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Review Article

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# A CONCISE REVIEW ON THE PREPARATION, BIOLOGICAL ACTIVITY AND MEDICINAL APPLICATIONS OF SUBSTITUTED IMIDAZOLES

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**ABSTRACT**

The objective of the review is to describe the synthesis and applications of some important substituted imidazoles which are found to exhibit medicinal value in recent years because of their bioactivity. Imidazole and its derivatives are important in the drug discovery. It occurs in purines & in histidine which is a proton source in the biochemical transformations, and as a part of many natural products such as: pilocarpin alkaloids and corrin based vitamin $B_{12}$. They are also found in tuna fish, milk products, egg yolk and marine sponges. This group of heterocycles have many biological functions; hence, find prime importance in pharmaceutical industry.

## 1. INTRODUCTION

Medicinal chemistry is concerned with determination of the chemical structure of the synthetic molecules and the chemical compounds derived from natural sources and their influence on the bioactivity. It involves preparation of new chemicals by the modification of known drugs and other bioactive molecules and then finding enhancement in their biological function,[1,2] and study of their mode of action.[3] Many synthetic and natural products have nitrogen based five-member heterocyclic rings in them.[4] The literature survey of the last two decades on such molecules reveals that, there is a lot of research and development work going on, which involves the modification of existing chemical matrices and molecular models towards the design of novel drugs.[5]

Debus *et al*., in the year 1858 reported the first synthesis of imidazole from ammonia, a molecule of aldehyde and a diketone; it was found to be amphoteric, and undergoes electrophilic and nucleophilic substitution reactions easily. It was found to be stable to heat, under acid and basic conditions, and towards reduction as well as oxidation reactions. Imidazole occurs in purines & in histidine which is one of the proton sources in the biochemical transformations, and as a part of many natural products such as: pilocarpin alkaloids and corrin based vitamin $B_{12}$ and in biotin.[6] They are also found in tuna fish, milk products, egg yolk and marine sponges.

Other imidazole based compounds have been known longer: allantoin (1800), parabanic acid (1837) prepared from uric acid. Since then, this particular heterocyclic group of compounds have been hugely investigated and imidazoles find tremendous applications today.[7]

Substituted imidazoles are important in the heterocyclic chemistry and have attracted attention in recent years due to their biological properties and application in medical and pharma industries.[8]

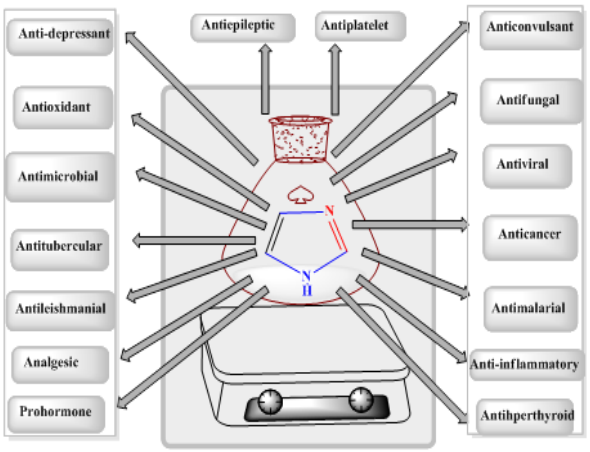


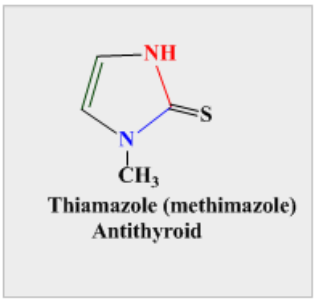

Figure-1: Imidazoles therapeutic uses

The imidazole based drugs have encouraged the organic chemists to prepare many novel chemotherapeutic agents throughout the world. These drug molecules have broadened their scope as clinical medicines as well. A variety of imidazole derivatives exhibit antileishmanial, antiviral, antibacterial, anti-depressant, anti-inflammatory, antidiabetic, antimalarial, anticancer, antitubercular, anticonvulsant, antioxidant, antifungal activity and act as anticoagulants (**Fig. 1**).[9–15]

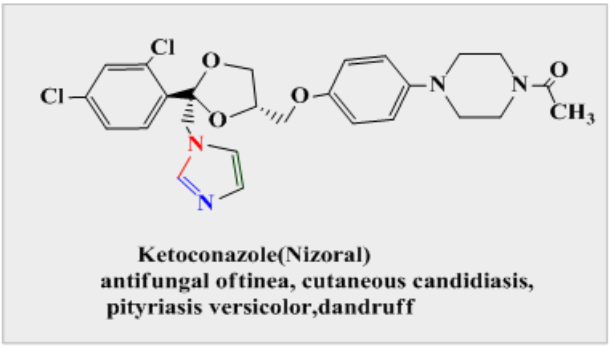
The mini-review presents a concise overview on the most relevant applications, synthetic routes, biological

properties and therapeutic uses of imidazole-derived heterocyclic systems which have encouraged numerous medicinal and organic chemists to develop various synthetic methods for a varied number of novel imidazole derivatives which are useful in chemotherapy.[16]

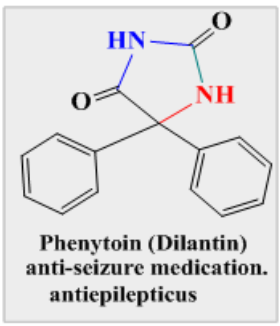
Various biologically active synthetic compounds having imidazole moiety in their structure are shown to exhibit analgesic, antiparasitic, platelet aggregation inhibiting and antiepileptic activities also.[17–21] Imidazole can be found in many other drugs such as: Clotrimazole (Canesten), Ketoconazole (Nizoral)[22], Phenytoin Dilantin, dacarbazine[23], Metronidazole[24], Cimetidine[25], Phenytoin[26], Thyroliberin[27], Methimazole[28], Pilocarpine[29], and Etomidate[30] as shown in the **Fig. 2**; which are used as antineoplastic, antibiotic, antiulcerative and as benzodiazepine antagonist agents. They are also used as prohormones, antiperthyroids, muscarinic receptor antagonists and as hypnotic agents.



