Part - A

(Part - 1)

Studies on Imidazolone Derivatives
INTRODUCTION

Imidazolinone, a five membered heterocycle having 2-nitrogen atoms at the 1 and 3-positions and C=O group at following positions: 2-oxo-imidazoline (I), 4-oxo-imidazoline (II), 5-oxo-imidazoline (III). Imidazolines are structurally related to guanidines and amidines.

Imidazolinone has been used extensively as a corrosion inhibitor of certain transition metals, such as copper. Preventing copper corrosion is important, especially in aqueous systems, where the conductivity of the copper decreases due to corrosion.

The discovery of the 2-substituted-5-imidazolines dates back to the year 1888, when A. W. Hoffmann for the first time discovered 5-oxo-imidazoline by heating N\textsuperscript{1} diacetyl ethylene diamine in a stream of dry hydrogen chloride and moreover the same compound was prepared by A. Ladenburg by the fusion of two equivalents of sodium acetate with one equivalent of ethylene diaminedihydrochloride.

SYNTHETIC ASPECT

Various methods have been reported for the synthesis of imidazolinones in literature. Aminolysis of oxazolone with amines led to the formation of imidazolinones which has been reported in literature.

1. Saxena et al. have synthesized new imidazolinone derivatives (IV) by the reaction of hydrazide with azalactone in dry pyridine.
2. X. Huang et al. ⁶ have synthesized some new imidazolinone derivatives (V) by the reaction of halide with acetonitrile in presence of K₂CO₃.

3. V. Patel et al. ⁷ have synthesized new imidazolinone derivatives by conventional method.

4. Z. Han et al. ⁸ have synthesized 5-imidazolinone derivatives with 2-bromo-acetic acid as a starting material.

5. V. Topuzyan et al. ⁹ have synthesized new imidazolone derivative (VI) by the reaction of corresponding amides with HMDS.

6. J. Benensek et al. ¹⁰ have synthesized simple one-pot imidazolone derivative.
Azalactone reacts with variety of compounds such as water, alcohols, amines and hydrogen halides. Amides of α-acylamino acrylic acids obtained from the condensation of azalactone and primary amine can be converted to imidazolinone as shown under.

The ring closer can be affected under a variety of conditions. Substituted anilides have been converted to imidazolinone derivatives by the action of POCl₃.
Naphazoline hydrochloride, xylometazoline hydrochloride etc. are various imidazolinone derivatives which have been used as adrenergic stimulants and tolazoline and phentolamine as adrenergic blocking agents. Various imidazolinones are known to exhibit a broad spectrum of biological activities such as:

1. Antitubercular\textsuperscript{11}
2. Antitumor\textsuperscript{12}
3. Insecticidal\textsuperscript{13}
4. Antiviral\textsuperscript{14}
5. Hypertensive\textsuperscript{15}
6. Antiinflammatory\textsuperscript{16}
7. Glucagon antagonists\textsuperscript{17}
8. Antimicrobial\textsuperscript{18}
9. Antihistaminic\textsuperscript{19}
10. Antidiabetic\textsuperscript{20}

P. Sah and coworkers\textsuperscript{21} have prepared some new imidazolinones and reported their antimicrobial and antileishmanial activities. K. M. Khan et al.\textsuperscript{22} have reported antibacterial and fungicidal activity of 5-oxo-imidazolines. Herbicidal activity of imidazolinone derivatives have been reported by Wang Ying et al.\textsuperscript{23} Y. Zhou et al.\textsuperscript{24} and A. Paiet al.\textsuperscript{25} have reported anticancer active analogues of 5-oxo-imidazolines. Imidazolinone derivatives which possess antifungal activity have been reported by M. D. Shah et al.\textsuperscript{26} Some new 5-oxoimidazolines as antimicrobial agents have been investigated P. S. Patel et al.\textsuperscript{27} V. Leroy and coworkers\textsuperscript{28} have prepared substituted imidazolone derivatives and reported their pharmaceutical use as inhibitors of protein kinases and antiproliferative agents. N. Xue et al.\textsuperscript{29} have synthesized and evaluated imidazol-2-one derivatives (VII) as potential antitumor agents.

