Heterocyclic Letters
Vol. 12| No.1|155-168|November -January|2022
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

MINI REVIEW ON BIOLOGICAL ACTIVITY OF IMIDAZOLE AND THEIR DERIVATIVES

F.M. Zahou[a] , Ruba A. Alolayan[b], Nadia A. A. Elkanzi[b, c*]

[a]Biology Department, college of Science, Jouf University, sakaka, 2014, Saudi Arabia
[b]Chemistry Department, college of Science, Jouf University, sakaka, 2014, Saudi Arabia
[c] Chemistry Department, Faculty of Science, Aswan University, Aswan, 81528, Egypt
Corresponding author (N.A.A.Elkanzi)
**e-mail: nahasan@ju.edu.sa & kanzi20@yahoo.com*

Abstract
This mini review summarizes the importance of imidazole derivatives as biomolecules. Our focus will be on the structure and pharmacological activities of imidazole and its derivatives.

Keywords: biomolecules, Imidazole derivatives, pharmacological activities, Biological activity, heterocyclic compounds.

Introduction

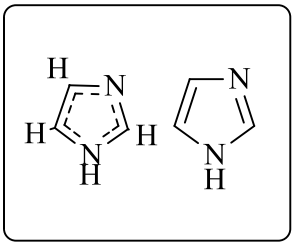
Imidazole derivatives are an important group of heterocyclic compounds that have biological, chemical properties and have been used for several years to treat parasitic illnesses produced by either protozoa or helminthes [I-III]. The imidazole ring is commonly create in highly important endogenous biomolecules comprising biotin, the essential amino acid histidine, and the autacoid histamine [IV]. Moreover, the imidazole nucleus is of significant importance in therapeutic chemistry research since numerous imidazole-comprising compounds show biological actions. on the other hand
heterocycles form by far the main of classical dissections of organic chemistry and are of immense use biologically and industrially. It is well recognized that the heterocycles are existent in all types of organic composites of interest in electronics, biology, optics, pharmacology, material sciences and so on. Heterocyclic nucleus reports a significant function in medicinal chemistry and attends as a key master for the growth of many therapeutic agents [V]. Mostly researchers have preserved their interest in sulfur and nitrogen-comprising heterocyclic compounds through decades of historical development

of organic synthesis [VI], but heterocycles with other heteroatoms such as oxygen [VII], phosphorus [VIII] and selenium [IX] also seems.

On the basis of various literature surveys Imidazole derivatives shows various biological activities such as anti -bacterial activity, anti-microbial activity, anti- helmintic activity , anti-inflammatory activity , anti- tubercular activity , anti-cancer activity ,anti-viral activity.

Structure and Pharmacological activities

Imidazole: Imidazoles are well known heterocyclic composites having significant feature of a variation of medicinal agents. Imidazole is a planar 5-membered ring. It is a very polar composite with dipole moment of 3.61 D. It is extremely soluble in water and also is soluble in other polar solvents. It exists in two equivalent tautomeric forms because the proton can be positioned on either of the two nitrogen atoms. Due to the presence of
a sextet of B-electrons the compound is categorized as aromatic. It contains of a pair of electrons from the protonated nitrogen atom and one from each of the lasting four atoms of the ring. Imidazole is amphoteric, i.e., it can function as both an acid and as a base [IX]. Structure of imidazole is shown in **Scheme 1**:



Imidazole

Scheme 1

Imidazo [2, 1-*a*] isoindole derivatives as anti-bacterial agents

Increasing resistance of pathogenic microorganisms toward the presently prevailing antibiotic drugs is main concern to the public health around the world. Hence, the treatment of microbial infections due to multidrug-resistant microbial pathogens becomes a major trial [X]. This has generated a substantial essential for the growth of new and more potent antimicrobial causes with broad spectrum of preventing activity, efficiency, and low toxicity. Therefore, it needs an effectual method to plan new antimicrobial causes with novel mechanism of action and structural modification to advance their target selectivity and efficiency. The high therapeutic characteristic of the imidazole-based drugs have stimulated the therapeutic chemists to create a great variety of novel chemotherapeutic causes [XI]. Furthermore, fused imidazole derivative such as imidazo [2,1-a]isoindole has emerged as an important heterocyclic scaffold with potentially therapeutic characteristics. One-pot creation of fused imidazo [2,1-a]isoindole products through in situ generation of amides from acid products and amines minimizes the hazards derived from their separation and handling. In the view of **[XII],** tetrahydroimidazo[2,1-a]isoindole derivatives consuming orthobenzoylbenzoic acid with ethylenediamine. In the study by **[XIII],** research group synthesized fused imidazo[2,1-a]isoindole using cyclic esters and ethylenediamine [XIII]. These fused imidazo[2,1-a]isoindoles have revealed strong

antiplasmodial activity. In the study by **[XIV],** fused imidazo[2,1-a]isoindole derivatives through intermolecular condensation of 2-formylbenzoic acid and α -aminoamides using a catalytic amount of toluene-p-sulfonic acid, which set the phase for the growth of a modular one-pot approach to fused imidazo[2,1-a] isoindole. In the view of [XV], fused 1H-imidazo[2,1-a] isoindole-2,5(3H,9bH)-dione derivatives by 2-formylbenzoic acid. One-pot synthesis of fused 2, 3-diaryl-5H-imidazo[2,1-a]isoindoles using 1,2-diketones, 2-formylbenzoic acids, and ammonium acetate is reported by **[XVI]**. Based on the above successful synthesis of fused imidazo[2,1-a]isoindoles and continuance of our research toward the creation of biologically strong heterocyclic compounds**,[XVII]**

