e- ISSN 0976-0342
Print ISSN 2229-7456

International Journal of Pharmacy & Therapeutics

Journal homepage: www.ijptjournal.com

Review article

CURRENT REVIEW ON IMPORTANCE OF IMIDAZOLE DERIVATIVES

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ABSTRACT

Imidazole motif is a vital part in many of the naturally and synthetically available medicinal compounds and they are well known for their biological significance because of its aptitude to tempt harmful cell inhibition in many of the diseases cell lines. The current review covers about past five years of period indole achievements in connection of its biological activities. The aim of review is addresses the importance of imidazole derivatives in the field of medicinal drug discovery.

Key Words:- Imidazole, Imidazole Derivatives, biological activities.

Access this article online

Home page: http://ijptjournal.com/

DOI: http://dx.doi.org/10.21276/ijpt.2018.9.2.3

Quick Response code

Received:25.03.2018 **Revised**:12.04.2018 **Accepted**:15.04.2018

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INTRODUCTION

Cyclic compounds which possess at least two different elements in its ring are known as heterocyclic compounds.Five membered cyclic compound with N,O and S as hetero atom are Pyrole, Furan, Thiophene respectively. It comes under the branch heterocyclic chemistry. Heterocyclic compounds are found to be significant in discoveries of different medicinal compounds (H. Z. Zhangv *et al* 2018). Examples: Indole, imidazole, pyridine, purine etc. It's a five membered heterocyclic compound having 2 nitrogen as hetero atoms at 1 and 3 positions. Imidazole(**Fig.1)** possess different therapeutic properties such as antifungal, anti-cancer, antimicrobial, enzyme inhibitor, anti-tubercular and many other pharmacological properties (Y. Hu *et al* 2018,G. F. Zhang*et al* 2018,Y. X. Xu *et al* 2018,X. L. Hu *et al* 2017,K. Wittine*et al* 2012, E. Serrao*et al* 2013, J. Z. Vlahakis *et al* 2006, Y. Q. Hu *et al* 2017,A. Bistrović *et al* 2018).

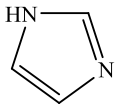


Fig.1

Imidazole ($C_3N_2H_4$) is an aromatic compound. Many drugs possess imidazole ring such as antifungals, sedatives, antibioticsetc. Imidazole can be seen in two tautomeric forms. Heinrich Debus, a German-British scientist first reported about imidazole in 1850s. In past few years few hundreds of imidazole derivatives and their hybrids were synthesized and also discovered and found useful in different formulation of drugs. Some hybrids like benzimidazole (**Fig.2**) derivatives were found to be anticancerous and anti-mycobacterial (Mantu D *et al.*,2016)

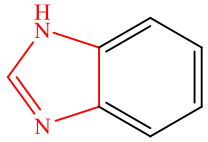


Fig. 2

1.1 Heterocycles related to imidazole

Benzimidazoles like Albendazole (**Fig.3a**), Mebendazole (**Fig.3b)**, Triclabendazole (**Fig. 3c)** etc, acts as antihelmintic.

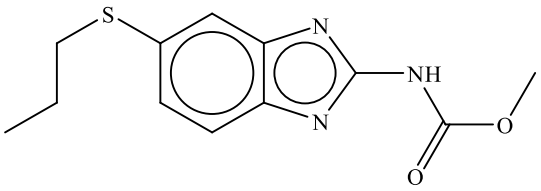


Fig.3a

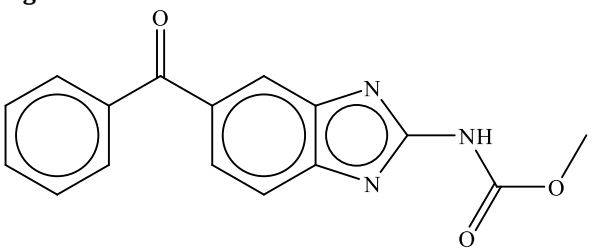


Fig.3b

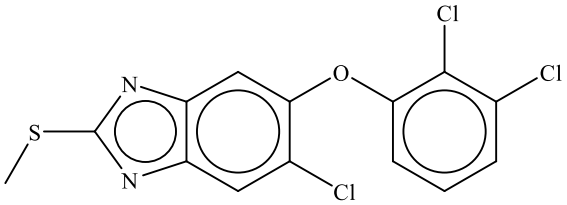


Fig.3c

Dihydroimidazole/imidazoline (**Fig.3d)** is found to be present in many drugs (Leon Shargel *et al* 2001)

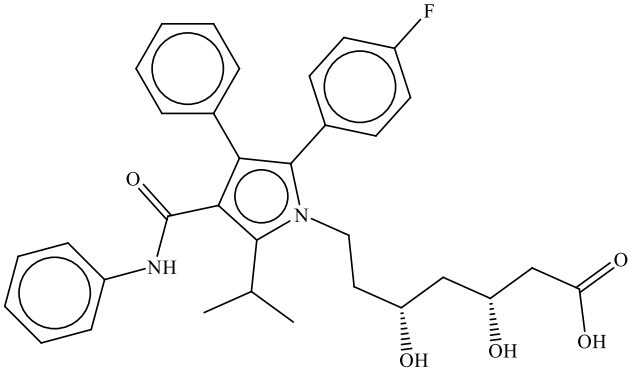


Fig.3d

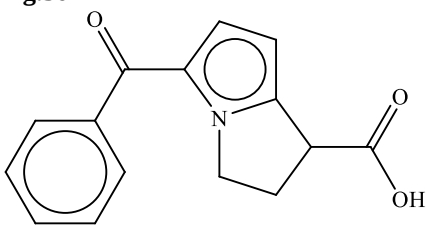


Fig.3e

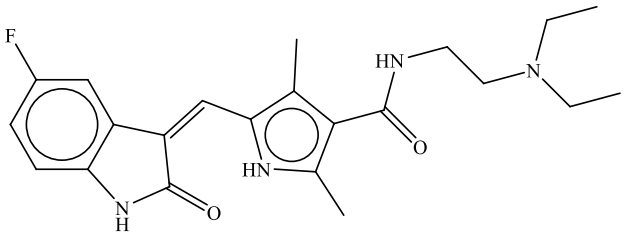
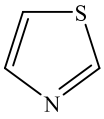


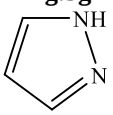
Fig. 3f

Pyroles (**Fig.3f**) are found in numerous drugs including atorvastatin**(Fig.3g**), ketorolac (**Fig.3h**) and sunitinib (**Fig.3i)**. *N*-Methylpyrrole is a precursor to *N*-methyl pyrrole carboxylic acid, a building-block in pharmaceutical chemistry (Sunderland *et al* 2014)



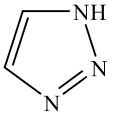
thiazole

Fig.3g



pyrazole

Fig.3h



triazole

Fig.3i

1.2 Biological importance

Histidine (**Fig. 4**), possess imidazole side chain which can be seen in many proteins and enzymes it has a vital role in binding of haemoglobin and in its structure.

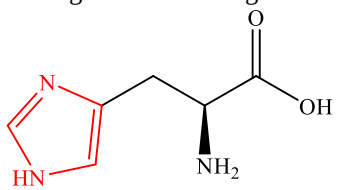


Fig.4a

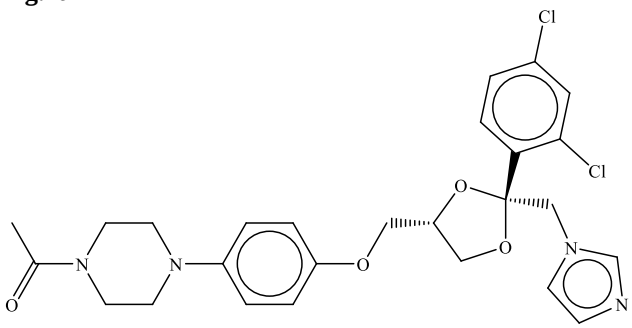


Fig.4b

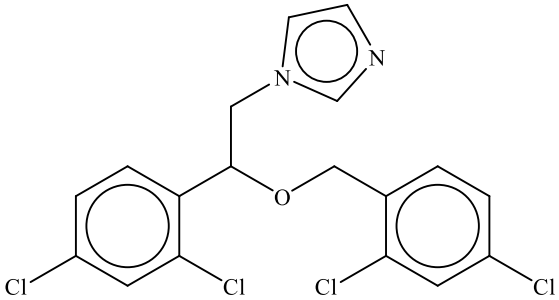


Fig.4c

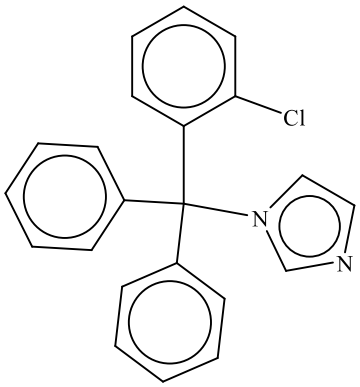


Fig.4d

Imidazole has its application in purification of His-tagged proteins in immobilised metal affinity chromatography (IMAC). Also in many pharmaceuticals imidazole acts as an important part. Synthetic imidazole has its roles in many fungicides and antifungal, antiprotozoal and antihypertensive medications. Imidazole as a part of theophylline molecule is present in the anticancer medication mercaptopurine which is used during leukaemia conditions. Imidazoles belong to the class of azole antifungals (Liu *et al* 2009), which includes ketoconazole **(Fig.4b)**, miconazole (**Fig.4c**) and clotrimazole (**Fig.4d)**. Some of imidazoles act against insects for example econazole nitrate with the common clothes moth *Tineolabisselliella* (Paal *et al* 1884)

1.2 Imidazole containing marketed drugs

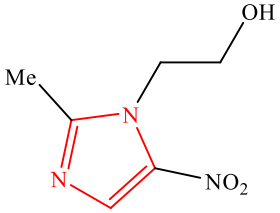


Fig. 5a

Metronidazole(Fig.5a) it is marketed in name Flagyl, it is an antibiotic and antiprotozoal agent.

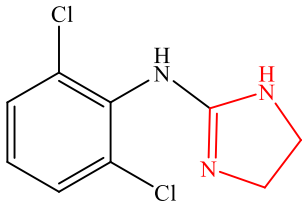


Fig. 5b

Clonidine(Fig.5b) it is marketed in following names, Catapres, Kapvay, Nexiclon.It is used to treat high BP and anxiety conditions.

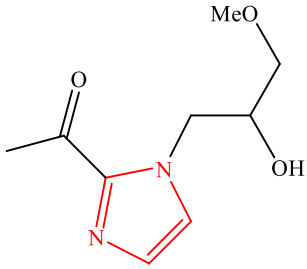


Fig. 5c

Misonidazole(Fig.5c) it has its role in converting normally resistant hypoxic tumor cells to become sensitive to treatment during radiation therapy.

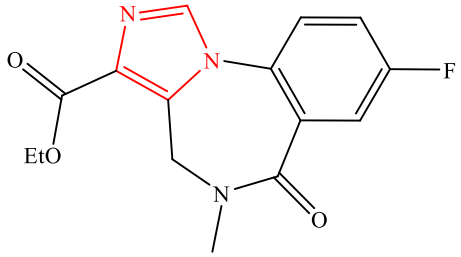


Fig.5d

Flumazenil(Fig.5d) possess antagonistic and antidote property to benzodiazepines through competitive inhibition.

2. Reviews

YadavS *et al* 2017 synthesized benzimidazole derivatives and also evaluated synthesized compounds for its invitro antimicrobial and anticancer activities. Out of all compounds evaluated anticancer activity was observed in **Fig.6** (IC_{50} = 0.0013 mM)it was found to be potent against breast cancer.

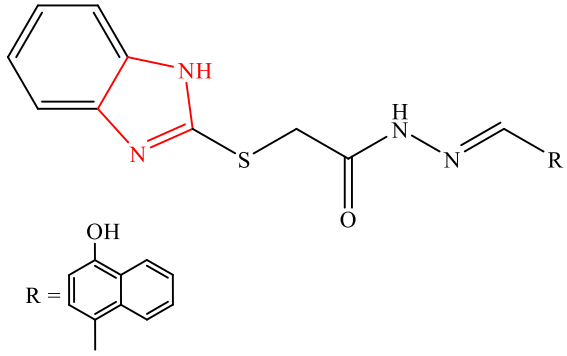


Fig.6

Akhtar J*et al* 2017 reviewed about methods for synthesizing nitrogen containing anticancer agents. According to which the broad range of biological activities was exhibited by synthetic compounds having N heterocyclic ring system as core structure. Studies done on nitrogen containing heterocyclic compounds among that imidazole derivatives**Fig.7** showed multiple mechanisms of antitumor activities.