M. K. Wong at al.\textsuperscript{30} have synthesized spiro - imidazolone (VIII) use for treatment and prevention of type - 2 diabetics and related conditions.
Literature survey reveals that the compounds bearing imidazolones moiety possess potential drug activity. Looking to the diversified biological activities we have synthesized some imidazolinone derivatives in order to achieving better therapeutic agents. These studies are described in following section.

SECTION-I: SYNTHESIS AND BIOLOGICAL EVALUATION OF (Z)-N-(4-(ARYL)-5-OXA-2-PHENYL-4,5-DIHYDRO-1H-IMIDAZOL-1-YL)-2-(3-(TRIFLUOROMETHYL)PHENYLAMINO) BENZAMIDES
Synthesis and biological evaluation of (Z)-N-(4-(Aryl)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino) benzamides
SECTION-I

SYNTHESIS AND BIOLOGICAL EVALUATION OF (Z)-N-(4-(ARYL)-5-OXA-2-PHENYL-4,5-DIHYDRO-1H-IMIDAZOL-1-YL)-2-(3-(TRIFLUOROMETHYL)PHENYLAMINO)BENZAMIDES

Various imidazolinone have resulted in many potential drugs and are known to possess a broad biological spectrum. In view of getting better therapeutic agents and considering the association of various biological activities with 2-(3-(trifluoromethyl)phenylamino)benzohydrazide nucleus, the preparation of imidazolone have been undertaken by the condensation of 2-(3-(trifluoromethyl)phenylamino)benzohydrazide with substituted azalactones by well known Ertenmeyer azalactone synthesis.

REACTION SCHEME

The constitution of all the synthesized compounds have been characterized by using elemental analysis, FT-IR, $^1$H NMR, $^{13}$C NMR spectroscopy and further supported by mass spectroscopy. Purity of all the compounds has been checked on thin layer chromatographic plate and HPLC technique.

All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and three fungal strains. The biological activities of the synthesized compounds have been compared with standard drugs.
EXPERIMENTAL SECTION

Melting points were determined in open capillary tubes and are uncorrected. Formation of the compounds was checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine and UV-245nm light. IR spectra were recorded on Bruker FT-IR instrument using KBr method. Mass spectra were recorded on Applied Biosystems API 2000 model using direct inlet probe technique. $^1$H NMR and $^{13}$C NMR were determined in DMSO-d$_6$ solution on Bruker 400 MHz spectrometer. Purity of the synthesized compounds was checked by Waters ACQUITY UPLC H-CLASS. Elemental analysis of the all the synthesized compounds were carried out on Euro EA 3000 elemental analyzer and the results are in agreements with the structures assigned.

[A] Synthesis of Methyl 2-(3-(trifluoromethyl)phenylamino)benzoate

2-(3-(trifluoromethyl)phenylamino)benzoic acid (2.81 gm, 0.01 mol) in methanol (10 mL) was stirred at room temperature for 5 minutes then added concentrated H$_2$SO$_4$ (0.5 mL, 0.01 mol) and stirred the reaction mixture at room temperature for 10 hours. The completion of the reaction was checked by TLC. Methanol removed in vacuo and then added dichloromethane (40 mL) and stirred it further for 10 minutes. The resulting solution was treated with saturated NaHCO$_3$ until pH become neutral. The neutral solution was treated with Na$_2$SO$_4$ and then organic layer was removed in vacuo. The crude product was collected.

[B] Synthesis of 2-(3-(Trifluoromethyl)phenylamino)benzohydrazide.$^{31}$

Methyl 2-(3-(trifluoromethyl)phenylamino)benzoate (2.95 gm, 0.01 mol) in absolute ethanol (25 mL) was refluxed with hydrazine hydrate (1.0 mL) for 2 hours. The completion of the reaction was checked by TLC and the reaction mixture was cooled to room temperature. The separated solid was filtered, washed with cold ethanol and crystallized from ethanol. Yield 98%, m.p 136-138°C.