Anti-microbial activity

On the other hand, antimicrobial resistance has become one of the most serious public health concern across the world. Antimicrobial resistance denotes to microorganism that has developed the capability to deactivate, reject, or block the inhibitory or fatal way of the antimicrobial causes [**XVIII**]. Structure–activity concept has emerged as a fruitful approach for the new drug discovery and is a quickly emerging theme in therapeutic chemistry. The 2-amino-4H-pyran are the model constructions, with their inherent affinity for diverse biological receptors, represent an ideal cause of core scaffolds and capping fragments for the scheme and creation of targeted molecules on a reasonable time scale [**XIX**]. Between them, 2-amino-4Hpyran-3-carbonitrile include a class of therapeutic compounds that apply a wide range of biological activities such as antitumor, antibacterial, antiviral, spasmolytic, and ant anaphylactic [**XX–XXIII**]. Literature survey showed that many 2-amino-4H-pyran derivatives displayed potent for the cure of Alzheimer, Schizophrenia, Myoclonus diseases [**XXIV**]. Green chemistry plays an important role in synthetic organic chemistry in current decades has been multicomponent reactions (MCRs) [**XXV, XXVI**]. The MCRs permit combination of more than two reactants in one-pot operations and permit direct admission to complex molecules and chemical libraries [**XXVII, XXVIII**]. Herein, we are recording an Imidazole catalyzed one-pot three-constituent coupling reaction under nonhazardous solvent, that is, mixture of EtOH and H_2O (1:1) at room temperature and synthesized composites were evaluated for antimicrobial analysis.

Imidazo [1, 2-a] pyridine analogues or derivatives as anti-helmintic drug

Helminths are parasites that live in the intestines of humans or other animals, and are mainly affected by polluted food or drinking water. There were several types of helminths, such as roundworm, pinworm, hookworm, tapeworm and whipworm **[XXIX- XXXI]**. The roundworm is the most broadly spread parasite in the world, and it is the most common parasite in humans. According to the World Health Organization (WHO) survey, about 25% of the world's population was infected with roundworms, and with an infection rate of more than 70% in individual areas **[XXXII-XXXV]**. Helminths are predominant in countries or areas where are tropical, economically undeveloped, warm and humid, and in poor sanitation. Anti-helminth drugs can destroy or eliminate the intestinal parasite (roundworm, pinworm, hookworm, whipworm and tapeworm) for human or other animals **[XXXVI – XXXVII].** They comprise the anti-roundworm drugs, anti-hookworm drugs, antipinworm drugs, anti-whipworm drugs and anti-tapeworm drugs. Some drugs can destroy or drove for a variety of helminth infection, too be recognized as extensive-

spectrum anti-helminth. Now, the medical used main anti-helminth drugs have imidazoles (Albendazole, Ciclobendazole, Obibendazole, Parbendazole, Mebendazole and Tiabendazole, **Figure 1**), piperazines (Phosphate and Citrate), piperidines (Pyrantel and Oxantel) and other drugs (Toosendanin and Agrimophol) **[XXXVIII – XL]**. These anti-helminth drugs essentially act on the intestinal, their chemical configuration was dissimilar, and they vary in the mechanism of action **[XLI – XLIII]**. However, the basic mechanism is generally in the neuromuscular system of paralytic body, affecting spasm or paralysis of the worm muscle, also producing the insect body to miss the adsorption ability of the intestinal wall and eject the polypide **[XLIV]**. Furthermore, the action mechanism of some drugs is to affect the biological action of the enzyme in the insect, which causes the loss of energy in the polypide because of the failure of glucose metabolism. The other drugs can directly digest the polypide **[XLV]**. In clinical, the imidazoles drugs are the most broadly used for anti-helmintic **[XLVI – XLVII]** because they can expel roundworm, hookworm, pinworm and whipworm. They are wide-spectrum of anti-helminth drugs. The pharmacological action of imidazole drugs selectively and irreversibly prevents the acceptance of glucose by the helminths, which leads to endogenous glycogen reduction of the helminths. The inhibition of the fumarate reductase [**XLVIII]** delays the creation of adenosine triphosphate, leading to the regular death of the helminths due to energy reduction. There are four binding places among fumarate reductase and imidazoles of drug **[XLVIII]**, which have strong capability of combination. For imidazole drugs of anti-helmintic, Albendazole is good in the clinical cure effect, it has a broad-spectrum of anti-helmintic, such as roundworm, hookworm, whipworm and pinworm, and it has good to destroy or diver influence for imago and egg. Albendazole is an oral absorption drug, and it has side-effects on human gastrointestinal, teratogenic and embryo toxic effects on pregnant women.

Using structural transformation and by modification with alkyl groups, this research used Albendazole as the lead compound to plan a novel of chain imidazo [1, 2-a] pyridine analogues or derivatives **(Figure 2)**. From the view of structure-activity relationship (SAR), the a new planned compounds (4a–4r) and Albendazole are like the imidazole ring construction, and may too have the influence of anti-helmintic. The adaptation with alkyl might influence to design the anti-helmintic drugs with broad-spectrum, less body to absorb, low poisonousness and low on the gastrointestinal mucosa irritation. This novel of series imidazo [1, 2-a] pyridine analogues or products were created by 2-hydrimidazo [1, 2-a] pyridin-2-amine (1a) as the initial material, and the target compounds were took by three steps of chlorination, amidation, and alkylation, correspondingly **(Scheme 2).** The synthetic way was characterized by simple process, high total yield and mild reaction circumstances.

