350.1 (M+1)+;

2.2 ANTIBACTERIAL BIOASSAY
The antibacterial activity of all the synthesized compounds (5a-m) were examined against different Gram-positive (Staphylococcus pyogens and Staphylococcus aureus) and Gram-negative (Escherichia coli and Pseudomonas aeruginosa) organisms by measuring zone of inhibition. The antibacterial activity was performed by Agar diffusion method at the concentration level of 5 \( \mu \)g/mL. Norfloxacin was used as standard drug at a concentration of 5 \( \mu \)g/mL. Nutrient agar was used as culture media and DMSO was used as solvent control.\[^{37-40}\] The results of the antibacterial activity are shown in Table 2.

3.0 RESULTS AND DISCUSSION
3.1 Chemistry
The synthesis of (\( E \))-N-substituted-3,4,5-trimethoxybenzamine Derivatives 5a-m is illustrated in Scheme-1. Methylation of Gallic acid was carried out using dimethyl carbonate in presence of borontrifluoride etherate in sealed tube at 120°C for 24h to afford 3,4,5-Trimethoxy benzoic acid 2. Reaction of acid 2 with iso-butyl chloroformate followed by
ammonium carbonate in presence of triethylamine at room temperature for 14h gave 3,4,5-
trimethoxybenzamide 3. Conversion of benzamide 3 to 3,4,5-trimethoxy aniline 4 was carried
out in presence of 12% NaOCl and 2M NaOH at 10-15°C for 5h and then later heating to
90°C for 1h resulted in the formation of 3,4,5-trimethoxy aniline 4. Condensation of 3,4,5-
Trimethoxyaniline 4 with aromatic aldehyde/Hetero-aromatic aldehyde a-m in presence of
ZnO Nano particles at room temperature resulted in the formation of N-substituted-3,4,5-
trimethoxybenzenamine derivatives 5a-m (Schiff bases).

The structural assignment of the newly synthesized Schiff base derivatives 5a-m was
determined by the spectroscopic techniques like 1H NMR, IR and mass spectral data. The
mass and IR spectral data of all the compounds are in agreement with the desired molecular
formulae. As an example, the 1H NMR interpretation of (E)-3,4,5-trimethoxy-N-((5-
nitrothiophen-3-yl)methylene)benzenamine 5a, is described here, the protons resonating at
8.68 ppm as a singlet with one proton integration corresponds to the imine group (-CH=N-),
while protons resonating at 8.50 ppm and 8.38 as doublets with two proton integration
corresponds to the thiophene ring. The characteristic protons resonating at 6.65 ppm (2H),
3.82 ppm (6H) and 3.67 pm (3H) as singlets is assigned to the 3,4,5-trimethoxy phenyl.

![Scheme 1: Synthesis of Schiff's base Derivatives from Gallic acid.](image)

**Experimental conditions**

(a) Dimethyl carbonate, Boron trifluoride etherate, 120°C, 24h; (b) iso-Butylchloroformate,
Triethylamine, Ammonium carbonate, room temperature, 14h; (c) 12% NaOCl, 2M NaOH, 10-15°C, 5h, 90°C, 1h; (d) ZnO (NP), Ethanol, room temperature, 13 h;
The green metrics evaluation data for the synthesized intermediate compounds and final compounds 5a-m is presented in Table 1. From table-1, it is observed that, there is a major variation in the AE for the compounds 2, 3 and 4, this variation is attributed to the various byproducts that are formed during the synthesis of compounds 2, 3 and 4. While in the case of final compounds 5a-m, AE is less than 100% owing to the formation of water as a by-product. In addition, since the product is formed in only one step, this synthesis is efficient in maintaining the reagent atoms in the product. There is a small variation in the AE for different products because the byproduct formed was water in all cases studied (Table 1).

RME calculation, offers a more practical evaluation of the synthetic procedures, it takes into account the yield of reaction and molar excess of the reactants / reagents requisite for the total conversion of the product. From the results in Table-1, the RME percentage of final compounds of 5a-m, varied between, 82.5% to 96.4%. In case of step 1 to step 3, the RME percentage is much lower i.e, 17.7, 23.8 and 40.5. This variation in RME is attributed to the factors such as number of reactants involved in the reaction, usage of excess molar equivalents of reactants and poor yields of the products.

Table 1: Green metrics evaluation data for the synthesized Schiff’s base derivatives 5a-m.