[C] Synthesis of 4-Arylidene-2-phenyl-5-oxazolinones.$^{32}$

These were prepared by the condensation of substituted benzaldehyde with benzoyl glyline in presence of sodium acetate and acetic anhydride as described by Vogel.
General procedure for the preparation of \((Z)-N-(4-(Aryl)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamides\)

To a mixture of 2-(3-(trifluoromethyl)phenylamino)benzohydrazide (2.95 gm, 0.01 mol) and different 4-arylidene-2-phenyl-5-oxazolinones (0.01 mol) in a pyridine (15 mL) was refluxed for 8-10 hours (monitoring by TLC). The excess of solvent was removed under reduced pressure and reaction mixture was poured on to crushed ice. The product was isolated and the resulting crude product was purified by column chromatography to give the pure product. The physical constants of the products are recorded in Table-1a.
Table-1a: Physical constant of (Z)-N-(4-(Aryl)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamides

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<th>Sr. No.</th>
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<th>M. F.</th>
<th>M. W.</th>
<th>Yield (%)</th>
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<td>556.53</td>
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<td>- HO</td>
<td>C30H20ClF3N4O2</td>
<td>542.50</td>
<td>68</td>
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</table>

TLC solvent system: - Ethyl acetate: Hexane = 3: 7
ANALYTICAL DATA

(Z)-N-(4-(4-hydroxy-3-methoxybenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (Ia). mp 125-127°C; Purity by UPLC: 98.48%; IR (KBr) : 3323(N-H str), 2923(C-H str), 1714(C=O, imidazole ring, str), 1639(C=O, amide, str), 1587(C=N str), 1514(Ar, C=C str), 1333(CF3, C-F str), 1262(C-H bending), 1071(C-N str) cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ ppm 3.85(s, 3H, OCH₃), 6.89-6.91 (d, J=8.4 Hz, 1H, CH), 7.03-7.05 (t, J=7.2 Hz, 1H, ArH), 7.23 (s, 1H, ArH), 7.25-7.27 (d, J=7.2 Hz, 1H, ArH), 7.34-7.36 (d, J=8.4 Hz, 1H, ArH), 7.40 (s, 2H, ArH), 7.45-7.51(m, 5H, ArH), 7.67-7.89 (d, J=8.0 Hz, 1H, ArH), 7.82-7.84(d, J=7.2 Hz, 1H, ArH) 8.01-8.03(d, J=7.2 Hz, 2H, ArH), 8.17(s, 1H, ArH), 9.21(s, 1H, NH), 10.02(s, 1H, OH), 11.68(s, 1H, NH); ¹³C NMR (100 MHz, DMSO-d₆): δ ppm 55.96, 115.91, 116.32, 117.24, 118.38, 120.37, 123.02, 126.00, 128.05, 128.35, 128.87, 130.13, 130.39, 132.83, 142.74, 144.14, 148.20, 150.79, 158.85, 167.57, 168.87; MS: m/z = 572.8[M⁺]; Anal. Calcd for C₃₁H₂₃F₃N₄O₄: C, 65.03; H, 4.05 N, 9.79%. Found: C, 64.84; H, 3.80; N, 9.55%.

