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Chapter

Potent Antibacterial Profile of 5-Oxo-Imidazolines in the New Millennium

Roshan D. Nasare, Mohammad Idrees, Satish S. Kola and Rajendra S. Dongre

Abstract

Pharmaceutics and therapeutics industries enforced chemists to seek/discover antibacterial novel heterocycles owing specific bioactivity and innate characteristics significance. This chapter summarized potent antibacterial profile of 5-oxo-imidazolines in the new millennium as an antibacterial against Gram-positive and Gram-negative bacteria viz. *B. thuringiensis*, *S. aureus*, *E. coli*, and *E. aerogenes* is presented in this chapter. 5-(H/Br benzofuran-2-yl)-1-phenyl 1H-pyrazole-3-carbohydrazides are condensed with 4-(arylidene)-2 phenyloxazol-5(4H)-one in acetic acid at elevated temperature to yield product 5-(H/Br benzofuran-2-yl)-N-(4-arylidene-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1H-pyrazole-3-carboxamides. Different substrates like 4-(arylidene)-2-phenyloxazol-5(4H)-one allowed to react with benzaldehyde hippuric acid to yield 5-oxo-imidazolines/5-oxo-4,5-dihydroimidazole. All synthesized 5-oxo-imidazolines were characterized via elemental analysis and FT-IR, ^{1}H-NMR and mass spectra techniques. All 5-oxo-imidazolines assayed in vitro for inherent antimicrobial activity at different concentration against stated bacterial strains and compared with standard chloramphenicol. 5-Oxo-imidazolines (**3a** and **3c**) with 125 μg/mL concentration showed excellent antibacterial profile against Gram-positive bacteria, *B. thuringiensis*, while other derivatives at different concentrations showed moderate antibacterial activity against Gram-positive bacteria, *S. aureus* and *B. thuringiensis*. Gram-negative bacteria like *E. coli* and *E. aerogenes* are tested at higher concentration (1000, 500, and 125 μg/mL) and found good-to-moderate antibacterial activity. Tested products found non-active against *E. aerogenes* for 125, 61, and 31 μg/mL concentration also inactive at conc. 31 μg/mL against *E. coli*.

Keywords: antibacterial, Gram positive/negative, *B. thuringiensis*, *S. aureus*, *E. coli*, *E. aerogenes*, 5-oxo-imidazoline, azlactones, medicinal

1. Introduction

Imidazole is a planer five-member ring with molecular formula $\mathbf{C_3N_2H_4}$, containing three carbon atoms and two nitrogen atoms in 1 and 3 skeletal positions as depicted in **Figure 1**. This is an aromatic heterocyclic ring that's classified as a diazole family owing non-adjacent nitrogens in its skeleton.

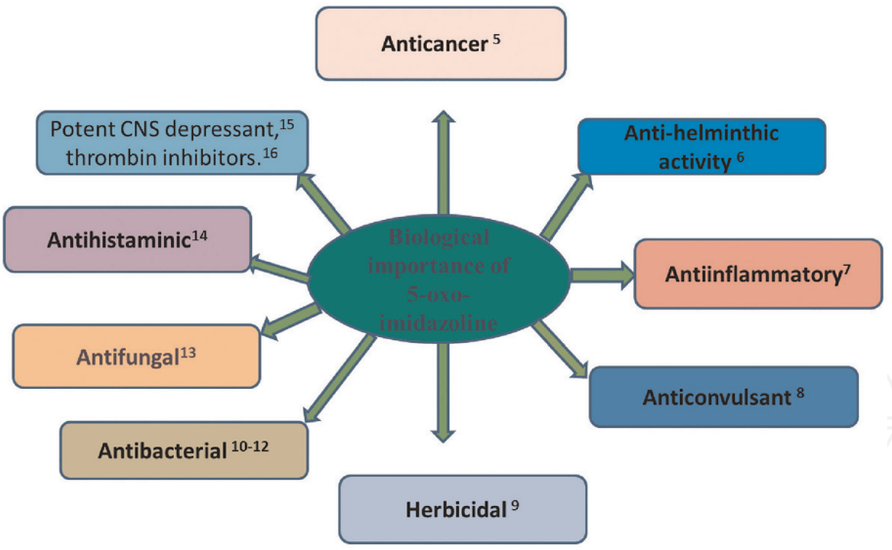
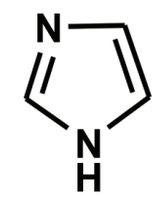
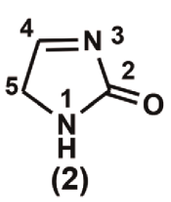


Figure 1.
Certain potent antibacterial profile of 5-oxo-imidazolines in the new millennium [5–16].

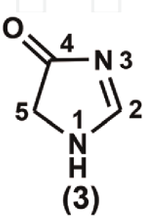


Imidazole
(1)

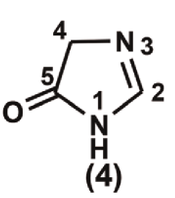
Assorted naturally occurring alkaloids own this imidazole moiety as vital biological building blocks viz; histidine and related hormone histamine. Various synthetic drugs are based on imidazole rings like antifungal, antibiotics: nitroimidazole and sedative: midazolam etc. Oxo-imidazoline derivatives are keto-dihydroimidazoles too, known as **imidazolinone** a five member ring system having 2-nitrogen situated at 1 and 3-positions and ─C═O at various positions like 2, 4 and 5 of ring. Three possible isomers of imidazolinone observed based on position of C═O substituent at skeleton namely: 2-oxo-imidazoline **(2)**, 4-oxo-imidazoline **(3)** and 5-oxo-imidazoline **(4)**.



(2)



(3)

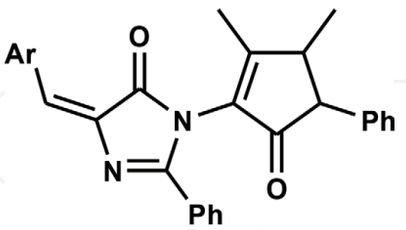


(4)

5-Oxo-4,5-dihydroimidazole derivative is called as 5-oxo-imidazoline, unsaturated system, in fact nitrogen analogues of azlactone/oxazolone can be converted into amino acids [1, 2] and also employed active pharmaceutical ingredient/API component in drugs [3]. 5-Oxo-imidazoline holds biological as well as chemical aspects for a long time; among the various heterocycles, it is preferred due to its wide antimicrobial profile. Certain imidazolines are useful intermediates in synthesis of many natural products as well as common building blocks in many biologically active moieties [4].