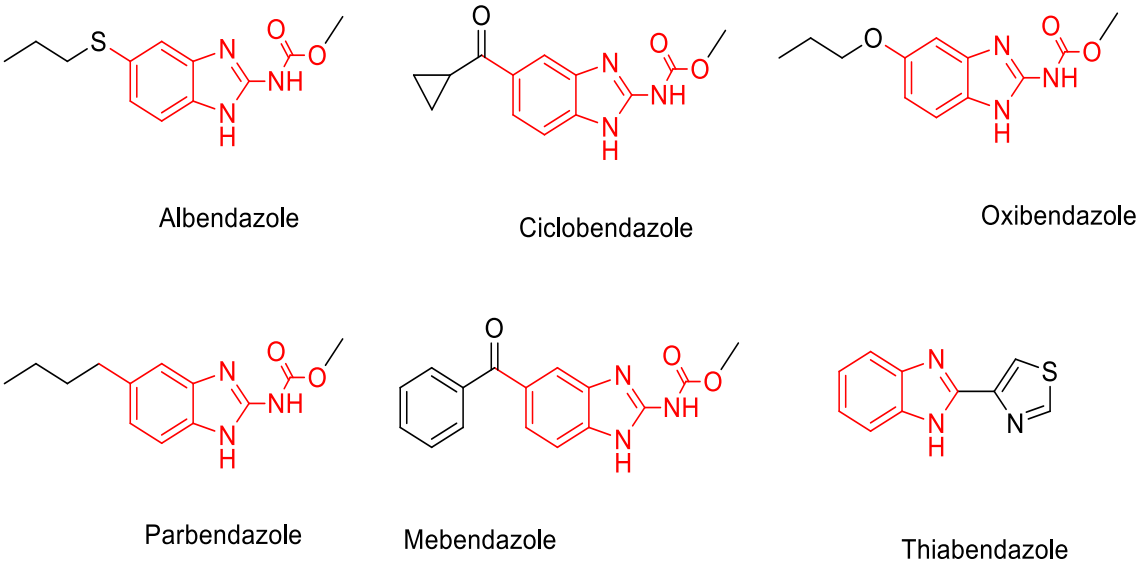
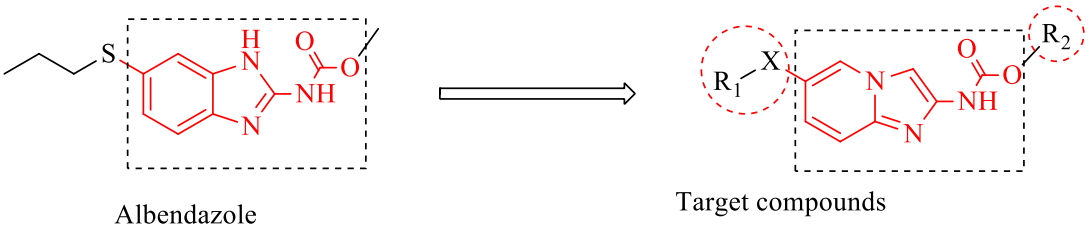
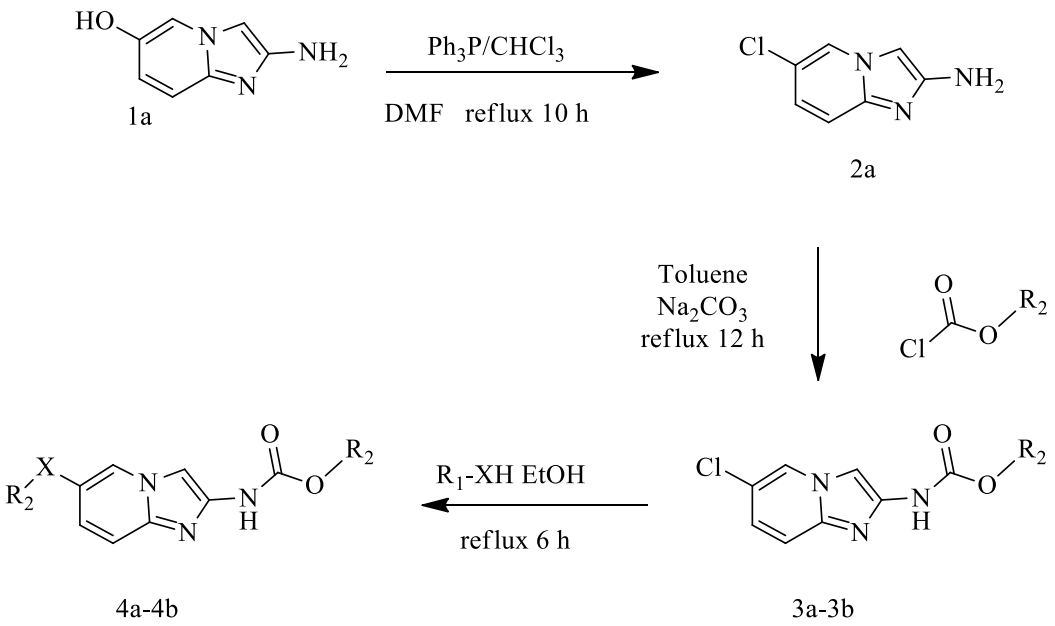


