Recent Developments and Biological Activities of 5-Oxo-Imidazolones Derivatives: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Heterocyclic compounds are essential primary units for both the synthetic and natural starting points. 5-oxo-imidazolone is a 5-member ring system that contains 3 carbons and 2 nitrogens that are arranged at 3 and 1 positions, and —C═O at the 5th position of the ring. 5-oxo-imidazolone is known as a privileged molecule because of its all biological potencies. This biological property increased the attention of many investigators to analyze this ring system and expose several activities. The present review aims to outline the various activities reported on the synthesis and the biological potencies of 5-oxo-imidazolone derivatives. 5-oxo-imidazolone is an important pharmacophore in modern drug discovery.

Keywords: 5-oxo-imidazolone; biological activities; pharmacophore.

1. INTRODUCTION

Imidazole (1) ring is a five-member aromatic heterocyclic ring system having molecular formula C₃N₂H₄. It consists of 3 carbon and 2 nitrogen atoms nomenclated at 1ˢᵗ and 3ʳᵈ positions. This aromatic heterocyclic ring is classified as a diazole family because of the

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presence of non-adjacent nitrogen in its ring system.

Ketodihydroimidazoles are oxo-imidazoline derivatives generally well known as imidazolinone, a 5 member ring containing 2-nitrogen atom at 1 and 3 position and −C=O at other positions like 2, 4 or 5 of the ring system. Generally 3 isomers of imidazolinone are reported based on the position of C=O (keto) group, 1H-imidizol-2(5H)-one (2), 1H-imidizol-5(4H)-one (3) and 1H-imidizol-245H)-one (4).

1H-imidizol-5(4H)-one (3) is a 5 member heterocyclic ring system containing nitrogen atoms at 3rd and 1st positions and a keto group at 5th position. It is found in various natural products like alkaloids, histamine, biotin, nucleic acids and forms a critical part in these phytochemical compounds [1].

1H-imidizol-5(4H)-one (3) is also known as 5-oxo-imidazoline which is an unsaturated ring system and the nitrogen analogues of azlactone/oxazolone can also be modified into various amino acids [2,3,4]. 5-Oxo-imidazoline is well established because of its wide antimicrobial activities. Certain imidazolines are valuable organic fragments in blend of numerous regular items just as basic structure blocks in numerous naturally dynamic moieties [5].

The discovery of 2-substituted-5-imidazolones were reported in the year 1988 when Hoffmann [6] synthesized 2-methyl-5-imidazoline (Lysodine) by heating N'-diacetyl ethylene diamine and by using a stream of dry HCL. Ladenburg [7] synthesized the said compounds by mixing 2 equivalents of Sodium salt of acetic acid and 1 equivalent of Ethylene diamine dihydrochloride.

Azalactones form an intermediate stage for synthesizing Imidazolones. The reaction of azalactones with different substituted aromatic amines has focused a great attention now a days for their wide range of pharmacological application and their biological activities.

1.1 Synthesis of Imidazolones

Azalactone readily reacts with various compounds like water, alcohol, amine and hydrogen halides. Azalactones have been widely investigated with various reactants like alcohol [7], thiophenol [8], hydrazinehydrate [9], phenyl hydrazine [10]; aromatic amino acid and ammonia to procure different Imidazolones [11-13].

1. According to one of these methods imidazolones was synthesized by the condensation of substituted azalactone and 1º amine under controlled dry conditions. Different Amides of acylamino acrylic acids was synthesized by the reaction of azalactone and primary amine (5).

The ring closure was found to be affected under a variety of conditions, when R' was H, the action of NaOH preferably converted the amide into the imidazolone [14,15]. When R' was CH₂R, heating is required above the melting point [16]. Various anilides (R'= -C₆H₄R) have been modified into imidazolone derivatives by the use of phosphorus oxychloride [17]. The modifications of amides of saturated α-acylaminoacid into respective imidazolones have not been reported extensively [18]. Benzoylphenylamine amide produced a poor yield, but benzoyl aminoisobutyric acid amide gives a better yield.

