Journal of Tropical Pharmacy and Chemistry

Journal homepage: https://jtpc.farmasi.unmul.ac.id

Synthesis, Chemical Characterization and Antibacterial Activity of Some Novel Triazole Substituted 5-Oxo-Imidazoline Derivatives

Yerra Rajeshwar

Department of Pharmacy, College of Medicine, Komar University of Science and Technology, Chaq-Chaq, Suleymaniyah, Kurdistan Region, Iraq
*Corresponding author: yerra.rajeshwar@komar.edu.iq

Abstract

5-oxo-imidazoline rings have been reported to possess various biological activities such as antibacterial, anticancer, antifungal, and anthelmintic activities. These activities also include anticonvulsant, and anthelmintic. These observations and findings prompted to synthesize the novel triazolo substituted 5-oxo-imidazoline derivatives. In the present investigation, a series of 10 new 1-trazolyl-5-oxo-imidazolinones were synthesized in good yield by using appropriate synthetic methods and have been established on the basis of their M.P., TLC, FT-IR, ^{1}H-NMR, ^{13}C-NMR data. Also, all the compounds were evaluated for the possible antibacterial activity by cup-plate agar diffusion method by measuring % zone of inhibition. Streptomycin at the concentration of 50µg/ml was used as standard drug. Of all the tested compounds, A6 exhibited significantly high potency against the various gram positive and gram negative organisms used in the investigation.

Keywords: 5-oxo-imidazolinone, triazole, antibacterial activity

Received: 12 November 2023 **Accepted**: 07 March 2024

DOI: https://doi.org/10.25026/jtpc.v8i1.617

How to Cite:

Rajeshwar, Y., 2024. Synthesis, Chemical Characterization and Antibacterial Activity of Some Novel Triazole Substituted 5-Oxo-Imidazoline Derivatives. *J. Trop. Pharm. Chem.* **8**(1). 10-16.
DOI: https://doi.org/10.25026/jtpc.v8i1.617

1 Introduction

Imidazole (molecular formula: $C_3H_4N_2$, molecular weight: 68.07) is a planar 5-membered heterocyclic ring system containing two nitrogen atoms (present at C1 and C3 skeletal positions) and three carbon atoms (present at C2, C4, and C-5) as depicted in Figure 1(a). It is an aromatic ring that is classified as a diazole family owing to its non-adjacent nitrogens in its skeleton. Imidazole is amphoteric in nature, and susceptible to electrophilic and nucleophilic attack. It is highly stable to thermal, acid, base, oxidation, and reduction reactions. The reduction products, named as other rings of five atoms, are imidazoline, imidazolidine, 5-oxo-imidazoline and their derivatives [1] (Figure 1(b), 1(c), and 1(d)).

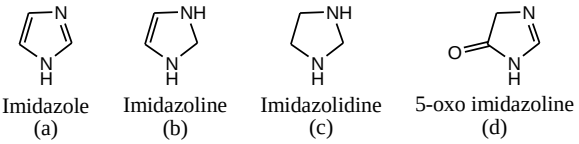


Figure 1: Structure of (a) Imidazole and (b-d) Imidazole reductive derivatives

The 5-oxo-imidazoline (Figure 1(d)) has two nitrogen atoms (present at C1, and C3 positions) and a carbonyl (>C=O) group present at C5 position. 2-substituted 5-oxo-imidazolines have been reported for the first time in 1888. A.W. Hoffman [2] was synthesized 2-methyl-5-imidazoline (Lysidine) by heating N_1-diacetylethylene-diamine in a stream of dry hydrogen chloride. A. Ladenburg [3] was prepared the same compound by fusing two equivalents of sodium acetate with one equivalent of ethylenediamine dihydrochloride. The imidazoline-4-one is believed to be more stable than 5-one because of the conjugated α, β-unsaturated carbonyl structure.

5-oxo-imidazoline is found to owe biological/clinical significance in a wide range of pharmacological activities. Anticancer activity of substituted 5-imidazolinones was studied by [4], [5]. Kumudine Bhanat *et al*., [6] and Sudhar Bharadwaj *et al*., [7] reported the synthesis and antimicrobial activity of imidazole-5-one derivatives. Anti-inflammatory activity was studied by [4], analgesic activity was investigated by [8], and anticonvulsant activity was evaluated by [9]. Monica Kachroo *et al*., [10] and R. Subramaniam *et al*., [11] evaluated the antioxidant activity of some thiazole- and pyrimidine-substituted imidazolinones, respectively. Moreover, the substituted imidazolinones were tested for antifungal [12], [13] and anthelmintic [1] activities. QSAR studies were also reported for these derivatives by [14]. Thiourea derivatives bearing imidazoline moiety were studied by [15].