<table>
<thead>
<tr>
<th>Compound No</th>
<th>Reaction time</th>
<th>Product Yield (%)</th>
<th>AE (%)</th>
<th>RME (%)</th>
</tr>
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<td>96</td>
<td>19.0</td>
<td>17.7</td>
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<td>49.6</td>
<td>40.5</td>
</tr>
<tr>
<td>5a</td>
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<td>98</td>
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<td>92.4</td>
</tr>
<tr>
<td>5b</td>
<td>5 min</td>
<td>97</td>
<td>94.4</td>
<td>92.4</td>
</tr>
<tr>
<td>5c</td>
<td>5 min</td>
<td>98</td>
<td>94.4</td>
<td>92.3</td>
</tr>
<tr>
<td>5d</td>
<td>10 min</td>
<td>92</td>
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<td>25 min</td>
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<td>5m</td>
<td>20 min</td>
<td>95</td>
<td>95.3</td>
<td>87.3</td>
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</table>
3.3 ANTIBACTERIAL ACTIVITY

The results of the antibacterial activity data of Schiff’s base derivatives 5a-m (Table 2) were compared with reference to the standard drug Norfloxacin for bacterial study against the bacterial pathogens viz., *Staphylococcus pyogens, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* respectively. From table 2, it is observed that in case of *E.coli* and *P.aeruginosa*: compounds 5c, 5d, 5e and 5f exhibited good antibacterial activity with zone of inhibition 15-21 mm while the compounds 5a, 5b, 5g, 5h, 5i and 5m showed moderate antibacterial activity with zone of inhibition 12-16 mm and the remaining compounds in series viz., 5j, 5k and 5l showed no anti-bacterial activity. Even in the case of *S.pyogens* and *S.aureus* these compounds responded in a similar manner. In general it is observed that Schiff’s base derivatives embedded with nitrogen heterocyclic ring (5c, 5d, 5e and 5f) was found to exhibit good anti-bacterial activity except compounds 5a and 5b while the schiff’s base (5g, 5h and 5i) embedded with substituted aromatic ring displayed moderate anti-bacterial activity.

Table 2: Results of Antibacterial and Antifungal activity of Compounds 5a-m.

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Gram negative bacteria</th>
<th>Gram positive bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><em>E. coli</em></td>
</tr>
<tr>
<td>5a</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>5b</td>
<td>14</td>
<td>13</td>
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<tr>
<td>5c</td>
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<td>13</td>
<td>14</td>
</tr>
<tr>
<td>5i</td>
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</tr>
<tr>
<td>5j</td>
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</tr>
<tr>
<td>5k</td>
<td>--</td>
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<td>5l</td>
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<td>5m</td>
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*Norfloxacin* 22, 18, 18, 19

* Concentration of Norfloxacin: 5 μg/mL; “--” NO ACTIVITY

4. CONCLUSION

Condensation of 3,4,5-Trimethoxyaniline 4 with aromatic aldehyde/Hetero-aromatic aldehyde a-m in presence of ZnO Nano particles resulted in the formation of the desired Schiff’s base derivatives 5a-m. The green metrics parameters such as AE and RME were
evaluated for these derivatives and also its associated intermediates. There is a major variation in the AE for the compounds 2, 3 and 4, this variation is attributed to the various byproducts that are formed during the synthesis of compounds 2, 3 and 4. While in the case of Schiff’s base derivatives 5a-m, AE is less than 100% owing to the formation of water as a by-product. The RME percentage of final compounds of 5a-m, varied between, 82.5% to 96.4%. In case of compounds 2,3 and 4 (step 1 to step 3) the RME percentage is much lower i.e, 17.7, 23.8 and 40.5. This variation in RME is attributed to the factors such as number of reactants involved in the reaction, usage of excess molar equivalents of reactants and poor yields of the products. The anti-bacterial activity results revealed that, in general it is observed that Schiff’s base derivatives embedded with nitrogen heterocyclic ring (5c, 5d, 5e and 5f) was found to exhibit good anti-bacterial activity except compounds 5a and 5b while the schiff’s base (5g, 5h and 5i) embedded with substituted aromatic ring displayed moderate anti-bacterial activity.

5. ACKNOWLEDGEMENT

One of the authors (BK), thanks the Director, Green Evolution Laboratories for helpful suggestions.

6.0 CONFLICT OF INTEREST

“The author(s) declare(s) that there is no conflict of interest regarding publication of this article”.

7.0 REFERENCE


