An Overview: Benzimidazole

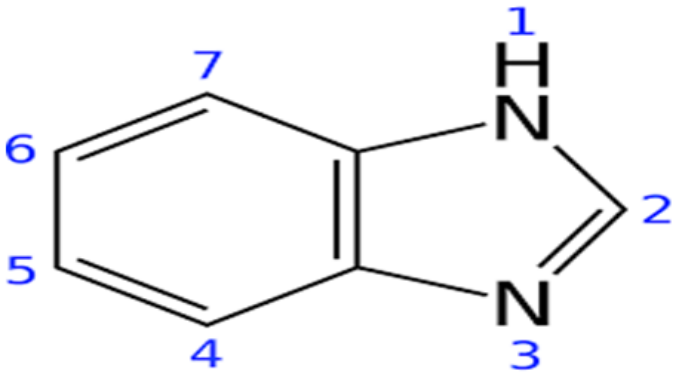
Nathiya Perumal[1], N. Ramanathan[2]
[1]Dept of of pharmaceutical chemistry
[2]Dept of of Pharmacy
[1, 2] Pallavan Pharmacy College, kanchipuram.

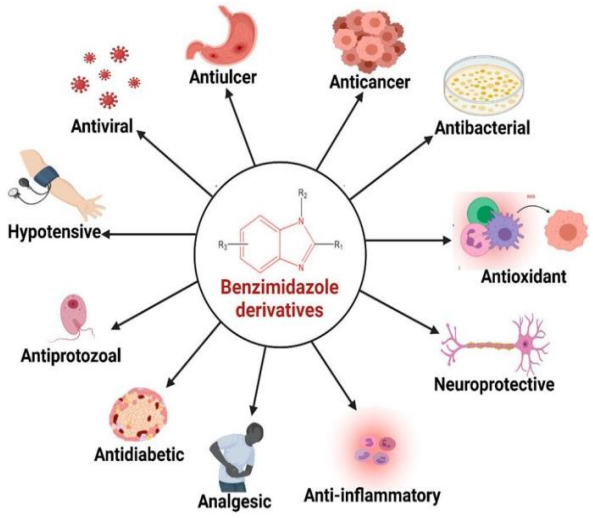
Abstract- *Benzomidazoles derivatives are useful in medicine because they have a wide range of pharmacological properties, including antibacterial, antiviral, antidiabetic, and anticancer properties. The discovery of some more significant and potent compounds was encouraged by the clinically effective medications' potency in treating microbial infections and other conditions. Benzimidazoles exhibit significant activity as potential antitumor agents, smooth muscle cell proliferation inhibitors, a treatment for intestinal cystitis, and in diverse area of chemistry*

I. INTRODUCTION

One type of heterocyclic aromatic organic chemical is benzomidazole. In medicinal chemistry, it is a privileged structure and a significant pharmacophore. This chemical is bicyclic, formed by the combination of imidazole with benzene. Currently, there exists a preferred moiety that has numerous pharmacological characteristics. N-ribosyl-dimethylbenzimidazole is the most well- known benzimidazole molecule found in nature. It functions as an axial ligand for cobalt in vitamin B12[1].

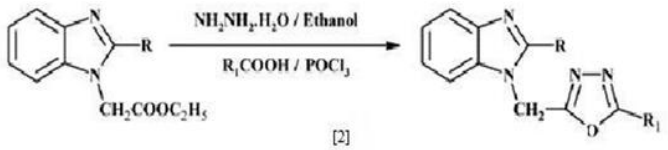
They wide range of pharmacological properties, including antibacterial, antiviral, antidiabetic, and anticancer effects, benimidazole derivatives are useful in the medical area. A various number of benzimidazole derivatives were created in 1990 by substituting cyclized molecules, propylene, tetrahydroquinoline, and fluorine[2,3]. Modern drug discovery depends extensively on the benzimidazole ring as a pharmacophor. Synthesis of benzimidazole derivatives has received more and more attention in the past several years. A major area of current medical research is the creation of new benzimidazole derivatives. The results of recent studies indicate that heterocyclic and substituted benzimidazoles interact easily with biopolymers and could cause fewer toxicities while used in treatment with chemotherapy treatment[25].





Anti bacterial and Anti microbial effects :

A review of the literature reveals that 2-substituted benzimidazole derivatives are pharmacologically more effective than other derivatives. As a result, designing and synthesizing 2-substituted benzimidazoles is a promising topic of study[4-6].