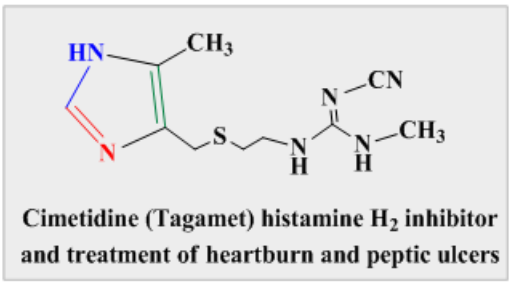
Thiamazole (methimazole)
Antithyroid



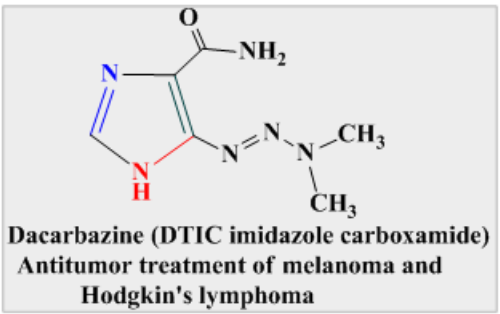
Ketoconazole(Nizoral)
antifungal oftinea, cutaneous candidiasis,
pityriasis versicolor,dandruff



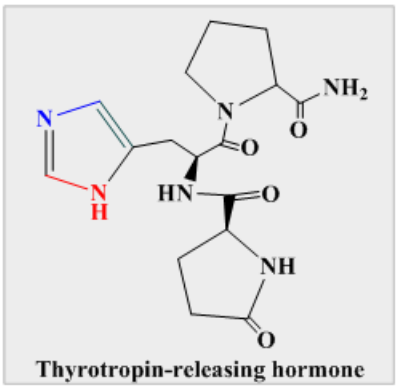
Phenytoin (Dilantin)
anti-seizure medication.
antiepilepticus



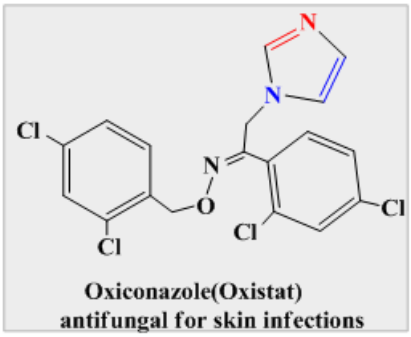
Cimetidine (Tagamet) histamine $H_2$ inhibitor
and treatment of heartburn and peptic ulcers



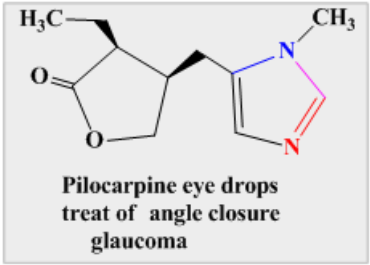
Dacarbazine (DTIC imidazole carboxamide)
Antitumor treatment of melanoma and
Hodgkin's lymphoma



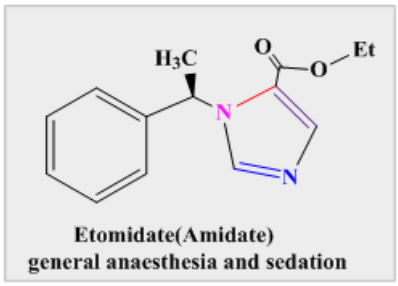
Thyrotropin-releasing hormone

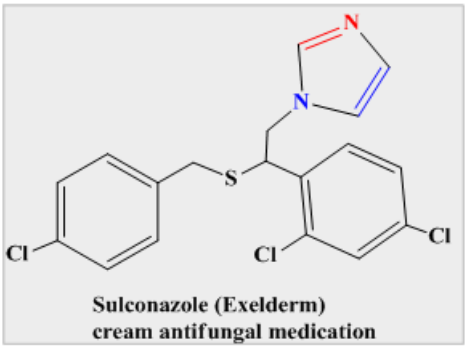


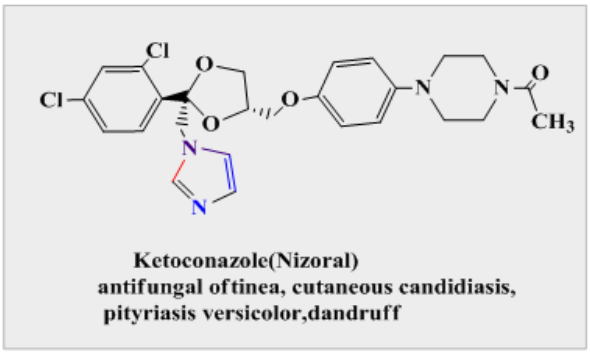
Oxiconazole(Oxistat)
antifungal for skin infections



Pilocarpine eye drops
treat of angle closure
glaucoma



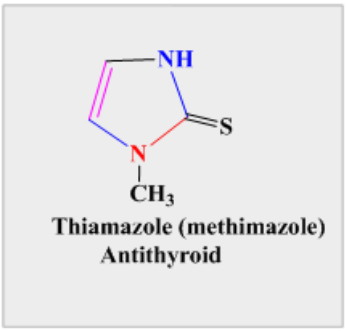
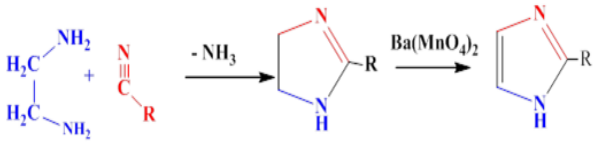




**Figure 2: Some important marketing Drug molecules containing imidazole scaffold.**

**Some general methods of synthesis of imidazole derivatives**

**1. *Imidazoline dehydrogenation***

Substituted nitriles and ethylenediamine react to give imidazolines, which on reaction with $Ba(MnO_4)_2$ yield 2-substituted imidazoles (**Scheme-1**).[31]



Scheme 1

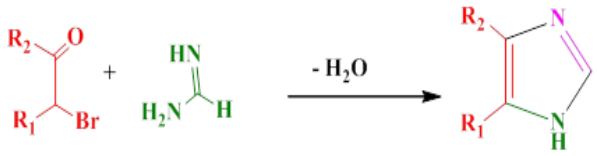
**2. *From α-amino ketones***

α-Amino ketones cyclise readily when treated with acetic anhydride in the presence of $NH_4OAc$ to give imidazoles as presented in the **Scheme-2**.[32]

