REVIEW ARTICLE

Antimicrobial of New 5, 6-dimethylbenzoimidazol Schiff Bases

Sura S. Raoof[1], Afrah Salman[2], Hiba A. Hasan[3*], Dina Saleem[1], Shams Khaleel[2]

[1]*Department of Pharmaceutical Chemistry, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq.*
[2]*Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq.*
[3]*Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq.*

Received: 20th October, 2022; Revised: 10th November, 2022; Accepted: 08th December, 2022; Available Online: 25th December, 2022

ABSTRACT

Organic chemistry is replete of heterocyclic compounds containing carbon and other elements like oxygen, nitrogen and/or sulfur. These compounds play an important role in biological activities. A new series of 5, 6-dimethylbenzoimidazol derivatives (3a-e) were synthesized by reaction of 2-amino-5, 6-dimethylbenzimidazole with different benzaldehydes. Spectroscopic methods such as fourier transform infrared (FTIR), proton nuclear magnetic resonance (^{1}H-NMR), and carbon-13 nuclear magnetic resonance (^{13}C-NMR) were used to characterize all compounds and they were identified by studying their physical properties such as melting points and R_f values. All compounds were magnificently prepared with a high yield 94–97%. The antibacterial activity of these derivatives against selected pathogenic bacteria were measured using well diffusion method. The results showed that all derivatives have antimicrobial activity against the selected pathogenic bacteria, including gram positive and negative bacteria, but these derivatives' activity against G-ve bacteria appeared to be higher than those against G + ve bacteria.

Keywords: 5,6-dimethylbenzoimidazol, Schiff bases, Antimicrobial.

International Journal of Drug Delivery Technology (2022); DOI: 10.25258/ijddt.12.4.67

How to cite this article: Raoof SS, Salman A, Hasan HA, Saleem D, Khaleel S, Antimicrobial of New 5, 6-dimethylbenzoimidazol Schiff Bases. International Journal of Drug Delivery Technology. 2022;12(4):1887-1891.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Heterocyclic compounds are cyclic compounds with ring containing carbon atoms and other elements, such as phosphorus, nitrogen, sulfur, oxygen, silicon, and boron and they combine them to form ring structure.[1] Heterocyclic compound can be divided into five-membered ring, such as pyrrole, furan and thiophene and six-membered ring such as pyridine and piperidine.[2] Heterocyclic compounds represent the vital importance of medicinal chemistry and have a wide range of applications in several fields such as pharmacology and are found in many drugs.[3,4] On the other hand, benzoimidazoles are heterocyclic organic compounds which present in many natural or synthetic derivatives.[5] They are bicyclic compounds formed from benzene and imidazole rings.[6,7] Their derivatives have a wide range of clinical and biological activities and many studies reported that they are considered as local analgesic, antihypertensive,[8] antioxidant, antiulcer,[9] anti-inflammatory,[10] and anticancer; bendamustine druge is one of its examples which is used in the treatment of chronic lymphocytic leukemia.[11] In 1864 Hugo Schiff had reported for the first time synthesis of a new compound called imine or azomethine by the reaction of primary amine and carbonyl compound.[12,13] These scaffolds, which contain an azomethine group (C=N-),[14] are named as ketamine when they are derived from ketone, or called aldiminies when they are derived from aldehyde.[15] These bases and their derivatives were reported to have wide biological activities like anti-inflammatory, antiviral, antibacterial, antifungal, antimalarial and antipyretic properties.[16-18] Moreover, these imine group are active against a wide range of organisms like (*Candida Albicans, Escherichia coli, Staphylococcus aureus, Bacillus polymxa*).[19,20]

Based on what has been mentioned above and depending on the effectiveness of these compounds, five new derivatives of benzimidazole imines were synthesized, purified and scanned for their antimicrobial activities.

MATERIALS AND METHODS

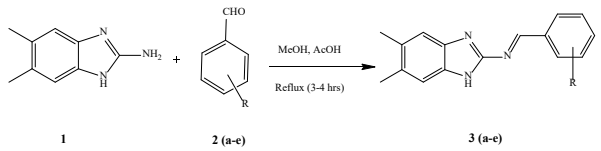
Materials

All chemicals used in this work are supplied from Sigma-Aldrich,Merck, Germany and BDH limited, England.