2. Formation of imidazolines (7) by aminolysis of the azalactone (6) with appropriate amine has been carried out as shown below [19,20].
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1H-imidazol-2(5H)-one

1H-imidazol-2(4H)-one

1H-imidazol-4(5H)-one

R' - NH₂

POCl₃

R_HC_\text{CONH}_R'\text{NH}_R'\text{CONH}_X

(5)

Ar-HC_\text{CONH}_X

NH₃

Heat

Ar-HC_\text{CONH}_X

(7)

R_HC_\text{CONH}_X

R' - NH₂

Dry Pyridine

R_HC_\text{CONH}_X

(9)
3. Various 5-oxazolones (8) when reacted with primary amines in the presence of pyridine produced respective 5-imidazolones (9) [21].

4. Srivastava et al. [22] reported a novel series of potent 5-imidazolones by fusing equimolar amount of substituted 5-oxazolinones and heterocyclic primary amines at 140°C.

5. New oxazolones were prepared in good yield by using benzoyl glycine, acetic anhydride and anhydrous sodium acetate and appropriate aldehydes. These particular oxazolones were modified to 5-oxo-imidazolines (10) by fusing with 4-methyl cinnamoyl hydrazine [23].

2. BIOLOGICAL IMPORTANCE OF 5-OXO-IMIDAZOLOONES

The 5-oxo-imidazoline ring has been included into a wide range of known biologically active compounds, either as a substituent group or as a replacement of another ring. There are several cases reported in the literature explaining the 5-oxo-imidazoline derivatives for their potent biological activities such as Anticonvulsant [24,25], Sedative and hypnotics [26], Potent CNS depressant [27,28], Antihistamine [29], Antiinflammatory [30,31], Mono Amino Oxidase (MAO) inhibitory [32], Local anaesthetic [33], Potent antiparkinsonian [34], Herbicidal [35], Insecticidal [36], Antibacterial [37,38], Antifungal [39,40].

2.1 Antibacterial and Antifungal Activity

5-Imidazolidinone having C-2, C-4 and N-1 substituted positions, possess different degrees of inhibitory activities against different species of bacteria and fungi. The drastically increasing multi-drug resistant microbes in the past few years have become a serious health issue. Around every one of the places of 5-Imidazolidinone have been investigated to increase the antibacterial and antifungal activity.

Hitendra et al. described in-vitro antimicrobial activity of oxazolidinone (11) and imidazolidinone (12) derivatives against Escherechia.coli, Pseudomonas aeruginosa, staphylococcus aureus, Streptococcus pyogenes and antifungal activity against Candida albicans, Aspergillus niger and Aspergillus clavatus by measuring in MBC and in MFC method in μg/ml. The synthesized compounds were evaluated against standard antibacterial drugs Gentamycin, Ampicillin, Chloramphenicol, Ciprofloxacin, Norfloxacin and antifungal drugs Nystatin and Griseofulvin. Antibacterial and antifungal activity was done by broth dilution method at various concentrations of 1000, 500, 250, 200, 125, 100, 62.5μg/ml respectively. The results proved that the selected compounds exhibited weak antibacterial and antifungal properties when compared with standard drugs Gentamycin, Ampicillin, Chloramphenicol, Ciprofloxacin, Norfloxacin and antifungal drugs Nystatin and Griseofulvin. Compounds (4j, 6f, 7a and 7c) showed better activity MBC of 62.5μg/ml against E.coli, P.aeruginosa and S.aureus when compared with the other all synthesized compounds [41].

Metha et al. produced new imidazolinone derivatives containing benzimidazole (13) and also evaluated their in-vitro antimicrobial potencies against Bacillus megaterium, Streptococcus citreus, Escherichia coli, Salmonella typhosa and Ampicillin using norfloxacin and chloramphenicol as a standard drug. The antifungal activity was performed against Aspergillus Niger using Greseofulvin as a standard agent. They noted that majority of the active compounds possessed a p- chlorophenyl, p- bromophenyl, 2-furyl and 3, 4- dimethoxy groups on the imidazolinone ring [42].
N.C. Desai et al. [43] performed green synthesis and evaluated the anti microbial activity of novel quinoline based imidazole derivatives [43] (14). All the novel compounds were evaluated for their antibacterial activities against different bacterial strains. Compound 3d and 3h having electron withdrawing groups, produced potent antibacterial activity (MIC was found to be 25 µg/mL) than standard molecule ampicillin against Gram-negative bacteria E. coli. Moreover, nitro, hydroxy and phenyl derivatives were found to be as potent as reference drug against E. coli.