(Z)-N-(4-(4-methoxybenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (Ib). mp 115-117°C; Purity by UPLC: 99.5%; IR (KBr) : 3350(N-H str), 3074(Ar, C-H str), 2923(C-H str), 1706(C=O, imidazole ring, str), 1669(C=O, amide, str), 1594(C=N str), 1517(Ar, C=C str), 1332(CF₃, C-F str), 1261(Ar, C-H bending), 1073(C-N str) cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆): δ ppm 3.84(s, 3H, OCH₃), 7.01-7.05(d, J=7.2 Hz, 1H, C-H), 7.09-7.11(d, J=7.2 Hz, 2H, ArH) 7.25-7.29(m, 2H, ArH), 7.34-7.36(m, J=8.4 Hz, 1H, ArH), 7.41(s, 2H, ArH), 7.45-7.55(m, 5H, ArH), 7.81-7.83(d, J=7.6 Hz, 1H, ArH), 8.00-8.02(d, J=7.2 Hz, 2H, ArH), 8.33-8.36(d, J=8.8 Hz, 2H, ArH), 9.17(s, 1H, NH), 11.69(s, 1H, NH); ¹³C NMR (100 MHz, DMSO-d₆): δ ppm 55.92, 114.72, 115.09, 115.83, 117.14, 118.40, 119.05, 120.36, 123.07, 125.78, 125.90, 126.50, 127.07, 127.89, 128.49, 128.66, 129.26, 129.35, 129.67, 130.40, 130.89, 132.51, 134.56, 135.24, 140.30, 142.73, 144.15, 159.58, 162.05, 167.70, 168.95. MS: m/z = 557.5 [M⁺]; Anal. Calcd for C₃₁H₂₃F₃N₄O₄: C, 66.90; H, 4.17; N, 10.07%. Found: C, 66.75; H, 4.01; N, 9.80%.
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(Z)-N-(4-(4-hydroxy-3,5-dimethoxybenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1c). mp 126-128 °C; IR (KBr) : 3340, 2922, 2851, 1709, 1642, 1590, 1515, 1332, 1262, 1072 cm⁻¹; MS: m/z = 602.9 [M]+; Anal. Calcd for C_{32}H_{25}F_{3}N_{4}O_{5}: C, 63.78; H, 4.18; N, 9.30%. Found: C, 63.40; H, 4.05; N, 9.05%.

(Z)-N-(4-(dimethylamino)benzylidene)-5-oxo-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1d). mp 130-132°C; IR (KBr) : 3338, 2930, 2850, 2800, 1709. 1642, 1589, 1515, 1333, 1260, 1070 cm⁻¹; MS: m/z = 569.9 [M]+; Anal. Calcd for C_{32}H_{26}F_{3}N_{5}O_{2}: C, 67.48; H, 4.40; N, 12.30%. Found: C, 67.20; H, 4.10; N, 12.05%.

(Z)-N-(4-(2-methoxybenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1e). mp 118-120°C; IR (KBr) : 3352, 3078, 2920, 2852, 1708, 1689, 1590, 1515, 1333, 1260, 1071 cm⁻¹; MS: m/z = 556.8 [M]+; Anal. Calcd for C_{31}H_{23}F_{3}N_{4}O_{3}: C, 66.90; H, 4.17; N, 10.07%. Found: C, 66.69; H, 3.88; N, 9.85%.

(Z)-N-(4-(3-nitrobenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1f). mp 112-114°C; IR (KBr): 3360, 3068, 2918, 2850, 1706, 1690, 1510, 1589, 1514, 1332, 1256, 1070, 837 cm⁻¹. MS: m/z = 571.80 [M]+; Anal. Calcd for C_{30}H_{20}F_{3}N_{5}O_{4}: C, 63.05; H, 3.53; N, 12.25%. Found: C, 62.85; H, 3.25; N, 12.01%.

(Z)-N-(4-(4-chlorobenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1g). mp 126-128°C; IR (KBr): 3325, 2950, 2850, 1710, 1638, 1588, 1515, 1334, 1260, 1070, 770 cm⁻¹. MS: m/z = 561.4 [M]+; Anal. Calcd for C_{30}H_{20}ClF_{3}N_{4}O_{2}: C, 64.23; H, 3.59; N, 9.99%. Found: C, 64.05; H, 3.25; N, 9.75%.

(Z)-N-(4-(2-chlorobenzylidene)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamide (1h). mp 124-126°C; IR (KBr): 3328, 2924, 2849, 1709, 1635, 1587, 1514, 1332, 1259, 1070, 770 cm⁻¹. MS: m/z = 561.5 [M]+; Anal. Calcd for C_{30}H_{20}ClF_{3}N_{4}O_{2}: C, 64.23; H, 3.59; N, 9.99%. Found: C,
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64.05; H, 3.25; N, 9.80%.