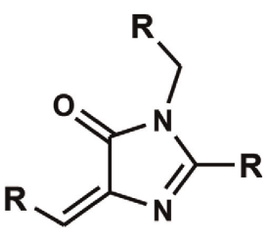
Biological importance of 5-oxo-imidazoline: Literature survey indicated that the synthetic drugs/molecules incorporated with 5-oxo-imidazoline found to owe assorted biological/clinical significance and wide range of pharmacological activities as mention below:

Solankee et al. [17] synthesized some 5-imidazolinones (**5**) and evaluated as anticancer agent.



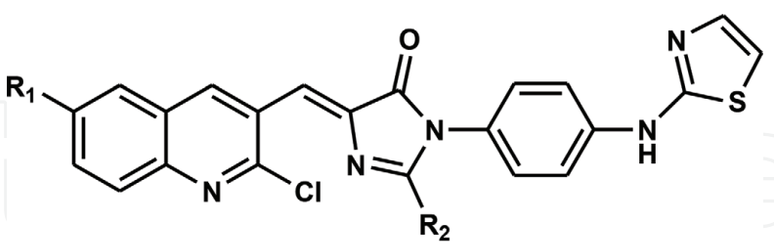
(5)

Mistry et al. [18] have synthesized imidazolinone (**6**) and studied antibacterial, antifungal activities.



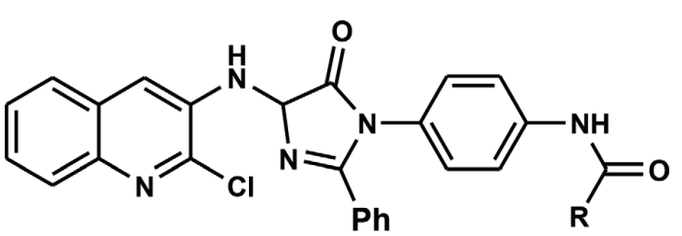
(6)

Kathrotiya et al. [19] and co-workers reported a series of some new quinoline based imidazole-5-one derivatives (**7**) and evaluated them as antibacterial and antifungal agent.



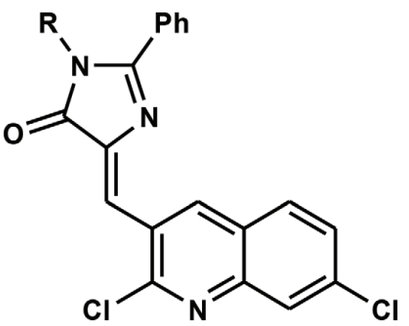
(7)

Desai et al. [20] also reported the synthesis of 5-oxo-imidazole amides derivatives including quinoline unit (**8**) and assessed their antibacterial and antifungal agent.



(8)

Mohammad and coworkers [21] have prepared some new imidazolinones and investigated their antimicrobial activities. Khan et al. [22] have also reported antibacterial and fungicidal activity of 5-oxo-imidazolines. Herbicidal activity of imidazolinone derivatives have been reported by Andreani et al. [23]. Moreover Zhou et al. [24] and Pai et al. [25] have reported anticancer active analogues of 5-oxo-imidazolines. Imidazolinone derivatives which possess antifungal activities have been reported by Shah et al. [26]. Some new 5-oxo-imidazolines as antimicrobial agents have been investigated by Patel et al. [27]. Rao [28] have prepared substituted imidazolone derivatives and reported their pharmaceutical use as inhibitors of p38 MAP Kinase and ERK-2 inhibitors. Xue et al. [29] have synthesized and evaluated imidazole-2-one derivatives as potential antitumor agents. Parekh and co-workers [30] have synthesized 5-oxo-imidazolines as novel bioactive compounds derived from benzimidazole. Kanjaria and co-workers [31] have described imidazolinones as potential antimicrobial agents. Joshi et al. [3] have synthesized imidazolinones as potent anticonvulsant agents. Acharya et al. [32] tested the imidazolinone **(9)** having quinolone nucleus for their antibacterial activity toward Gram-positive and Gram-negative bacteria and antifungal activity toward *Aspergillus niger* at a concentration of 40 μg, they found active against microorganism.



(9)

In view of potent antimicrobial and other pharmacological activities exhibited by 5-oxo-imidazolines, a variety of novel imidazolone analogs (**3a**-**g**) were synthesized by the condensation of different substituted oxazolines (**2a**-**g**) with hetero-aromatic amines (**1a**-**b**). All the synthesized compounds were screened for in vitro activities against a panel of Gram-positive and Gram-negative bacteria.

2. Materials and method

Melting points of all synthesized compounds were recorded in open capillary tube and are uncorrected. IR was recorded on a Shimadzu IR Spectrophotometer in KBr pellets. 1H-NMR recorded on a Bruker AM 400 model (400 MHz) using tetramethylsilane (TMS) as an internal reference and DMSO-d6 as solvent. Chemical shifts are given in parts per million (ppm). Positive-ion electrospray ionization (ESI) mass spectra were obtained with a Waters MicromassQ–TOF Micro, Mass Spectrophotometer. Elemental analysis was done on Vario EL III Elemental Analyzer, all compounds showed satisfactory elemental analysis. Reactions were

monitored by E. Merck TLC aluminum sheet silica gel 60F254 and seen spot in UV light and iodine chamber.

3. Experimental

(I) **Synthesis of benzoyl glycine [33]:** A solution of glycine (0.33 mol) in 10% NaOH (250 mL) of was prepared and benzoyl chloride (45 mL, 0.385 mol) was added to the above solution in portions. The mixture was shaken vigorously after each addition until all the chlorides have been reacted. The mixture was cooled by adding few grams of crushed ice and was acidified by adding conc. HCl slowly with constant stirring. The resulting crystalline precipitate of benzoyl glycine was filtered and washed with cold water and dried. The solid was treated with hot CCl_4 in order to remove benzoic acid. The dried product was recrystallized with boiling water.

(II) **Synthesis of 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones [33] (2a-g)**: Benzoyl glycine (0.0476 mmol), aryl aldehydes (0.0476 mol), acetic anhydride (14 mL, 0.146 mmol) and anhydrous sodium acetate (0.0476 mmol) were placed in a 250 mL conical flask. It was heated on electric hot plate with constant shaking until the mixture liquefies completely. Then it was refluxed for 2 h on water bath. Then ethanol (10 mL) was added and mixture was allowed to stand overnight. The crystalline precipitate was filtered, washed with ice-cold alcohol and boiling water. The product was dried and recrystallized using benzene.