Figure 1: the structure of imidazoles drugs with anti-helminth



R_1: C_2H_5-, n-C_3H_7-, n-C_4H_9-
R_2: CH_3-, C_2H_5-
X: NH, O, S

Figure 2: Design of imidazole [1, 2-a] pyridine analogues or derivatives



R1: C2H5-, n-C3H7-, n-C4H9-
R2: CH3-, C2H5-
X: NH, O, S

Scheme 2: The synthetic route of imidazo [1-2a] pyridine analogues or derivatives

Anti-inflammatory and Anti-microbial Activity of Novel Indolyl Chalcone Derivatives

Heterocyclic compounds containing nitrogen have been pronounced for their biological action against different microorganisms. The indole unit is the key structure block for variability of compounds, which have vital roles in the roles of biologically significant molecules [**XLIX**, **L**]. Introduction of varies groups to the adapted indole construction can yield a sequence of composites with multiple actions. Various 3-substituted indoles had been used as beginning resources for the creation of a number of alkaloids, agrochemicals, pharmaceuticals, and perfumes. Also, 3-substituted indole derivatives have different kinds of extensive spectrum's biological actions such as antimicrobial, antitumor, hypoglycemic, anti-inflammatory, analgesic, and antipyretic activities [**LI**, **LII**]. Additionally, the replacement at the 3-position of the indole circle can take place by presenting an extra heterocyclic ring, for example imidazole (topsentins, nortopsentins) [**LIII**, **LIV**], dihydroimidazole (discodermindole) [**LV**], oxazole [**LVI**, **LVII**], thiazole [**LVIII**], quinazoline [**LIX**], pyrimidine [**LX**, **LXI**] as shown in Figure 3, and pyrazoline [**LXII**]. Therefore, 3-substituted indoles still characterize an important synthetic task. In view of the important biological properties of the indole ring, we have scheduled to synthesize a new series of 3-chloro-2-substituted indole products bearing side chains with altered constructions; as such products could own interesting and beneficial antimicrobial and anti-inflammatory actions.

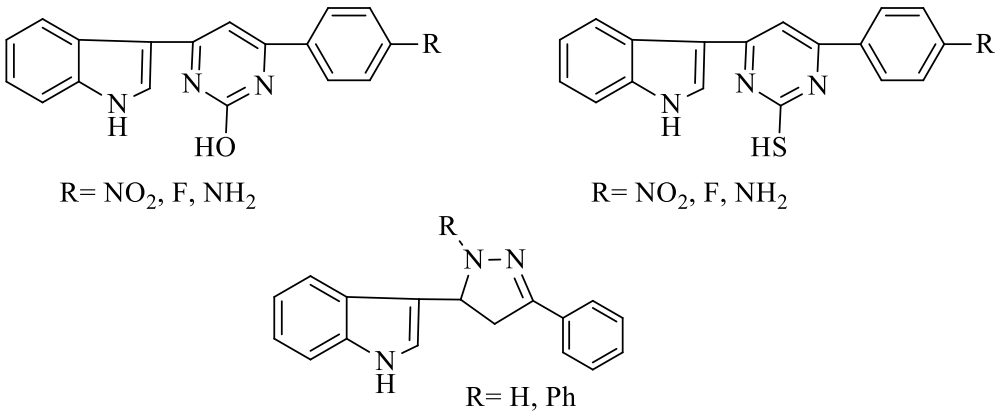
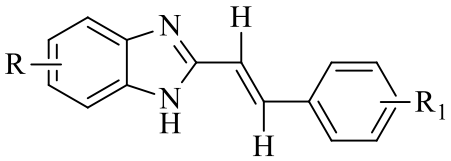


Figure 3: pyrimidinyl and pyrazolylindole as bioactive moleculesAnti-tubercular activity

The [**LXIII**] created sequence of novel 5-(nitro/bromo)-styryl-2-benzimidazoles derivatives and screened for in vitro anti-tubercular action against *Mycobacterium tuberculosis*, and these compounds exhibited good antitubercular actions. Streptomycin was used as reference drug.



A, R=Br, R_1=H
B, R=Br, R_1= 3,4-OCH_3
C, R=Br, R_1= 4-CH_3
D, R=Br, R_1= 2,4-Cl

Fig-4

The [**LXIV**] described anti-mycobacterium tuberculosis actions of ring substituted -1Himidazole-4-carboxylic acid products and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid products against durg-sensetive and durg-resistent *M. tuberculosis* strains. (Fig.**5**) compounds were most strong compound.

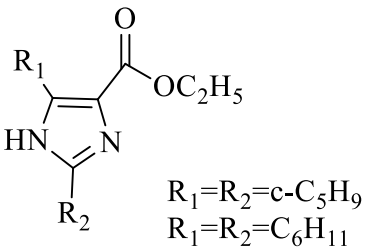


Fig-5

The [**LXV**] created a series of imidazole derivatives and compounds were screened against *M .tuberculosis* where this compound exhibited good antitubercular activity.