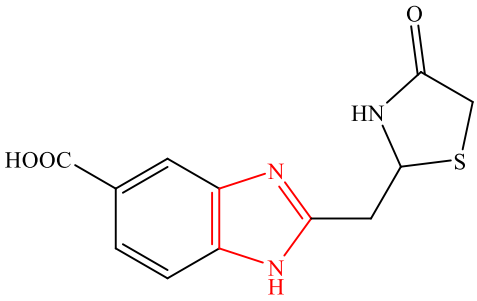
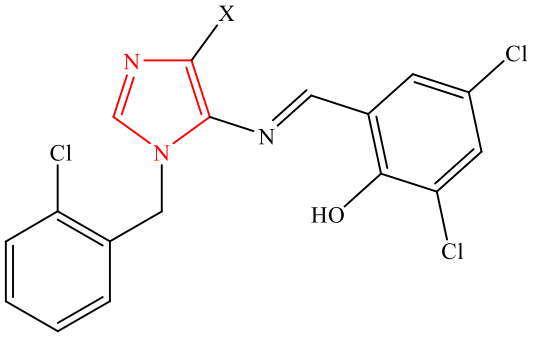


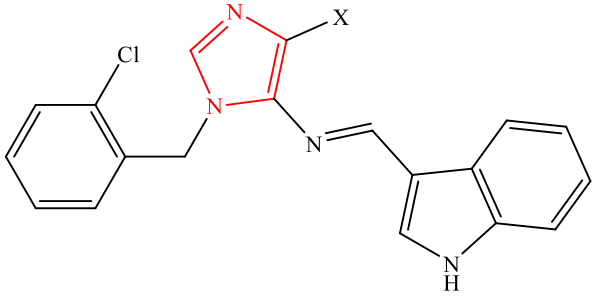
Fig.7

Negi A *et al* 2015 for first time discovered and reported anticancer property of novel imine/amide- imidazole conjugates derived from 5-amino-4-cyano-N1-substituted benzyl imidazole using seven cancer cell lines. By using cancer cell lines they discovered acceptable antiproliferative activity of some compounds like **Fig. 8a**, **8b** and **8c** against some selected cancer cell lines. They also found out there is a chance that compounds might induce apoptosis.



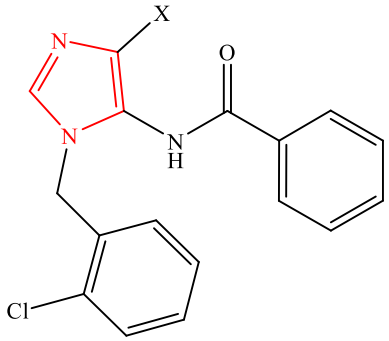
X=CN

Fig.8a



X=CN

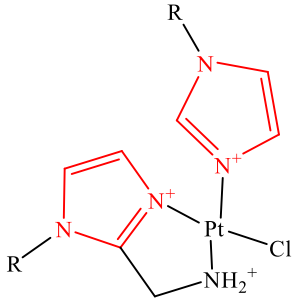
Fig.8b



X=CN

Fig.8c

Rimoldi *et al* 2017 conducted research on cytotoxic activity of cationic platinum (II) complexes by testing it on triple negative breast cancer MDA-MB-231 cell line. The group of researchers found that most potent cytotoxic agent in MDA-MB-231 was **Fig.9**, it was more effective. By testing told that 4 is a cytotoxic agent with acceptable antitumor activity.



R=C_6H_{13}

Fig.9

Ghanbarimasir Z *et al* 2017 designed and synthesized quinoxaline derivatives containing 2-aminoimidazole in search of antiproliferatives. They confirmed the synthesized compound structures using IR, NMR and other spectral techniques. The synthesized compounds were evaluated for anticancer potency using cancer cell lines. The group of researchers found that some of compounds synthesized acted as antiproliferative agents with percentage inhibition of 50%. Among some antiproliferative compound synthesized compound (E)-4phenyl-1-((quinoxalin-2-ylmethylene)amino)-1H-imidazol-2-amine **Fig.10** was found to be most active with highest inhibition for cancer cell lines.

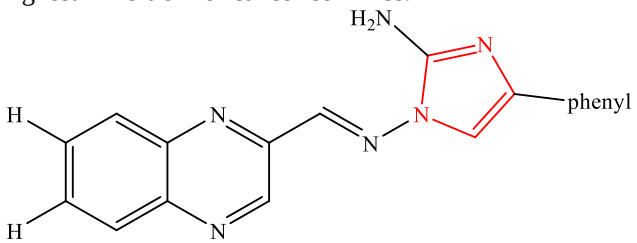


Fig.10

CorreiaC *et al* 2014 synthesized and assessed the radical scavenging activity of novel hydroxylated benzylidine

amino imidazole derivatives against DPPH and hydroxyl radicals. High activity of imidazoles **Fig.11** were seen against hydroxyl radicals and showed high ability to chelate iron ions.

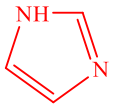
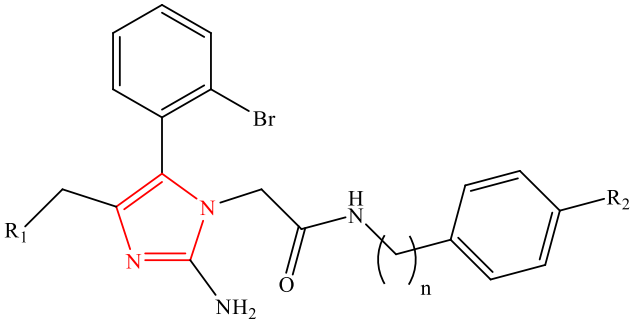


Fig.11

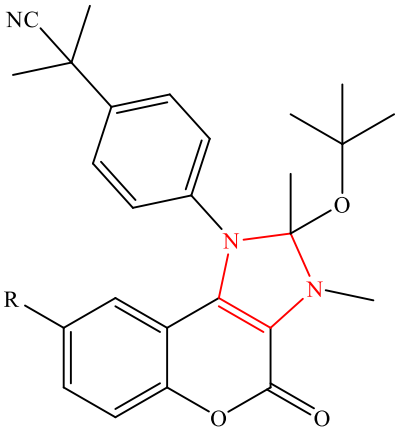
Gill RK *et al* 2017 found out that biofilm formation along with their natural tolerancy to antibiotics is reason for many bacterial infections and their treatments. They told that compounds which possess anti biofilm activity could be usefull in chemotherapic treatment. So they synthesized series of aminoimidazoles and evaluated them for their antiproliferative potency against various cancer cell lines. By the various evaluations they found out that antiproliferative activity can be increased by indroduction of p-methyl group at carboxamide ring. After series of evaluation studies the highest antiproliferative activity was found in **Fig. 12a** and **12b.**



12a;R1=H,R2=p-OCH_3-C_6H_4
12b;R1=CH_3;R2=p-tolyl

Fig.12

Han X *et al* 2016 synthesized and evaluated biological activities of molecules containing chromeno [3,4-d] imidazol-4(1H)-one. Out of all the compounds synthesized showed its ability to arrestG0/G1 cell-cycle and cancer cell migration was also blocked by this compound. Researchers also found that the tumor implanted in mice was also inhibited by this compound. After all studies they told that **Fig.13** can be considered as promising anticancer agent.



R=quinolyn-3-yl

Fig.13

Kerru N *et al* 2017 in their study told that cancer is still fatal disease and it is also a prominent cause of death despite development of lot of anticancer agents. Present anticancer agents are known to possess resistance against many drugs along with side effects. So in recent days many of researchers are working on combination techniques for cancer therapy with less side effects as well as more affinity and activity in comparison to single target drugs or parent molecules. Mainly these combination drugs have less chemoresistance along with better specificity and patient compliance. Based on this factor combination drugs like Curcumin-imidazol hybrids and some other drugs were developed in 2015-16. Curcumin-imidazol hybrids (**Fig.14**) were found to be potent antiproliferative agents.

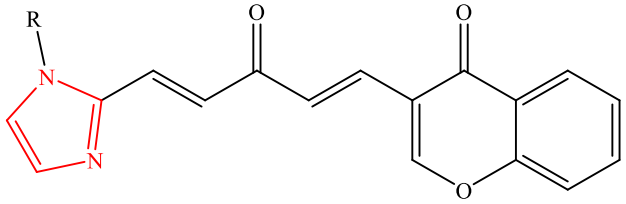
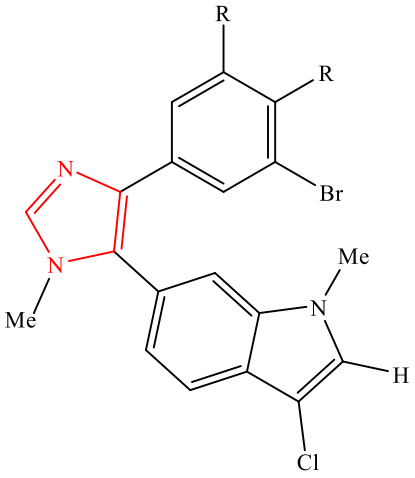


Fig.14

R=methyl, ethyl, propyl, butyl, pentyl, isopropyl, sec-butyl, isopentyl, pentan-2-yl,pentan-3-yl

Mahal K *et al* 2016 prepared 5-(1-Methyl-4-phenyl-imidazol-5-yl) indoles and they were tested. Researchers found out that 3-bromo-4,5-dimethoxyphenyl derivative (**Fig.15**) was comparatively highly active when compared with other drug against multidrug resistant carcinoma cells. Cytoskeleton of cancer cells were completely disrupted by indole.I t was found that indole killed red blood cells in both chorioallantoic membranes (CAM) of fertilized chicken eggs as well as tumor in mice without causing any harm to embryo or mouse. Indole showed less toxicity to body cells. The retarded growths of tumors in mice were observed during first trial with indole.



R=MeO

Fig.15

Parekh NM *et al* 2017 constructed new series of multi-heterocyclic Schiff base which is converted and reacted with other compounds to generate imidazolylphenyl heterocyclic-2-ylmethylenethiazole-2-amines. In vitro cytotoxicity efficacies of new bases obtained were evaluated against cancer cell lines like MCF7, HCT116, DU145 and normal skin fibroblast. During evaluation studies cytotoxic actions were produced by synthetic derivatives obtained against individual cancer cell lines but showed weak actions against skin fibroblast. SAR suggested that variations in pharmacological effects are caused by difference in characteristics of substituents attached to Schiff's base. Structural analysis for final potent anticancer Schiff base (**Fig.16**) was performed using various spectral techniques.

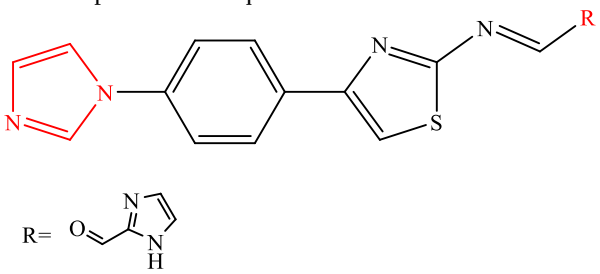
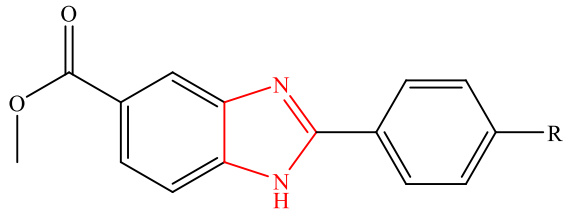


Fig.16

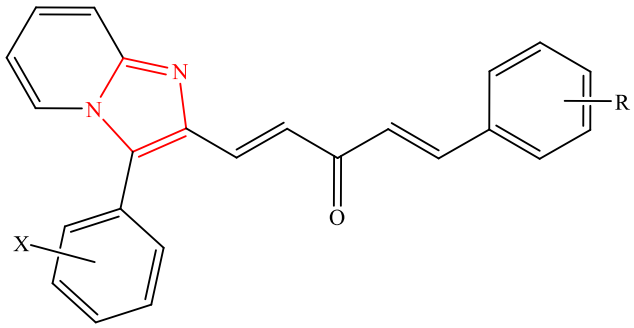
Karthikeyan C *et al* 2017 synthesized and examined group of novel substituted 2-(phenyl)-3H-benzo[d]imidazole-5-carboxylic acids and its methyl esters and their antiproliferative effects were evaluated in vitro using breast cancer cell lines. Researchers used cisplatin as reference compound with which the antiproliferative effects of synthesizes compounds were compared. Most active compound among group of synthesized compounds **Fig.17** was found to be having5-fluoro-2-hydroxyphenyl substituent against breast cancer cell lines.



R=2-OH, 5-F

Fig.17

Ramya PS *et al* 2018 prepared a group of (1E,4E)-1-phenyl-5-(3-phenylimidazo[1,2-a]pyridin-2-yl)penta-1,4-dien3-ones as tubulin polymerization inhibitors with an aim to develop new potent anticancer agents. Researchers evaluated the cytotoxic potential using six cancer cell lines. Among evaluated compounds potent growth inhibition was shown by some compounds. Among these researchers found out that **Fig.18** easily inhibited tubulin polymerization and reactive oxygen species (ROS) levels showed its ability of removal of apoptosis.



X=2,4,6-tri-OCH_3,R=3,4-difluro

Fig.18

Shaik SP *et al* 2017 synthesized group of imidazo[2,1-b]thiazole associated triazole conjugates and utilizing some human cancer cell lines they examined synthesized conjugates for their antiproliferative activity. Researchers found that among synthesized conjugates **Fig.19a** and **19b** showed significant antiproliferative potency.

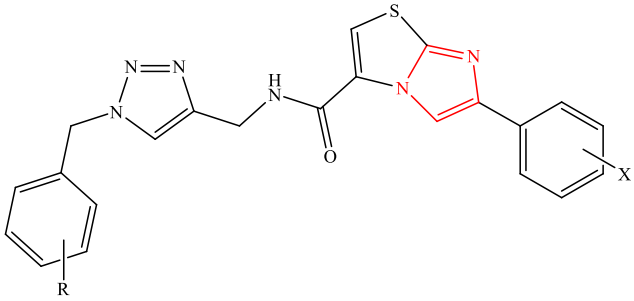


Fig.19

19a: X= 4-0Me;R= 3-OH,4-OMe

19b: X= 4-0Me;R= 3,4-di OMe

Shao KP *et al* 2014 prepared group of pyrimidine-benzimidazol hybrids. They selected four human cancer cell lines for examination of synthesized hybrids to know its anticancer activity. Among prepared hybrids anticancer

activity was shown by few compounds against some cancer cell lines. Among compounds more effective activity was shown by **Fig.20a** and **20b**.