Solankee et al. studied potential antimicrobial agents of 5-imidazolones (15) and showed that compounds 3a, 3d, 3e, 3f and 3i having very good activity (25-150 µg/ml) against gram positive bacterial strain S. aureus and S. pyrogenes evaluated against standard drug.
ampicillin, compounds 3d and 3f showed better activity activity (25-125 µg/ml) against gram negative bacterial strain *E. coli* and *P. aeruginosa*. All other molecules produced moderately active results against all bacterial strains. Compounds 3d, 3g, 3h and 3j showed very good antifungal activity *C. albicans* when compared with standard drug griseofulvin [44].

Novel 1-N-4'-4''-difluoro diphenyl-methyl]piperazine-1'-yl]-4-arylidene-2-phenyl-5-oxo-imidizoline derivatives (16) reported by M D Savaliya et al. [45] were found to inhibit the growth of various bacterial and fungal species. The results confirmed that compounds 3a, 3d, 3f, 3h, 3i and 3j exhibited better antibacterial and antifungal activity as compared to standard antibiotics ampicillin, chloramphenicol, norfloxacin and griseofulvin at the concentration of 50 mg/mL.

Osman et al. synthesized various derivatives containing both aryl sulfonate and imidazolone moieties (17-22) in the same molecule and checked their antimicrobial activity [46]. All the compounds were exposed to biological screening and they showed potent antibacterial and antifungal activity which were comparable to standard drugs. The results for antibacterial activities revealed that, most compounds exhibited good activities against the reference chemotherapeutics, where 3, 5b, 5c, 6a, 7b, 7c, and 8a exhibited good activities against *Bacillus Thuringenesis* and compounds 3, 5a, 5c, 6a, 7b, and 8a exhibited good activities against *Klebsiella Pneumonia*. Antifungal activities of compounds 3, 4, 6a, 6b, 6c, 7c, 8a, and 8c exhibited good activities against the *Trichoderma Herzianum* and *Trichoderma Virdi*. A comparison of antibacterial and antifungal activities of compounds with their structures revealed that, the compounds that bearing aryl sulfonate and imidazolone moieties in the same molecule exhibited significant activity against *Bacillus Thuringenesis*, *Klebsiella Pneumonia*, *Trichoderma Herzianum* and *Trichoderma Virdi*.

![Diagram](image-url)

Where R = Substituted phenyl (3a-j)
Harshad et al. synthesized twenty four 3'-quinolinyl substituted imidazole-5-one derivatives and evaluated for antimicrobial activities against *E. coli, B. Subtilis, B. Cereus, A. Parasiticus, S. rolfsii* [47]. Most of the prepared imidazole-5-one derivatives (23, 24) revealed good to moderate antibacterial inhibition against tested strains taking ampicillin as a reference drug, except compound 6q (R1 = OCH3, R2 = Ph, X = N−
CH$_2$CH$_3$) found potent against bacterial species *E. coli*.

Antibacterial activity of some novel 5-imidazolones had been studied by Anjani Solanki *et al.* against *S. aureus*, *B. subtilis*, gram positive bacteria and *E. coli*, *S. paratyphi*-B gram negative bacteria [48]. The results demonstrated that introduction of a chloro group at 2$^{nd}$ position (25) decreases the antibacterial activity of the compound for all bacterial strains. Addition of chloro group at 3$^{rd}$ and 4$^{th}$ position gives satisfactory results. In case of Gram-positive bacteria, substitution of methoxy group at 4$^{th}$ position increases antibacterial activity of the compounds. In case of Gram-negative bacteria, substitution of methoxy group at 4$^{th}$ position decreases the antibacterial activity of compounds.

Murlidhar *et al.* evaluated the biological activities of novel 5-oxo-imidazolines containing azo linkage (26) and proposed that these compounds are having good activity against the human pathogenic species like *B. magatherium*, *B. subtilis*, *E. coli*, *P. vulgaris*. Most of compound exhibited moderate activity against both gram positive and gram negative bacteria. Few of them had poor activity and the other compounds were inactive against *Protius vulgaris* [49].