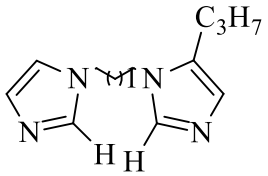
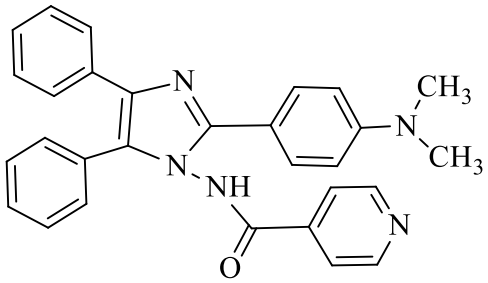


Fig- 6

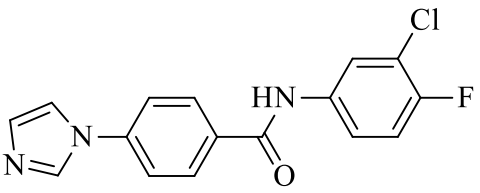
Anti-cancer activity

Ten new aryl imidazoles combined with chemotherapeutic pharmacophores have been created and assessed for their anti-bacterial and short term anti-cancer activity. All the manufactured substituted imidazoles have revealed good antibacterial action against gram negative bacterial strains *Klebsiella pneumoniae* and *Escherichia coli*. The produced imidazole derivatives have important cytotoxic action against Ehrich's Ascites Carcinoma (EAC) cell lines and Dalton's Lymphoma Ascites (DLA) cell lines. Compound 1 exhibited the best anti-cancer action with CTC_{50} value of 98.56 and 31.25 μg Ml [**LXVI**] against DLA and EAC cell line [**LXVII**].

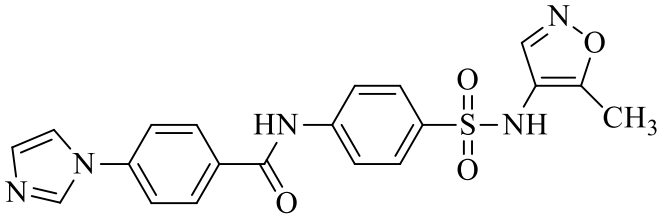


1

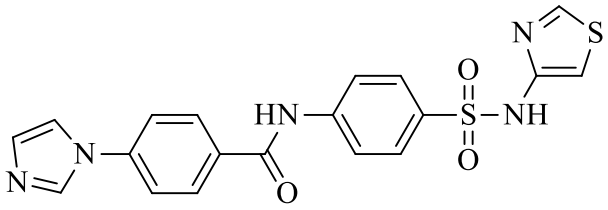
A new series of 1-substituted imidazole products have been created by taking altered anilines and sulfonamides as substitutions [**LXVIII**]. The compounds were screened for their anticancer and antimicrobial activities. Compound 2 exhibited highest activity against cervical cancer. Compound 3 showed good antifungal activity while compound 4 showed good antibacterial activity.



2



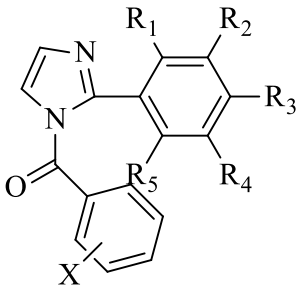
3



4

Anti-viral activity

The [**LXIX**] created imidazole derivatives and the antiviral screening of (substituted phenyl)-[2-(substituted phenyl)-imidazol-1-yl]-methanones against viral strains showed that compounds A and B selected as the most potent antiviral agents. Ribavirin was used as standard drug.



For compound A, R_1=H,R_2=H,R_3=Cl,R_4=H,R_5=H,X=4-NO_2
B, R_1=H,R_2=H,R_3=NO_2,R_4=H,R_5=H,X=4-NO_2
Fig- 7

The [**LXX**] created seventy six 2-phenylbenzimidazole derivatives and assessed for cytotoxicity and anti-viral activity against a panel of RNA and DNA viruses. Compound ([5,6- dichloro-2-(4-nitrophenyl) benzimidazole]) revealed a high activity resulting more strong than reference drugs smycophenolic acid and 6-azauridine.

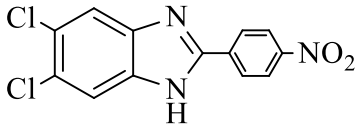


Fig- 8
5,6-dichloro-2-(4-nitrophenyl)-1H-benzo[d]imidazole

Conclusion

Imidazole derivatives have several antimicrobial activities such as anti -bacterial activity , anti-microbial activity, anti- helmintic activity, anti-inflammatory activity,anti- tubercular activity,anti-cancer activity,anti-viral activity.

Acknowledgements

The financial support from Jouf University, Saudi Arabia.

References:

[I] M.F. Malkin, R.M. Camacho, The effect of thiabendazole on fumarate reductase from thiabendazole-sensitive and resistant Haemonchus contortus, J. Parasitol. 58 (1972) 845e846. PMID: 5057246.
[II] R.K. Prichard, The fumarate reductase reaction of Haemonchus contortus and the mode of action of some anthelmintics, Int. J. Parasitol. 3 (1973) 409e417, http://dx.doi.org/10.1016/0020-7519(73)90121-5.
[III] J.J. Marr, R. Docampo, Chemotherapy for Chagas'disease: a perspective of current therapy and considerations for future research, Clin. Infect. Dis. 8 (1986) 884e903, http://dx.doi.org/10.1093/clinids/8.6.884.
[IV] A.R. Katritzky, Comprehensive Heterocyclic Chemistry, vol. V, Pergamon, Exeter, UK, 1984, pp. 469e498. Med. Chem. Res. 20 (2011) 1119e1140, http://dx.doi.org/10.1007/s00044-010-9472-5 and references therein.