Instrumentation

Digital Stuart scientific SMP30 melting point apparatus (UK) was used to measure melting points for all derivatives. Furthermore, Agilent Technologies NMR 500MHz, USA, was used to analyze the ^{1}H-NMR (500 MHz) and the ^{13}C NMR (125 MHz)

**Author for Correspondence: hibaalichemist@uomustansiriyah.edu.iq*



R= **a**: 3-OCH$_2$-C$_6$H$_5$, 4-OCH$_3$; **b**: 2-OH, 5-NO$_2$; **c**: 3-OCH$_2$CH$_3$, 4-OH; **d**: 2,3-di-OH; **e**: 2-OH, 5-CH$_3$

Scheme 1: General scheme for synthesis of 5, 6-dimethylbenzoimidazol Schiff bases (3a-e).

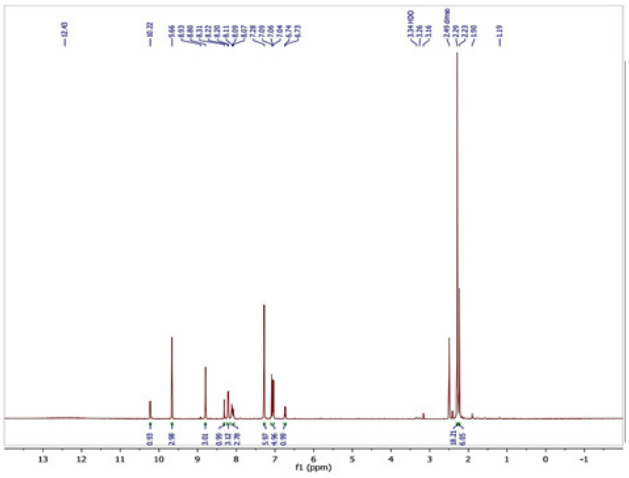


Figure 1: ^{1}H- NMR of (E)-2-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino)methyl)-4-nitrophenol (3b).

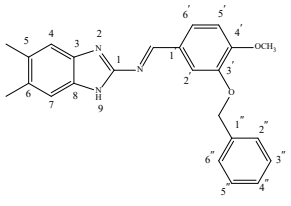
spectra for all scaffolds while the fourier transform infrared (FTIR) analysis was performed using FTIR-800 (SHIMADZU, Japan).

Synthesis and Characterization

Five new derivatives of 5, 6-dimethyl-1H-benzo[*d*]imidazol-2-yl)imino)methyl **(3a-e)** were synthesized according to the following Scheme 1.

The reflux method was performed according to Hasan *et al*. 2020 [20] and Hasan *et al*. 2021.[21] 1.2 mmol of each selected aldehyde was dissolved in one milliliter of methanol and mixed with 2-amino-5, 6-dimethylbenzimidazole (1 mmol, 0.16 g) in 50 mL round bottom flask and followed by 2 drops of acetic acid as catalyst. Oil bath was used to help in mixture reflux for 3 to 4 hours and TLC was performed to monitor the reaction progress. After completion the reaction, the mixture were cooled down to room temperature, dried, and washed with suitable solvent to furnish the final product with 94–97% yield.

(E)-1-(3-(benzyloxy)-4-methoxyphenyl)-N-(5, 6-dimethyl-1H benzo[d]imidazol-2-yl)methanimine (3a).



Following the conventional reflux method (2.3) using 3-benzyloxy-4-methoxybenzaldehyde (0.24 g, 1.2 mmole), new

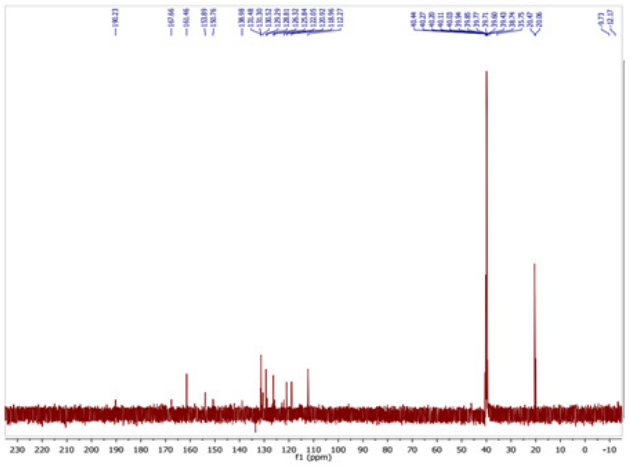


Figure 2: ^{13}C-NMR of (E)-2-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino)methyl)-4-nitrophenol (3b).