Scheme 2

**3. *From imidine and α-bromoketones***

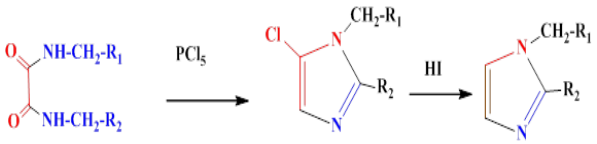
The reaction between imidine and α-bromoketones takes place to give diphenylimidazoles readily (**Scheme-3**). Phenacyl bromide reacts with benzimidine to afford 4,5-diphenylimidazole in high yield.[31]



Scheme3

**4. *Wallach synthesis***

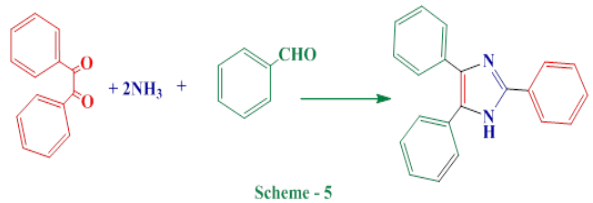
*N*,*N*-Dimethyloxamide and its derivatives with $PCl_5$ give a chlorine containing intermediate which on treatment with HI give *N*-substituted imidazoles as shown in the **Scheme-4**.[33–36]



Scheme 4

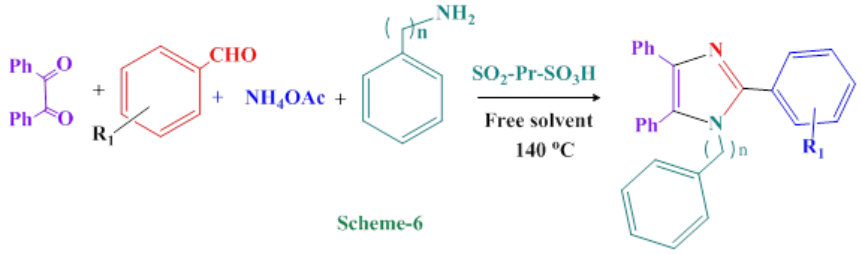
**5. *Radziszewski synthesis***

In this reaction, condensation of benzil with benzaldehyde in the presence of excess ammonia yields 2,4,5-triphenylimidazole as presented in the **Scheme-5**.[37,38]



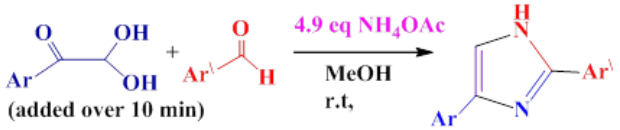
Scheme - 5

6. $SiO_2$-Pr-$SO_3H$ has been used by Ziarani *et al*., as a catalyst in the synthesis of 1,2,4,5-tetrasubstituted imidazoles by a one-pot four-component reaction of benzil, substituted benzaldehydes, substituted primary amines and ammonium acetate under solvent-free condition as shown in the **Scheme-6**.[39]



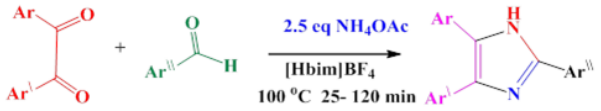

Scheme-6

7. Biologically active 2,4(5)-diarylimidazoles are prepared by a simple and efficient approach by a one-pot three-component reaction from α-keto-*gem*-diol, an araldehyde and 4.9 eq. $NH_4OAc$ is also reported (**Scheme-7**).[40]




Scheme-7

8. Siddiqui, S. A. *et al*., (2005) have synthesised 2,4,5-triarylimidazoles by a rapid one-pot three-component synthesis from 1,2-diaryl-1,2-diketones, arylaldehydes and 2.5 eq. $NH_4OAc$ in the presence of an ionic liquid. This one-pot methodology offers recycling of the ionic liquid (**Scheme-8**).[41]




Scheme-8

**Literature survey on the biological activity and therapeutic uses of imidazole derivatives**

Imidazole and its derivatives are most widely used as therapeutic agents and have shown a broad spectrum of activities against several pathogens. Drugs which contain the imidazole nucleus such as: ketoconazole, metronidazole and cimetidine, are used to treat fungal infections, bacterial infections and gastric ulcers respectively. On the basis of literature survey, imidazole derivatives have shown different pharmacological activities and therapeutic uses when compared with other five membered heterocycles.

***Antibacterial Activity***

1. Vijesh *et al*., (2011) have synthesized, characterized and studied the antimicrobial activity of some new pyrazole incorporated imidazoles, and carried out the *in vitro* antibacterial activity of the synthesized compounds. *Salmonella typhimvrium*, *Escherichia coli*, *Clostridium perfringens*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus subtilis* were investigated for the activity. The antibacterial showed that, some of the prepared compounds exhibited good inhibition against the mentioned microbial strains (**Fig. 3**).[42]

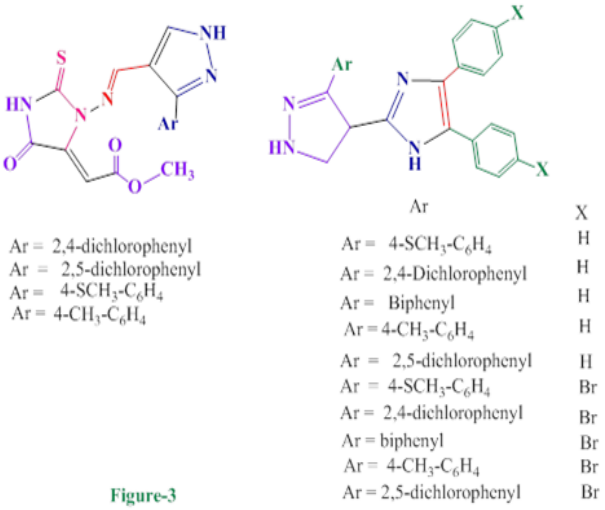
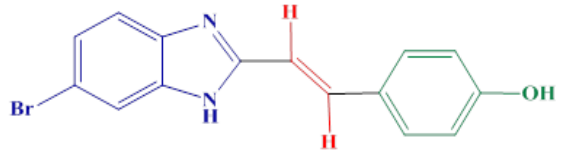