\((Z)-N-(4\text{-}benzylidene\text{-}5\text{-}oxa\text{-}2\text{-}phenyl\text{-}4,5\text{-}dihydro\text{-}1H\text{-}imidazol\text{-}1\text{-}yl})\text{-}2\text{-}(3\text{-}(trifluoromethyl)phenylamino)benzamide(II).\) mp 120-122°C; IR (KBr): 3324, 2922, 2837, 1706, 1638, 1588, 1517, 1333, 1260, 1072 cm\(^{-1}\); MS: \(m/z = 526.7[M]^{+}\); Anal. Calcd for C\(_{30}\)H\(_{21}\)F\(_{3}\)N\(_{4}\)O\(_{2}\): C, 68.44; H, 4.02; N, 10.64%. Found: C, 68.12; H, 3.98; N, 10.05%.

\((Z)-N-(4\text{-}(2\text{-}hydroxybenzylidene)\text{-}5\text{-}oxa\text{-}2\text{-}phenyl\text{-}4,5\text{-}dihydro\text{-}1H\text{-}imidazol\text{-}1\text{-}yl})\text{-}2\text{-}(3\text{-}(trifluoromethyl)phenylamino)benzamide(Ij).\) mp 128-130°C; IR (KBr): 3530, 3340, 2922, 2851, 1709, 1642, 1589, 1514, 1332, 1262, 1072 3324, 2922, 2837, 1706, 1638, 1588, 1517, 1333, 1260, 1072 cm\(^{-1}\); MS: \(m/z = 542.7 [M]^{+}\); Anal. Calcd for C\(_{30}\)H\(_{21}\)F\(_{3}\)N\(_{4}\)O\(_{3}\): C, 66.42; H, 3.90; N, 10.33%. Found: C, 66.10; H, 3.67; N 10.03%.

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SPECTRAL STUDY OF SYNTHESIZED COMPOUNDS

IR spectra of compound 1a.

![IR spectrum of compound 1a](image)

IR spectra of compound 1b.

![IR spectrum of compound 1b](image)

Imidazolone derivatives...
Mass spectrum of compound 1a.

Mass spectrum of compound 1b.

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UPLC spectrum of compound 1a.

**SAMPLE INFORMATION**

- Sample Name: 1a-572
- Sample Type: Unknown
- Visk: 1:0:0
- Injection #: 1
- Injection Volume: 2.00 ul
- Run Time: 5.0 Minutes
- Data Acquired: 12/22/2010 3:15:59 IST
- Data Processed: 12/22/2010 3:29:48 IST

**Peak Results**

Channel: PDA Spectrum

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**Peak Results**

Channel: SQ 1: MS Scan

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**Warning**

- Sample Name: 1a-572
- Sample Type: Unknown
- Visk: 1:0:0
- Injection #: 1
- Injection Volume: 2.00 ul
- Run Time: 5.0 Minutes
- Data Acquired: 12/22/2010 3:15:59 IST
- Data Processed: 12/22/2010 3:29:48 IST

**Imidazolone derivatives...**
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\[^1\text{H} \text{NMR spectrum of compound 1a.}\]

\[
\begin{array}{c}
\text{Expanded spectrum of compound 1a.}
\end{array}
\]
Studies on heterocyclic...
Studies on heterocyclic...  

$^{13}$C NMR spectrum of compound 1a.

![Image of $^{13}$C NMR spectrum of compound 1a.]

$^{13}$C NMR spectrum of compound 1b.

![Image of $^{13}$C NMR spectrum of compound 1b.]

Imidazolone derivatives...
ANTIMICROBIAL ACTIVITY

Biological evaluation of (Z)-N-(4-(Aryl)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamides.

All of the synthesized compounds (Ia-j) were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria Staphylococcus aureus MTCC-96 and Streptococcus pyogenes MTCC 442, two Gram-negative bacteria Escherichia coli MTCC 443 and Pseudomonas aeruginosa MTCC 441 and three fungal strains Candida albicans MTCC 227, Aspergillus Niger MTCC 282 and Aspergillus clavatus MTCC 1323 taking gentamycin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and griseofulvin as a standard drugs. The standard strains were procured from the Microbial Type Culture Collection (MTCC), Institute of Microbial Technology, Chandigarh, India.