From the above investigations and findings, it is understood that 5-oxo-imidazoline moiety seemed to be a possible pharmacophore in designing safer medicinal agents. Thus, we underwent in continuation of the work on the same nucleus and synthesized some new triazole substituted 5-oxo-imidazolinone derivatives and tested for the antibacterial activity by using various gram-positive and gram-negative microorganisms.

2 Materials and Methods

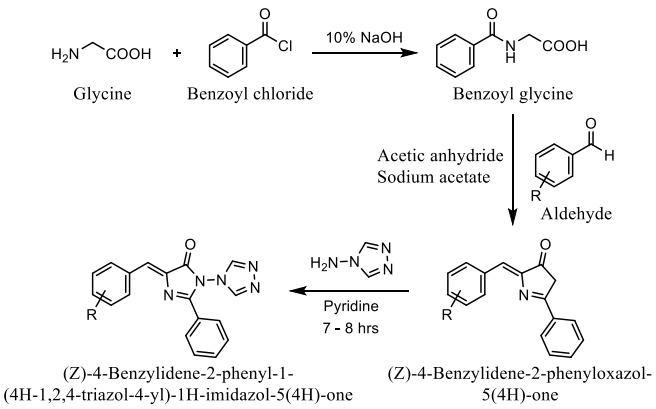
Melting points of all the synthesized compounds were recorded in open capillary tubes on Thermionic Melting Point apparatus and are uncorrected. The Infrared (IR) spectra (cm^{-1}) for the synthesized compounds were recorded on Fourier Transform IR Spectrometer (Model: Shimadzu 8700) in the range of 400-4000 using KBr pellets and the values of ν_{max} are reported in cm^{-1}. Nuclear Magnetic Resonance (^{1}H-NMR) spectra were recorded on DMM X-200 MHz NMR, Bruken Daltonics, Karsruhe, Germany using DMSO and

chemical shifts were reported in parts per million (δ ppm) with Tetramethylsilane (TMS) as an internal standard.

Elemental analysis was undertaken using an Elemental Analyzer model Vario El III. The purity of compounds was checked by Thin Layer Chromatography (TLC) using silica gel G as stationary phase and various combinations of n-hexane : ethyl acetate mobile phase. The spots resolved were visualized by using Iodine and UV chamber.

The chemicals used were of AR grade and IR grade. They were purchased from SD Fine, Spectrochem, Sisco Research Laboratory, and Qualichem.

2.1 General procedure for the synthesis of 1-triazole substituted 5-oxo-imidazoline derivatives



R	Substituent
H	Benzaldehyde
4-N(CH_3)$_2$	N,N-Dimethylaminobenzaldehyde
3-OH, 4-OCH_3	Vanillin
3,4-Dimethoxy	Veratraldehyde
4-CH_3	4-Methylbenzaldehyde
4-Cl	4-Chlorobenzaldehyde
4-OCH_3	Anisaldehyde
3-Phenylallylidene	Cinnamaldehyde
4-OH	4-Hydroxybenzaldehyde

Figure 2. Synthesis of 1-triazole substituted 5-oxo-imidazoline derivatives

2.2 Antibacterial activity

One of the most frequently encountered heterocycles in Medicinal Chemistry (MC) is 5-imidazolinone with wide applications including antibacterial activity [16], [17], [18].

All the synthesized compounds have been screened for antibacterial activity using cup-plate agar diffusion method by measuring the zone of inhibition in mm (Table 2). Streptomycin (50 µg/ml) was used as a standard drug. All the compounds were screened for antibacterial activity against both gram positive bacteria such as *Lactobacillus, Streptococcus pyogenes, Staphylococcus aureus, Bacillus megaterium and Bacillus subtilis; and* gram-negative bacteria like *Proteus vulgaris*, *Salmonella paratyphi*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *Escherichia coli*, in nutrient agar medium. These sterilized agar media were cooled and added with bacterial suspension in individual portions and poured into Petri-dishes and allowed to solidify. A stainless-steel cylinder of 8 mm diameter (pre-sterilized) was used to bore cavities.