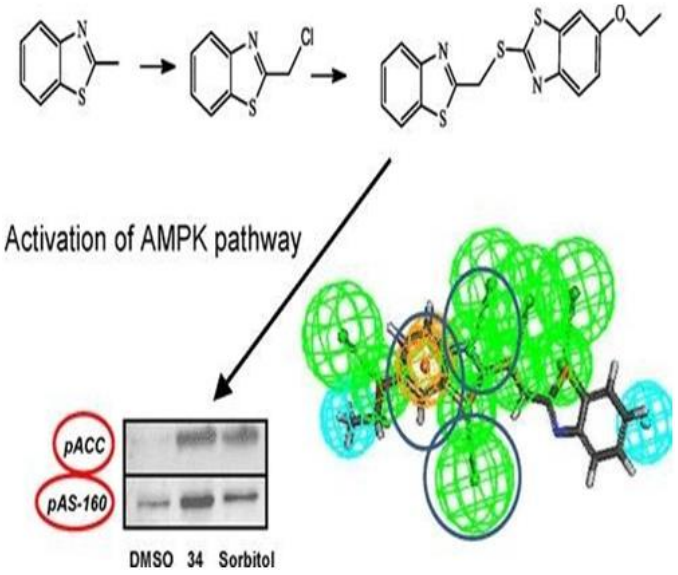
Some widely used antibacterial drugs such as furacilin, furazolidone and ftivazide are known to contain this

group. In past decades, hydrazones have received much attention and many studies[7]

Have been reported due to their chemotherapeutic value in the development of novel anti- microbial agents.

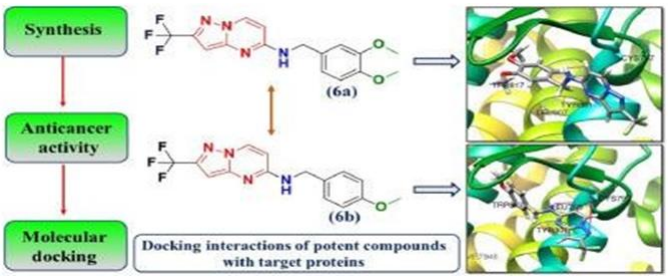
HYPOGLYCEMIC E FFECT:

This substance's hypoglycemic effect was linked to its effects on insulin secretion, improvement of glucose utilization in peripheral tissues, and prolongation of the hypoglycemic action of insulin. These effects were observed in both test animals with experimental alloxan- induced diabetes and in intact animals of various kinds[16-18].



ANTI CANCER ACTIVITY:

The synthesis of aromatic aldehydes with matching 2-aminobenzimidazoles produced a unique series of Schiff bases substituted with benzimidazole. When examined for antiproliferative activity in vitro, the synthesized Schiff bases showed non-specific antiproliferative action on the tested cell lines at the maximum tested dose[19].



ANTI HYPERTENSIVE AGENTS :

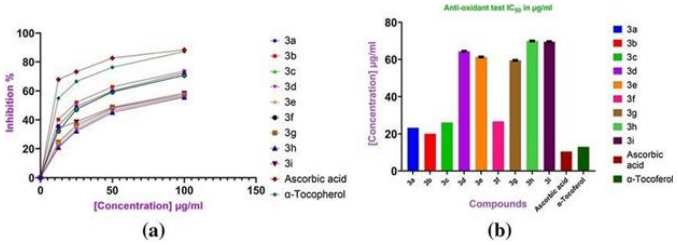
The biphenyl position is essential for the activity, and the biphenylbenzimidazoles exhibit stronger antihypertensive effects than the earlier related treatments because they are more readily available when taken orally.Compared to angiotensin-II AT1 receptor antagonistic activity[20]

Compound	Experimental animal (Sprague dawley)rat	After 1 hour			After 3 hour		
		SBP	DBP	MBP	SBP	DBP	MBP
1a	1	149	102	118	142	102	115
	2	145	105	118	139	103	115
	3	135	109	118	137	109	118
	4	144	112	123	142	105	117
	5	142	116	125	145	113	124
1b	1	148	112	124	149	113	125
	2	144	109	121	143	105	118
	3	149	112	124	145	110	122
	4	139	104	116	143	106	118
	5	150	101	117	148	104	119
1c	1	152	109	123	150	109	123
	2	147	106	120	144	100	115
	3	146	103	117	140	101	114
	4	133	103	113	140	102	115
	5	142	113	123	140	110	120
(Control) Losartan	1	141	110	120	144	112	123
	2	143	105	118	140	103	115
	3	134	109	117	138	109	119
	4	145	107	120	146	103	117
	5	149	110	123	145	105	118

.