The minimal inhibitory concentration (MIC) values for all the newly synthesized compounds, defined as the lowest concentration of the compound preventing the visible growth, were determined by using micro dilution broth method according to NCCLS standards.33

Minimal Inhibition Concentration [MIC]

The main advantage of the Broth Dilution Method for MIC determination lies in the fact that it can readily be converted to determine the MIC as well.
1. Serial dilutions were prepared in primary and secondary screening.
2. The control tube containing no antibiotic is immediately subcultured (before inoculation) by spreading a loopful evenly over a quarter of plate of medium suitable for the growth of the test organism and put for incubation at 37°C overnight.
3. The MIC of the control organism is read to check the accuracy of the drug concentrations.
4. The lowest concentration inhibiting growth of the organism is recorded as the MIC.
5. The amount of growth from the control tube before incubation (which
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represents the original inoculums) is compared.

Methods used for primary and secondary screening.

Each synthesized compounds were diluted in DMSO to obtain 2000 µg mL⁻¹ concentration, as a stock solution. Inoculum size for test strain was adjusted to 10⁸ cfu (colony forming unit) per milliliter by comparing the turbidity.

**Primary screen:** In primary screening 1000 µg mL⁻¹, 500 µg mL⁻¹ and 250 µg mL⁻¹ concentrations of the synthesized compounds were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution against all microorganisms.

**Secondary screen:** The compounds found active in primary screening were similarly diluted to obtain 200 µg mL⁻¹, 100 µg mL⁻¹, 50 µg mL⁻¹, 25 µg mL⁻¹, 12.5 µg mL⁻¹, and 6.25 µg mL⁻¹ concentrations.

**Reading Result:** The highest dilution showing at least 99 % inhibition zone is taken as MIC. The result of this is much affected by the size of the inoculums. The test mixture should contain 10⁸ organism/mL. The results obtained from antimicrobial susceptibility testing are depicted in Table 1b.
Table-1b: Antimicrobial activity of (Z)-1V-(4-(Aryl)-5-oxa-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)-2-(3-(trifluoromethyl)phenylamino)benzamides.

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<td>Minimal bactericidal concentration μg/mL</td>
<td>Minimal fungicidal concentration μg/mL</td>
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<td>Gram +Ve Bacteria</td>
<td>Gram -Ve Bacteria</td>
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<tr>
<td>S. aureus</td>
<td>S. pyogenus</td>
<td>E. coli</td>
</tr>
<tr>
<td>1a</td>
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<td>50</td>
</tr>
<tr>
<td>1b</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>1c</td>
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<td>250</td>
</tr>
<tr>
<td>1d</td>
<td>500</td>
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</tr>
<tr>
<td>1e</td>
<td>250</td>
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</tr>
<tr>
<td>1f</td>
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<td>100</td>
</tr>
<tr>
<td>1g</td>
<td>200</td>
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</tr>
<tr>
<td>1h</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>1i</td>
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<td>500</td>
</tr>
<tr>
<td>1j</td>
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<td>500</td>
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</table>

MINIMAL INHIBITION CONCENTRATION

<table>
<thead>
<tr>
<th>Standard Drugs</th>
<th>S. aureus</th>
<th>S. pyogenus</th>
<th>E. coli</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
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<td>0.5</td>
<td>0.05</td>
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<tr>
<td>Ampicillin</td>
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<td>Chloramphenicol</td>
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<td>Ciprofloxacin</td>
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<td>25</td>
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<td>Norfloxacin</td>
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MINIMAL FUNGICIDAL CONCENTRATION

<table>
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<th>Standard Drugs</th>
<th>C. albicans</th>
<th>A. niger</th>
<th>A. clavatus</th>
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<tbody>
<tr>
<td>Nystatin</td>
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<tr>
<td>Greseofulvin</td>
<td>500</td>
<td>100</td>
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</tbody>
</table>

Imidazolone derivatives...
REFERENCES

Studies on heterocyclic...


33. National Committee for Clinical and Laboratory Standards, Method for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically
Studies on heterocyclic...