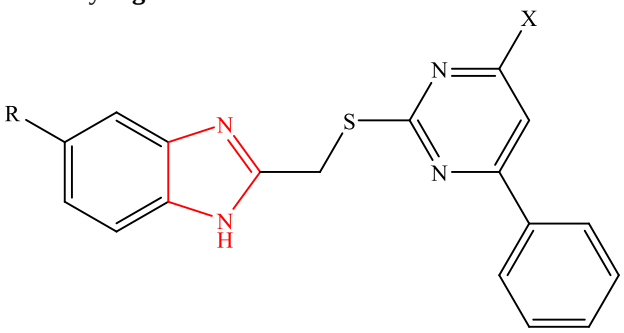


Fig.20

20a= R=H;X=4-$CH_3OC_6H_5NH$

20b= R=H;X=4-$CH_3OC_6H_5NH$

Sharma P *et al* 2016 synthesized (E)-benzo[d]imidazol-2-yl)methylene)indolin-2-one and checked for their cytotoxic activity by using cancer cell lines together with normal breast epithelial cells. Among the compounds tested, **Fig.21** was found to be showing significant cytotoxic activity against cancer cell lines. On normal breast epithelial cells they were found to be safer and less toxic. The apoptosis induced by compound was characterized by staining techniques.

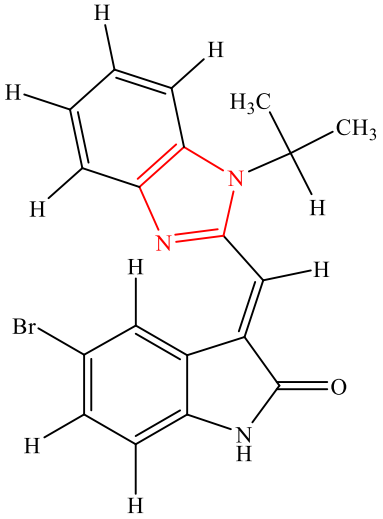


Fig.21

Sharma P *et al* 2017 used conventional and microwave-assisted methods for synthesizing benzimidazole bearing thiazolidinedione derivatives. These techniques caused improvement in yield and decrease in reaction time. Compounds obtained were examined in vitro against human cancer cell lines along with normal kidney cells to check their cytotoxic potency. It was observed that among synthesized compounds **Fig.22a** and **22b** were found to be comparatively more potent and showed apoptic morphological features.

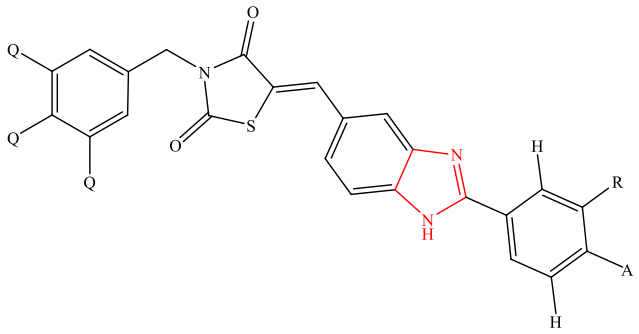


Fig.22

22a; Q=methoxy, R,A=Methoxy

22b; Q=methoxy, R=Methoxy, A=1-isobutoxy

Wei Q *et al* 2018 by structural combination of YM155 with stilbenoids designed and synthesized two series of novel 2-arylvinyl-naphtho[2,3-d]imidazol-3-ium iodide derivatives and 2-arylvinyl-naphtho[2,3-d]imidazol-3-ium bromide derivatives. The compounds synthesized were examined for their antiproliferative activity against some human cancer cell lines. On evaluation one compound was found to be more effective with more potency. Researchers noticed that along with antiproliferative potency antitumor activity was also shown by (E)-2-(2-(1H-indol-3-yl)vinyl)-1-benzyl-3-(2-methoxyethyl)-4,9-dioxo-4,9-dihydro -1H-naphtho [2 ,3-d]imidazol-3-ium bromide **Fig. 23**.

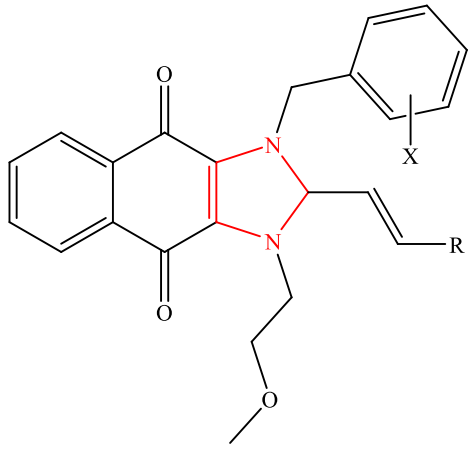


Fig. 23

X=H;R=indoyl

Kirwen EM *et al* 2017 studied about developing novel anticancer and anti-inflammatory agents including a diaryl pharmacophore by examining the suitability of the 3H-imidazo[4,5-b]pyridine ring system. Cytotoxic activity of eight 2,3-diaryl-3H-imidazo[4,5-b]pyridine derivatives against cancer cell lines. The results of evaluation showed that among eight derivatives **Fig. 24** showed high anticancer activity.

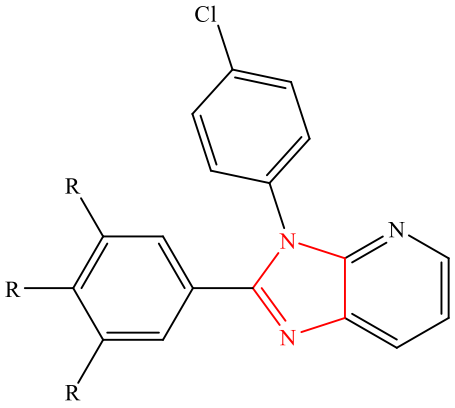


Fig. 24

R=OCH_3

Sharma P *et al* 2016 prepared and examined series of new benzimidazole-thiazolidinedione hybrids for their cytotoxic strength against cancer cell lines. Among those of synthesized hybrids promising cytotoxicity was exhibited by **Fig. 25**. Different tests and studies showed that **Fig. 25** induces apoptosis in lung cancer cell lines.

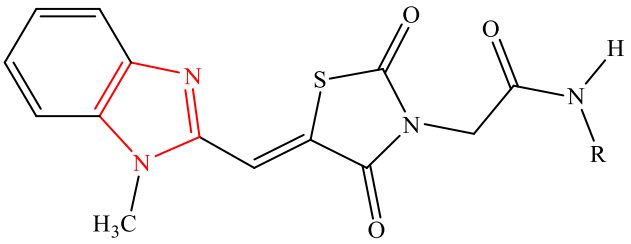


Fig. 25

R=4-phenylthiazol

Ali AR *et al* 2014by the reaction of 6-hydrazinylimidazo[2,1-b] thiazoles with different b-dicarbonyl compounds synthesized imidazo[2,1-b]thiazoles having pyrazole moieties. Synthesized compounds were screened for their anticancer activity at a single dose at National Cancer Institute (NCI), USA. Through evaluation researchers observed that **Fig. 26a** and **Fig. 26b-26d**showed high potency in in vitro anticancer evaluation. **Fig. 26a** and **Fig. 26b-26d** gave promising results of assessment of toxicities, drug score profile during evaluation.

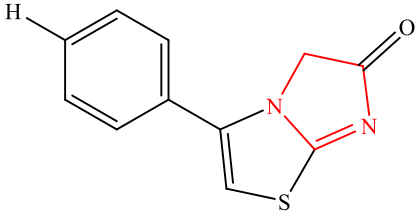


Fig. 26a

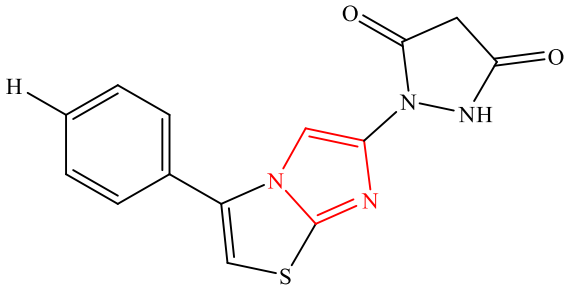


Fig. 26b

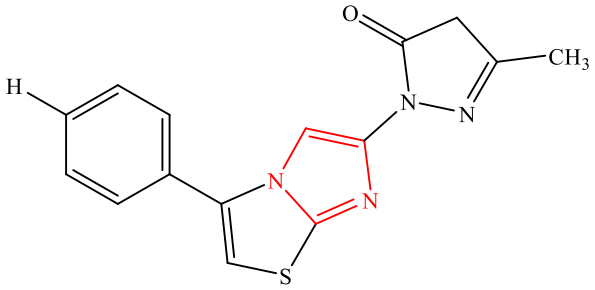


Fig.26c

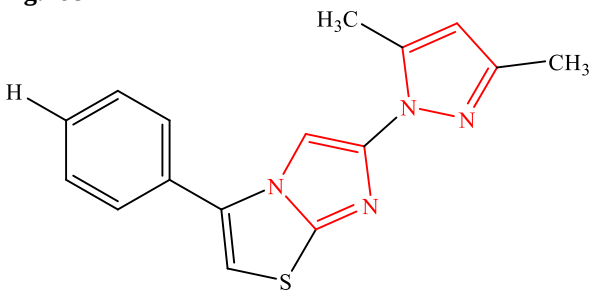


Fig.26d

Bellina F *et al* 2015 replaced C-C double bond of the natural derivative in novel trans-restricted analogues of resveratrol by diaryl-substituted imidazole analogues. Researchers successfully carried out synthesis of 1,4-, 2,4- and 2-5-diarylimidazoles **Fig. 27** by regioselective sequential transition metal-catalyzed arylations of simple, commercially available imidazole precursors. Using human cancer cell lines selected analogues were evaluated for their anticancer activity.

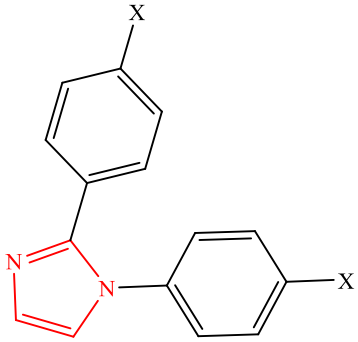


Fig. 27

X=OH,OMe

Karlık Ö *et al* 2018 by the interaction of 1-benzyl-3H-benzimidazolium p-toluene sulfonate derivatives and Ag_2O

synthesized novel benzimidazole-silver (I) complexes with the intention of checking their anticancer property. Researchers by MTT test investigated cytotoxic effects of compounds using human cancer cell lines and non cancer mouse cell lines. After evaluation researchers found that **Fig. 28** containing chlorine was found out to be most active among synthesized complexes but was found to be non selective for non cancer mouse cell lines. **Fig. 28** was observed to be equally cytotoxic as cisplatin against non cancer mouse cell lines. So for colorectal cancer **Fig. 28** was found to be a promising complex.

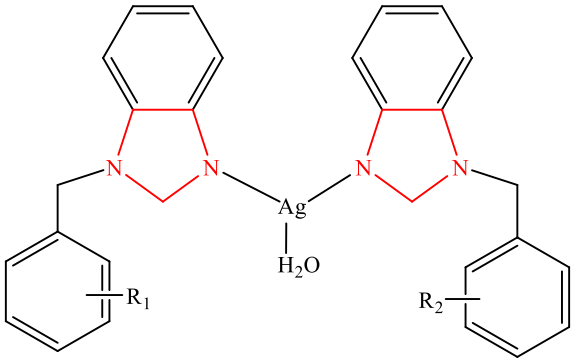


Fig. 28

b=R=2-CH_3; d=R=2-Cl

Since benzimidazole scaffold is rarely exposed for α-amylase inhibitory activity Adegboye AA *et al* 2018 synthesized2-aryl benzimidazole derivatives **Fig. 29** and evaluated for in vitro α-amylase inhibitory activity. Researchers deduced the structures of synthesized compounds by using spectral techniques. Acarbose was considered as standard and compared with synthesized compounds for their inhibition potential. In silico study was performed in order to explain the binding interactions of most active compounds with the active site of α-amylase enzyme.