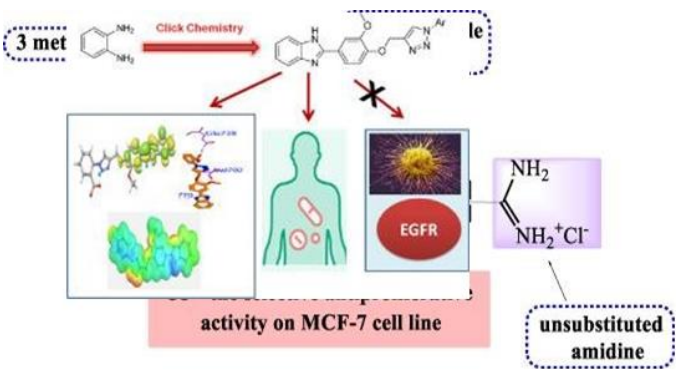
ANTI OXIDANT ACTIVITY :

It has also been found that certain compounds with dihydrochlorides have antioxidant properties; these salts also exhibit modest antiaggregant activity against platelets and erythrocytes[21]. By inhibiting 5-lipoxygenase, it was shown that combining a trimethyl group with benzimidazole also added antioxidative function[22].



ANTI PROLIFERATE ACTIVITY :

It has been reported that a novel Schiff base is derived from 2-aminobenzimidazole and modified aromatic aldehydes. After the compounds were reduced by NaBH4, 2-benzylaminobenzimidazoles were produced. Cinnamoyl chloride then acylated the compounds to produce 2-(obromobenzylamino)-1-cinnamoylbenzimidazole. The antiproliferative activity of the substances was assessed in vitro[23].



ANTI TUMOR ACTIVITY :

It has been observed that a number of novel nitrobenzimidazoles exhibit cytotoxic action against breast cancer. It was also discovered in the published research that substances such as imidazoles, tetrazole, thiadiazole, and triazines have the activity[24].

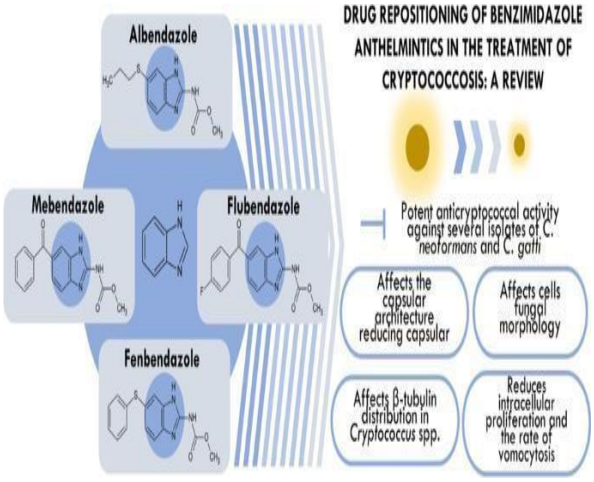
gastric cancer cell lines) with mean GI_{50}.

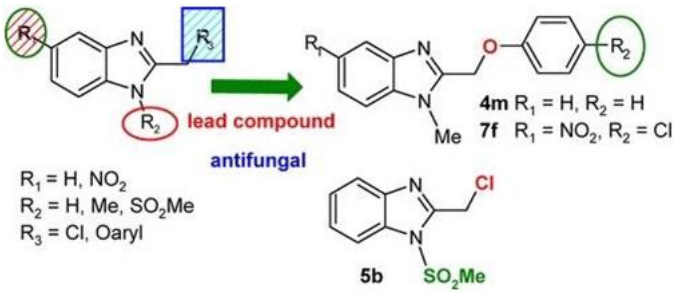
Compound #	Mean GI_{50}[a]
1	>100 μM
2	17 μM
3	22 μM
4	47 μM
5	>100 μM
6	0.095 μM
7	0.163 μM
8	0.091 μM
9	0.174 μM
Etoposide	1.3 μM
Doxorubicin	0.065 μM
SN-38	0.066 μM
Cisplatin	3.9 μM

[a] GI_{50}: 50% inhibition of cell growth (GI_{50}; the concentration needed to reduce the growth of treated cells to half that of untreated [i.e., control] cells).