Figure-3

2. Ramya, V. and others (2009) have prepared a series of novel substituted benzimidazoles and subjected them for antibacterial property of *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Enterococcus faecalis*; and anti-fungal property of *Aspergillus fumigates* and *Candida albicans* which showed reasonably good activity when compared to the standard of reference ciprofloxacin (**Fig. 4**).[43]



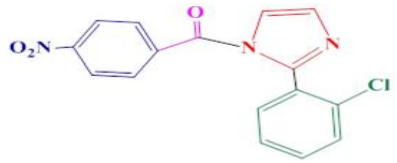

4-((E)-2-(6-bromo-1H-benzo[d]imidazol-2-yl)vinyl)phenol

Figure -4

***Anti fungal activity***

1. Deepika, S. *et al*., (2009) have reported the synthesis of substituted-1H-imidazole and substituted imidazolyl menthanone derivatives and have been shown to exhibit antimicrobial activity towards gram negative, gram positive bacteria and fungi using Norfloxacin

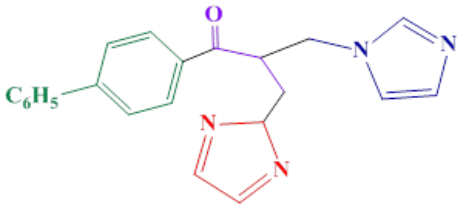
as a reference compound and the compound presented in the **Fig. 5** is found to be the most active molecule.[44]



(2-(2-chlorophenyl)-1*H*-imidazol-1-yl)(4-nitrophenyl)methanone

**Figure -5**

2. Daniele , Z. *et al*., (2007) have prepared the 1*H*-imidazol-1-yl 2*H*- imidazole-2-yl derivative (**Fig. 6**), and verified its anti-mycobacterial and antifungal activities. The prepared compound showed the best result against *Candida glabrata* and *Candida albicans* when compared with the Miconazole which was used as a standard drug.[45]

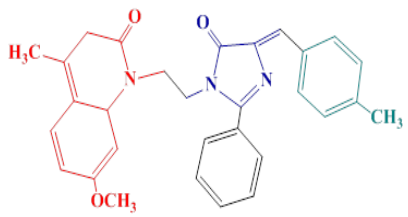


2-((1*H*-imidazol-1-yl)methyl)-1-([1,1'-biphenyl]-4-yl)-3-(2*H*-imidazol-2-yl)propan-1-one

**Figure -6**

***Anti-inflammatory, Analgesic and COX-2 Inhibitor activity***

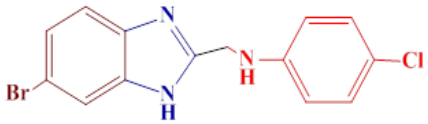
1. Raghavendra *et al*., (2011) have synthesized an imidazoloquinoline analogue which was subjected for ulecerogenic and anti-inflammatory activity determination; and showed to be a potent drug towards inflammation when compared with the standard.[46]



(*Z*)-7-methoxy-4-methyl-1-(2-(4-(4-methylbenzylidene)-5-oxo-2-phenyl-4,5-dihydro-1*H*-imidazol-1-yl)ethyl)-1,8a-dihydroquinolin-2(3*H*)-one

**Figure- 7**

2. Kavitha, C. S. *et al*., (2010) reported the preparation of a number of 2-methylaminophenyl benzimidazoles and the newly synthesized compound (**Fig. 8**) was screened for anti-inflammatory and analgesic activity and found to show considerably high analgesic property when compared to the standard drug nimesulide.[47]



*N*-((6-bromo-1*H*-benzo[*d*]imidazol-2-yl)methyl)-4-chloroaniline

**Figure- 8**

3. Husain, A. *et al*., (2013) have prepared and studied the biological evaluation of di- and tri-substituted imidazoles; and the following 1*H*-imidazole (**Fig. 9**) exhibited good and safer anti-inflammatory and antifungal activity.[48]

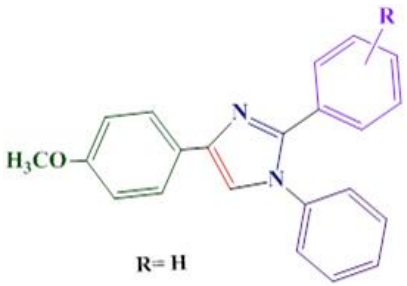
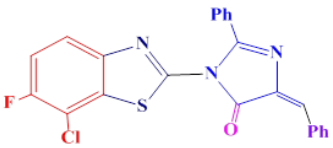


**Figure- 9:** 4-(4-methoxyphenyl)-1,2-diphenyl-1*H*-imidazole

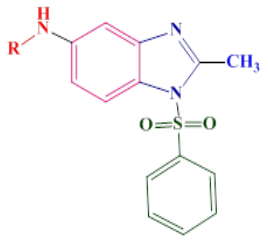
4. Sathe, B. S. *et al*., (2011) have reported the synthesis of new fluorinated benzoimidazole compounds such as 2-imidazolo benzothiazole (**Fig.10**) and screened its *in–vitro* anti-inflammatory activity.[49]



(*E*)-4-benzylidene-1-(7-chloro-6-fluorobenzo[*d*]thiazol-2-yl)-2-phenyl-1*H*-imidazol-5(4*H*)-one

**Figure- 10**

5. Gaba, M. *et al*., (2010) have synthesized novel 5-substituted-2-methylbenzimidazoles and found their analgesic properties. The following three derivatives showed good analgesic activity (**Fig. 11**).[50]

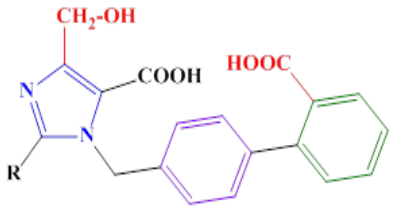



2-methyl-5-(2-phenylhydrazinyl)-1-(phenylsulfonyl)-1*H*-benzo[*d*]imidazole

Figure - 11 :