N. C. Desai *et al.* reported a new series of novel 5-imidazolinones (27, 28) and investigated their antimicrobial activity [50]. Among all compound 4a, 4b, 4i, 4j, 4k, 4q and 5e were active against *E. coli* and compound 4b and 5e were active against *P. aeruginosa*. Compound 4k was active against *S. aureus* and 6m was also active against *S. pyogens*. Moreover compound 4f, 5b, 6f, 6l, and 6m were active against fungi strains. Based on these results they reported that presence of groups like OH, OCH$_3$, NO$_2$, Cl and Br increased the antibacterial and antifungal activities.
2.2 Anticancer Activity

Heba et al. tested a series of 4-(3-Bromo-4-hydroxybenzylidene)-2-aryl-1H-1-phenyl-imidazol-5(4H)-ones (3a, b) and its acetate derivatives (4a, b) for possible cytotoxic activity in human breast tumour cells (MCF-7) and human liver carcinogenic cells (HePG2)[51]. Molecules 3a, 3b (29) were found to be moderately potent against HePG2 cells (IC\textsubscript{50} = 10.9 to 15.8 µg/ml) and compounds 4a, 4b (30) were found to be least potent against MCF-7 and HePG2 cells when compared with the standard drug vinblastine.

Sudheer et al. proposed the synthesis and evaluations of imidazolidinidine analogues of 2-aminochromones [52]. The in vitro cytotoxicity studies were carried out by using MTT assay on two cell lines, which revealed that the conversion to imidazolidinones has increased the cytotoxic activities of aminochromone. Among all, the compound 6c [4-(3,4-dimethoxybenzylidene)-1-(4-oxo-2-phenyl-4H-chromen-6-yl)-2-phenyl-1H-imidazol-5-5(4H)-one, (31) showed potent activity with an IC\textsubscript{50} value 19.78µg/ml. It is worth mentioning here, that the most promising compound had two methoxy groups in their structure.

Sudheer et al. revealed the synthesis of imidazolidinidine analogues of 2-aminoflavone and their derivatives, also evaluated their cytotoxic activity [53]. Fundamental in vitro cytotoxicity considers did utilizing MTT and SRB tests on 2 distinctive cell lines uncover that the transformation to the imidazolidinidine analogues upgraded the cytotoxic capability of aminoflavone. Of the analogues tested, compound 7d [4-(3,4-dimethoxybenzylidene)-1-(4-oxo-2-phenyl-4H-chromen-6-yl)-2-phenyl-1H-imidazol-5-5(4H)-one] (32) showed promising degrees of action with an IC\textsubscript{50} worth of 9.87 µg/mL. It is critical that the most dynamic compound had two methoxy bunches in its design.

Solankee et al. synthesized some new 1-(2',3'-dimethyl-1'-phenyl-3'-pyrazoline-5'-one-4'-yl)-2-phenyl-4-(substitutedbenzylidene)-5-imidazolones (33) are prepared by refluxing the mixture of 5-oxazolone derivatives with 4-amino antipyrine in pyridine. The synthesised compounds are tested for their anticancer activity [54].
Pai et al. synthesized and reported various substitutions of imidazolones, their in vitro anticancer activity on human cervical cancer cell lines (HeLa) by using MTT method at various concentrations of 12.5 – 100 µg/mL. Compound 3CBRS (34) showed IC$_{50}$ value of 14.56 µg/mL, which was comparable against standard Cisplatin (6.58 µg/ml). Other derivatives showed IC$_{50}$ value above 100. The compound 3CBRS displayed a good growth inhibitory activity.
because of the presence of halogen substituted thiazol ring on Imidazolone ring. This compound was also reported to be active in preventing the growth of tumor cells [55].

**2.3 Anticonvulsant Activity**

Sudha et al. proposed a novel series of substituted imidazolinone derivatives (35) and evaluated their in vivo anticonvulsant activity by maximal electroshock (M.E.S) model using phenytoin as standard drug. Among all, the compounds 3b, 3c and 3g compounds showed promising anticonvulsant activities. The finding revealed that the presence of electron withdrawing groups at the para position of aromatic ring in 3b, 3g compounds and also 4c derivative show good activities near to the standard phenytoin because of the presence electron donating (4-OCH₃) group at para position increases electron density in benzene ring [56].