ANTI FUNGAL ACTIVITY :

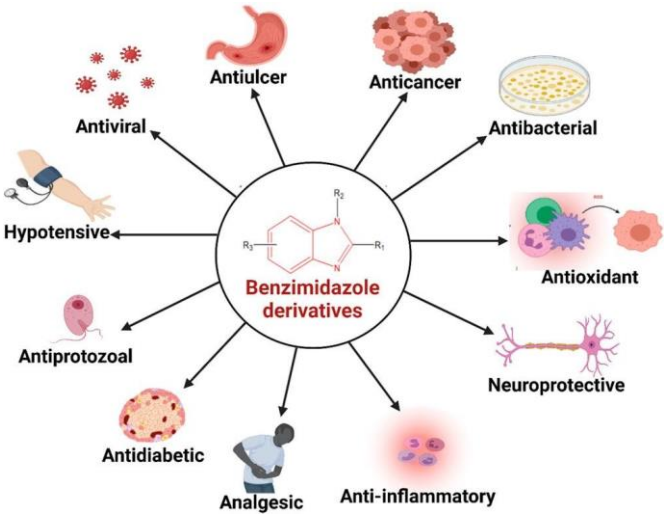
In the past several years, infectious illnesses have been considered a significant and increasing threat to human health. Additionally, resistance to various medications is becoming more common for particular microbes, particularly Grampositive bacteria and some stubborn fungi, and the susceptibility of a wide range of diseases to anti-microbial agents has been declining[26] .





II. CONCLUSION

The benzimidazole ring is an important pharmacophore in modern drug discovery. Attention has been increasingly given to the synthesis of benzimidazole derivatives as a source of new antimicrobial agents. The Benzimidazole derivatives are a resource for medicinal research. Whether it involves biological activities, such as anti-microbial, antiviral, anti-diabetic, and anti- cancer properties, benzomidazoles have been considered to be a promising class of heterocyclic chemicals.



REFERENCES

[1] Barker HA, Smyth RD, Weissbach H, Toohey JI, Ladd JN and Volcani BE. Isolation and properties of crystalline cobamide coenzymes containing Benzimidazole or 5,6-Dimethylbenzimidazole. Journal of Biological Chemistry. 1960;235(2):480- 488

[2] Kubo K, Oda K, Kaneko T, Satoh H and Nohara A. Synthesis of 2-(4- Fluoroalkoxy-2-pyridyl) methyl] sulfinyl]-1H-benzimidazoles as Antiulcer Agents. Chem Pharm Bull. 1990;38(10):2853-2858.

[3] Uchida M, Chihiro M, Morita S, Yamashita H, Yamasaki K, Kanbe T, Yabuuchi Y and Nakagawz K. Synthesis and Antiulcer Activity of 4- Substituted 8-[(2-Benzimidazolyl) N N R 1 R 2 R 3 IJRPC 2011, 1(3)

Ramanpreet et al. ISSN: 2231□2781 571 sulfinylmethyl]-1, 2, 3, 4-tetrahydroquinolines and Related Compounds. Chem Pharm Bull. 1990;38(6):1575-1586.

[4] Preston PN. Benzimidazoles and Congeneric Tricyclic Compounds Part 2.Wiley Interscience New York, 1980:531.

[5] Foks H, Ksepko DP, Kuzmierkiewicz W, Zwolska Z, Augustynowicz EK, and Janowiec M. Synthesis and tuberculostatic activity of new benzimidazole derivatives. Chem Het Comp. 2006;42:611-614.

[6] Ansari KF and Lal C. Synthesis, physicochemical properties and antimicrobial activity of some new Benzimidazole derivatives. European Journal of Medicinal Chemistry. 2009;44:4028–4033.

[7] Chornous VA, Bratenko MK, Vovk MV and Sidorchuk II. Synthesis and Antimicrobial Activity of Pyrazole-4-carboxylic Acid Hydrazides and N-(4-Pyrazoyl)hydrazones of Aromatic and Heteroaromatic Aldehydes. Pharmaceutical Chemistry Journal. 2001;35(4):203-205

[8] Rollas S, Gulerman N and Erdeniz H. Synthesis and antimicrobial activity of some new hydrazones of 4-fluorobenzoic acid hydrazide and 3- acetyl-2,5-disubstituted-1,3,4- oxadiazolines. Farmaco. 2002;57:171- 174. 27. Papakonstantinou GS, Pouli N, Marakos P and Chytyroglou LA. Synthesis antimicrobial and antifungal activity of some new 3-substituted derivatives of 4-(2, 4-dichlorophenyl)- 5-adamantyl-1H-1,2,4-triazole. Farmaco. 2002;57:973- 977.

[9] Vicini P, Zani F, Cozzini P and Doytchinova I. Hydrazones of 1, 2- benzisothiazole hydrazides: synthesis, antimicrobial activity and QSAR investigations. Eur J Med Chem. 2002;37:553- 564.

[10] Loncle C, Brunel JM, Dherbomez M, and Letourneux Y. Synthesis and antifungal activity of cholesterolhydrazone derivatives. Eur J Med Chem. 2004;39:1067-1071.