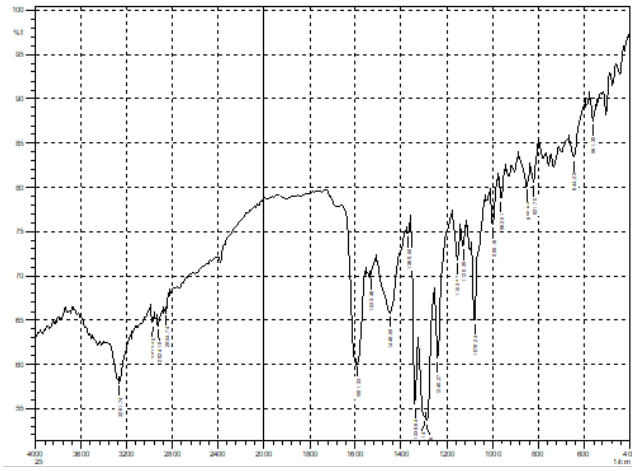


Figure 3: FTIR of ((E)-2-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl) imino)methyl)-4-nitrophenol (3b).

compound (3a) was obtained as a yellow solid (0.36 g, 94%); m.p.: 270–273°C; R_f: 0.63 in hexane: ethylcetate (1:1) solvent system. FT-IR (KBr, cm^{-1}): 3427 (=C-H sp^2), 2968 (-C-H sp^3 stretching), 1689 (C=N stretching), 1263 (C-O stretching). ^{1}H NMR (500 MHz, *DMSO-d6*) δ ppm 2.29 (s, 6H, CH$_3$), 3.87 (s, 3H, OCH3), 5.06 (s, 1H, NH), 5.17 (s, 1H, CH$_2$), 6.97 (d, 1H , H-5'), 7.35 (d, 1H, H-4,7), 7.38 (d, 1H, H-3'',4'',5''), 7.40 (d, 1H, H-6'), 7.48 (d, 1H, H-2'',6'') , 7.61 (s, H, H-2'), 9.30 (s, 1H, -N=CH). ^{13}C NMR (125 MHz, *DMSO-d6*) δ ppm 20.2 (2x**C**H$_3$), 56.2 (OCH3), 70.2 (CH$_2$), 111.8 (C-2',5'), 112.2(C-4,7), 126 (C-6'), 127 (C-2'', 4'', 6''), 128.4 (C-3'', 5''), 132.9 (C-5,6), 132.9(C-1'), 137.1 (C-3, 8), 148.5(C-3', 4'), 164.1 (N=CH).

(E)-2-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino) methyl)-4-nitrophenol (3b).

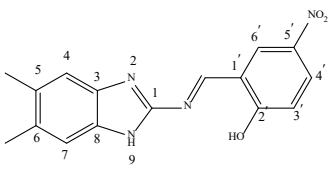


Table 1: Physical properties of 5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino)methyl derivatives (3a-e).

Compounds	*Molecular formula*	*Molecular weight*	*Melting point °C*	*Coluor*	*yield%*
3a	$C_{24}H_{23}N_3O_2$	385.47	270–273	yellow	94
3b	$C_{16}H_{14}N_4O_3$	310.31	140–142	Orang	97
3c	$C_{18}H_{19}N_3O_2$	309.37	195–197	Orang	94
3d	$C_{16}H_{15}N_3O_2$	281.32	153–155	Brown	97
3e	$C_{16}H_{14}N_4O_3$	310.31	156–158	Yellow	97

Table 2: The most important 1H-NMR signals of 5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino)methyl derivatives (3a-e).

Compound	*^{1}H-NMR chemical shifts(δ, ppm)*	
	CH_3 (s)	*-N=CH (s)*
3a	2.29	9.20
3b	2.29	8.80
3c	2.20	8.63
3d	2.31	9.55
3e	2.30	7.61

Table 3: The most important ^{13}C-NMR signals of 5, 6-dimethyl-1H-benzo[*d*]imidazol-2-yl)imino)methyl derivatives **(3a-e)**.