All compounds (labelled A1-A10) were placed serially in the cavities with the help of micropipette and allowed to diffuse for 1.0 hr. DMSO was used as a solvent for all the compounds, and as a control. These plates were incubated at 37°C for 24 hr, for antibacterial activity. The zone of inhibition observed around the cups after respective incubations were measured [19].

3 Results and Discussion

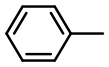
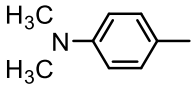
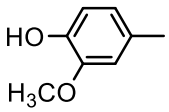
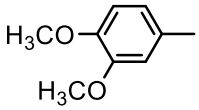
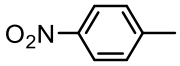
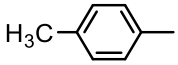
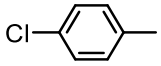
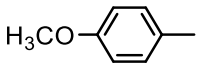
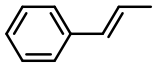
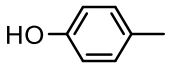
Ten new (1-triazolyl) or triazole substituted 5-oxo-imidazolinone compounds were synthesized by using appropriate synthetic methods as mentioned in the above section (Figure 2). The synthesized compounds were characterized by both physical and spectral data like ^{1}H-NMR, ^{13}C-NMR, and FT-IR and the results are illustrated in Table 1.

The compounds were also evaluated for antibacterial activity using various bacterial gram-positive and gram-negative strains and the results were shown in Table 2.

3.1 Characterization of compounds

The newly synthesized compounds (A1-A10) physical data has been presented in the Table 1.

Table 1: Physical parameters of synthesized compounds

Compound Code	R	Molecular formula	Molecular weight ($gmol^{-1}$)	MP (°C)	% yield	R_f
A1		$C_{18}H_{13}N_5O$	315.33	190-192	47.60	0.61
A2		$C_{20}H_{18}N_6O$	358.40	146-150	33.50	0.56
A3		$C_{19}H_{15}N_5O_3$	361.35	180-182	49.80	0.62
A4		$C_{20}H_{17}N_5O_3$	375.38	128-130	40.00	0.57
A5		$C_{18}H_{12}N_6O_3$	360.33	164-165	50.00	0.71
A6		$C_{19}H_{15}N_5O$	329.36	200-203	54.70	0.64
A7		$C_{18}H_{12}ClN_5O$	349.77	186-189	51.50	
A8		$C_{19}H_{15}N_5O_2$	345.35	128-130	50.00	0.72
A9		$C_{20}H_{15}N_5O$	341.37	170-174	52.70	0.66
A10		$C_{18}H_{13}N_5O_2$	331.33	154-158	52.80	0.72

All the compounds (A1-A10) are found to be soluble in Ethanol, methanol, and DMSO; and the TLC system employed was $CHCl_3$:Ethyl acetate (3:1).

All the compounds (A1-A10) are found to be soluble in Ethanol, methanol, and DMSO; and the TLC system employed was $CHCl_3$:Ethyl acetate (3:1).

Compound A1: *4-Benzylidene-2-phenyl-1-(4H-1,2,4-trizol-4-yl)-1H-imidazol-5(4H)-one*

IR (KBr, cm^{-1}): 1793 (C=O), 1651 (C=N), 3037 (C-H), 1448 (C=C Ar), 1163 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.2-8.4 (s, 2H, triazole-H), 8.0-8.25 (dd, 3H, benzylidene-H and Ar-H), 7.25-7.8 (m, 8H, Ar-H)

EI-MS (m/z): 314(100%), 315(25%), 316(60%)

Compound A2: *4-(4-Dimethylamino)benzylidene-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one*

IR (KBr, cm^{-1}): 1607 (C=O), 1523 (C=N), 3060 (C-H), 1443 (C=C), 1168 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.1-8.3 (s, 2H, triazole-H), 7.8 (s, 1H, benzylidene-H), 6.6-7.6 (m, 9H, Ar-H)

EI-MS (m/z): 358(100%)