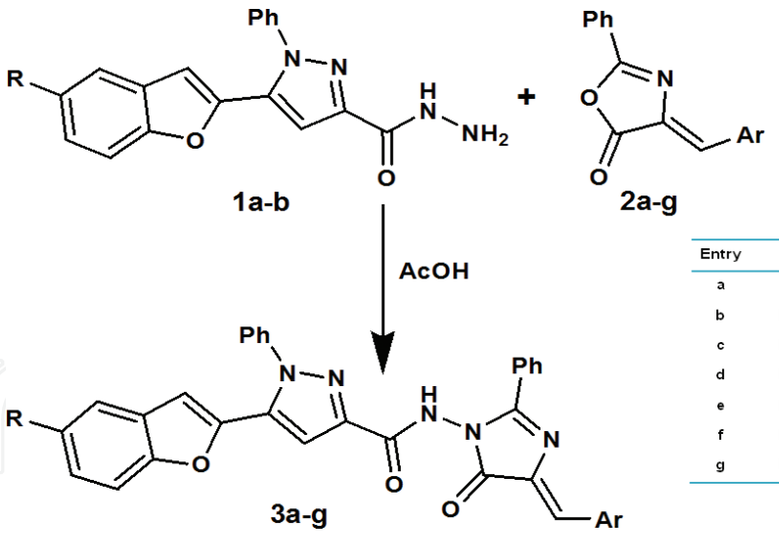
(III) **Preparation of 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole carbohydrazide (1a-b):** Synthesis of (5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazides (**1a-b)** were prepared in laboratory in quantitative yield according to reference method [34].

(IV) **General procedure for the synthesis of 5-(5-H/Br benzofuran-2-yl)-*N*-(4-arylidene-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3 carboxamide (3a-g):** To a mixture of 4-benzylidene-2-phenyloxazol-5(4*H*)-one, **2a** (0.002 mol) and 5-(benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazide **1a** (0.002 mol), acetic acid (20 mL) were added and the contents were refluxed for 9 h. Resulting mass was poured onto crushed ice, filtered and the product was recrystallized from ethanol to give **3a**.

Similarly, other 5-(bromobenzofuran-2-yl)-*N*-(4-arylidene-5-oxo-2-phenyl-4,5-dihydro imidazole-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide **3b-g** were synthesized from **1b** and **2b-g** by extending the same procedure followed for **3a**.

- **Reaction scheme:**

See **Figures 2** and **3**.



Entry	R	Ar
a	H	$-C_6H_5$
b	Br	$4\text{-}OMe\text{-}C_6H_4$
c	Br	$2\text{-}Cl\text{-}C_6H_4$
d	Br	$1\text{-}C_{10}H_7$
e	Br	$4\text{-}OCH_2C_6H_5\text{-}C_6H_4$
f	Br	$-CH{=}CH\text{-}C_6H_5$
g	Br	2-Furfuryl

Figure 2.
Reaction scheme for 5-oxo-imidazoline derivatives.

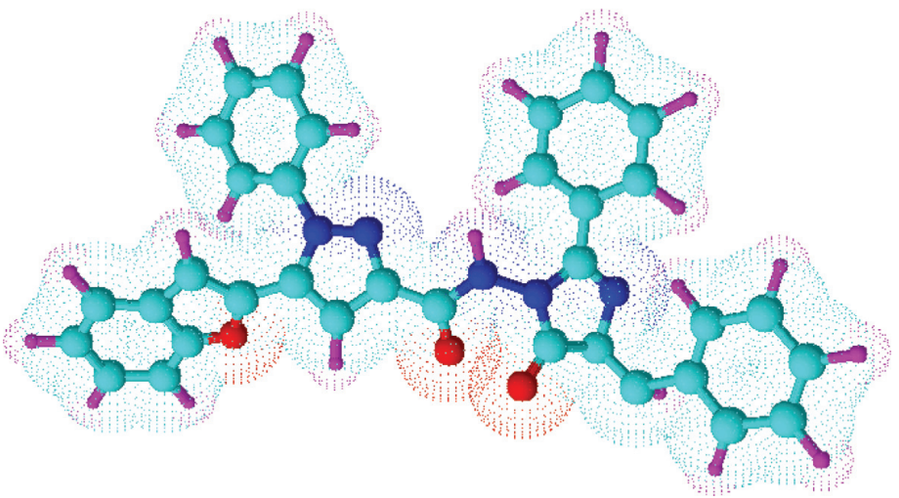


Figure 3.
*3D representation of 5-(benzofuran-2-yl)-*N*-(4-benzylidene-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (compound **3a**).*

4. Results and discussion

4.1 Spectral, elemental and physical data of synthesized compounds

5-(Benzofuran-2-yl)-*N*-(4-benzylidene-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3a): Yellow crystalline solid; mp. 200–204°C; yield, 90%.

IR (KBr, v max in cm^{-1}): 3197 (NH), 3062 (ArH), 1793, 1719 (C═O imidazole), 1597, 1525, 1496, 1448, (C═C), 1207, 1292, 1028 (C—O—C), 1164 (C—N—C stretch), 1640 (C═O in amide group), 1525 (C═N), 1110 (C—N).

^{1}H-NMR (DMSO-d_6): δ (ppm) 6.53 (s, 1H, C_4 of pyrazole ring), 11.65 (s, 1H, NH of amide group), 7.22–8.37 (m, 21H, ArH + benzofuran ring).

MS: *m/z*550 $[M+H]^+$, 551 $[M+2]^+$, 572 $[M+Na]^+$, 573 $[(M+H)+Na]^+$.

Elemental analysis: Calcd: for $C_{34}H_{23}N_5O_3$, calculated: C, 74.30; H, 4.22; N, 12.74; found: C, 74.16; H, 4.05; N, 12.37.

4-(4-Methoxybenzylidene)-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-5-(5-bromo benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3b): Yellow crystalline solid; recrystallization solvent, Ethanol; mp. 132–135°C; yield, 78%; IR (KBr, v max in cm^{-1}): 3315 (NH), 3063 (ArH), 1779, 1720 (C═O imidazole), 1502, 1438 (C═C), 1257, 998 (C—O—C), 1159 (C—N—C stretch), 1649 (C═O in amide group), 1595 (C═N), 1106 (C—N). Elemental anal. calcd: for $C_{35}H_{24}BrN_5O_4$; calculated: N, 10.64; found: N, 10.03.