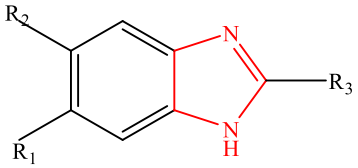


Fig. 29

R1=R2=H

R1=R2=CH_3

R1=H,R2=F

R1=H,R2=Cl

R1=H,R2=NO_2

Che Z *et al* 2015 synthesized a new complex [Zn(bbb)Cl2] DMF, where bbb is 2-(2-(1H-benzo[d]imidazol-2-yl) benzyl)-1Hbenzo[d]imidazole and characterized the new synthesized complex by different elemental analysis like X-ray and NMR. Two nitrogen atoms from 2- (2-(1H-benzo[d]imidazol-2-yl)benzyl)-1H-benzo[d]imidazole and two Cl coordinated distortion of tetrahedron geometry by Zn^{2+}. In DMF solution either maximal emission peak at550 nm complex emits yellow green luminescence. It was observed by researchers that with IC_{50} value of 8.9 ± 1.1 lM complex (25) exhibits inhibition on the growth of Eca109 cancer cell, it was comparatively lower than that of cisplatin. Hence, researchers told that in treatment of esophageal cancer the synthesized complex **Fig. 30b** has wide applications. (**Fig.30a**-ligand)

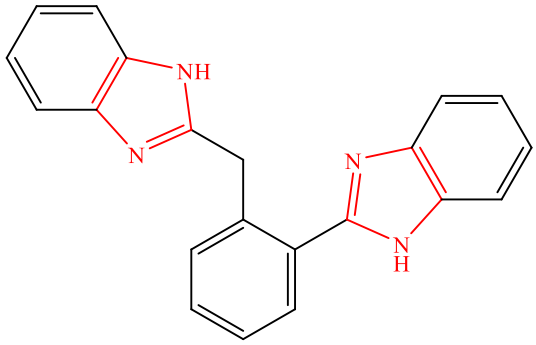


Fig.30a

Fig. 30b

By the reaction of N-arylcyanothioformamides with arylisocyanate derivatives a group of new imidazolidine iminothione derivatives were synthesized by Moussa Z *et al* 2016 with various halogenated and alkylated aromatic substituents at N-(1) and at N-(3). Their structures were deduced on basis of different spectral techniques. Synthesized compounds were evaluated for their antitumor activity. Highest cytotoxic activity was resulted due to existence of 3,5-dichlorophenyl moiety at N-(1) and trichlorophenyl moiety on N-(3) **Fig.31**. Lowest cytotoxicity was observed due to existence of 9H-fluorenyl moiety on N-(3).

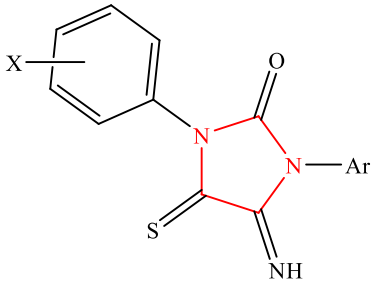


Fig.31

X=3,5-Cl_2

Ar=$C_6H_2Cl_3$-2,4,5

Bistrović A *et al* 2018 by implementation of microwave and ultrasound irradiation in click reaction and subsequent condensation of thus obtained 4-(1,2,3-triazol-1-yl) benzaldehyde with o-phenylenediamines synthesized series of novel amidino 2-substituted benzimidazoles linked to` 1,4-disubstituted 1,2,3-triazoles . By performing in vitro antiproliferative screening of compounds on human cancer cells it was revealed that benzyl-substituted 1,2,3-triazolyl imidazoline **Fig.32** and pchlorophenyl-substituted 1,2,3-triazolyl N-isopropylamidine **Fig.32** benzimidazole

possess potent cytostatic and selective activity against non-small lung cancer cell line in low nM range.

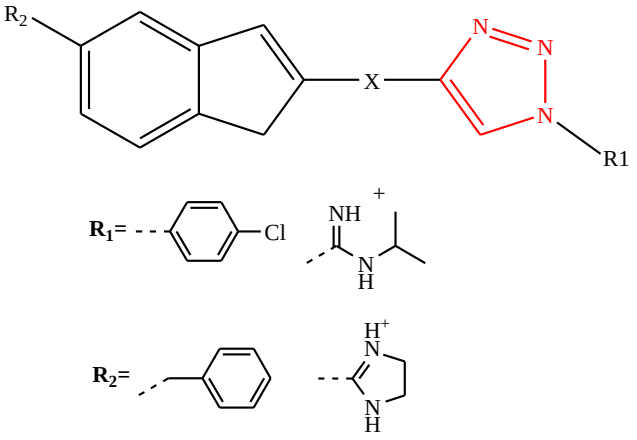


Fig. 32

Esteghamat-Panah R *et al* 2017 synthesized a new mononuclear rhodium (III) complex, [Rh(bzimpy) Cl3] (bzimpy = 2,6-bis (2-benzimidazolyl) pyridine) and the synthesized compounds were characterized by elemental analysis and spectral methods. Researchers confirmed the molecular structure of synthesized complex by single crystal X-ray crystallography. The evaluation of cytotoxic properties of synthesized complex Rh(III) was done against MCF-7, K562, and HT-29 cell lines by comparing with those of the free ligand (bzimpy) **Fig.33**. Researchers found that anticancer activity was significantly improved by complexation process.

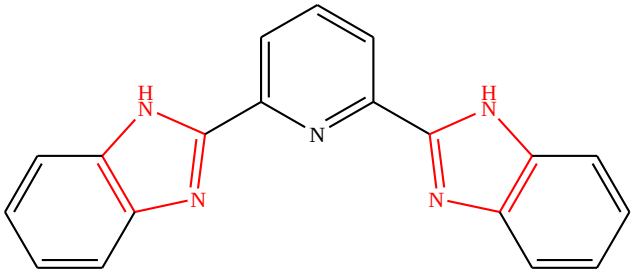


Fig.33

A series of five new mononuclear neutral gold (I) complexes containing N-heterocyclic carbenes (NHCs) were synthesized by Zhang C *et al* 2018 and these synthesized complexes were characterized by spectral techniques. Evaluation of all these five gold complexes was done in vitro against Leishmania infantum promastigotes and axenic amastigotes. Except one complex all other complexes showed potent activity against L. infantum amastigote. **Fig.34** exhibited very high and selective activity.

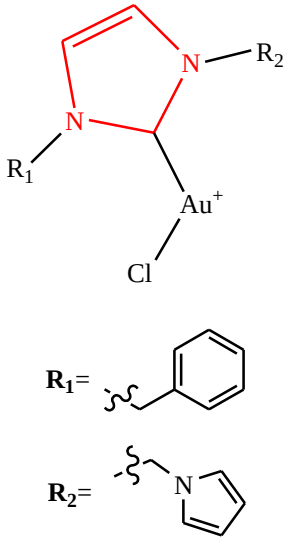


Fig. 34

Chen J *et al* 2011 did wide SAR studies on ABI-I scaffold in order to know more about structural requirements for potency of ABI analogs, to know about its metabolic stability. Researchers have previously reported about discovery of 2-aryl-4-benzoyl-imidazoles (ABI-I) as effective antiproliferative against melanoma. This time they synthesized ABI-II analogs and found out that these newly synthesized analogs have lower potency compared to previously discovered ABI-I. Researchers found that some new analogs have comparable effect to most active compounds of previous analogs when they were tested against two melanoma and four prostate cancer cell lines. Tested **Fig.35a** and **Fig.35b** were found to be equally active against highly paclitaxel resistant cancer cell lines and their parent cell lines, which indicated that ABI-I analog drugs may have therapeutic advantages over paclitaxel in treatment of resistant tumors. Researchers found that **Fig.35a** failed to extend stability. Researchers told about possibility of modifications on imidazole ring for further lead.

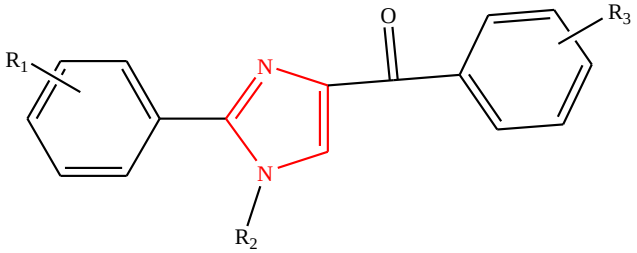


Fig. 35a

R_1=4-CH_3; R_2=CH_3; R_3=3,4,5-$(OCH_3)_3$

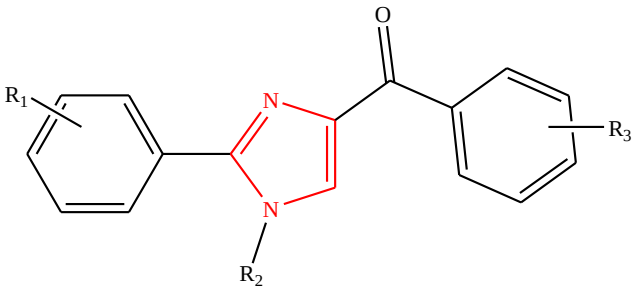


Fig. 35b

R_1=4-Br;R_2=H;R_3=3,4,5-$(OCH_3)_3$

A series of new 1H-benzo[d]imidazole derivatives of dehydroabietic acid were designed and synthesized by Gu W*et al* 2017 as potent antitumor agents. Structures were characterized using various spectral techniques. On performing in vitro cytotoxic assay most of compounds showed reduced cytotoxicity against noncancerous human hepatocyte (LO2) and significant cytotoxicity against two hepatocarcinoma cells (SMMC-7721 and HepG2). Out of these compounds, **Fig.36a** and **36b**exhibited best cytotoxicity against SMMC-7721 and HepG2 respectively.

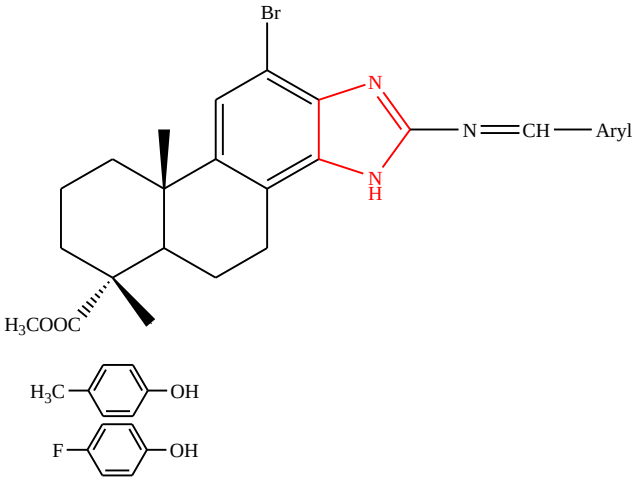


Fig.36

Oksala R *et al* 2018 reported discovery of a novel nonsteroidal dual-action compound, ODM-204 **Fig.37** it has therapeutic action against an advanced form of prostate cancer called castration-resistant prostate cancer (CRPC), characterized by by high androgen receptor (AR) expression and in this case AR signaling axis is persistently activated by residual tissue androgens. The compound inhibits CYP17A1 which inturn dampens androgenic stimuli in the body and it also blocks AR with high affinity and specificity. Researchers in their study observed inhibition of proliferation of androgen-dependent VCaP and LNCaP cells in vitro by ODM-204 and it significantly reduced tumor growth in a murine VCaP xenograft model in vivo. Researchers obtained similar results on testing it with human chorionic gonadotropin treated male rats and cynomologus monkeys. Hence the researchers found out that for the men having CPRC ODM-204 **Fig.37** can be an effective therapeutic.

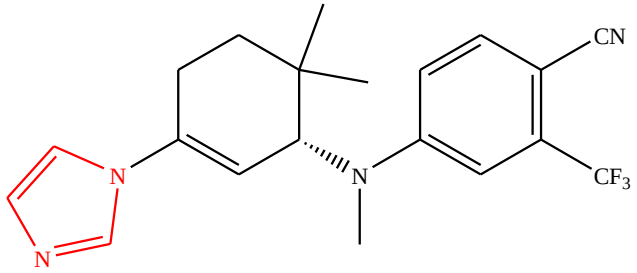


Fig.37

Chen CL *et al* 2013 synthesized a series of anthra[1,2-d]imidazole-6,11-dione derivatives and those synthesized derivatives were examined for suppression of cancer cell growth in vitro, for their ability to inhibit telomerase and hTERT expression. Selected compounds after testing were chosen by NCI screening. Among the compounds selected by NCI **Fig.38a, 38b** and **38c** showed selectivity towards hTERT expression without affecting cell growth.

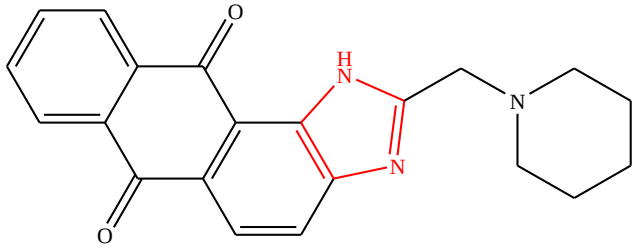


Fig.38a

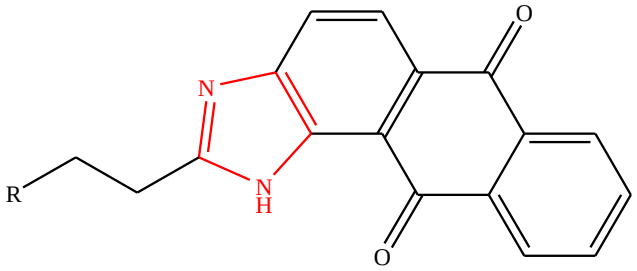
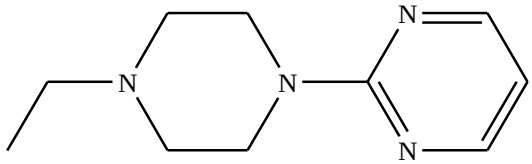


Fig.38b

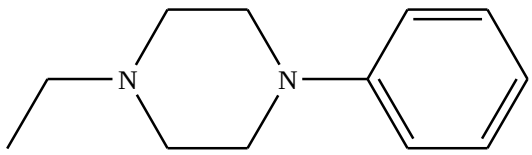
38b

R=



38c

R=



Salerno L *et al* 2013synthesized A novel series of aryloxyalkyl derivatives of imidazole and 1,2,4-triazole which act as inhibitors of heme oxygenase-1 (HO-1) and heme oxygenase-2 (HO-2). The compounds that carrying imidazole moiety as azolyl group and a 3-bromo or 4-iodophenyl as aryl moiety were found to be good inhibitors of HO-1. **Fig. 39a** and **39b** were found to be most potent and they were studied for their antitumor properties in a model of LAMA-84 R cell line overexpressing HO1 which is resistant to imatinibmesylate (IM). IM is used in treatment of cancer which acts as a tyrosine-kinase inhibitor. Researchers found out that compounds showed good antitumor properties of IM and sensitized model cell line.