Compound A3: 4-(4-Hydroxy-3-methoxybenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1793 (C=O), 1651 (C=N), 3037 (C-H), 1448 (C=C Ar), 1163 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.2-8.4 (s, 2H, triazole-H), 8.0-8.25 (dd, 3H, benzylidene-H and Ar-H), 7.25-7.8 (m, 8H, Ar-H)

EI-MS (m/z): 314(100%), 315(25%), 316(60%)

Compound A4: 4-(3,4-Dimethoxybenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1698 (C=O), 1639 (C=N), 2920 (C-H, aliphatic), 3250 (C-H Ar), 1143 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.0-8.2 (s, 2H, triazole-H), 6.5-7.6 (m, 7H, Ar-H), 7.8 (m, 2H, benzylidene-H and Ar-H), 3.6-3.9 (s, 6H, O-CH_3)

EI-MS (m/z): 375(100%)

Compound A5: 4-(3-nitrobenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1600 (C=O), 1750 (C=N), 3200 (C-H), 1350 (C=C Ar), 1151 (C-N), 1525.35 (Ar-NO_2)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.3 (s, 3H, triazole-H), 7.5-8.1 (m, 8H, Ar-H), 7.7 (m, 1H, benzylidene-H, Ar-H)

EI-MS (m/z): 360 (100%)

Compound A6: 4-(4-Methylbenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1690 (C=O), 1725 (C=N), 3095 (C-H), 1345 (C=C Ar), 1170 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.29 (s, 2H, triazole-H), 7.1-7.8 (m, 9H, Ar-H), 7.5 (s, 1H, benzylidene-H), 2.4 (s, 3H, Ar-H)

EI-MS (m/z): 362 (100%)

Compound A7: 4-(4-Chlorobenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1730 (C=O), 1555 (C=N), 3120 (C-H), 1490 (C=C Ar)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.29 (s, 2H, triazole-H), 7.4-7.9 (m, 9H, Ar-H), 7.5 (s, 1H, benzylidene-H)

EI-MS (m/z): 349 (100%), 351 (32%), 350 (19%)

Compound A8: 4-(4-Methoxybenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1690 (C=O), 1630 (C=N), 3150 (C-H), 1525 (C=C Ar), 1158 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.29 (s, 2H, triazole-H), 6.8-7.8 (m, 9H, Ar-H), 7.5 (s, 1H, benzylidene-H), 3.8 (s, 3H, -OCH_3)

EI-MS (m/z): 345 (100%), 346 (20%), 347 (2.5%)

Compound A9: 2-Phenyl-4-[(E)-3-phenylallylidene)-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1678 (C=O), 1622 (C=N), 3014 (C-H), 1560 (C=C Ar), 1174 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 8.29 (s, 2H, triazole-H), 7.3-7.8 (m, 10H, Ar-H), 7.4 (d, 1H, benzylidene-H), 6.7 (t, 1H, allylidene), 7.2 (m, 1H, allylidene)

EI-MS (m/z): 341 (100%), 342 (21%), 343 (2.8%)

Compound A10: 4-(4-Hydroxybenzylidene)-2-phenyl-1-(4H-1,2,4-triazol-4-yl)-1H-imidazol-5(4H)-one

IR (KBr, cm^{-1}): 1675 (C=O), 1735 (C=N), 3120 (C-H), 1498 (C=C Ar), 1168 (C-N)

^{1}H-NMR (DMSO-d_6, δ ppm): 9.4 (s, 1H, Ar-OH), 8.29 (s, 2H, triazol-H), 6.4-7.8 (m, 9H, Ar-H), 7.5 (s, 1H, benzylidene-H)

EI-MS (m/z): 331 (100%), 332 (19%), 333 (2.6%)

3.2 Antibacterial activity

It could be evidenced from the results of the present investigation that irrespective to their nature, none of the test compounds are comparable with the standard drug, Streptomycin, in their antibacterial activity.