4-(2-Chlorobenzylidene)-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-5-(5-bromobenzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3c): Yellow crystalline solid; re-crystallization solvent, ethanol; mp. 155–158°C; yield, 82%; IR (KBr, v max in cm^{-1}): 3417 (NH), 1786, 1715 (C═O imidazole), 1501, 1433 (C═C), 1243, 1060 (C—O—C), 1155 (C—N—C stretch), 1643 (C═O in amide group), 1595 (C═N), 1106 (C—N). Elemental anal. calcd: for $C_{34}H_{21}BrClN_5O_3$; calculated: N, 10.56; found: N, 10.11.

5-(5-Bromobenzofuran-2-yl)-N-(4-(naphthalen-1-ylmethylene)-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3d): Yellow crystalline solid; recrystallization solvent, ethanol; mp. 136–138°C; yield, 76%; IR (KBr, v max in cm^{-1}): 3378 (NH), 3005 (ArH), 1778, (C═O imidazole), 1489, 1431 (C═C), 1236, 1069 (C—O—C), 1151 (C—N—C stretch), 1689 (C═O in amide group), 1593 (C═N), 1151 (C—N). Elemental anal. calcd: for $C_{38}H_{24}BrN_5O_3$; calculated: N, 10.32; found: N, 10.40.

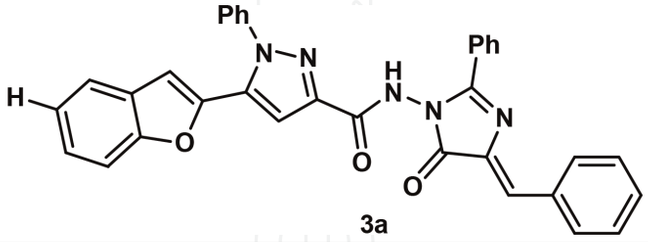
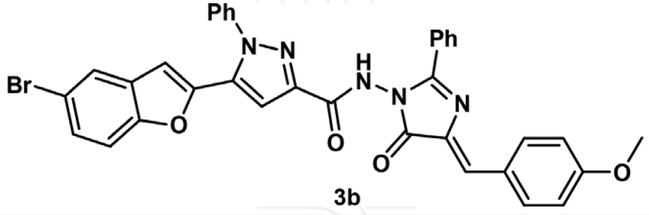
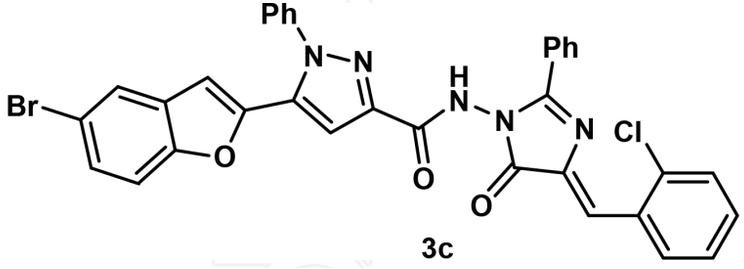
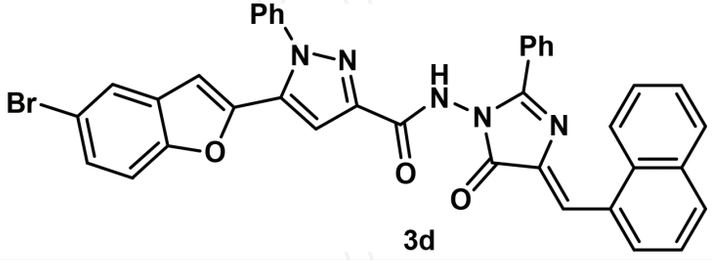
4-(4-(Benzyloxy)benzylidene)-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-5-(5 bromobenzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3e): Yellow crystalline solid; recrystallization solvent, ethanol; mp. 155–157°C; yield, 80%; IR (KBr, v max in cm^{-1}): 3432 (NH), 3062, 2986 (ArH), 1786, 1716 (C═O imidazole), 1501, 1438 (C═C), 1249, 998 (C—O—C), 1160 (C—N—C stretch), 1642 (C═O in amide group), 1595 (C═N), 1110 (C—N). Elemental anal. calcd: for $C_{41}H_{28}BrN_5O_4$; calculated: N, 9.53; found: N, 9.07.

5-(5-Bromobenzofuran-2-yl)-N-(−5-oxo-2-phenyl-4-((E)-3-phenylallylidene)-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide (3f): Yellow crystalline solid; recrystallization solvent, ethanol; mp. 158–160°C; yield, 84%; IR (KBr, v max in cm^{-1}): 3342 (NH), 3034 (ArH), 1783 (C═O imidazole), 1493, 1439 (C═C), 1237, 1068 (C—O—C), 1158 (C—N—C stretch), 1627 (C═O in amide group), 1597 (C═N), 1105 (C—N). Elemental anal. calcd: for $C_{36}H_{24}BrN_5O_3$; calculated: N, 10.70; found: N, 10.25.

5-(5-Bromobenzofuran-2-yl)-N-(4-(furan-2-ylmethylene)-5-oxo-2-phenyl-4,5-dihydroimidazol-1-yl)-1-phenyl-1*H*-pyrazole-3-carboxamide(3g): Yellow crystalline solid; recrystallization solvent, ethanol; mp. 148–150°C; yield, 83%; IR (KBr, v max in cm^{-1}): 3431 (NH), 3062(ArH), 1783 (C═O imidazole), 1496, 1450 (C═C), 1231, 1008 (C—O—C), 1153 (C—N—C stretch), 1641 (C═O in amide group), 1525 (C═N in imidazole), 1079 (C—N). Elemental anal. calcd: for $C_{32}H_{20}BrN_5O_4$; calculated: N, 11.32; found: N, 10.96.

4.2 Common examination of the product

The newly synthesized compounds are soluble in following solvents which are listed in table also identification of newly synthesized compounds has been further confirmed by Lassaigne's test for nitrogen, all compound gives positive test. **Table 1** represents the structure of all derivatives along with solubility solvent and Lassaigne's test.