[V] Kashyap, S.J., P.K. Sharma, V.K. Garg, R. Dudhe and N. Kumar, 2011. Review on synthesis and various biological potential of thiazolopyrimidine derivatives. J. Adv. Sci. Res., 2: 18-24.
[VI] Valverde, M.G. and T. Torroba, 2005. Sulfur- Nitrogen heterocycles. Molecules, 10: 318-320.
[VII] Liu, R.S., 2001. Synthesis of oxygen heterocycles via alkynyltungsten compounds. Pure Appl. Chem., 73: 265-269.
[VIII] Reddy, P.V.G., Y.B. Kiran, C.S. Reddy and C.D. Reddy, 2004. Synthesis and antimicrobial activity of novel phosphorus heterocycles with exocyclic p-C link. Chem. Pharm. Bull., 52: 307-310.
[IX] Abdel-Hafez, S.H., 2008. Selenium containing heterocycles: Synthesis, anti-inflammatory, analgesic and anti- microbial activities of some new 4-Cyanopyridazine- 3(2H) selenone derivatives. Eur. J. Med. Chem., 43: 1971-1977.
[X] (a) Muroi, H.; Nihei, K.; Tsujimoto, K.; Kubo, I. Bioorg. Med. Chem. 2004, 12, 583–587; (b) Pfeltz, R. F.; Wilkinson, B. J. Curr. Drug Targets Infect. Disord. 2004, 4, 273–294; (c) Tenover, F. C.; Mc Donald, L. C. Curr. Opin. Infect. Dis. 2005, 18, 300–305.
[XI] (a) Congio, C.; Cocco, M. T.; Onnis, V. Bioorg. Med. Chem. Lett. 2008, 18, 989–993; (b) Emami, S.; Foroumadi, A.; Falahati, M.; Lotfali, E.; Rajabalian, S.; Ebrahimi, S.; Farahyar, S.; Shafiee, A. Bioorg. Med. Chem. Lett. 2008, 18, 141–146; (c) Ujjinamatada, R. K.; Baier, A.; Borowski, P.; Hosmane, R. S. Bioorg. Med. Chem. Lett. 2007, 17, 2285–2288; (d) Zampieri, D.; Mamolo, M. G.; Laurini, E.; Scialino, G.; Banfati, E.; Vio, L. Bioorg. Med. Chem. 2008, 16, 4516–4522; (e) Crane, L.; Anastassiadour, M.; Hage, S. E.; Stigliani, J. L.; Mouysset, G. B.; Payard, M.; Leger, J. M.; Bizot-Espiard, J.; Ktorza, A.; Caignard, D.; Renard, P. Bioorg. Med. Chem. 2006, 14, 7419–7433; (f) Valhhakis, J. Z.; Kinobe, R. T.; Nakatsu, K.; Szarek, W. A.; Crandall, I. E. Bioorg. Med. Chem. Lett. 2006, 16, 2396–2406; (g) Venkatesan, A. M.; Agarwal, A.; Abe, T.; 932 S. NARSIMHA ET AL. Ushirogochi, H. O.; Santos, D.; Li, Z.; Francisco, G.; Lin, Y. I.; Peterson, P. J.; Yang, Y.;Weiss, W. J.; Shales, D. M.; Mansour, T. S. Bioorg. Med. Chem. 2008, 16, 1890–1902.
[XII] Metlesics, W.; Anton, T.; Sternba, L. H. J. Org. Chem. 1967, 32, 2185–2187.
[XIII] Olmo, E. D.; Armas, M. G.; Ybarra, M.; Lopez, J. L.; Oporto, P.; Gimenez, A.;Deharoe, E.; Felicianoa, A. S. Bioorg. Med. Chem. Lett. 2003, 13, 2769–2772.
[XIV] Katritzky, A. R.; Xu, Y.-J.; He, H.-Y.; Steel, P. J. J. Chem. Soc. Perkin Trans. 2001, 1, 1767–1770.
[XV] Gomes, P.; Araujo, M. J.; Rodrigues, M.; Azevedo, N. V. Z.; Iley, J.; Chambel, P.; Moraisd, J.; Moreira, R. Tetrahedron 2004, 60, 5551–5562.
[XVI] Maryam, S. H. Z.; Mohammad, M.; Mina, S.; Mehdi, A.; Shahrzad, J.; Abbas, S.; Foroumadi, A. Tetrahedron Lett. 2012, 53, 3448–3451.
[XVII] (a) Narsimha, S.; Kumar, T. R.; Kumar, N. S.; Yakub, S.; Reddy, N. V. Med. Chem. Res. 2014, 23, 5321–5327; (b) Kumar, T. R.; Narsimha, S.; Kumara Swamy, B.; Chary, V. R.; Estari, M.; Reddy, N. V. J. Saud. Chem. Soc. 2015. doi:10.1016/j.jscs.2015.12.001; (c) Kumara Swamy, B.; Narsimha, S.; Reddy, N. V.; Priyanka, B.; Srinivasa Rao, M. J. Serb. Chem. Soc. 2016, 81 (3), 233–242; (d) Narsimha, S.; Kumar, N. S.; Kumara Swamy, B.; Reddy, N. V.; Althaf Hussain, S. K.; Srinivasa Rao, M. Bioorg. Med. Chem. Lett. 2016, 26, 1639–1644; (e) Narsimha, S.; Kumara Swamy, B.; Sudhakar, L.; Reddy, N. V.; Altaf Hussain, S. K. Phosphorus Sulfur Silicon Relat. Elem.