[11] Salgın-Goksen U, Gokhan-Kelekci U, Goktas O, Koysal Y, Kılıc E, Isik S, Aktay G and Ozalp M. 1-Acylthiosemicarbazides, 1, 2, 4- triazole-5(4H)-thiones, 1, 3, 4- thiadiazoles and hydrazones containing 5-methyl-2-benzoxazolinones: synthesis, analgesic-anti-inflammatory and antimicrobial activities. Bioorg Med Chem. 2007;15:5738-5751.

[12] Masunari A and Tavares LC. A new class of nifuroxazide analogues: synthesis of 5- nitrothiophene derivatives with antimicrobial activity against multidrug-resistant Staphylococcus aureus. Bioorg Med Chem. 2007;15:4229-4236.

[13] A.A. Spasov, G. P. Dudchenko, A. F. Turchaeva, et al., Vestn. Volgograd, Med. Akad., No. 1, 33 -36 (1995)

[14] T. B. Sibiryakova, A. F. Turchaeva, and 1~. V. Besedina, Current Problems in Medicine. Proc. 49th Sci. Session [in Russian], Volgograd (1995), pp. 79- 80.

[15] T. B. Sibiryakova, P. A. Bakumov, N. P. Larionov, and A. A. Spasov, Abstracts of Papers. All- Russia Sci. Conj "Creation o.I" Drugs" (Moscow, 26-30 Octobet, 1996) [in Russian], Moscow (1996), pp. 171 – 172.

[16] A.A. Spasov, G. P. Dudchenko, A. F. Turchaeva, et al., Vestn. Volgograd, Med. Akad., No. 1, 33 -36 (1995)

[17] T. B. Sibiryakova, A. F. Turchaeva, and 1~. V. Besedina, Current Problems in Medicine. Proc. 49th Sci. Session [in Russian], Volgograd (1995), pp. 79- 80.

[18] T. B. Sibiryakova, P. A. Bakumov, N. P. Larionov, and A. A. Spasov, Abstracts of Papers. All- Russia Sci. Conj "Creation o.I" Drugs" (Moscow, 26-30 Octobet, 1996) [in Russian], Moscow (1996), pp. 171 – 172.

[19] Hranjec, M., Starcevic, K., Pavelic, S.K., Lucin, P., Pavelic, K., Zamola, G.K., 2011. Synthesis, spectroscopic characterization and antiproliferative evaluation in vitro of novel Schiff bases related to benzimidazoles. Eur. J. Med Chem. 46, 2274

[20] Shah DI, Sharma M, Bansal Y, Bansal G and Singh M. Angiotensin II--AT1 receptor antagonists: design, synthesis and evaluation of substituted carboxamido benzimidazole derivatives. Eur J Med Chem. 2007;20:1-5

[21] Anisimova VA, Spasov AA, Kosolapov VA, Tolpygin IE, Kucheryavenko AF, Sysoeva VA, Tibirkova EV and Eltsova LV. Synthesis and pharmacological activity of 3-(2,2,2-trichloro-1- hydroxyethyl) imidazo[1,2- a]Benzimidazole dihydrochlorides. Pharmaceutical Chemistry Journal. 2009;43:491-494.

[22] Nikano H and Inoue T. Synthesis of Benzimidazole derivatives as antiallergic agents with 5- lipoxygenase inhibiting action. Chem Pharm Bull. 1999;47(11):1573.

[23] Nawrocka W, Sztuba B, Kowalska M W, Liszkiewicz H, Wietrzyk J, Nasulewicz A, Pełczynska M and Opolski A. Synthesis and antiproliferative activity in vitro of 2- aminobenzimidazole derivatives. IL Farmaco. 2004;59:83–91.

[24] Salgın-Goksen U, Gokhan-Kelekci U, Goktas O, Koysal Y, Kılıc E, Isik S, Aktay G and OzalpM. 1-Acylthiosemicarbazides, 1, 2, 4- triazole-5(4H)-thiones, 1, 3, 4- thiadiazoles and hydrazones containing 5-methyl-2-benzoxazolinones: synthesis, analgesic-anti-inflammatory and antimicrobial activities. Bioorg Med Chem. 2007;15:5738-5751.

[25] Haugwitz, R.D. (1982). Anti-parasitic agents Synthesis and anti-helmintic activities of novel 2-

substituted isothiocyanatobenzoxazoles and benzimidazole. J. Med. Chem. 25: 969-974. DOI PMid:7120286.

[26] Fang, B., Zhou, C.H., Rao, X.C. (2010). Synthesis and biological activities of novel amine- derived bis-azoles as potential anti-bacterial and anti-fungal agents. Eur. J. Med. Chem. 45: 4388-4398. DOI PMid:20598399