Table 2: Antibacterial activity by % inhibition

Microorganism	A1	A2	A3	A4	A5	A6	A7	A8	A9	A10	Streptomycin
Proteus vulgaris	35.0	-	-	-	35.00	41.25	44.37	52.62	38.12	50.62	100
Lactobacillus	35.0	-	49.28	-	45.71	63.57	42.14	45.70	49.28	52.80	100
Streptococcus pyrogenes	36.6	-	36.60	36.60	50.00	46.66	40.00	60.00	43.30	46.60	100
Salmonella paratyphi	36.6	-	33.30	43.30	50.00	70.00	53.33	56.60	50.00	40.00	100
Enterobacter aerogenes	44.2	-	41.50	38.90	52.31	49.40	38.90	44.20	36.30	41.50	100
Staphylococcus aureus	44.2	30.0	41.40	47.10	52.80	50.00	35.70	44.20	35.70	47.10	100
Proteus mirabilis	34.2	31.1	40.30	37.20	49.30	43.33	55.40	40.30	37.20	43.30	100
Klebsiella pneumonia	30.0	33.3	36.60	46.60	43.30	56.60	50.00	46.60	13.30	53.30	100
Pseudomonas aeruginosa	31.4	-	-	17.00	-	21.00	23.00	24.00	63.50	20.00	28
Bacillus megeterium	32.8	-	30.00	32.80	-	30.00	38.50	44.20	50.00	38.50	100
E. coli	41.2	35.0	29.70	63.10	47.50	66.20	44.30	56.80	56.80	44.30	100
Bacillus subtilis	35.0	-	32.50	35.00	37.50	42.50	35.00	42.50	45.00	47.50	100

25-40: poor activity; 46-60: moderate activity; >60: strong activity; -: No activity.
All values are mean of three experiments and expressed as % inhibition;
Concentration of all compounds = 50 µg/mL

Antibacterial activity among the test compounds is illustrated in Table 2. All the compounds (A1-A10) showed a varied degree of antibacterial activity against various gram-positive and gram-negative strains employed in the investigation. However, among this series of compounds, A6 showed strong antibacterial inhibitory activity against *Salmonella paratyphi* (70.00%), *E. coli* (66.20%), and *Lactobacillus* (63.57%), while the test compounds A4, A8, A9 and A10 exhibited strong activity against *E. coli* (63.1%), *Streptococcus pyrogenes* (60%), and *Pseudomonas aeruginosa* (63.5%), respectively. Other triazolyl 5-oxo-imidazoline derivatives A1, A2, and A3 have shown poor to moderate activity against the test organisms employed. However, the zone of inhibition varied with the test compound and the test bacterium. Among the test compounds employed, A2 exhibited relatively mild or poor activity. The compounds A7, A8, A9 and A10 showed moderate to strong activity.

4 Conclusions

A series of new 2-phenyl-4-(substituted benzylidene)-1-(1,2,4-triazol)yl-5-oxo-imidzolines were synthesized and evaluated for their possible antibacterial activity. All these molecules were characterized by FT-IR, ^{1}H-NMR and Mass spectral analysis along with physical data. Agar diffusion method was used to evaluate the antibacterial activity against various gram positive and gram-negative bacterial strains by measuring zone of inhibition. Streptomycin was used as a standard drug. All the test compounds (A1 to A10) showed a varied degree of antibacterial activity against all the gram positive and gram-negative bacterial strains employed.

Currently, we are also undergoing the biological activities such as anthelmintic, antifungal and antioxidant activities of all the synthesized compounds and the findings will be reported soon.

5 Declarations

5.1 Funding Statement

This research was not supported by any funding sources.

5.2 Conflicts of Interest

The authors declare no conflict of interest.

6 References

[1] Kaplesh Patel, Jayachandran E, Shah R, Javali V, and Sreenivasa GM, 2010. Synthesis, characterization and anthelmintic activity (*Perituma posthuman*) of new oxadiazole incorporated with imidazole and pyrazole, *International Journal of Pharma and Bio Sciences*, 1(3), 1-13.

[2] Hoffman AW, 1880. *Ber*., 21, 2332.

[3] Ladenburg A, 1894. *Ibid*., 27, 295.

[4] Safinaz E Abbas, Nagwa M Abdel Gawad, Hanan H Georgey, and Jalal H Abdullah, 2010. New Quinazolinone derivatives: Synthesis, antiinflammatory and antitumor activities, *International Journal of ChemTech Research*, 2(3), 1560-1578.

[5] Solankee A, Kapadia K, Upadhyay K, and Patel J, 2001. Synthesis and anticancer activity of some 1-(2',3'-dimethyl-1'-phenyl-3'-pyrazoline-5'-one-4'-yl)-2-phenyl-4-(substituted benzylidene)-5-imidazolinones, *Oriental Journal of Chemistry*, 17(2), 315.