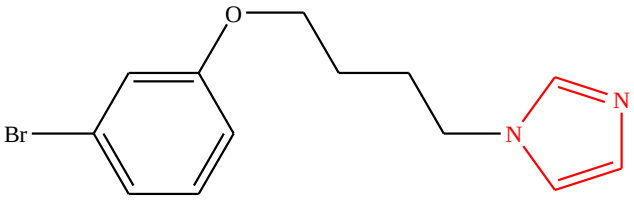


Fig.39a

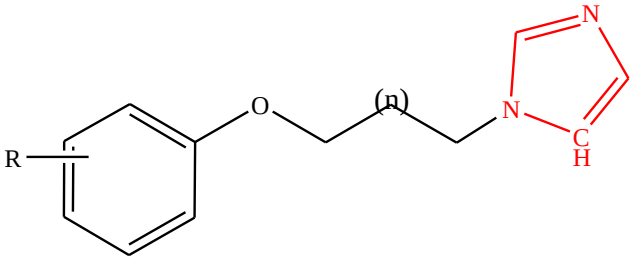


Fig. 39b
R=4-I
n=2

Chen X *et al* 2018 told that in repairing of DNA damaged by endogenous and exogenous process The nuclear protein poly (ADP-ribose) polymerases-1/2 (PARP-1/2) and in a past decadeit has been proved that in repairment of DNA PARP-1/2 inhibitors are clinically efficacious. So researchers developed a series of 4,5,6,7-tetrahydro thieno pyridin-2-yl benzimidazole carboxamides as novel and potent PARP-1/2 inhibitors. The compound with best PARP-1 and PARP-2 inhibitory activity among series of synthesized compounds was found to be **Fig.40** with IC_{50} of 18 nM and 42 nM. Moreover the selected **Fig.40** can selectively kill BRCA2 deficient V-C8 cells and shows single-agent activity and is well tolerated in BRCA 1 mutant model. After all evaluation process **Fig.40** was selected as lead candidate.

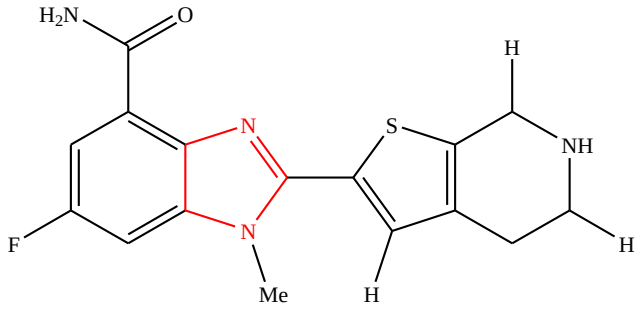


Fig.40

An abnormal increase in glucocorticoid levels will result in different pathological disorders and selective inhibition of appropriate enzymes is a validated strategy to restore them to their normal levels. So on studies on CYP11B Gobbi S *et al* (2017) by using datas from previously reported series of derivatives and from a performed docking study synthesized a small series of 6-substituted 3-imidazolylmethylxanthones **Fig.41**. The synthesized compounds were found to be potent inhibitors of CYP11B compared to previously reported compounds.

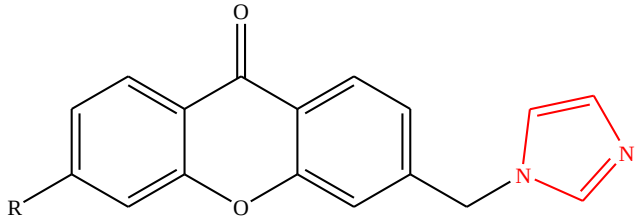


Fig.41

Jeanmart S *et al* 2018 told that against plant pathogens *Alternaria solani*, *Botryotinia fuckeliana*, *Erysiphe necator* and *Zymoseptoria tritici* novel imidazole-based ketene dithioacetals **Fig.42** show impressive in planta activity. Here especially, the control of phytopathogens is exhibited by derivatives of the topical antifungal lanoconazole, which possess an alkynyloxy or a heteroaryl group in the para-position of the phenyl ring. Thus obtained compounds in sterol biosynthesis pathway of fungi inhibit 14a-demethylase.

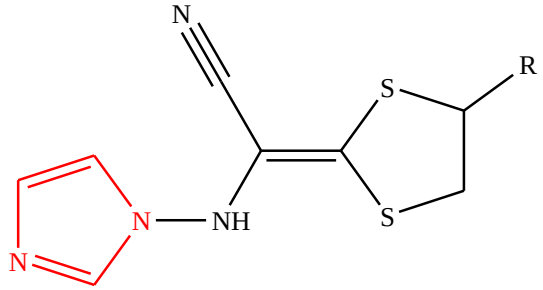


Fig. 42

Papadopoulou MV *et al* 2017 synthesized limited number of novel 3-nitrotriazole- and 2-nitroimidazole-linked quinolines and quinazolines they were evaluated for their in vitro antitrypanosomal and antitubercular as well as cytotoxic activities in normal cell. Among synthesized

compound all were active against T. cruziamastigotes, but against T. b. rhodesiense all but one were active or they were moderately active. But among synthesized compounds only two chloroquinolines exhibited satisfactory selectivity indices against T. cruzi, against T. b. rhodesiense only one compound showed satisfactory selectivity indices. Out of all synthesized compounds against hypoxic Mtb (MIC-2.89-9.18 µM) the 2-nitroimidazole-based analogs were active. By all data's researchers found out that 2-nitroimidazole **Fig.43a** and **43b** based aromatic amines are selectively active against nonreplicating Mtb.

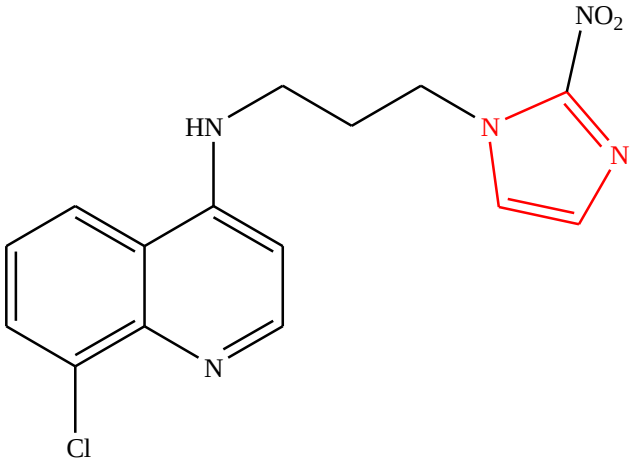


Fig. 43a

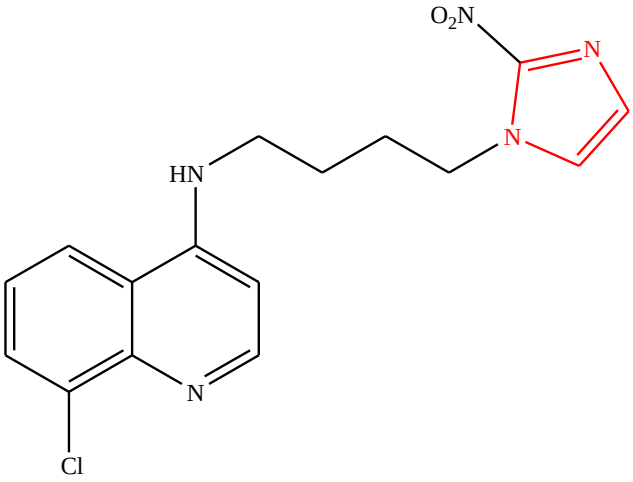


Fig. 43b

In chronic and acute inflammatory diseases the transcription nuclear factor NF-κB plays an important role. Among different strategies of inhibiting NF-κB, the development of IKK inhibitors was found to be most effective. In order to enhance the activity of inhibitors Cindy Patinote C *et al* 2017 synthesized different compounds based on the imidazo[1,2-a]pyrazine **Fig.44** (i.e3-bromo-8-chloroimidazo[1,2- a]pyrazine), imidazo [1,5-a] quinoxaline or pyrazolo [1,5- a] quinoxaline structures and evaluated their ability to inhibit activities of IKK1 and IKK2.

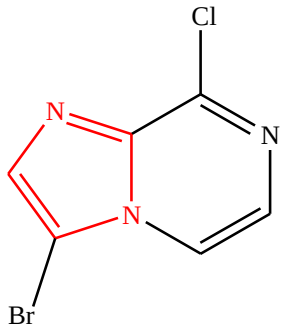


Fig.44

Rajesh R *et al* 2017 synthesized a series of substituted methoxybenzyl-sulfonyl-1Hbenzo[d] imidazole derivatives **Fig.45** and evaluated for their anti-ulcer therapeutics. Since it plays an important role in ulcer development a preliminary binding assay was carried out against H+ /K+ -ATPase from goat gastric mucosa. A molecular docking was carried out in order to know best binding affinities. Researchers found that many of synthesized compounds had proposed activity. In molecular docking study least inhibitory constant (ki) values of synthesized compounds were found in range 0.02-1.8 µM which was correlated in in the H+ /K+ -ATPase inhibition assay (IC50 0.14-1.29 µM). The compounds showed activity percentage of 72-92%. Safety and suitability/alternative towards anti-ulcer therapy was ensured from efficient HRBC membrane stabilization.

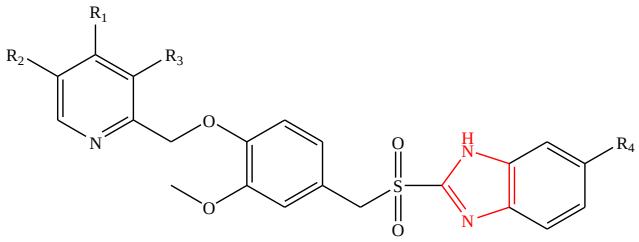


Fig.45

By reaction of imidazole with aryldiazonium salts, followed by ultrasound-assisted alkylation Salerno A *et al* 2017synthesizedseries of 2-arylazoimidazole derivatives. Spectral techniques were used in order to determine structure of synthesized compounds. The synthesized compounds were evaluated for anti-Trypanosomacruzi activity. Among synthesized compounds **Fig.46** were found to be effective inhibitors of epimastigote proliferation that are compounds which had piperidino substituents in the carboxamide moiety, remaining compounds showed low cytotoxicity. A mice was protected in vivo condition against lethal strain of Trypanosomacruzi. These result obtained tells us to use 2-arylazoimidazoles against Chagas' disease.

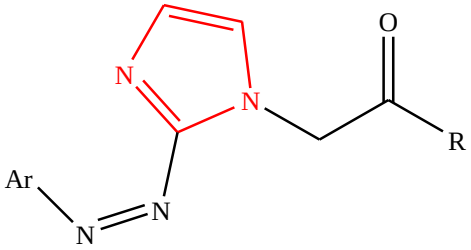


Fig.46

By the substitution reaction of cyanuric chloride with imidazole (IM), 2-methylimidazole (2MI), 2-ethylimidazole (2EI) and 2-ethyl-4-methylimidazole (EMI) Yang S*et al* 2018successfully prepared series of novel s-triazine based tri-imidazole derivatives **Fig.47**. To find the curing behaviors and thermal latency synthesized tri-imidazole derivatives were applied in epoxy resin (EP). EP systems containing s-triazine based tri-imidazole derivatives were shifted to high temperature regions, they showed higher storage stability at room temperature. The s-triazine structure with strong electron withdrawing effect resulted in suppression of reactivity of the modified imidazole derivatives towards EP at room temperature since their srong electron withdrawing effect reduced nucleophilicity of pyridine-like nitrogen atom of imidazole ring. At elevated temperatures s-triazine based tri-imidazole derivatives regained fast curing performance towards EP.

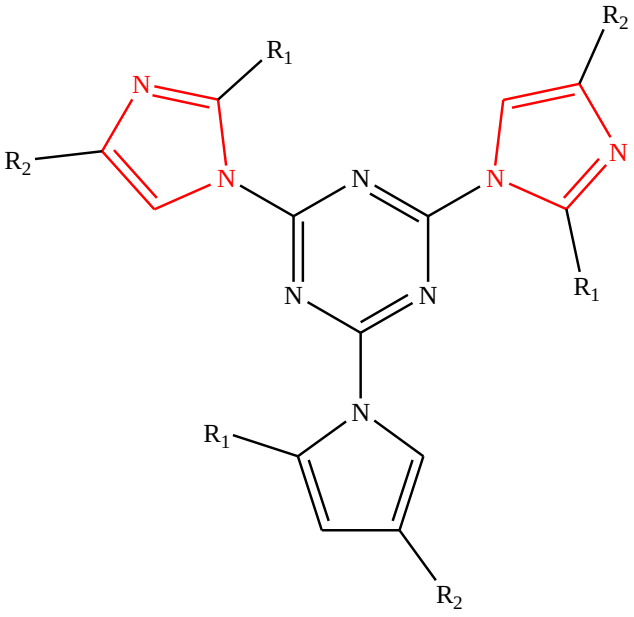


Fig.47

Zhou J *et al* 2017 synthesized novel 1H-benzo [d] immidazole-4-carboxamide derivatives bearing five-membered or six-membered N heterocyclic moieties at the 2-position as PARP-1 inhibitors. Many potent PARP-1 inhibitors having IC50 values in the single or double digit nanomolar level were obtained by structure activity relationships. Some of PARP-1 inhibitors also had inhibitory property against PARP-2. Among compounds synthesized strong potentiation effects on temozolomide (TMZ) in MX-1 cells was shown by **Fig.48a** and **48b.** In vivo it was found that **Fig.48a** could strongly potentiate cytotoxicity of TMZ in MX-1 xenograft tumor model, it was done in combination of **Fig.48a** with TMZ.