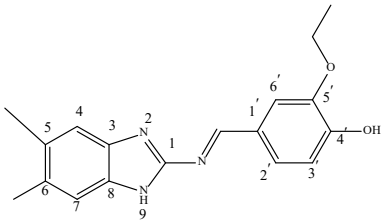
Compound	*^{13}C-NMR chemical shifts (δ, ppm)*	
	CH_3	*-N=CH*
3a	20.2	164.1
3b	20.0	161.4
3c	22.31	173.71
3d	20.19	165.82
3e	20.2	164.8

Table 4: Infrared frequencies of the major functional groups of 5, 6-dimethyl-1H-benzo[*d*]imidazol-2-yl)imino)methyl derivatives **(3a-e)**.

Compound	*FTIR spectral data of compounds (3a-e) (vmax in cm^{-1})*					
	=C-H sp^2	*-C-H sp^3*	*OH*	*C=N*	*C-O*	*N=O*
3a	3427	2968	-	1689	1263	-
3b	3450	2972	3261	1591	1314	1448
3c	3221	2729	3059	1699	1411	-
3d	3225	2733	3-68	1698	14111	-
3e	3254	3731	3051	1699	1411	-

Following the conventional reflux method (2.3) using 2-hydroxy-5-nitrobenzaldehyde (0.17 g, 1.2 mmole), new compound (**3b**) was obtained as a orange solid (0.30 g, 97%); m.p.: 140-142°C; R_f: 0.63 in hexane: ethylcetate (1:1) solvent system. FT-IR (KBr, cm^{-1}): 3450 (=C-H sp^2), 3261 (O-H stretching), 2972 (-C-H sp^3 stretching), 1591 (C=N stretching, N=O asymmetric stretching), 1448 (N=O symmetric stretching), 1314 (C-O stretching). ^{1}H NMR (500 MHz, *DMSO-d6*) δ ppm 2.29 (s, 6H, CH_3), 6.73 (s, 1H, NH), 7.28 (s, 1H, H-4, 7), 7.09 (d, 1H, H-3'), 8.09 (d, 1H, H-4'), 8.30 (s, 1H, H-6'), 8.80 (s, 1H, N=CH) , 9.66 (br. s, 1H, OH). ^{13}C NMR (125 MHz, *DMSO-d6*) δ ppm 20.0 (2 x **C**H_3), 112.2 (C-4, 7),118.9(C-1'), 120.9 (C-3'), 129.2 (C-4', 6'),130.5 (C-5, 6), 138.9 (C-3, 8), 150.7(C-5'),161.4 (N=CH), 167.6 (C-2')

(E)-4-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino) methyl)-2-ethoxyphenol (3c).



Following the conventional reflux method (2.3) using 3-ethoxy-4-hydroxybenzaldehyde (0.17 g, 1.2 mmole), new compound (3c) was obtained as a orange solid (0.29 g, 94%); m.p.: 195-197°C; R_f: 0.63 in hexane: ethylcetate (1:1) solvent system. FT-IR (KBr, cm^{-1}): 3221 (=C-H sp^2), 3068 (O-H stretching), 2729 (-C-H sp^3 stretching), 1699 (C=N stretching), 1411 (C-O stretching). ^{1}H NMR (500 MHz, *DMSO-d6*) δ ppm 1.34 (t, 3H, OCH_2CH_3), 2.20 (s, 6H, CH_3), 3.87 (s, 3H, OCH3), 4.8 (t, 2H, OCH_2CH_3) 6.55 (s, 1H, NH), 6.88 (s, 1H, OH), 6.92 (d,1H , H-3'), 7.37 (s, 1H, H-4,7), 7.39 (s, 1H, H-2'), 7.41 (s, 1H, H-6'), 8.63 (s, 1H, -N=CH). ^{13}C NMR (125 MHz, *DMSO-d6*) δ ppm 20.19 (OCH_2CH_3), 22.31 (2 x CH_3) 112.70 (C-4, 7), 135.72 (C-3, 8), 154.74 (C-4'), 173.71 (N=CH).

(E)-3-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino) methyl)benzene-1,2-diol (3d).

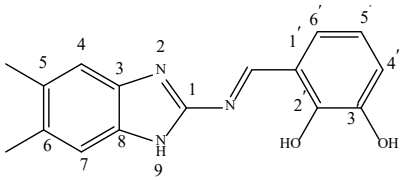
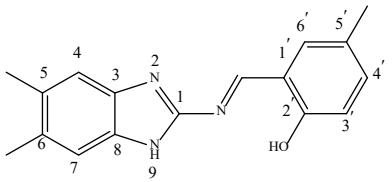


Table 5: The antimicrobial activity of the highest and lowest concentrations (7 and 0.875 mg/mL) of the synthesized derivatives against pathogenic bacteria. The measurement of inhibition zone of bacteria in millimeter. The diameter of well is 8 mm.