Sr. no.	Structure and compound code	Solubility	Lassaigne's test for nitrogen
1.	 3a	1,4-Dioxane, DMSO, THF	Prussian blue coloration
2.	 3b	1,4-Dioxane, DMSO, THF	Prussian blue coloration
3.	 3c	1,4-Dioxane, DMSO, THF	Prussian blue coloration
4.	 3d	1,4-Dioxane, DMSO, THF	Prussian blue coloration

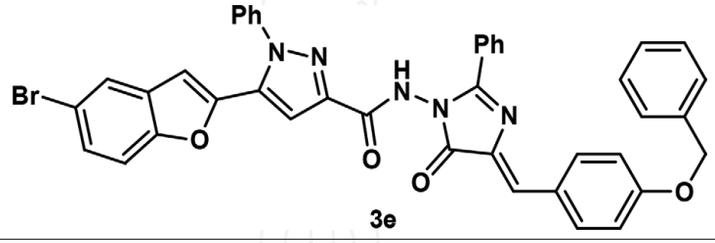
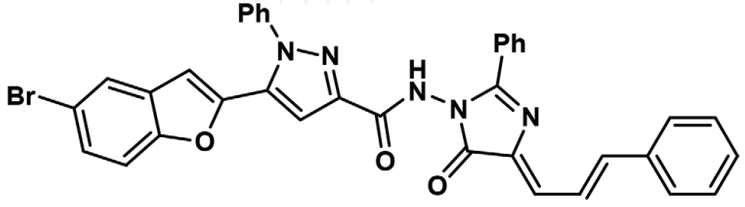
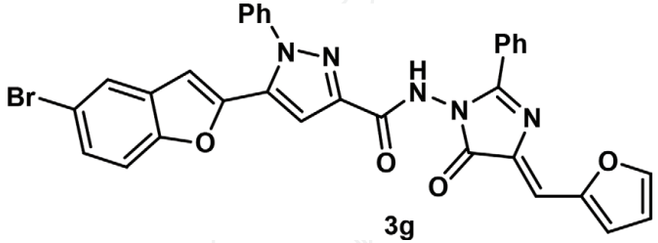
Sr. no.	Structure and compound code	Solubility	Lassaigne's test for nitrogen
5.	 3e	1,4-Dioxane, DMSO, THF	Prussian blue coloration
6.	 3f	1,4-Dioxane, DMSO, THF	Prussian blue coloration
7.	 3g	1,4-Dioxane, DMSO, THF	Prussian blue coloration

Table 1.
Analysis characteristics.

4.3 Physico-chemical characterization

The synthesis of the novel compounds **3a-g** is described in the reaction schemes. Purity of the compounds was monitored by TLC technique. The structures of the newly synthesized compounds were confirmed using chemical transformation reaction, physical data, elemental analysis and different spectroscopic techniques such as IR, ^{1}H NMR and mass. The synthesis of the starting compound, 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazides **(1a-b)** and 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones **(2a-g)** achieved in quantitative yields according to the reference method. The reaction of **1a-b** with **2a-g** (4-(arylidene)-2-phenyloxazol-5(4*H*)-ones) in acetic acid solvent yields compounds **3a-g**.

IR spectrum of this **3a** showed absorption bands at 3197 cm^{-1} due to —NH stretching, disappearance of absorption band due to —NH_2 stretching and two absorption bands at 1719 and 1640 cm^{-1} for two carbonyl groups of imidazoline and aryl amide respectively indicated that 4-(arylidene)-2-phenyloxazol-5(4*H*)-ones has condensed with 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazides to form **3a**. In addition, ^{1}H NMR spectrum of **3a** showed singlet at δ 10.65 ppm for —NH group and disappearance of signal due to —NH_2 group in the synthesized compound **3a** which is expected in carbohydrazide **1a** and also exhibited multiplet at δ 7.22–8.37 ppm due to 21 aromatic protons is in consistent with aromatic protons of **3a**. The % of elements in **3a** was C 74.16, H 4.05 and N 12.37, while its mass spectrum shows molecular ion peaks at *m/z* 550 $[M+H]^+$, 551 $[M+2]^+$, 572 $[M+Na]^+$, 573 $[(M+H)+Na].^+$ which is in good agreement with the proposed structure and molecular formula $C_{34}H_{23}N_5O_3$.

Similarly other imidazolinones (**3b-g**) were also identified on the basis of chemical transformation reaction, physical data, IR and elemental detection. IR spectra of each compound showed characteristics absorption bands for —NH stretching and disappearance of absorption band due to —NH_2 stretching, also showed corresponding band for carbonyl group. Elemental analysis was carried for nitrogen and sulfur of all compounds is found to be in good agreement with the calculated values.

4.4 Antimicrobial activity/profile

Antimicrobial activity means activity of any agent or drug against microbial organism. Microbial organism includes bacteria, viruses, fungi and protozoa. On the basis of their activity against specific microbial organism they termed as like antibacterial (against bacteria) that means they are capable to inhibit the growth of bacteria or to kill the bacteria. Other term is antifungal (against fungi), antiviral (against virus), antiprotozoal (against protozoa). Heterocyclic entities possess different antimicrobial activity. Activity changes by changing structural unit. It is very interesting thing to check out antimicrobial activity of newly synthesized compound. We carried out antibacterial activity of the novel compound (**Figure 4**).

4.5 Potent antibacterial/inhibition profile of 5-oxo-imidazolines (at different concentration) by agar disc-diffusion method

Test solutions were prepared with known weight of compound in DMSO and half diluted suitably to give the resultant concentration of 31–1000 μg/mL [35]. Whatman No. 1 sterile filter paper discs (6 mm) were impregnated with solution and allowed to dry at room temperature. *In-vitro* antibacterial activity was determined by using Mueller Hinton Agar obtained from Himedia Ltd., Mumbai. Petri plates were prepared by pouring 10 mL of Mueller Hinton Agar for bacteria