[6] Kumudini Bhanat, Narendra Parashar, Khushboo Jain, and Sharma VK, 2011. Synthesis and antimicrobial study of 4-benzylidene-2-phenyl-1-(5-phenylthiazole-2-yl)-1H-imidazol-5(4H)-one, *Asian Journal of Biochemical and Pharmaceutical Research*. 1(1), 83-91.

[7] Sudhir Bharadwaj, Dimple K Rathore, Bharat Parashar, and Sharma VK, 2010. Synthesis and antimicrobial study of 4-benzylidene-2-phenyl-1-(5-phenylthiazol-2-yl)-1H-imidazol-5(4H)-one, *Journal of Chemical and Pharmaceutical Research*, 2(5), 392-398.

[8] Maha M Khalifa and Naiya A Abdelbaky, 2007. Synthesis of new imidazolyl acetic acid derivatives of potential anti-inflammatory and analgesic activities. *Al-Azhar Journal of Pharmaceutical Sciences*. 35.

[9] Hashmukh Joshi, Paresh Upadhyay, Denish Karia, and Baxi AJ, 2003. Synthesis of some novel imidazolinones as potent anticonvulsant agents. *European Journal of Medicinal Chemistry*, 38(9), 837-840.

[10] Monica Kachroo , Gopal Krishna Rao, Rajasekaran S, Sanjay Pai PN, and Hemalatha YR, 2011. Synthesis, antibacterial and antioxidant activity of N-[(4E)-arylidene-5-oxo-2-phenyl-4,5-dihydro-1H-imidazol-1-yl]-2-(2-methyl-1,3-thiazol-4-yl) acetamide. *Der Pharma Chemica*, 3(3), 241-245.

[11] R. Subramaniam, Gopal Krishna Rao, Sanjay Pai, Gurpreet Kaur, Virya L, and Gurpreet Singh Sodhi, 2010. Synthesis and *in vitro* study of biological activity of 2,3-substituted quinazolin-4-(3H)-ones, *Journal of chemical and Pharmaceutical Research*. 2(2), 462-468.

[12] Rakesh N Mistry and Desai KR, 2005. Studies on synthesis of some novel heterocyclic azlactone derivatives and imidazolinone derivatives and their antimicrobial activity. E-Journal of Chemistry, 2(1), 42-51.

[13] Harshad G Kathrotiya, Nilav A Patel, Ranjan G Patel, and Manish P Patel, 2012. An efficient synthesis of 3'-quinolinyl substituted imidazole-5-one derivatives catalyzed by zeolite and their antimicrobial activity. *Chinese Chemical Letters*, 23, 273-276.

[14] Desai NC, Maheta AS, Rajpara KM, Joshi VV, Vaghani HV, and Satodiya HM, 2014. Green synthesis of novel quinoline based imidazole derivatives and evaluation of their antimicrobial activity. *Journal of Saudi Chemical Society*, 18(6), 963-971.

[15] Mohammad Amir, Mir M Shahroz, and Anees A Siddiqui, 2006. Synthesis and antimicrobial activity of some new thiourea derivatives bearing imidazoline moiety. *Oriental Journal of Chemistry*, 22(1).

[16] Biplab De, Jayanta Kumar Gupta, and Venkatapuram Sampath Saravanan, 2005. Synthesis of some oxazolinones and imidazolinones and their antimicrobial screening. *Acta Pharmaceutica*, 55, 287-296.

[17] Desai NC, Bhavsar AM, and Baldaniya BB, 2009. Synthesis and antimicrobial activity of 5-imidazolinone derivatives. *Indian Journal of Pharmaceutical Sciences*, 71(1), 90-94.

[18] Omar A Miqdad, Nada M Abunada, Hamdi M Hassaneen, and Ahmad SM Abu Samaha, 2011. Synthesis and biological activity evaluation of some new heterocyclic spirocompounds with imidazolinone and pyrazoline moieties. *International Journal of Chemistry*, 3(4), 20.

[19] Amir Md, Arun Kumar, Ali I, and Khan SA, 2009. Synthesis of pharmaceutically important 1,3,4-thiadiazole and imidazolinone derivatives as antimicrobials. *Indian Journal of Chemistry*, 48B: 1288-1293.