2016, 191, 1118–1122; (f) Narsimha, S.; Kumara Swamy, B.; Kumar, N. S.; Ramesh, G.; Reddy, Y. N.; Reddy, N. V. RSC Adv. 2016, 6, 74332–74339; (g) Kumara Swamy, B.; Narsimha, S.; Reddy, N. V.; Srinivasa Rao, M. J. Serb. Chem. Soc. 2016. doi:10.2298/ JSC151222088B.
[XVIII] Tolaro, K.; Tolaro, A. Foundation of Microbiology, Dubuque ed.; W C Brown Publisher: Pasadena, CA, 1993; Vol 3, p. 326.
[XIX] Bunch, L.; Erichsen, M. N.; Huynh, T. H. V.; Abrahamsen, B. J Med Chem 2010, 53, 7180.
[XX] Wang, J. L.; Liu, D.; Zhang, Z. J.; et al. Proc Natl Acad Sci U S A 2000, 97, 7124.
[XXI] Martinez Grau, A.; Marco, J. L. Bioorganic & Medicinal Chemistry Letters 1997, 7, 3165.
[XXII] Bonsignore, L.; Loy, G.; Secci, D.; Calignano, A. Eur J Med Chem 1993, 28, 517.
[XXIII] Kumar, D.; Reddy, V. B.; Sharad, S.; Dube, U.; Kapur, S. Eur J Med Chem 2009, 44, 3805.
[XXIV] Konkoy C S, Fick D B, Cai S X, Lan N C & Keana J F W, Chemical abstracts, 134, Article ID 29313a, 2001, International Application WO 00/75123 A1, 2000.
[XXV] Childers, K. K.; Haidle, A. M.; Machacek, M. R.; Rogers, J. P.; Romeo, E. A. Tetrahedron Lett 2013, 54, 2506.
[XXVI] Dömling, A.; Wang, W.; Wang, K. Chem Soc Rev 2012, 112, 3083.
[XXVII] Slobbe, P.; Ruijter, E.; Orru, R. V. A. Med Chem Commun 2012, 3, 1189.
[XXVIII] Perreault, S.; Rovis, T. Chem Soc Rev 2009, 38, 3149.
[XXIX] Borgonie, G., Garcia, A., Litthauer, D., Bert, W., Bester, A., van Heerden, E., Onstott, T. C. (**2011**). Nematoda from the terrestrial deep subsurface of South Africa. *Nature*, *474*(7349), 79–82. https:/ doi.org/10.1038/nature09974.
[XXX] Danovaro, R., Gambi, C., Dell, A., Corinaldesi, C., Fraschetti, S., Vanreusel, A., Gooday, A. J. (2008). Exponential decline of deep-sea ecosystem functioning linked to benthic biodiversity loss. Current Biology, 18(1), 1–8. https://doi.org/10.1016/j. cub.2007.11.056
[XXXI] Zhang, Z. (2013). An outline of higher-level classification and survey of taxonomic richness. Zootaxa, 3703(1), 5–11. https://doi. org/10.11646/zootaxa.3703.1.
[XXXII]Holterman, M., Wurff, A., Elsen, S., van Megen, H., Bongers, T., Holovachov, O., Helder, J. (2006). Phylum-wide analysis of SSU rDNA reveals deep phylogenetic relationships among nematodes and accelerated evolution toward crown Clades. Molecular Biology and Evolution, 23(9), 1792–1800. https://doi.org/10.1093/molbev/ msl044
[XXXIII] Kavlie, R., Kernan, M., & Eberl, D. (2010). Hearing in Drosophila requires TilB, a conserved protein associated with ciliary motility. Genetics, 185, 177–188. https://doi.org/10.1534/genetics.110.114009
[XXXIV] Laloševiæ, V., Laloševiæ, D., Capo, I., Simin, V., Galfi, A., & Traversa, D. (2013). High infection rate of zoonotic Eucoleus aerophilus infection in foxes from Serbia. Parasite, 20, 3.
[XXXV] LiuG, Shao R., Li, J., Zhou, D. H., Li, H., & Zhu, X. Q. (2013). The complete mitochondrial genomes of three parasitic nematodes of birds: A unique gene order and insights into nematode phylogeny. BMC Genomics, 14(1), 414