***Anti hypertensive and Angiotension II receptor Antagonist activity***

Arunkumar, S. S. (2015) has reported that, imidazole derivatives act as an antagonist against Angiotension II receptor. The substituents at the 4th and 5th positions in the imidazole moiety of the following compounds are favourable for the bioactivity (**Fig. 12**).[51]




1-((2'-carboxy-[1,1'-biphenyl]-4-yl)methyl)-2-ethyl-4-(hydroxymethyl)-1*H*-imidazole-5-carboxylic acid

Figure- 12

***Anti-tuberculosis activity***

Anti-tubercular agents are used for the treatment of the most infectious disease tuberculosis.[52]

1. Lee *et al*., (2011) have prepared nitroimidazoles having anti-tubercular property against Mtb H37Rv, which has been found by micro dilution Alamar blue assay method. The methoxy-nitroimidazole-1-phenylethanol was found to be highly active when compared with other derivatives (**Fig. 13**).[53]

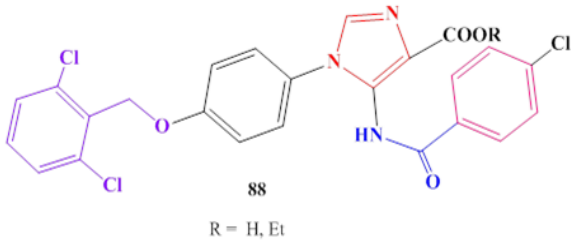
| $R_1$ | $R_2$ |
|---|---|
| 2,4-Dichloro | H |
| 2,4-Dichloro | Br |
| 2,4-Dichloro | Br |
| 4-F | Br |
| 4-Cl | Br |
| $4-NO_2$ | Br |
| H | Br |
| 2,4-Dimethyl | Br |

| $R_1$ |
|---|
| 2,4-Difluoro |
| 2,4-Dichloro |
| 4-F |
| 4-Cl |
| $4-NO_2$ |
| 4-Phenyl |
| H |
| 2,4-Dimethyl |

2-(2-methoxy-4-nitro-1*H*-imidazol-1-yl)-1-phenylethanol

Figure- 13:

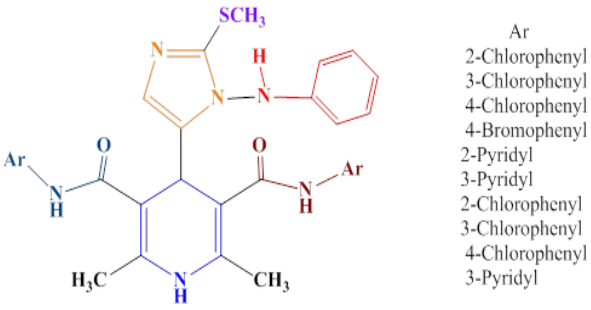
2. Lu *et al*., (2012) have prepared of a number of substituted imidazole. The following imidazole based derivatives (**Fig. 14**) have been examined for *in vitro* antitubercular activity of Mycobacterium tuberculosis H37Rv strain and found to give very good activity.[54]




ethyl 5-(4-chlorobenzamido)-1-(4-((2,6-dichlorobenzyl)oxy)phenyl)-1*H*-imidazole-4-carboxylate

Figure - 14

3. Fassihi and others have prepared a series of 4-substituted imidazolyl-dicarboxamides (**Fig. 15**) and subjected them to *in vitro* activity against Mycobacterium tuberculosis H37RV strain ATCC 27294 which is susceptible to rifampicin and isoniazid drugs.[55]



| Ar |
|---|
| 2-Chlorophenyl |
| 3-Chlorophenyl |
| 4-Chlorophenyl |
| 4-Bromophenyl |
| 2-Pyridyl |
| 3-Pyridyl |
| 2-Chlorophenyl |
| 3-Chlorophenyl |
| 4-Chlorophenyl |
| 3-Pyridyl |

$N^3$,$N^5$-diaryl-2,6-dimethyl-4-(2-(methylthio)-1-(phenylamino)-1*H*-imidazol-5-yl)-1,4-dihydropyridine-3,5-dicarboxamide

Figure- 15

4. Patel *et al*., (2013) have synthesized new imidazothiadiazoles and conducted their *in vitro* antitubercular studies against Mycobacterium tubercular H37RV strain. In the imidazothiadiazole series the 3-nitro and 4-nitrophenyl derivatives showed potential antitubercular activity (**Fig. 16**).[56]

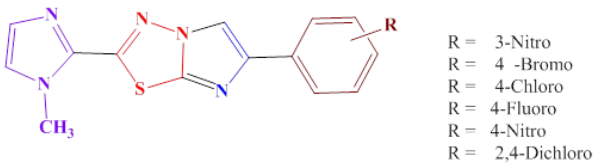



Figure - 16

5. Ranjith *et al*., (2014) have synthesised and characterized new 1*H*- imidazolyl-methoxyphenyl amide (A) and 1*H*-imidazolyl- methoxyphenyl sulfonamide (B) derivatives were found to exhibit the antitubercular activity of Mycobacterium tuberculosis

H37RV, Mycobacterium smegmatis, Mycobacterium fortuitum and MDR-tubercular strains (**Fig**. **17**).[57]


**Figure- 17**

***Antidepressant and anti-convulsant activity***

1. Hadi Zadeh F *et al*., (2008) have obtained new moclobemides by replacing the moclobemide phenyl ring with imidazole ring (**Fig. 18**) and determined their antidepressant property by using forced swimming test. All the prepared compounds were highly active when compared with the standard moclobemide.[58]

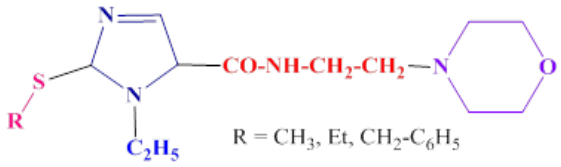



**Figure- 18**

2. Bastaki *et al*., (2018) have reported the study of anticonvulsant effect and safety of H3R 2-18 antagonist (**Fig. 19**) and found that, the imidazole-containing H3R antagonist has high *in vitro* antagonist affinity, selectivity and *in vivo* antagonist activity in mice using antiepileptic drug: valproic acid as a standard of reference.[59]