Some novel imidazolinone derivatives were also reported by Moorthy et al. and predicted in silico metabolic and toxicity as potent anticonvulsant agents. The anticonvulsant activity of the compounds was reported. Among all the compounds tested, maximal protection was reported for compounds with p-OCH₃ (IVa), p-OH (IIIa) (36) substitution in phenyl ring on the 4th positions of the imidazolinone ring of series bearing sulfamethoxazole moiety, and p-OCH₃ (IVb), o-Cl (Vb) (37). It is important to mention that the majority of the compounds produced significant activity [57].

Mohamad et al. synthesized 1H-Imidazol-5(4H)-one derivatives (38) with low neurotoxicity property. The compounds with benzylidene a furfurylidene groups at R¹ has contributed significantly to the protection against seizures. Therefore the anticonvulsant activity deemed less sensitive to variations at R² group [58].

Joshi et al. synthesized some novel imidazolinone derivatives (39). These compounds are evaluated for their anticonvulsant activity [59]. Out of 15 compounds 13 compounds were tested for their in vitro anticonvulsant activity [60]. It revealed that compound IIb, IIc and IVf were most potent with maximum protection and minimum mortality rate. Compounds Ila, IIIb and IIIe displayed significant activity (provided 80% protectivity) while other compounds exhibited moderate activity.

Pandey et al. synthesized 1, 2, 4-Trisubstituted-5-Imidazolones (40) and reported their anticonvulsant activity. These results showed that introduction of a substituent in the phenyl nucleus of benzylidene moiety increased the anticonvulsant activity [61].

Anticonvulsant Properties of 1, 2, 4-Trisubstituted 5-Imidazolones (41) were studied using pentylenetetrazole-induced convulsions. Verma et al. noted that anticonvulsant activity of these compounds and their 24 hr pentylenetetrazole-induced mortality had not shown any association between increased protection from convulsions and decreased mortality in experimental animals [62].

![Chemical structure](image-url)

3a= -H, 3b= -4-NO₂, 3c= -4-OCH₃, 3d= -4-Cl, 3e= -3-NO₂, 3f= -3,4-diOCH₃, 3g= -N(CH₃)₂, 3h= -2-OH

(35)
Structures: I = H, II = p-dimethylamino, III = p-OH, IV = p-OCH₃, V = o-Cl, VI = o-OH

R¹ = Phenyl, 4-chlorophenyl, 4-methoxyphenyl, 2-furyl
R² = phenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 4-fluorophenyl, benzyl
2.4 Anti-Inflammatory and Analgesic Activity

Inflammation constitutes a complex biological response to the harmful stimuli and is associated with many other pathophysiological conditions. In response to the stimuli, macrophages release various pro-inflammatory molecules like free radical nitric oxide (NO). After the introduction of various successful anti-inflammatory medicines on world markets belonging to the selective COX-2 inhibitors like Celecoxib, Rofecoxib, Valdecoxib, Lumiracoxib and Etoricoxib, Rofecoxib (Vioxx)™ and valdecoxib (Bextra)™ were removed subsequent to evidence of atherothrombotic cardiovascular adverse effects (AEs) [63]. Rofecoxib caused the accumulation of oxidized LDL and 20-HETE, two biomarkers that are involved in atherosclerotic events. Celecoxib was not found to produce same metabolic products and hence, less cardiovascular associated risk was reported. To solve the above mentioned side effects the research moved towards development of new chemical classes of anti-inflammatory molecules which are made to act through inhibition of COX-2 [64]. Rapid progress in the discovery of novel anti-inflammatory agents may depend on their in vivo anti-inflammatory activities compared to ulcerogenic and other side effects [65]. Moustafa et al. synthesized novel 1, 2-diaryl-4-ylidene-5-4H-imidazolone with comparable anti-inflammatory potencies to reference NSAIDs, but with controlled ulcerogenic properties [66]. Interestingly compound (42) which was sub substituted with fluoro group at 4th position of aryl ring was as potent as the reference meloxicam with minimum ulcerogenic side effects on rats at 10mg/kg.

Series of 4-benzylidene-1-(4-oxo-4H-chromen-2-yl)-2-phenyl-1H-imidazol-5(4H)-one exhibited significant carrageenan-induced paw and rats pleurisy edema models of acute inflammation. 4-(3, 4-dimethoxybenzylidene)-1-(4-oxo-4H-chromen-2-yl)-2-phenyl-1H-imidazol-5(4H)-one (43) highly active compound among the imidazolidinone analogues synthesized with a % inhibition value of 52.17. The % inhibition values obtained with these active compounds were very much comparable with that of the standard drug ibuprofen (67.14%). It was noticed that the analogue which contain two methoxy groups registered the highest activity in comparison with other analogues. The results obtained suggest that the presence of methoxy and hydroxy
groups have an influence on the anti-inflammatory activity [67].