Derivatives	*3a*		*3b*		*3c*		*3d*		*3e*		*Cefamadol antibiotic*
E. coli	15	10	22	-	18	10	24	14	27	13	R
Klebsiella spp	18	13	14	10	20	13	22	13	18	10	R
S. aureus	15	-	14	10	28	-	14	-	12	-	10

Following the conventional reflux method (2.3) using 2, 3-dihydroxybenzaldehyde (0.14 g, 1.2 mmole), new compound (**3d**) was obtained as a brown solid (0.27 g, 96%); m.p.: 153-155°C; R_f: 0.63 in hexane: ethylcetate (1:1) solvent system. FT-IR (KBr, cm^{-1}): 3225 (=**C-H** sp^2), 3059 (**O-H** stretching), 2733 (-**C-H** sp^3 stretching), 1698 (**C=N** stretching), 1411 (**C-O** stretching). ^{1}H NMR (500 MHz, *DMSO-d6*) δ ppm 2.31 (s, 6H, C**H**$_3$), 6.39 (s, 1H, N**H**), 6.81 (s, 1H, **OH 2',3'**), 6.83(s,1H **, H-5'**), 6.84 (, 1H, **H-4'**), 7.26 (s, 1H, **H-6'**), 7.31 (s, 1H, 4,7) ,9.55 (s, 1H, -N=C**H**). ^{13}C NMR (125 MHz, *DMSO-d6*) δ ppm 20.19 (2x**C**H$_3$), 112.76(**C-4,7**), 119.77 (**C**-1'), 120.3 (**C-4'**), 123.28 (**C-5'**), 127.47 (**C-6'**), 131.14 (**C-5,6**), 136.10 (**C-3,8**), 146.24 (**C-3'**), 153.38 (**C-2'**), 154.74 (**C-1**), 165.82 (N=**C**H).

(E)-2-(((5, 6-dimethyl-1H-benzo[d]imidazol-2-yl)imino) methyl)-4-methylphenol (3e).



Following the conventional reflux method (2.3) using 2-hydroxy-5-methylbenzaldehyde (0.14 g, 1.2 mmole), new compound (**3e**) was obtained as a yellow solid (0.30 g, 97%); m.p.: 156-158°C; R_f: 0.63 in hexane: ethylcetate (1:1) solvent system. FT-IR (KBr, cm^{-1}): 3254 (=C-H sp^2), 3051 (O-H stretching), 2731 (-C-H sp^3 stretching), 1699 (C=N stretching), 1411 (C-O stretching). ^{1}H NMR (500 MHz, *DMSO-d6*) δ ppm 2.30 (s, 6H, CH_3), 6.33 (s, 1H, NH), 6.92 (d, 1H, H-3'), 7.28 (d, 2H, H-4'), 7.29 (s, 1H, H-4, 7), 7.61 (s, 1H, -CH=N), 9.54 (br. s, 1H, OH). ^{13}C NMR (125 MHz, *DMSO-d6*) δ ppm 20.2(2x**C**H$_3$), 112.7 (C-4, 7), 117.1 (C-3'), 119.5 (C-1'), 131.1 (C-5, 6, 6'), 132 (C-5'), 134.7 (C-4'), 136.3 (C-3, 8), 158.8 (C-2'), 164.8 (-N=CH).

Antimicrobial Activity

The antimicrobial activity of the synthesized compounds was evaluated using well diffusion methods. This method produced a loan of bacteria treated with 2 fold dilution of compound in (DMSO) by spreading a particular amount of the bacterial inoculum all over the agar surface.[22] Cefamandol antibiotic, which belongs to cephalosporin and has activity against a wide range of gram-positive and gram-negative organisms,[23] was used as a reference standard.

RESULT AND DISCUSSION

A series of five derivatives of 5, 6-dimethyl-1H-benzo[d] imidazol-2-yl)imino)methyl compounds (**3a-e**) were synthesized by reaction of 2-amino-5,6-dimethylbenzimidazole with different benzaldehyde derivatives using glacial acetic acid and methanol as a catalyst and as a solvent, respectively as shown in Scheme 1. TLC was performed to confirm the purity of all synthesized compounds and proved by different R_f values. The physical properties for all derivatives are given in Table 1. In addition, the identification of the studied products was performed by spectroscopic analysis, which includes FTIR, ^{1}H-NMR and ^{13}C-NMR, and the most important peaks of ^{1}H and ^{13}C NMR are given in Tables 2 and 3, respectively.