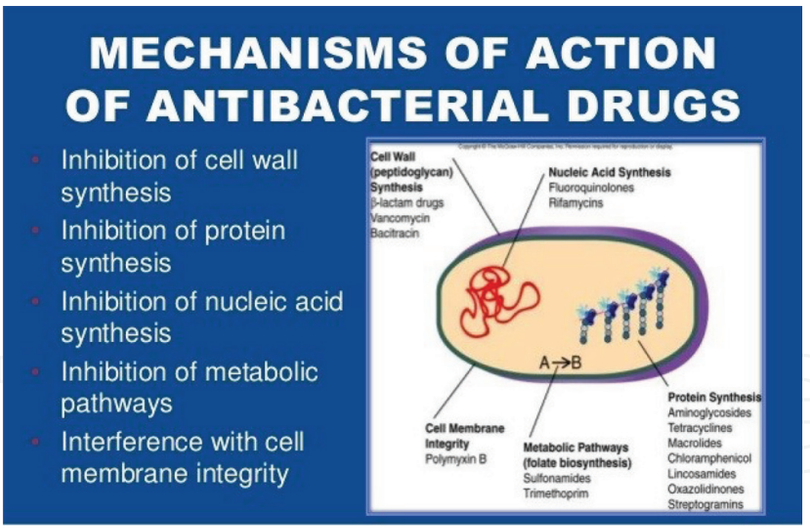


Figure 4.
Antibacterial drug mechanism in cell wall of microbe. Source: Google image.

containing microbial culture was allowed to solidify. The discs were then applied and the plates were incubated at 37°C for 24 h (bacteria) and the inhibition zone was measured as diameter in four directions and expressed as mean. The results were compared using chloramphenicol as a standard antibacterial agent. The results of antibacterial activity (i.e. zone of inhibition in mm) are given in the **Tables 2** and **3**.

4.6 Inhibition profile zone for Gram-positive bacterial strains of tested compound-3a-g

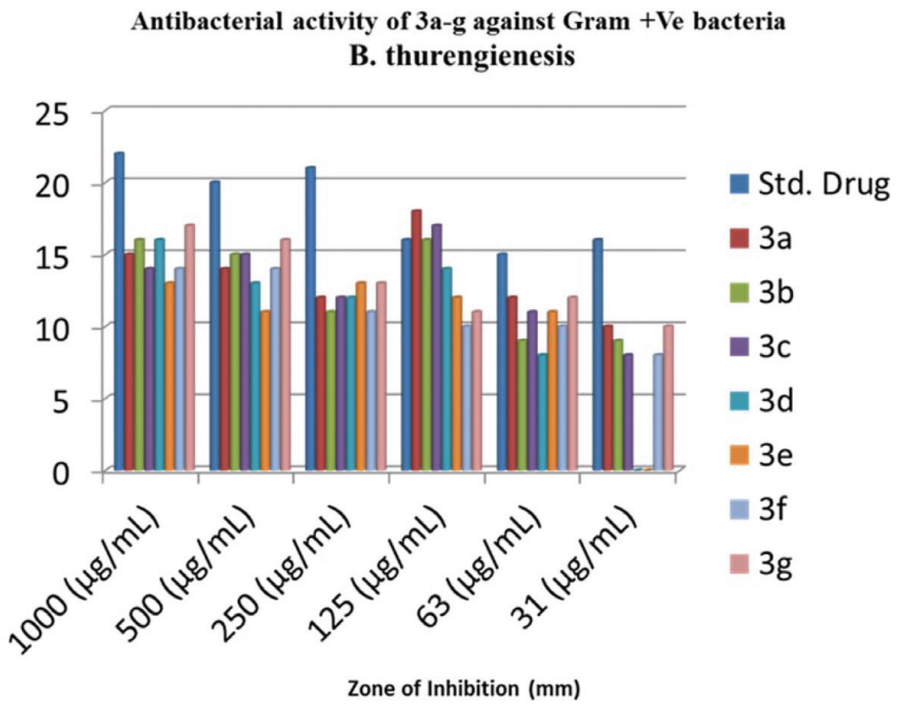
The synthesized compounds **3a-g** were screened for their *in vitro* antimicrobial activity using agar disc-diffusion method against two Gram-positive bacterial

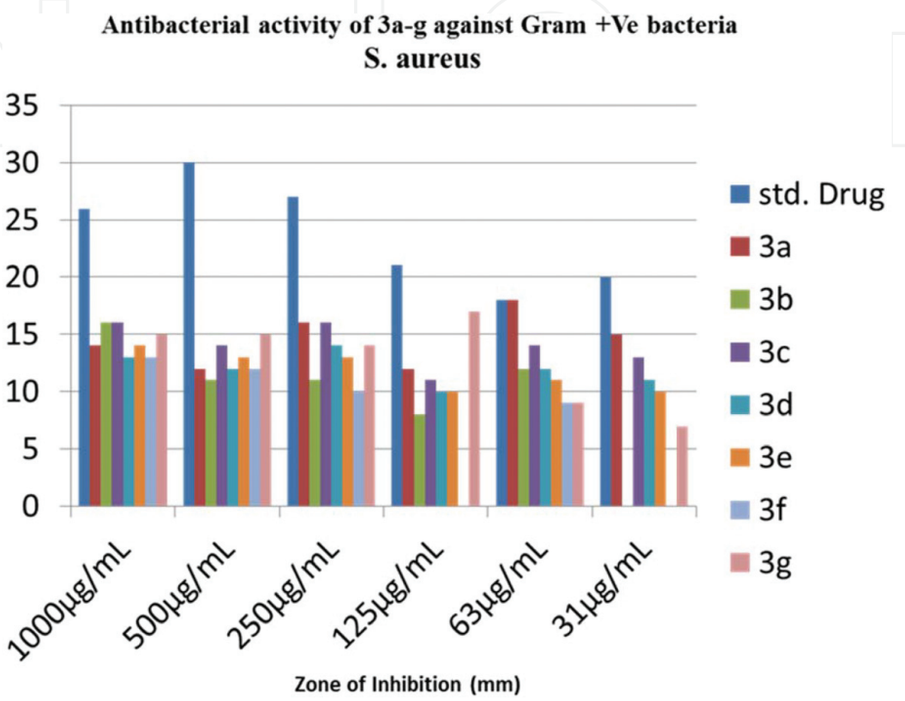
Compd. code	Zone of inhibition (mm)											
	Gram-positive bacteria											
	B. thuringiensis						*S. aureus*					
	Conc. (μg/mL)						Conc. (μg/mL)					
	1000	500	250	125	63	31	1000	500	250	125	63	31
3a	15	14	12	**18**	12	10	14	12	16	12	**18**	15
3b	16	15	11	**16**	9	9	16	11	11	8	12	—
3c	14	15	12	**17**	11	8	16	14	16	11	14	13
3d	16	13	12	14	8	—	13	12	14	10	12	11
3e	13	11	13	12	11	—	14	13	13	10	11	10
3f	14	14	11	10	10	8	13	12	10	—	9	—
3 g	17	16	13	11	12	10	15	15	14	17	9	7
Std. drug	**22**	**20**	**21**	**16**	**15**	**16**	**26**	**30**	**27**	**21**	**18**	**20**

Standard drug: chloramphenicol.
Bold value indicates activity of tested compound is equal or high than standard drug.