4-(3,4-dimethoxybenzylidene)-1-(4-oxo-2-phenyl-4H-chromen-6-yl)-2-phenyl-1Himidazol-5-one (44) was found to be associated with lesser degree of anti-inflammatory activity among the all of the imidazolidinone analogues with reduction of paw volume as low as 0.23 mL [68].
2.5 Anthelmintic Activity

Yellasubbaiah et al. synthesized some novel imidazolidinone derivatives (45) and tested for the in vitro anthelmintic activity. Among the all synthesized compounds, compound 3g showed most potent activity. The compound 3b, 3d, 3f demonstrated paralysis as well as death of worms at a time comparable to albendazole at 62.5 μg/ml, 125 μg/ml, 250μg/ml, and 500μg/ml &1000 μg/ml concentrations [69].

Maneshwar, et al. investigated 4-(4-Methyl-benzyldene)-5-oxo-2-phenyl-imidazolidine-1-carbothioic acid (2-oxo-1,2-dihydro-indol-3-ylidene)-hydrazide derivatives (46) which showed interesting stereoselective anthelmintic activities. All the synthesized compounds were screened for in vitro anthelmintic activity was carried out on earthworms. The compounds with electron withdrawing groups like Cl, NO₂ at the para position of the aryl ring exhibited higher in vitro anthelmintic activity [70].

Srinivas et al. Synthesized novel Fluorobenzothiazole comprising sulfonamido imidazolinone derivatives (47,48) and screened for in vitro anthelmintic activity. Among the compounds tested; V A1, V A3, V A4, V A11, V A12 and VII A1, VII A9, VII A11, VII A12 showed significant paralytic time of earthworms, compared to standard drug albendazole, at all 0.1, 0.2, 0.5 % concentrations of compounds [71].

\[ \text{R} = \text{-H, -OCH}_3, \text{-Cl, -NO}_2, \text{-CH}_3 \quad \text{R}_1 = \text{H, -OCH}_3 \quad \text{R}_2 = \text{-H, -Cl} \]

(44)

(45)
3. CONCLUSION

5-oxo-imidazoline nucleus is a heterocyclic compound which is an important pharmacophore in modern drug discovery, the synthesis of novel 5-oxo-imidazoline derivatives remains the main focus of medicinal research since past and found potent in various pharmacological and pathological conditions. This review has highlighted the use of 5-oxo-imidazoline derivatives having antimicrobial activity, anticancer activity, anticonvulsant activity, anti-inflammatory activity and anthelmintic activity.

The antimicrobial activity of 5-oxo-imidazoline proved to be a varied degrees of inhibition against Gram-positive and Gram-negative bacteria showing inhibition as good as to the standard drugs in some of the 5-oxo-imidazoline derivatives with electron withdrawing substitution on aromatic ring on C-4 position and C-1 positions.

Anticancer activity of 5-oxo-imidazoline derivatives on various human breast tumour cells (MCF-7) and human hepatocellular cancer cells (HePG2), HeLa cancer cell lines and in vitro cytotoxicity studies carried out using MTT assay. From the literature it can be concluded that 5-oxo-imidazolines with various substitutions like methoxy and halogen on aromatic ring at C-4 positions exhibit more potent anticancer activity.

5-oxo-imidazolines also explored for their anticonvulsant activity by maximal electroshock (M.E.S) model using phenytoin as standard drug. Most of the derivatives showed good anticonvulsant activity.

The anti-inflammatory and anthelmintic profile of 5-oxo-imidazolines was studied but very few of the derivatives showed potent anti-inflammatory and anthelmintic activity.

From these findings, the importance of nucleus is exposed. But there are various other potencies yet to be revealed in this promising moiety as a number of other molecular targets are available for 5-oxo-imidazoline. Present literature review revealed that 5-oxo-imidazoline has diverse biological activity, and interesting synthetic routes have increased the attention of various researchers.

CONTENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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