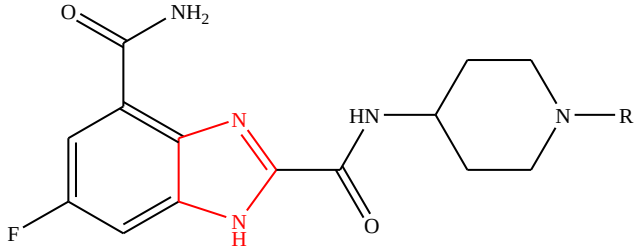


Fig.48a

R=neo-pentyl

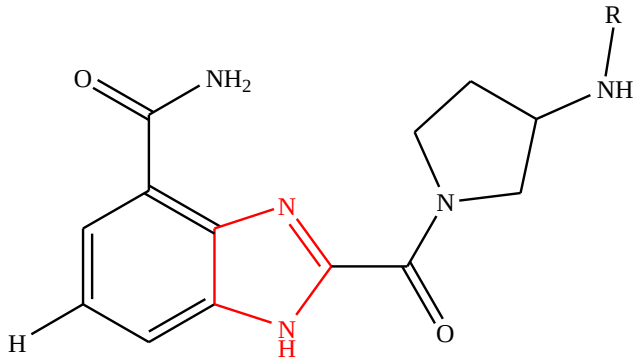


Fig.48b

R=cyclohexyl

In cancer immunotherapy Indoleamine-2,3-dioxygenase-1 (IDO1) is an attractive target. Zou Y *et al* 2017 synthesized series of novel imidazole isoindole derivatives and evaluated their ability to inhibit IDO1. Among derivatives synthesized derivative **Fig.49a** showed negligible cellular toxicity and it was found to be most active compound with nanomolar potency in the Hela cell-based assay. Spectral study showed that compound **Fig.49a** and **49b** bound to IDO1 and coordinated with the heme iron. In order to understand interaction of compounds to IDO1 protein, induced fit docking (IFD) and quantum mechanics /molecular mechanics (QM/MM) calculation were performed. The compounds could promote T cell proliferation, increase IFN-γ production, and reduce the numbers of Foxp3+ regulatory T cells.

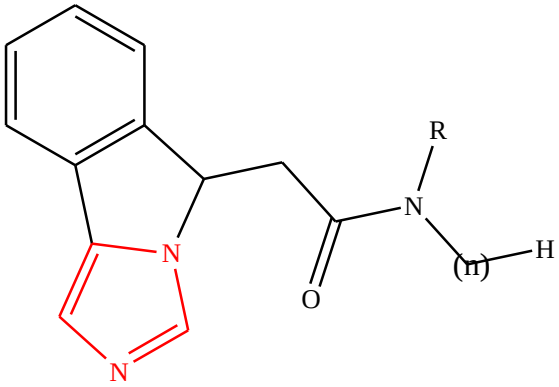
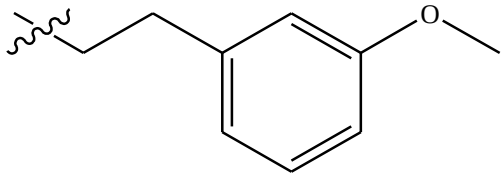
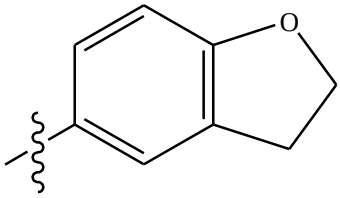


Fig.49

49a,R=



49b,R=



Patel HM *et al* 2017synthesized, a series of imidazo[2,1-b] [1,3,4] thiadiazole derivatives ,they were characterized by spectral techniques. Under direction of the US National Institutes of Health, the NIAID division by using Alamar Blue susceptibility test as a part of TAACF TB screening programme the synthesized compounds were evaluated against Mycobacterium tuberculosis H37Rv strain for their for their in vitro antitubercular activity. Among tested compounds 2-(1-methyl -1H- imidazol -2-yl) -6- (4-nitro phenyl) imidazo [2,1-b][1,3,4] thiadiazole **Fig.50** showed highest inhibitory activity as compared to other compounds. This revealed that these synthesized compounds have antitubercular activity at non cytotoxic concentrations.

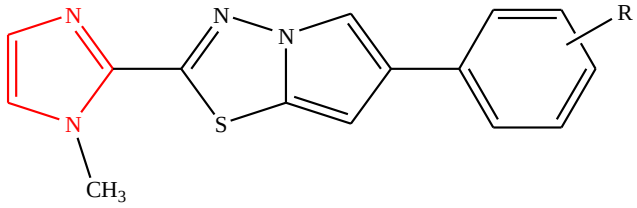


Fig.50

R=4-nitro

Because of its important role in promoting cancer growth and metastasis inhibition of angiogenesis through inhibition of vascular endothelial growth factor receptor 2 (VEGFR-2) has been applied in cancer therapy. Abdullaziz MA *et al* 2017 through facile synthetic pathways synthesized a series of benzimidazol-furan hybrids. To know in vitro cytotoxic activity of compounds they were evaluated against breast (MCF-7) and hepatocellular (HepG2) carcinoma cell lines. Two of conjugates showed potent antiproliferative properties against MCF7 cell line in comparison to tamoxifen. Against liver carcinoma cell line HepG2 some compounds showed promising potency when compared to that of cisplatin. **Fig.51** was found to have good VEGFR-2 inhibitory activity compared to that of sorafenib. Molecular docking was performed to know about binding of newly obtained compounds with VEGFR-2 active site. It showed their good inhibitory activity.

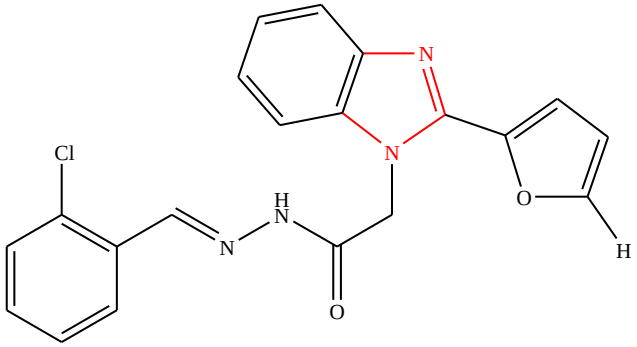


Fig.51

Liu J *et al* 2017 synthesized novel series of 2-(1H-pyrazol-4-yl)-1H-imidazo[4,5-f] [1,10] phenanthrolines and the synthesized compounds were evaluated against lung adenocarcinoma for their antitumor activity by CCK-8 assay,UV-melting study, wound healing assay, electrophoretic mobility shift assay (EMSA) and docking study. Synthesized compounds showed good inhibitory activities during evaluation. **Fig.52** was found to be more potent inhibitor than cisplatin, this compound showed potential antiproliferative activity against A549 cell line. Further experiments suggested that synthesized compounds can strongly interact with telomeric DNA to stabilize G-quadruplex DNA. Thus it showed that growth inhibition of A549 cells mediated by phenanthroline derivatives are correlated to their interaction with telomeric G quadruplexs.

Wani MY *et al* 2015 synthesized a series of compounds in which 2-(4-ethyl-2-pyridyl)-1H-imidazole was clubbed with substituted 1,3,4-oxadiazole and evaluated for its antifungal activity. In vitro assays done against different strains of laboratory and clinically isolated Candida species showed that several clubbed derivatives had excellent antifungal activity. According to SAR studies antifungalability of the compounds is guided by presence and position of substituents on the phenyl ring of the 1,3,4-oxadiazole, **Fig.53** were found to be active against all strains of fungi. Mechanisms of antifungal action of these compounds is revealed by impairment of ergosterol biosynthesis.

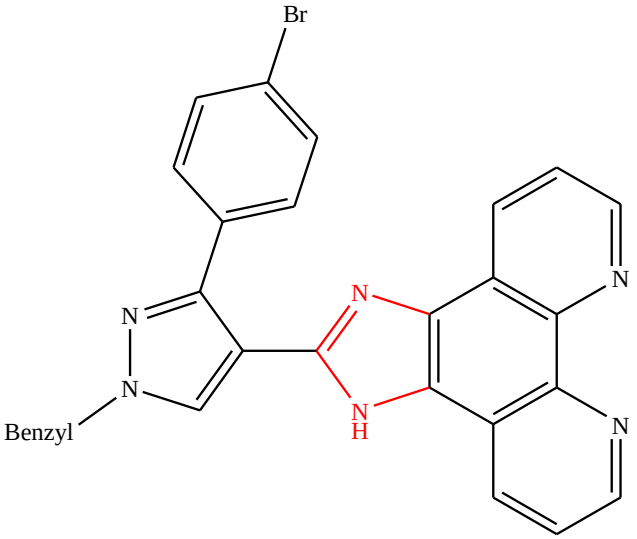


Fig.52

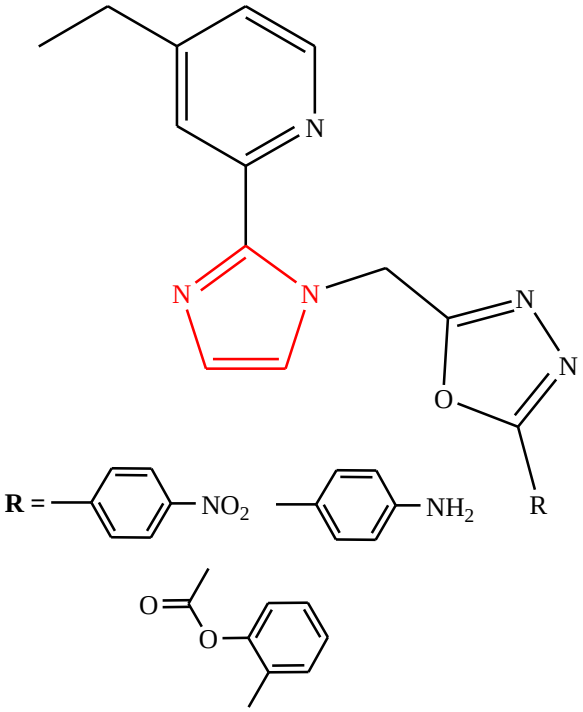


Fig.53

Kerscher-Hack S *et al* 2016 reported about synthesis and biological examination of new mGAT3 inhibitors in form of series of 1,5- and 1,4- substituted derivatives of 1H-imidazol-4-ylacetic acid, a series of 1,2-substituted 3-(1H-imidazol-2-yl) propanoic acid and an N-substituted (2E)-3-(1H-imidazol-2-yl) prop-2-enoic acid. Synthesized compounds were checked for inhibitory activities at mouse GABA transporter proteins mGAT1-mGAT4. Among 1,2-substituted compounds at mGAT3compound **Fig.54** (N-alkylated (2E)-3-(1H-imidazol2-yl)prop-2-enoic acid) exhibited pIC value of 5.13 ± 0.04,but for this GABA transporter it was devoid of significant selectivity. However compound **Fig.54** exhibited higher inhibitory activity than that of SNAP-5294.

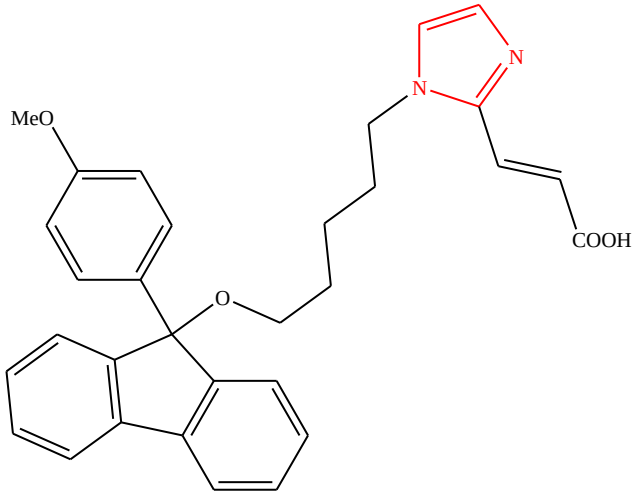


Fig.54

Dong J *et al* 2016 previously reported a potent compound that inhibits the wild-type influenza A virus A/HK/68 (H3N2) and A/M2-S31N mutant viruses A/WS/33 (H1N1) but its activity was found to be weak. So, to increase its ability on series of imidazole-linked pinanamine derivatives researchers carried out a structure-activity relationship study by modifying imidazole ring of a compound. Among several compounds tested **Fig.55** was found to be most potent, it was identified to be active on an amantadine-sensitive virus through blocking of the viral M2 ion channel. This compound also inhibited amantadine resistant virus and it is observed that activity of **Fig.55** was increased almost 24 times compared to previously reported compound.