The formation of the azomethine compounds (3a-e) was confirmed by ^{1}H-NMR analysis of all compounds, which displayed the most significant peaks at the ranges of 2.29–2.30 and 7.61–9.20 ppm for CH_3 protons and imine groups (-N=CH), respectively, as shown in Table 2.

New compounds (3b) ^{1}H-NMR spectrum is an example of the synthesized compounds (3a-e), which displayed two sharp resonances at 2.29 and 8.80 ppm for CH_3 and -N=CH protons, respectively. This proton NMR spectrum showed other characteristic signals such as doublets at 7.09 and 8.09 ppm for H-3' and H-4', respectively, as shown in Figure 1.

The ^{13}C-NMR spectra for the same compounds exhibited the most significant resonances at the range of 20.0–20.2 and 161.4–164.8 ppm for **C**H$_3$ and–NH=**C**H carbons, respectively, which affirm the structure of imines (3a-e) formation, as shown in Table 3. For instance, different signals at different chemical shifts were displayed by compound 3b (Figure 2).

FTIR spectra presented essential absorption bands between 1591-1699 cm^{-1} for all aromatic 5, 6-dimethylbenzoimidazol derivatives, which belong to C=N stretching vibrations. The parent primary amine was reacted and converted into imine compound, which was proved by disappearing primary NH_2 bands and replacing by C=N band.

Furthermore, distinctive peaks around 3221-2450, 2729-2972, 1591-1699 and 1263-1411cm^{-1} regions were shown by FTIR spectra which corresponded to =C-H sp^2, -C-H sp^3, C=N, C-O, stretching, respectively (see Table 4). FTIR spectrum for 3b derivative is displayed in Figure 3.

The measurements of antimicrobial activity of the new synthesized chemical compounds against the selected pathogenic bacterial strain were conducted using agar diffusion method.

The results showed that all the synthesized compounds in the current study appears to have antimicrobial characteristics against gram negative and positive bacterial strains as they can inhibit the growth of these strains by producing a zone of inhibition around the wells (Table 5). Each well was filled with different concentration of synthesized compounds prepared by tow fold dilution (7, 3.5, 1.75, 0.875 mg/mL, respectively). This activity is higher than the activity of the standard antibiotic used in the current study. However, the activity of these compounds (in all concentration used in the current study) against gram negative bacteria including *E. coli* and *Klebseilla spp.* appeared to be higher than the activity against gram positive bacteria, *S. areus*, which only appeared to be effective in the highest concentration, except 3b, which was effective in all concentrations used.

ACKNOWLEDGMENT

All Authors would like to thank Mustansiriyah University, Baghdad-Iraq for its support in the present work.

REFERENCES

1. Entesar OA, Sura SA and Aymen AD, Synthesis of Poly Azo Heterocyclic from Modification of Poly Methyl Acrylate, (IOSR-