Table 2.
Antibacterial activity of 3a-g.

strains such as *B. thuringiensis, S. aureus.* Chloramphenicol was used as standard drug for bacteria. According to antibacterial data obtained the test compounds **3a**–**c** at 125 µg/mL conc. showed excellent activity i.e. equal or higher than the standard drug and other derivatives viz. **3d**–**g** at 125 µg/mL conc. showed good inhibitory activity against *B. thuringiensis*. At conc. 1000, 500, and 250 µg/mL imidazolinone derivatives 3a-g showed good to moderate activity against *B. thuringiensis*, whereas **3d** and **3e** are found to be inactive at 31 µg/mL against Gram-positive bacteria, *B. thuringiensis*. In case of *S. aureus* **3a** exhibit with excellent activity at 63 µg/mL conc. While at 1000, 500, 250 µg/mL concentrations **3a-g** possesses good to moderate activity. Whereas **3b & 3f** are found to be inactive at 31 µg/mL also **3f** found to be inactive at 125 µg/mL against *S. aureus*. Obtained results of *in-vitro* antimicrobial activities of **3a-h** are summarized in **Table 2**.





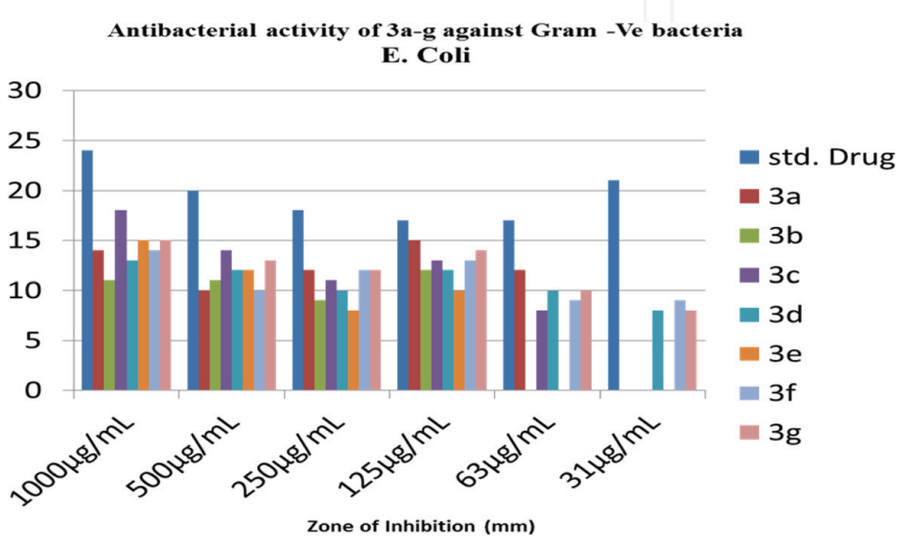
4.7 Inhibition profile zone for Gram-negative bacterial strains of tested compound-3a-g

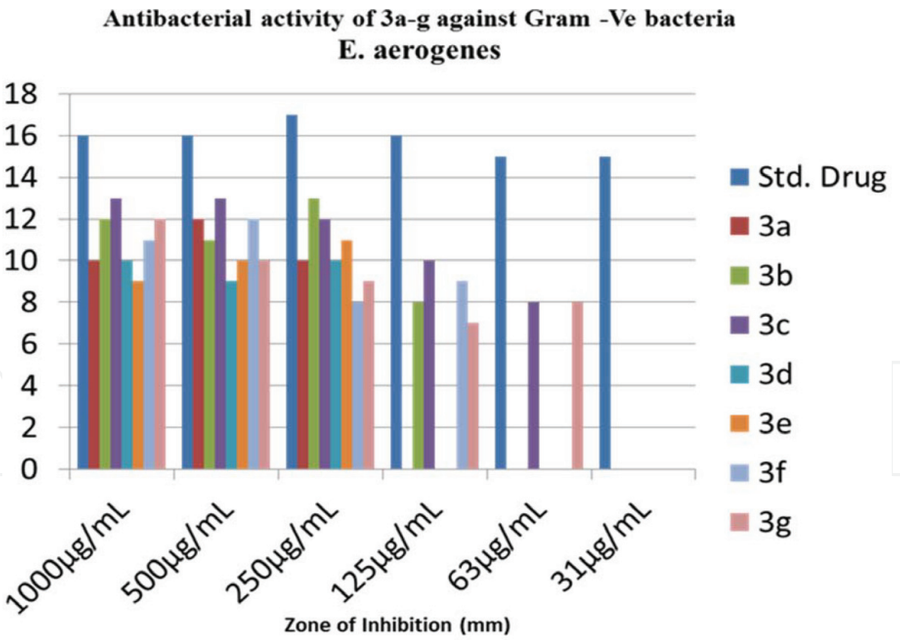
The synthesized compounds **3a-g** were screened for their *in vitro* antimicrobial activity using agar disc-diffusion method against two Gram-negative bacterial strains such as *E. coli, E. aerogenes.* Chloramphenicol was used as standard drug for bacteria. According to antibacterial data obtained the test compounds **3a-g** possesses good to moderate activity at higher concentrations, i.e. 1000, 500, 250 and 125 μg/mL against Gram-negative bacteria *E. coli.* At conc. 63 μg/mL **3a-g** showed good activity while **3b** & **3e** found to be inactive against *E. coli*. At conc. 31 μg/mL **3d, 3f & 3g** showed moderate activity whereas **3a, 3b, 3c & 3e** found to be inactive against *E. coli*. In case of *E. aerogenes,* tested compounds showed moderate activity at higher concentrations while poor activity at lower concentrations. At conc. 125 μg/mL **3a, 3d, 3e** and at 63 μg/mL **3a, 3b, 3d, 3e, 3f** found to be inactive. All the compounds were inactive at a concentration of 31 μg/mL against *E. aerogenes.* Obtained results of *in-vitro* antimicrobial activities of synthesized 5-oxo-imidazolines (**3a-g)** are summarized in **Table 3**.