[XXXVI] Loothfar, R., & Tony, S. (2005). Suppression of root knot nematode (Meloidogyne javanica) after incorporation of Indian mustard cv. Nemfix as green manure and seed meal in vineyards. Australasian Plant Pathology, 34(1), 77–83.
[XXXVII] Yanoviak, S., Kaspari, M., Dudley, R., & Poinar, G. Jr (2008). Parasiteinduced fruit mimicry in a tropical canopy ant. American Naturalist, 171(4), 536–544. https://doi.org/10.1086/528968
[XXXVIII] Bogitsh, J., Carter, E., & Oeltmann, N. (2012). General characteristics of the nematoda (Chapter 15), Intestinal nematodes (Chapter 16). Human Parasitology, 000, 269–345.
[XXXIX] Maya, C., Torner, F., Lucario, E., Hernández, E., & Jiménez, B. (2012). Viability of six species of larval and non-larval helminth eggs for different conditions of temperature, pH and dryness. Water Research, 46(15), 4770–4782. https://doi.org/10.1016/j. watres.2012.06.014
[XL] Szewczyk, J., Mancinelli, L., McLamb, W., Reed, D., Blumberg, B. S., & Conley, C. A. (2005). Caenorhabditis eleganssurvives atmospheric breakup of STS–107, space shuttle columbia. Astrobiology, 5(6), 690–705. https://doi.org/10.1089/ast.2005.5.690
[XLI] Alouini, Z., & Jemli, M. (2001). Destruction of helminth eggs by photosensitized porphyrin [J]. Journal of Environmental Monitoring, 3, 548–551. https://doi.org/10.1039/b103471p
[XLII] Banas, S. (2006). In situ characterisation of a microorganism surface by Raman microspectroscopy: The shell of Ascaris eggs. Analytical and Bioanalytical Chemistry, 386, 249–255.
[XLIII] Keraita, B., Jiménez, B., & Drechsel, P. (2008). Extent and implications of agricultural reuse of untreated, partly treated and diluted waste water in developing countries. Nutrition and Natural Resources, 3(58), 15–27.
[XLIV]Capizzi, S., Deloge, M., Remy, M., & Schwartzbrod, J. (2004). Liming as an advanced treatment for sludge sanitisation: Helminth eggs elimination - Ascaris eggs as mode. Water Research, 38(14–15), 3251–3258. https://doi.org/10.1016/j.watres.2004.04.015
[XLV] Jiménez, B., Maya, C., & Salgado, G. (2001). The elimination of Helminth Ova, Fecal Coliforms, Salmonella and protozoan cysts by various physicochemical processes in wastewater and sludge. Water Science and Technology, 43(12), 179–182. https://doi.org/10.2166/ wst.2001.0733
[XLVI] Anelia, M., Stefan, D., Dimitar, V., Anichina, K., & Yancheva, D. (2018). Antihelminthic Activity of Some 2-Substituted Thieno[2,3-d] pyrimidin-4-ones. Letters in Drug Design & Discovery, 15(8), 887–894.
[XLVII] Deep, A., Bhatia, R., Kaur, R., Kumar, S., Jain, U. K., Singh, H., Deb, P. K. (2017). Imidazo[1,2-a]pyridine scaffold as prospective therapeutic agents. Current Topics in Medicinal Chemistry, 17(2), 238–250.
[XLVIII] Iverson, T., Luna, C., Cecchini, G., & Rees, D. C. (1999). Structure of the Escherichia coli fumarate reductase respiratory complex. Science, 284(5422), 1961–1966. https://doi.org/10.1126/ science.284.5422.1961
[XLIX] Kaniwa, K.; Arai, M. A.; Li, X.; Ishibashi, M. Bioorg & Med Chem Lett 2014, 17, 4254.
[L] Saundane, A. R.; Walmik, P.; Yarlakatti, M.; Katkar, V.; Verma, V. A. J. Heterocyclic Chem 2014, 15, 303.

[LI] Deokar, H.; Chaskar, J.; Chaskar, A. J. Heterocyclic Chem 2014, 51, 719.
[LII] Chavan, R. S.; More, H. N.; Bhosale, A. V. Trop J Pharm Res 2014, 10, 463.
[LIII] Kawasaki, I.; Katsuma, H.; Nakayama, Y.; Yamashita, M. Y.; Ohta, S. Heterocycles 2007, 48, 1887.
[LIV] Kawasaki, I.; Yamashita, M. Y.; Ohta, S. Chem Pharm Bull 1996, 44, 1831.
[LV] Sun, H. H.; Sakemi, J. J. Org. Chem 1991, 56, 4307.
[LVI] Raju, R.; Gromyko, O.; Fedorenko, V.; Luzhetskyy, A.; Müler, R. Tetrahedron Lett 2012, 53, 3009.
[LVII] Fresneda, P. M.; Castaneda, M.; Blug, M.; Molina, P. Synlett 2007, 15, 324.
[LVIII] Aaron, M. S.; Richard, A. L.; David, C. R. J Nat Produ 2009, 70, 1793.
[LIX] Gao, X.; Chooi, Y.-H.; Ames, B. D.; Wang, P.; Walsh, C. T.; Tang, Y. J Am Chem Soc 2011, 133, 2729.
[LX] Mohamed, A. R.; Mahmound, E. S. Bioorg & Med chem let 2007, 15, 1206.
[LXI] Panda, S. S.; Chowdary, P. V. Ind. J Pharm Sci 2008, 70, 208.
[LXII] Shroff, M.; Daharwal, S. British Biomed Bull 2017, 5, 298.
[LXIII] R. V. Shingalapur, K. M. Hosamani, R.S. Keri, *European Journal of Medicinal Chemistry*., **2009**, 44, 4244–4248.
[LXIV] P. Gupta, S. Hameed, R. Jain, *European Journal of Medicinal Chemistr*y., **2004**, 39,805–814.
[LXV] P. jyoti, T. K. Vinod, V. S.Shyam, C. Vinita, S. Bhatnagar , S Sinha ,A.N. Gaikwad and R. P. Tripathi, *European Journal of Medicinal Chemistry* ., **2009**, 44, 3350-3355.
[LXVI] Kashyap, S.J., P.K. Sharma, V.K. Garg, R. Dudhe and N. Kumar, 2011. Review on synthesis and various biological potential of thiazolopyrimidine derivatives. J. Adv. Sci. Res., 2: 18-24.
[LXVII] Sharma, G.K., N.K. Sharma and D. Pathak, 2013. Microwave assisted synthesis of some substituted imidazole derivatives as potential antibacterial and anti-cancer agents. Indian J. Chem., 52B: 266-272.
[LXVIII] Prasanthy, G., K. Venkata Ramana, V. Koti Reddy, K. Nirmala and N. Ramesh Kumar,. Synthesis and biological evaluation of 1- substituted imidazole derivatives. Int. J. Pharma., **2011**, 1: 92-99.
[LXIX] D. Sharma, B. Narasimhan, P. Kumar, V. Judge, R. Narang, E. De Clercq, J. Balzarini, *European Journal of Medicinal Chemistry*., **2009**, 44, 2347–2353.
[LXX] M. Tonelli , M. Simone , B. Tasso , F. Novelli , V. Boido , *Bioorganic & Medicinal Chemistry*., **2010,** 18, 2937–2953.

Received on August 20, 2021.