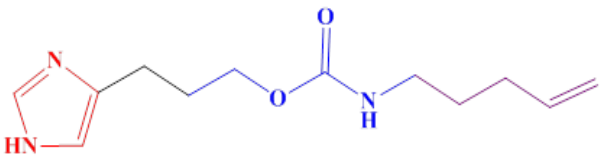



**Figure- 19**

***Anticancer activity***

1. Yusuf, O. *et al*., (2010) have synthesized many novel imidazole-(benz)-azole and its derivatives (**Fig**. **20**) and evaluated their anticancer activity and found that, these derivatives were the most active compounds when compared with the standard Cisplatin.[60]

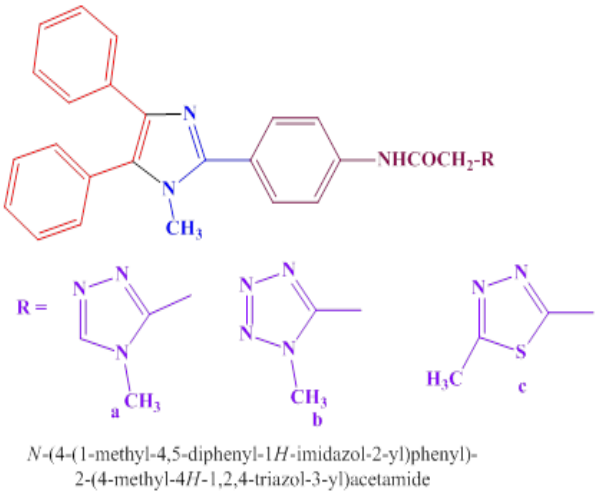



**Figure- 20**

2. Li, W.T. *et al*., (2010) have synthesized 2-amino-1-arylmethylideniminoimidazoles and studied their biological activity as orally active anticancer agents (**Fig. 21**).[61]

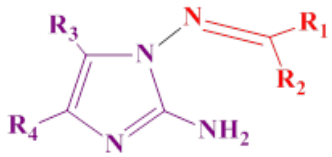



**Figure- 21**

3. Hanan, M. R. *et al*., (2010) have reported the synthesis of a series of 2-substituted benzimidazoles. Several of the synthesized products have been subjected for anticancer screening and found that, the tested compounds (**Fig. 22**) exhibited human hepatocellular carcinoma activity, and were found to be effective against breast cancer cell, adenocarcinoma and human colon cancer. Some of the prepared compounds are found to be very effective against certain other types of cancers.[62]

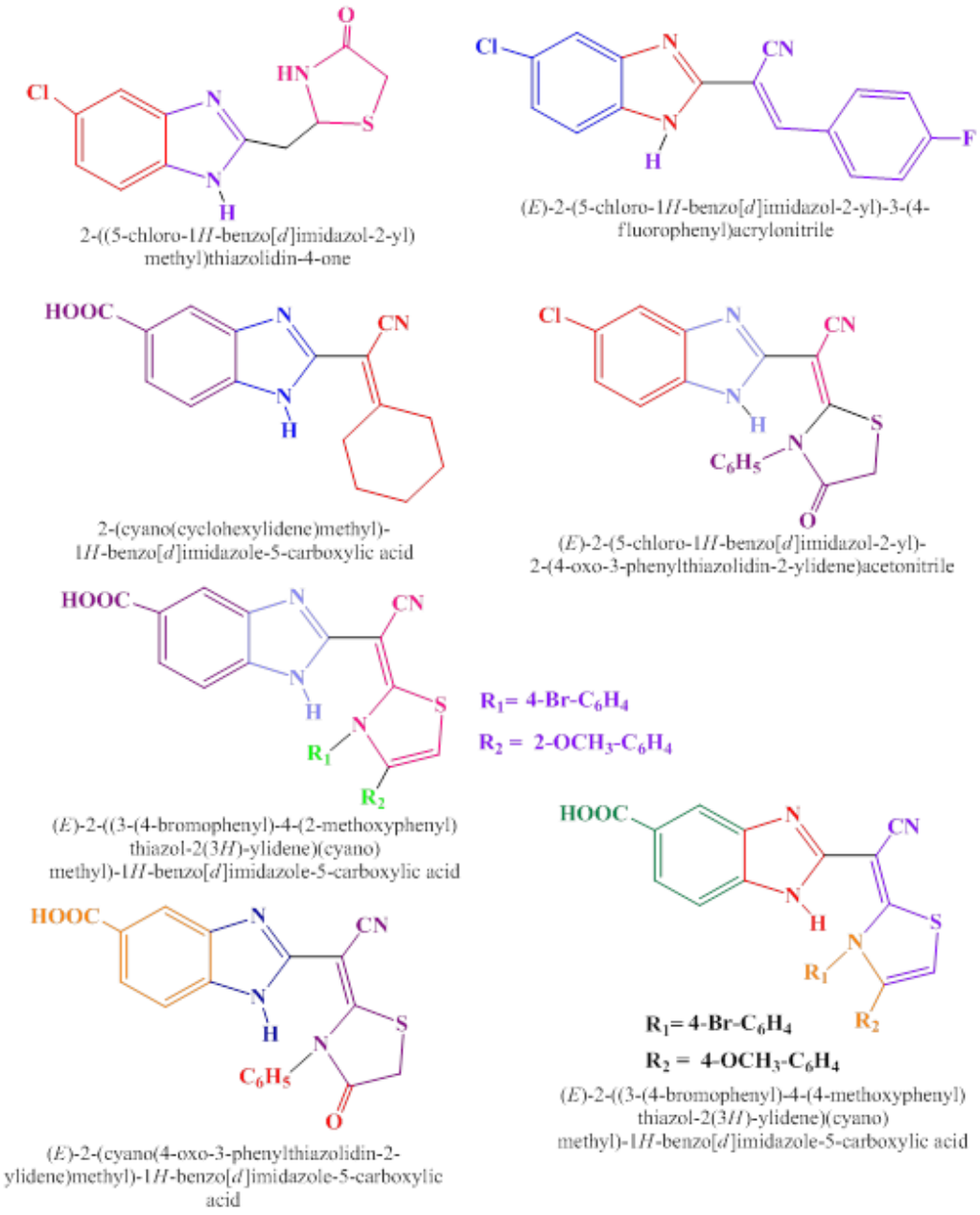



**Figure - 22**

***Antiviral activity***

Antiviral agents are used for the treatment a specific type of viral infection;[24] broad spectrum antiviral drugs are effective towards the treatment of a wide variety of viruses.[25]