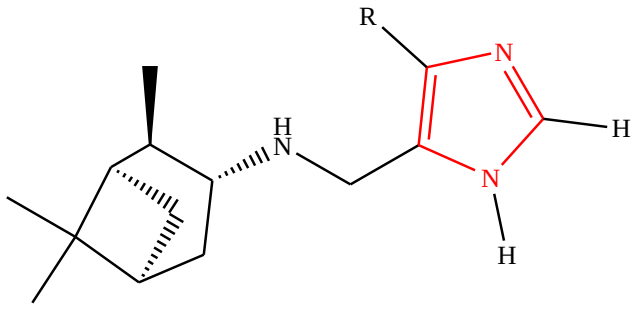


Fig.55

R=n-Pr

Tarazi H *et al* 2017 identified potent β-secretase inhibitors i.e, potent isophthalic acid derivatives armed with imidazol and indolyl groups. As measured by FRET (Fluorescence Resonance Energy Transfer) and cell-based (ELISA) assays most effective analogs demonstrated low nano-molar potency for the BACE1 (β-secretase cleaving enzyme). Researchers design method was supported by molecular modeling studies depending on previously reported hydroxyethylene transition state inhibitor derived

from isophthalic acid I and they followed traditional SAR approach. Most potent compound in FRET assay **Fig.56a** displayed an IC50 value for BACE1 of 75 nM and this compound cellular activity with an EC50 value of 0.81 µM. In cell-based assay **Fig.56b** was found to be most potent with an EC50 value of 0.29 µM.

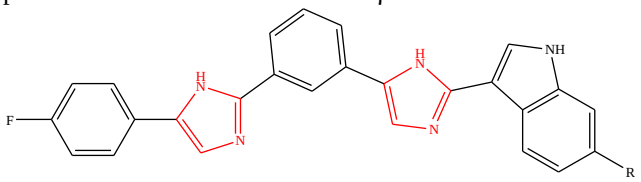


Fig. 56
56a:R=F
56b:R=OCF_3

Alwan WS *et al* 2015 reported synthesis of twenty five novel hybrid derivatives of imidazo [2,1-b]-1,3,4-thiadiazole containing chalcones and Schiff bases and carried out in vitro antimicrobial evaluation of synthesized compounds against three fungal strains (Candida albicans, Cryptococcus neoformans and Aspergillus niger). **Fig.57a, 57b** and **57c** exhibited promising activity against Cryptococcus neoformans at a MIC 1.56 µg/mL. IN addition to that researchers found out that **Fig.57c** displayed significant antifungal activity against clinical isolates of Cryptococcus neoformans at MIC 3.125 µg/mL. But these compounds exhibited moderate activity against four bacterial strains (Staphylococcus aureus, Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa) and Mycobacterium tuberculosis (H37Rv).

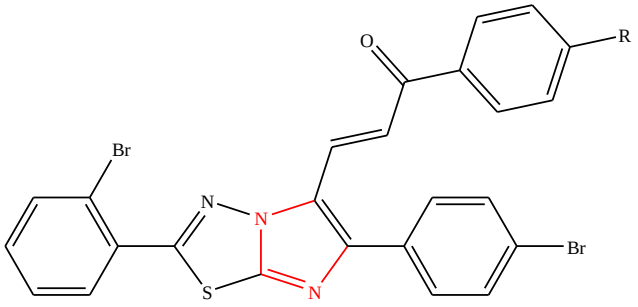


Fig.57
57a:R=H
57b:R=CH_3

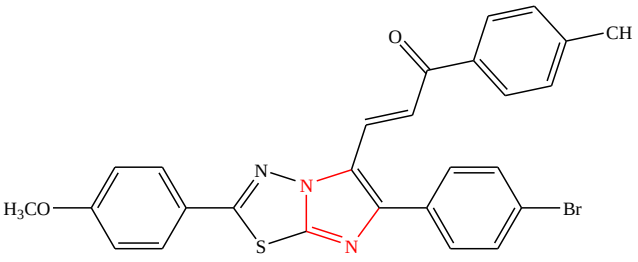


Fig. 57c

Kumar S *et al* 2016 described simple and efficient method to synthesize the hitherto unknown imidazo [1,2-a] pyridine selenides by reaction of 2-chloroimidazo[1,2-a]pyridines with aryl/heteroarylselenols, generated in situ by reduction of various diselenides with hypophosphorous acid. -ray crystallography was employed to confirm crystal structures of 3-nitro-2-(phenylselanyl)-imidazo[1,2-a]pyridine **Fig.58a**, 2-(mesitylselanyl)-3-nitro-imidazo [1, 2-a] pyridine and 3-nitro-2-(pyridin-2- ylselanyl)-imidazo [1,2-a]pyridine **Fig.58b** and to determine various structural parameters that are correlated eith X-ray crystal structures DFT calculations were performed. Antimicrobial evaluation were done in which it was found that **Fig.58a** and **58c** were active against gram negative bacterium E. coli and **Fig.58b** was found to be active against different fungal strains.In order to understand microbial activity of synthesized compounds time kill assay was performed and they were evaluated against human cell lines for their toxicity. Synergistic effects of active **Fig.58a** and **58b** were tested.

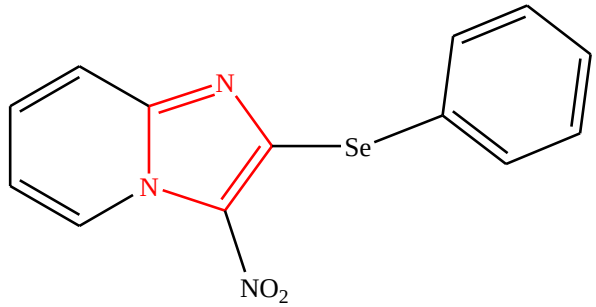


Fig.58a

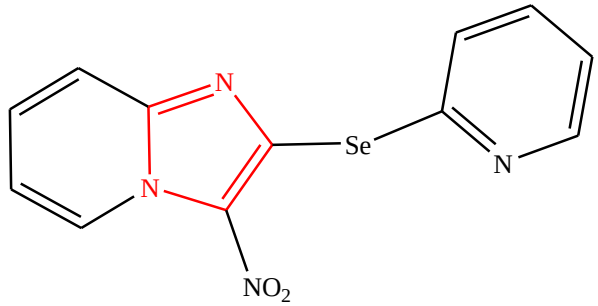


Fig.58b

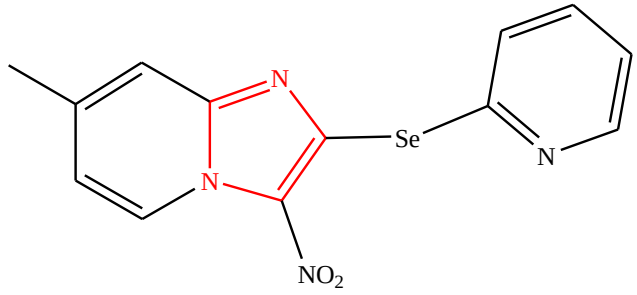


Fig.58c

In immunity, inflammation and cancer inhibition of the NF-κB-dependent pathways by IKK inhibitors plays an important role. Moarbess G *et al* 2016 using microwave assistance prepared new imidazoquinoxalines tricyclic derivatives and described their biological activities as IKK inhibitors. Researchers found that **Fig.59** possess potent

inhibition activity and selectivity for IKK2. Potent IKK2 inhibition activity and selectivity of compound was explained docking studies in IKK2 binding site.

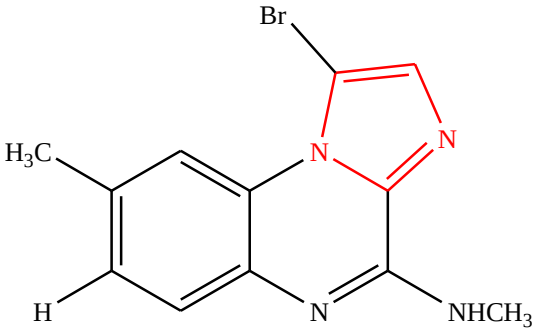


Fig.59

Stepanov AI *et al* 2015 using aminofurazanyl hydroximoyl chlorides and o-diaminobenzenes prepared series of 4-(1H-benzo[d]imidazol-2-yl)-furazan-3-amines (BIFAs) were prepared in good yields. This was performed under mild reaction conditions and , it was robust and did not require extensive purification of intermediates or final products. Biological evaluation of prepared compounds were done in order to reveal their antiproliferative effects in the sea urchin embryo model and human cancer cell lines. Out of examined compounds most active was **Fig.60**bearing the 2-chlorophenyl acetamide substituent at the nitrogen atom of the imidazole ring.

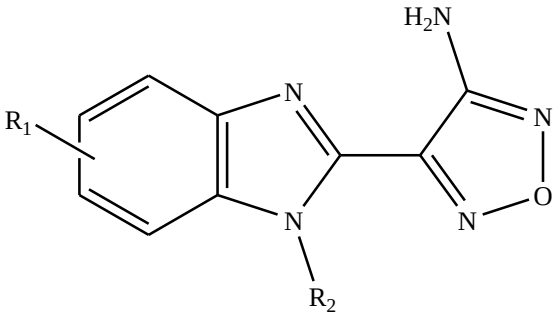
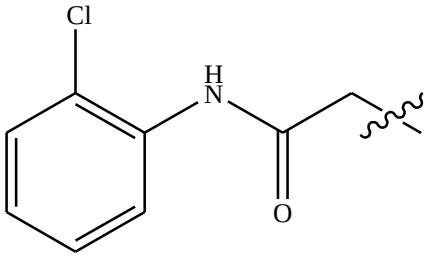


Fig.60

R_1=H



R_2=

Tuberculosis(TB) is caused by Mycobacterium tuberculosis (MTB) ,it primarily affects lungs i.e pulmonary TB. TB is a life threatening chronic deadliest infectious disease. In recent decades, drug-resistant TB (DR-TB), multidrug-resistant TB (MDR-TB), extensively drug-resistant TB (XDR-TB) and the recently cases of totally drug resistant (TDR) towards currently accessible drugs have emerged. In search of new anti-TB agents many derivatives have been synthesized and evaluated for their anti-TB activity. One of most important class of natural products that exhibit various biological activities is coumarin**Fig.61**, and its derivatives which are considered as new class of anti-TB agents with potential anti-TB activity. Due to this property coumarin has attracted great interest in developing new anti-TB agents. Hu YQ *et al* 2018 reviewed advances in application of coumarin-containing derivatives as anti-TB agents and about their design and structure-activity relationship.

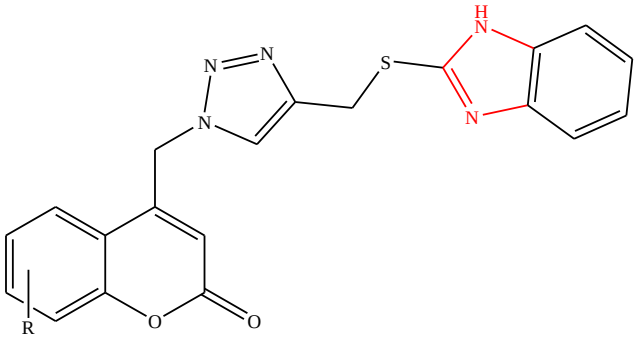


Fig.61

R=5,7-diMe or 7,8-diMe

Yoon YK *et al* 2015 under relatively mild reaction condition synthesized 51 novel benzimidazoles by a 4-step reaction starting from basic compound 4-fluoro-3-nitrobenzoic acid. Structures of synthesized compounds were confirmed by spectroscopic analysis and data. Among synthesized compounds 42 were evaluated against M. tuberculosis H37Rv strain using BacTiter-Glo™ Microbial Cell Viability (BTG) method for their antimycobacterial activity. Among evaluated compounds ethyl 2-(4-(trifluoromethyl)phenyl)-1-(2-morpholinoethyl)-1H benzo[d] imidazole-5-carboxylate **Fig.62** was found to be most active.

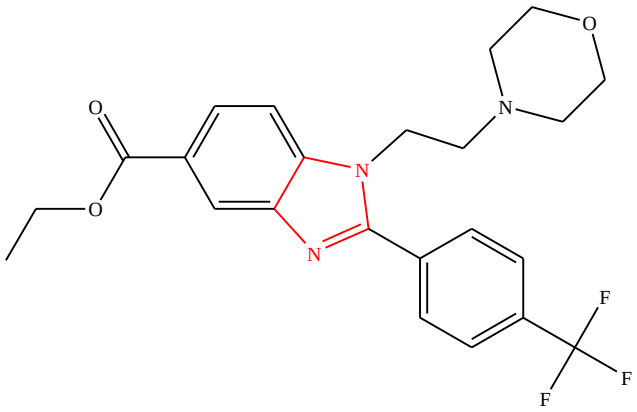


Fig.62

In search of new selective anti-cancer agents Singh K *et al* 2014 regioselectively synthesized a series of sixteen novel

2-aminoimidazole quinoline hybrid compounds Synthesized compounds were characterized extensively using spectral methods. During cytotoxic evaluation of synthesized compounds against different cancer cell lines **Fig.63** (Imd-Ph) emerged as potent cytotoxic compound. **Fig.63** was found non cytotoxic to breast cancer cells (MDA-MB231) as well as to normal primary endothelial cells (HUVEC), whereas it showed selective anticancer activity against human colon cancer cell line (HCT-116, DLD-1). Differential and selective toxicities exerted by the different derivatives against cancer and normal cells was revealed by structure activity relationship of imidazole-quinoline hybrid scaffold.