Compd. code	Zone of inhibition (mm)											
	Gram-negative bacteria											
	E. coli						*E. aerogenes*					
	Conc. (μg/mL)						Conc. (μg/mL)					
	1000	500	250	125	63	31	1000	500	250	125	63	31
3a	14	10	12	15	12	—	10	12	10	—	—	—
3b	11	11	9	12	—	—	12	11	13	8	—	—
3c	18	14	11	13	8	—	13	13	12	10	8	—
3d	13	12	10	12	10	8	10	9	10	—	—	—
3e	15	12	8	10	—	—	9	10	11	—	—	—
3f	14	10	12	13	9	9	11	12	8	9	—	—
3 g	15	13	12	14	10	8	12	10	9	7	8	—
Std. drug	**24**	**20**	**18**	**17**	**17**	**21**	**16**	**16**	**17**	**16**	**15**	**15**

Standard drug: chloramphenicol.
Bold value indicates activity of tested compound is equal or high than standard drug.

Table 3.
Antibacterial activity of 5-oxo-imidazoline compounds (3a-g).





4.8 Mechanism of inhibition/prohibition

Gram-negative bacteria habitually owe low susceptibility as outer membrane of their cell wall not gets blocked/penetrated by drugs easily and factors like amount of peptidoglycan, receptors, and lipids availability, nature of cross-linking, autolytic enzymes activity greatly influence the bio-activity, permeation, and incorporation of the antibacterial drugs. 5-Oxo-imidazoles showed their specificity for polysaccharides, thats present in the outer membrane of many Gram-negative bacteria and so acted selectively toxic for series of *B. thuringiensis*, *S. aureus* bacteria. Mechanistically, once alliance with lipopolysaccharide substrate in outer membrane of *B. thuringiensis*, *S. aureus* bacteria, synthesized imidazolinone: potent antibacterial agent changes their membrane structure, thus enhances permeability and disruption of osmotic balance that ultimately results higher physiological effects.

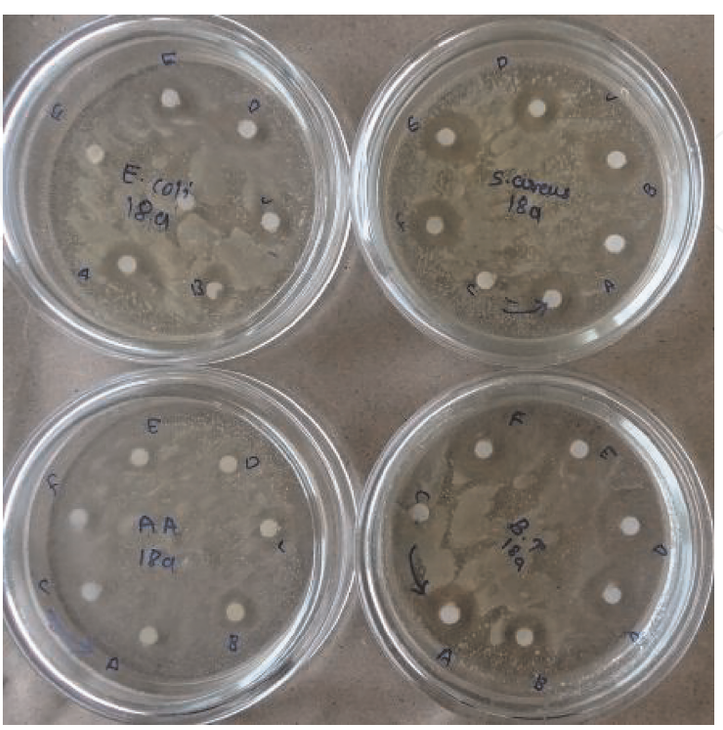


Figure 5.
Inhibition profile zone for four different bacterial strains of tested compound-3a (at different concentration).

Also, alteration like discharge of molecules from interior of *B. thuringiensis*, *S. aureus* bacterial cell inhibits respiration and increased water uptake may leads to cell death. Gram-positive bacteria own too thick cell wall and deny easy access of 5-oxo-imidazoles via their bacterial cell membrane, thus less effective on *E. coli* and *E. aerogenes* series of bacteria. The inhibition profile zone for four different bacterial strains of tested compound-**3a** (at different concentration) 5-oxo-imidazoline compounds are shown in **Figure 5**.

5. Conclusion

Assorted antibacterial agents own certain limitations viz.; resistance/potency, vast types and numbers own different structures besides slightly dissimilar pattern of activity which made it necessary to discover/explore the existing class and functions of almost all the antibacterial agents. Thus, futuristic pathogenic bacterial infections/diseases can be easily cured via promising antibacterial chemotherapeutic agents derive from 5-oxo-Imidazole skeleton. Pursued chapter described antibacterial resistance of 5-oxo-imidazoles mostly against Gram-positive series like *B. thuringiensis*, *S. aureus*. 5-Oxo-imidazoles can act onto simple one-celled bacterial organism that could kill, inhibit, or at least slower down their growth and ultimately can inhibit concern diseases/infections. This chapter focused on helping futuristic researchers, clinicians, and academicians involved in synthesizing and corresponding biological screening of innate activity of certain novel imidazolinone heterocycles. These synthesized 5-oxo-imidazoles restrain potent antibacterial activity may own prospective different therapeutic behavior if developed as advanced drug moiety. Therefore, chapter focus on the basis of chemical structure of 5-oxo-imidazoles. Gram-positive and Gram-negative bacteria showed varied response/susceptibility toward 5-oxo-imidazoles.

Targeted 5-oxo-imidazolines (**3a-g**) a class of imidazolinones are successfully synthesized in good yields and purity checked by physical, analytical and spectral data. Antibacterial screening of 5-oxo-imidazolines (**3a-g**) exhibited a potent bactericidal. Thus, 5-oxo-imidazolines could be powerfully stimulates major advances in remarkable significant chemotherapeutics in medicine, biology and pharmacy. Overall these imidazolinones disturb macromolecules like cytoplasmic membrane covering cytoplasm which acts selective barrier to control internal composition of cell. 5-Oxo-imidazoles in particular interrupted such functional roles of cytoplasmic membrane and ionic outflow that resulted cell destruction/death. Synthesized potent bioactive 5-oxo-imidazoles may open new possibilities in the successful treatment of several diseases due to promising antibacterial profile. So, ample scope exists in further research of imidazolinones especially innate selectivity of 5-oxo-imidazoles needs to carry out their chemotherapy as potent antibacterial aims to target cell membrane of range of Gram-negative bacteria as to derive novel drugs of new millennium.

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