1. Liu, C. *et al.*, (2012) have synthesized (3-bromo-3-deazaneplanocin) imidazole derivatives. These derivatives have shown promising antiviral activity (**Fig. 23**).[63]

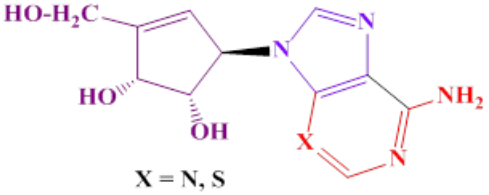
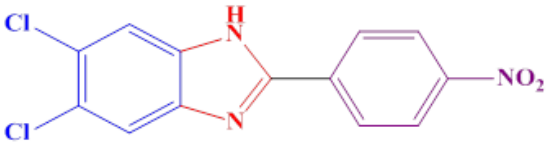



**Figure - 23**

2. Michele, T. *et al*., (2010) have synthesized many 2-phenylbenzimidazoles and found their cytotoxicity and antiviral activity against a panel of RNA and DNA viruses. The 2-(4-nitrophenyl) benzimidazole derivative (**Fig. 24**) was found to be a more potential drug than the standards of reference smycophenolic acid and 6-azauridine.[64]



5,6-dichloro-2-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole

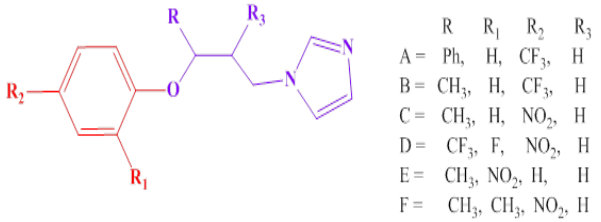
**Figure- 24**

***Antileishmanial activity***

Leishmaniasis is a vector-borne disease people get infected by protozoan parasites. The disease spreads by the bite of the infected female phlebotomine flies.[65]

Leishmaniasis is a complex disease and is classified into: i). visceral leishmaniasis or kala azar (black fever); ii). cutaneous leishmaniasis is most serious and common form, and is long-lasting; iii). diffuse cutaneous leishmaniasis resembles leprosy, which can destroy the membranes of the nose, throat and mouth.[66]

Kalpana, B. *et al*., (2010) have prepared a series of substituted imidazoles and determined their *in vitro* activity. All the synthesized compounds (**Fig. 25**) exhibited excellent inhibition of *Leshmania donovani*.[67]



| | R | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|---|
| A = | Ph, | H, | $CF_3$, | H |
| B = | $CH_3$, | H, | $CF_3$, | H |
| C = | $CH_3$, | H, | $NO_2$, | H |
| D = | $CF_3$, | F, | $NO_2$, | H |
| E = | $CH_3$, | $NO_2$, | H, | H |
| F = | $CH_3$, | $CH_3$, | $NO_2$, | H |

1-(3-phenoxypropyl)-1*H*-imidazole

**Figure - 25**

***Antioxidant activity***

Free-radicals are harmful to the cells; by attacking the healthy cells they can cause damage to the vital molecules such as: DNAs, RNAs, proteins, vitamins and enzymes etc. The ability of antioxidants to curb the production of the free-radicals depends primarily on the age of a person and the health status. The human body generally depends on the diet to obtain the required antioxidants.

Free-radicals also cause other diseases such as: Alzheimer's disease, cardiovascular disease, alcohol-induced liver disease and neural disorders. Hence, synthesis of novel antioxidants has attracted much attention in recent years.

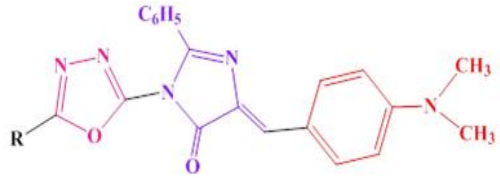
Abdel-Wahab, B. F. *et al*., (2011) have synthesized 2-cyano-3-(4-fluorophenyl)-*N*′-[1-(5-methyl-2-phenyl-1*H*-imidazol-4-yl)ethylidene]acrylohydrazine (**Fig. 26**) and tested for its antimicrobial, antioxidant, anti-hemolytic and cytotoxic activities.[68]

(2*Z*,*N*′*E*)-2-cyano-3-(4-fluorophenyl)-*N*′-(1-(5-methyl-2-phenyl-1*H*-imidazol-4-yl)ethylidene)acrylohydrazide

**Figure - 26**

***Anthelmintic activity***

1. Sreenivasa, G. M. *et al*., (2010) have reported the synthesis and characterization of (5Z)-5-[4-(dimethylamino)benzylidene]-3-(5-substituted-1,3,4-oxadiazol-2-yl)-2-phenyl-3,5-dihydro-4*H*-imidazol-4-ones and then, tested the anthelmintic activity against Pheretima posthuma (**Fig. 27**).[69]

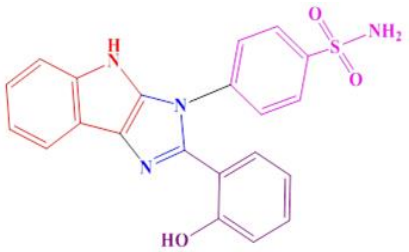


R = H, $NO_2$ , F, Br , Cl, OH

(*Z*)-4-(4-(dimethylamino)benzylidene)-1-(1,3,4-oxadiazol-2-yl)-2-phenyl-1*H*-imidazol-5(4*H*)-one

**Figure- 27**

2. Prabhu, M. *et al*., (2012) have synthesised, characterized and evaluated the antibacterial and anthelmintic activity of the novel 4-[2-(2-hydroxyphenyl)imidazo[4,5-b]indol-3(4*H*)-yl]benzenesulfonamide (**Fig. 28**).[70]