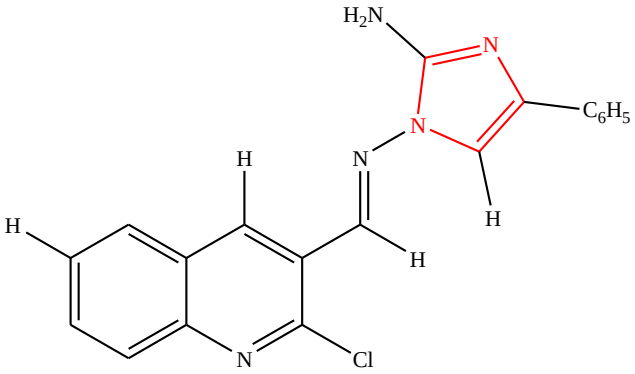


Fig.63

Olmo F *et al* 2015 prepared a series of new phthalazine derivatives containing imidazole rings and functionalized with nitro groups in the benzene ring of the phthalazine moiety, synthesized derivatives were identified on basis of their MS, elemental analysis and spectral datas, they were tested for their trypanocidal activity. In vitro the 8-nitrosubstituted compound **Fig.64** was found to be more active against T.cruzi when compared to reference drug benznidazole and in amastigote form it showed 47-fold better SI value than reference drug. It decreased the reactivation of parasitemia in immunodeficient mice and also remarkably reduced infectivity rate in Vero cells. **Fig.64** also resulted in decreased cardiac damage in mice. Despite presence of potentially toxic nitro group the livers, hearts, and kidneys of treated mice were unaffected by **Fig.64**. Researchers also found the inhibition of antioxidant parasite enzyme Fe–superoxide dismutase (Fe–SOD) by **Fig.64** in comparison with human CuZn–SOD.

By high-throughput screening assay with the use of dengue virus-2 replicon results showed that high dengue virus inhibitory activity was observed in imidazole 4,5-dicarboxamide (I45DC) derivative. Considering it as a lead, Saudi M *et al* 2014 synthesized a novel class of both disubstituted I45DCs and the resembling pyrazine 2,3-dicarboxamides (P23DCs). Researchers here reported on in vitro inhibitory activity of compounds against dengue virus (DENV) and yellow fever virus (YFV), in micromolecular range some of first generation compounds exhibited their activity against both virus. Among synthesized compounds **Fig. 65a** showed highest antiviral potency against YFV and **Fig.65b** and **65c** inhibited replication of DENV in Vero cells

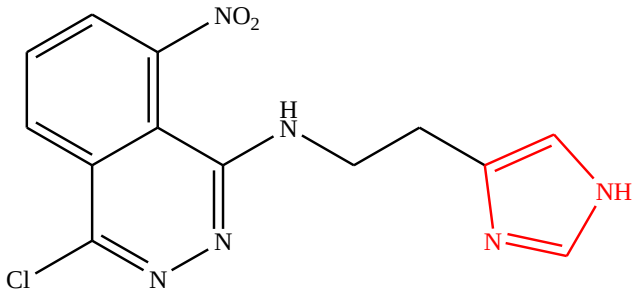


Fig.64

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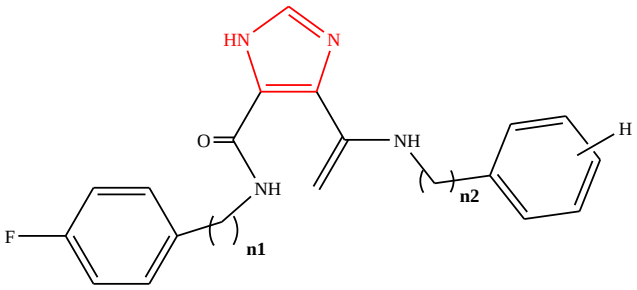

Fig.65a

n1=0, n2=0

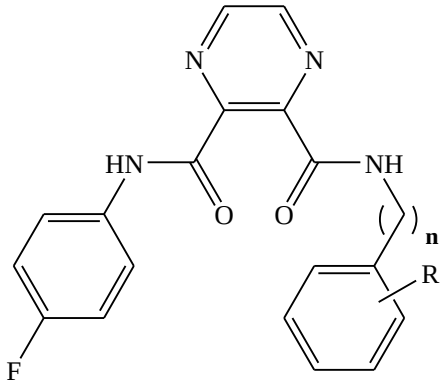

Fig.65b

65b:R=H,n=1

65c:R=p-methyl,n=0

Yan G*et al* 2017 developed b-secretase (BACE-1) inhibitors i.e a series of 2-substituted-thio-N-(4-substituted- thiazol/ 1H-imidazol-2-yl) acetamide derivatives. A small library of derivatives was designed supported by docking study and they were biologically evaluated in vitro. Selected synthesized compounds were evaluated with affinity (KD) towards BACE-1, blood brain barrier (BBB) permeability and cytotoxicity. From studies, most potent was found to be **Fig.66** which could serve as lead since it had high predicted BBB permeability and low cellular cytotoxicity.

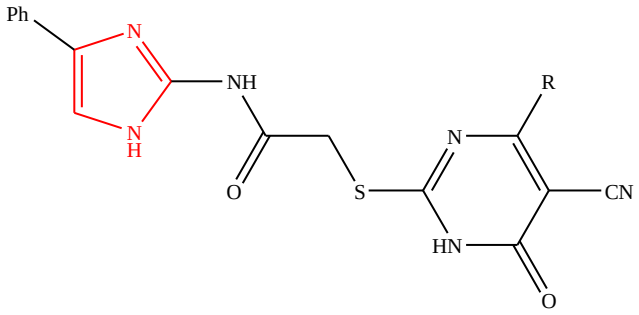

Fig.66

R=m-EtOPh

Bosc D *et al* 2016 modified their previously developed 3-arylthiophene series of inhibitors in search of new protein farnesyltransferase inhibitors with advanced antiparasitic activities by replacing the thioisopropyl group by different substituted imidazolyl methanamino moieties. Researchers synthesized twenty four new derivatives and evaluated them against human and parasite farnesyltransferases and determined their anti-parasitic activity against Plasmodium falciparum, Trypanosoma brucei **Fig.67a**, Trypano somacruzi **Fig.67b**, and Leishmania donovani. Significant increase in inhibition of parasite proliferation in the submicromolar range was observed by introduction of a N-p-substituted-benzylimidazole. Three compounds showed same IC50 values as that of reference miltefosine against Leishmania donovani proliferation and researchers found new derivatives possessing high level of anti-trypanosomal activity against T. cruzi, which was higher or in same order of magnitude as that of reference benznidazole and nifurtimox.

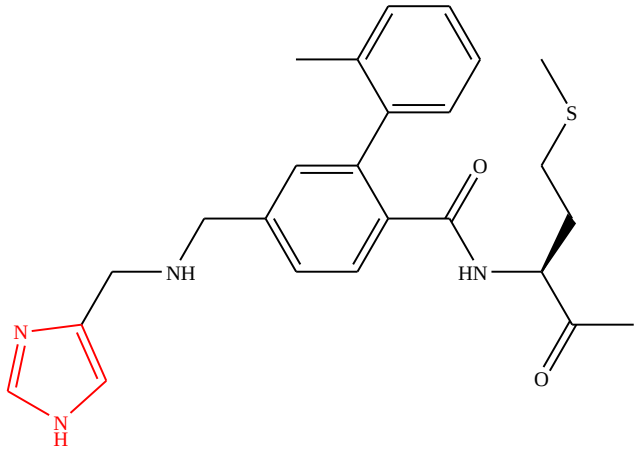

Fig.67a

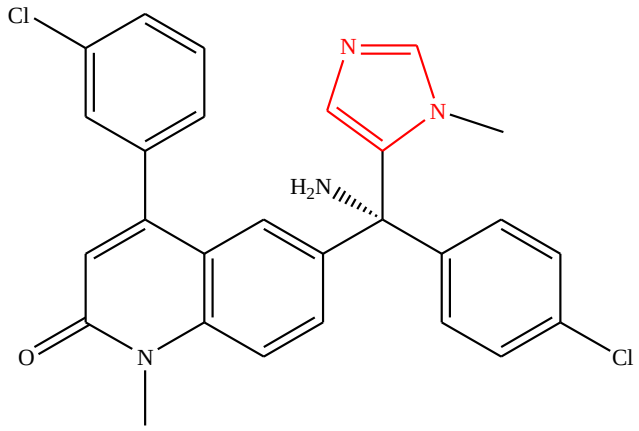

Fig.67b

Jeyakkumar P *et al* 2016 conveniently and efficiently synthesized series of novel berberine-benzimidazole derivatives and they were characterized by spectral techniques. In contrast with clinical norfloxacin, chloromycin and fluconazole many of synthesized compounds showed effective antimicrobial activity. Among synthesized compounds **Fig.68** exhibited good anti-MRSA, anti-E. coli, and anti-S. typhi activity with low MIC values, which is comparable or superior to reference drug. The primary evaluation revealed that **Fig.68** can effectively intercalate into DNA to form DNA complex and cleave DNA by agarose gel electrophoresis. Researchers also found that the most effective **Fig.68** was able to permeabilize the membranes of both Gram-positive (MRSA) and Gram-negative (E. coli DH52) bacteria efficiently. Experiments performed and molecular docking studies revealed that human serum albumin (HSA) could effectively transport **Fig.68**.

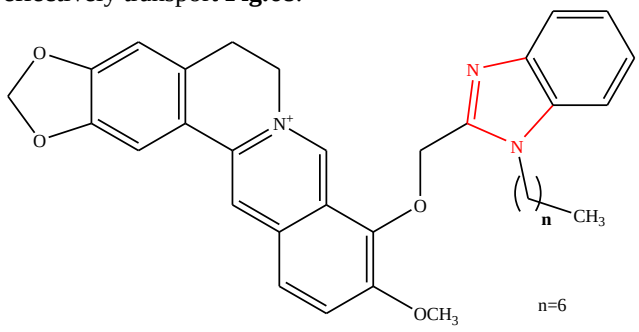

Fig.68

To Fig.ht against diabetic complications aldose reductase (ALR2) inhibitors provide a viable mode. Gopinath G *et al* 2016 based on natural isoflavonoids synthesized a novel series of amino acid conjugates of chromene-3-imidazoles. Identification of compounds is done on basis of spectral data and these compounds were tested for their inhibitory activity in vitro with IC50 value ranges from 0.031 ± 0.082 mM to 4.29 ± 0.55 mM. In silico and biochemical studies done by researchers confirmed that among synthesized

compounds **Fig.69** possess best inhibition activity with high selectivity index against Aldehyde reductase (ALR1).

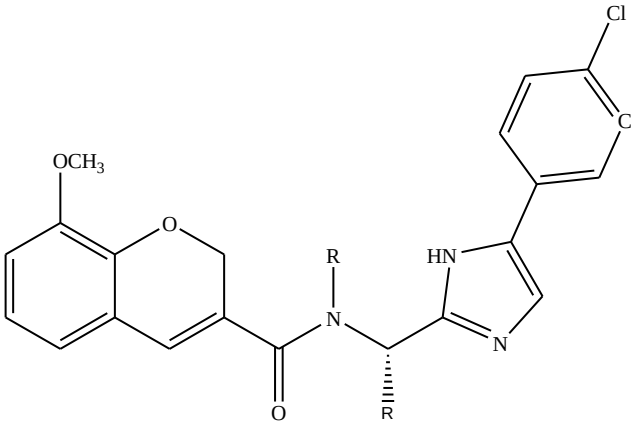

Fig.69

R=-CH_2-CH_2-CH_2-

Azoles are used for eradication of systemic candidiasis and also they are potent inhibitors of fungal lanosterol 14α demethylase (CYP51). Doğan İS *et al* 2017 reported about synthesis of series of 1-phenyl/1-(4-chlorophenyl)-2-(1H-imidazol-1-yl)ethanol esters and their evaluation. Synthesized compounds like **Fig.70** was found to be potent against resistant C. glabrata. The antifungal efficiency of compounds were confirmed by antibiofilm test. They also performed safety tests by cytotoxic assay against human monocytes.

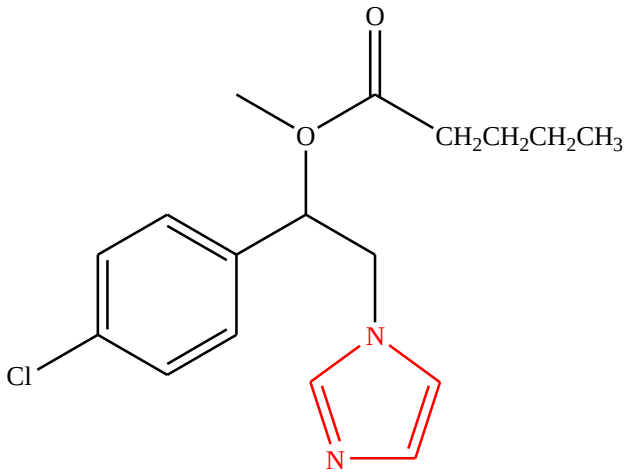

Fig.70

CONCLUSION

Heterocyclic compound imidazole possess variety of activities which can be used for betterment of medical techniques or to increase the ability of particular drugs. Imidazole has potential to Fig.ht against many diseases and infections which is proved by variety of techniques and doing evaluation studies using living species. So in coming few years, many of imidazoles can be used as drugs to increase medical standards.

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Cite this article:
Theivendren Panneerselvam, Adarsha Govinda K, Sajan Francis P, Current Review on Importance of Imidazole Derivatives. *International Journal of Pharmacy & Therapeutics*, 9(2), 2018, 42-65.
DOI: http://dx.doi.org/10.21276/ijpt.2018.9.2.3