JPBS), Volume 12, Issue 2 Ver. I (Mar. - Apr.2017), pp 06-12 .
2. Kwa CD and Fayad S, Heterocycles, their Synthesis and Industrial Applications: A Review, IJRASET,2020, 8. 36-55.
3. Nayak SG, Poojary B. Synthesis of novel Schiff bases containing arylpyrimidines as promising antibacterial agents. Heliyon. 2019 Aug 1;5(8):e02318.
4. Patil J. Versatile applications of heterocyclic compounds: special attention to nanomaterials in cancer therapy. J Pharmacovigil. 2016;4:e164.
5. Neelima Shrivastava, Mohd. Javed Naim, Md. Jahangir Alam, Farah Nawaz, Shujauddin Ahmed, and Ozair Alam, Benzimidazole Scaffold as Anticancer Agent: Synthetic Approaches and Structure–Activity Relationship, Arch. Pharm. Chem. Life Sci. 2017, 350, e1700040.
6. VANDANA BABAN SHINDE, MANISH ASHOK RASKAR, Synthesis and Biological Evaluation of Benzimidazol Derivatives as Antimicrobial agents, International Journal of Current Pharmaceutical Research, Vol 11, Issue 6, 2019.
7. Abdel –Amir M. Fenjan, Sahar T.Adday, Synthesis and Characterization of Some New Benzimidazole Derivatives, Baghdad Science Journal, Vol.13(1)2016.
8. Prabhu PP, Panneerselvam T, Shastry CS, Sivakumar A, Pande SS. Synthesis and anticancer evaluation of 2-phenyl thiaolidinone substituted 2-phenyl benzothiazole-6-carboxylic acid derivatives. Journal of Saudi Chemical Society. 2015 Mar 1;19(2):181-5.
9. Kucukbay H, Durmaz R, Sireci N, Gunal S. Synthesis, antibacterial and antifungal activities of new bis-5 (6)-nitrobenzimidazoles. Asian Journal of Chemistry. 2010 Apr 20;22(4):2816.
10. Sreena K, Ratheesh R, Rachana M, Poornima M, Shyni C. Synthesis and anthelmintic activity of benzimidazole derivatives.
11. Sugumaran M, Kumar MY. Synthesis and biological activity of novel 2, 5-disubstituted benzimidazole derivatives. International Journal of Pharmaceutical Sciences and Drug Research. 2012;4(1):80-3.
12. Qin W, Long S, Panunzio M, Biondi S. Schiff bases: A short survey on an evergreen chemistry tool. Molecules. 2013 Oct 8;18(10):12264-89.
13. Miroslaw B. Homo-and Hetero-Oligonuclear Complexes of Platinum Group Metals (PGM) Coordinated by Imine Schiff Base Ligands. International journal of molecular sciences. 2020 May 15;21(10):3493.
14. Omidi S, Kakanejadifard A. A review on biological activities of Schiff base, hydrazone, and oxime derivatives of curcumin. RSC advances. 2020;10(50):30186-202.
15. Khalifa ME, Gobouri AA, Kabli FM, Altalhi TA, Almalki AS, Mohamed MA. Synthesis, antibacterial, and anti HepG2 cell line human hepatocyte carcinoma activity of some new potentially benzimidazole-5-(aryldiazenyl) thiazole derivatives. Molecules. 2018 Dec 11;23(12):3285.
16. Mumtaz A, Mahmud T, Elsegood MR, Weaver GW. Synthesis and characterization of new Schiff base transition metal complexes derived from drug together with biological potential study. J Nucl Med Radiat Ther. 2016;7(310):2.
17. Hasan HA, Abdulmalek E, Saleh TA, Rahman MB, Shaari KB, Yamin BM, Chan KW. Synthesis of novel 6-substituted-5, 6-Dihydrobenzo [4, 5] Imidazo [1, 2-c] quinazoline compounds and evaluation of their properties. Journal of Molecular Structure. 2019 Oct 5;1193:482-94.
18. Hasan HA, Abdulmalek E, Rahman MB, Shaari KB, Yamin BM, Chan KW. Microwave synthesis, crystal structure, antioxidant, and antimicrobial study of new 6-heptyl-5, 6-dihydrobenzo [4, 5] imidazo [1, 2-c] quinazoline compound. Chemistry Central Journal. 2018 Dec;12(1):1-5.
19. Malakyan M, Babayan N, Grigoryan R, Sarkisyan N, Tonoyan V, Tadevosyan D, Matosyan V, Aroutiounian R, Arakelyan A. Synthesis, characterization and toxicity studies of pyridine-carboxaldehydes and L-tryptophan derived Schiff bases and corresponding copper (II) complexes. F1000Research. 2016;5.
20. Hasan HA, Raoof SS, Abd Razik BM. Synthesis, Characterization and Molecular Docking Simulation of Thioxothiazolidin-4-One Derivatives as Acetylcholinesterase Inhibitors. Systematic Reviews in Pharmacy. 2020;11(12):1920-6.
21. Hasan HA, Salman A, Abdulmalek E. Anticancer activity and high content screening of new 6-substituted-5, 6-dihydrobenzo [4, 5] imidazo [1, 2-c] quinazoline derivatives. Research Journal of Pharmacy and Technology. 2021 May 1;14(5):2397-405.
22. Valgas C, Souza SM, Smânia EF, Smânia Jr A. Screening methods to determine antibacterial activity of natural products. Brazilian journal of microbiology. 2007;38:369-80.
23. Valentovic M. xPharm: The Comprehensive Pharmacology Reference.