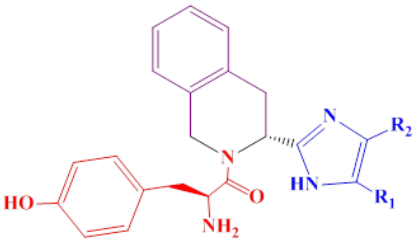


4-[2-(2-hydroxyphenyl)imidazo[4,5-b]indol-3(4H)-yl]benzenesulfonamide

**Figure - 28**

***Antiulcer Agents & Agonist (Gastrointestinal Disorder) activity***

Henry, J. B. *et al*., (2004) have reported the synthesis of novel substituted imidazoles (**Fig. 29**) as opioid receptor agonists for gastrointestinal disorders.[71]



$R_1$ =Me, $R_2$ = Ph, n-pr

(*S*)-2-amino-3-(4-hydroxyphenyl)-1-((*R*)-3-(5-methyl-4-phenyl-1*H*-imidazol-2-yl)-3,4-dihydroisoquinolin-2(1*H*)-yl)propan-1-one

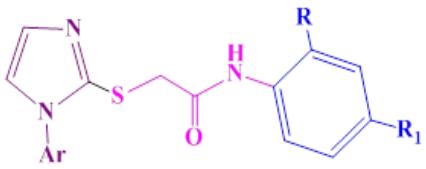
**Figure- 29**

***Anti-HIV activity***

Human Immunodeficiency Virus type-1 (HIV-1) causes Acquired Immunodeficiency Syndrome (AIDS).[72]

HIV-1 virus destroys the 'helper cells: lymphocytes' which fight the infectious diseases in human beings.[73]

1. Zhan, P. *et al*., (2009) have reported the synthesis of a series of 2-(1-aryl-1*H*-imidazol-2-yl-thio)acetamide [imidazole thioacetanilide (ITA)] derivatives and evaluated as potent inhibitors of HIV-1. They found that, all the newly synthesized imidazole thioacetanilides showed higher anti-HIV-1 activity (**Fig. 30**).[74]

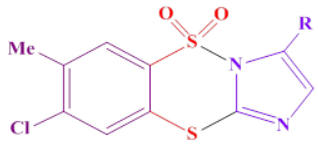


2-((1-aryl-1*H*-imidazol-2-yl)thio)-*N*-phenylacetamide

**Figure- 30**

| Ar | R | $R_1$ |
|---|---|---|
| Naphthalen-1-yl | F | H |
| Naphthalen-1-yl | Cl | H |
| Naphthalen-1-yl | Br | H |
| Naphthalen-1-yl | Br | Me |
| Naphthalen-1-yl | $NO_2$ | H |
| -Tolyl | $NO_2$ | H |

2. Brzozowski, Z. *et al*., (2006) synthesised novel series of 2,3-dihydroimidazo[1,2-b][1,4,2]benzodithiazines and tested their anti-HIV-1 activity (**Fig. 31**).[75]



R = H , $C_6H_5$, Ar , Me , Et

8-chloro-7-methylbenzo[*e*]imidazo[1,2-*b*][1,4,2]dithiazine 5,5-dioxide

**Figure - 31**

3. Serrao, *et al*., (2013) have discovered novel 5-formyl-1*H*-imidazole-4-carboxamides which have the potent inhibitor activity for HIV-1 integrase–LEDGF/p75 (**Fig. 32**).[76]

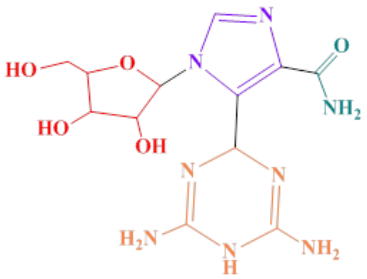
5-formyl-1*H*-imidazole-4-carboxamide

Figue - 32

***Anti-hepatitis C activity***

Today, the world is facing problems related to generate drugs which can work against the hepatitis C virus (HCV). Nearly, 1.70 crore people in the world are affected by the hepatitis C disease. Generally, ribavirin with pegylated interferon alpha is used for the treatment of hepatitis C. Unfortunately, a combination of ribavirin with pegylated interferon alpha are active only against type-2 and type-3 hepatitis viruses and found to be inactive towards 1 and 4 types of HCV viruses. Due to lack of activity, certain very severe side effects are noticed in the patients suffering from hepatitis C, and in order to overcome this, there is an urgent need for the development of novel drugs.[77]

1. Ujjinamatad, *et al*., (2007) have prepared imidazole derivatives and evaluated their *in vitro* activity against Flaviviridae family viruses: hepatitis C virus (HCV), the Japanese encephalitis virus (JEV), dengue virus (DENV) and West Nile virus (WNV) by employing RNA and a DNA substrate. The compound shown in the Fig. 33 exhibited maximum activity against WNV and HCV with an $IC_{50}$ value of 23 and 37l M respectively in the presence of DNA substrate.[78]



5-(4,6-diamino-2,5-dihydro-1,3,5-triazin-2-yl)-1-(3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-1*H*-imidazole-4-carboxamide

**Figure- 33**

2. Windisch and co-workers (2014) reported the synthesis and characterization of 2-iminobenzimidazole (IBI) which is found to be an effective hepatitis C enzyme inhibitor. It showed a maximum inhibition, and a novel mechanism of action has been proposed by the investigators (**Fig. 34**).[79]


2-Iminobenzimidazole

**Figure- 34**

## CONCLUSION

On basis of the literature survey, in this review, we conclude that, imidazoles are very effective pharmacological compounds, their design and preparation is a very attractive area of research. It has been observed that, modifications of the substituents on the imidazole ring are the structural isosters and bioisosters of nucleotides which can interact readily with the biopolymers such as: nucleic acids, proteins, enzymes, lipids and vitamins. They possess high potency and low toxicity which can make them vary safe chemotherapeutic agents for human beings and display very valuable bioactivities and therapeutic uses. It is important to note that, these modified compounds can be considered as potential drugs in the coming years. The bioactivity patterns of this new generation of imidazoles would represent an amazing scaffold for the further research studies and discovery of the best new medical and pharmaceutical compounds. Studies have clearly indicated that, imidazoles have various activities such as: anti-HIV, anticancer, analgesic, antimicrobial, antituberular, anti-inflammatory and other activities. We strongly feel that, the search for new imidazole based drugs and their utilization in the treatment of several diseases will continue in future as they are found to exhibit a variety of pharmaceutical applications.

## ACKNOWLEDGEMENTS

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