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Review Article

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LITERATURE REVIEW ON BIOLOGICAL ACTIVITY OF NOVEL 2-SUBSTITUTED BENZIMIDAZOLE SCHIFF'S BASES AND ITS AZETIDINONE AND THIAZOLIDINONE DERIVATIVES

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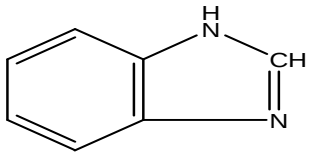
ABSTRACT

The Benzimidazole ring is an omnipresent structural feature of many synthetic compounds with diversified therapeutic efficacy. A large volume of published literature over the last few decades on 2-substituted benzimidazole Schiff's bases derivatives preludes a comprehensive review. The major activities exhibited by the 2-substituted benzimidazole Schiff's bases derivatives are, antibacterial, antifungal, antiviral, anti-tubercular, analgesic, anti-inflammatory, anti-helminthic, sedative, hypnotic, anticonvulsant etc. The article presents a comprehensive review on the biological activities of some novel derivatives of 2-substituted benzimidazole Schiff's bases.

KEY WORDS: Benzimidazole, Schiff's base, antibacterial, analgesic, anticonvulsant.

INTRODUCTION

Benzimidazole is a fused ring heterocyclic compound containing a benzene ring attached with one face of the imidazole ring. It contains two nitrogen atoms, one of which is not bonded to hydrogen and has its lone pair in as sp^2 orbital that is not involved in the aromatic system. Such lone pair is basic. The other nitrogen atom uses its third sp^2 orbital to bond to hydrogen and its lone pair is part of the aromatic sextet. Benzimidazole is more important than imidazole as the former occurs in the core structure of Vitamin B_{12} as well lead molecule in numerous bioactive compounds.



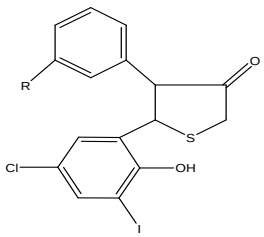
1*H*-benzo[*d*]imidazole

Benzimidazole and their substituted derivatives are important biological agents. They are used as antibacterial and antifungal, antiviral, anti-tubercular and insecticidal agents. Some of these compounds have also shown anti-inflammatory, anti-diabetic and analgesic properties. This review article highlights the recent work that has been carried out on 2-substituted benzimidazole Schiff's base derivatives shows the diversified biological importance.

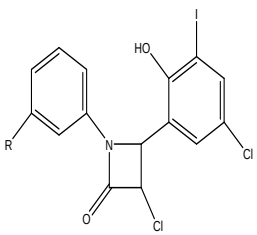
LITERATURE REVIEW

Atmakuru Ramesh *et al.*, (2001)[1] reported the synthesis of Schiff bases by reacting isatin and the appropriate aromatic primary amine / hydrazines and evaluated for analgesic, anti-inflammatory and anti-pyretic activities.

R. P. Pawar *et al.*,(2002)[2] reported the synthesis 4-thiazolidinones and 2-azetidinone and evaluated for antibacterial activity.

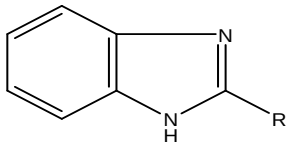


(I)

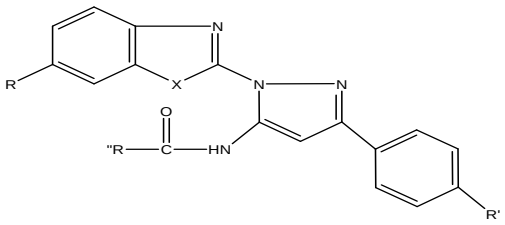


(II)

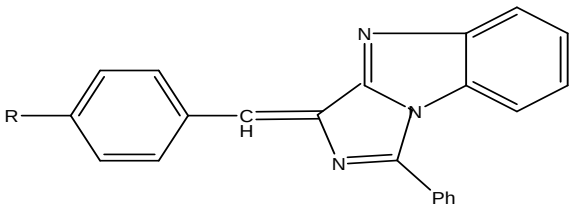
G.K. Trivedi *et al.*, (1990)[3] reported the synthesis of benzeimidazoles by condensation reaction between arylalkanoic acids with O-Phenylenediamine. The compounds have been screened for anti-inflammatory, antibacterial and antifungal activities.



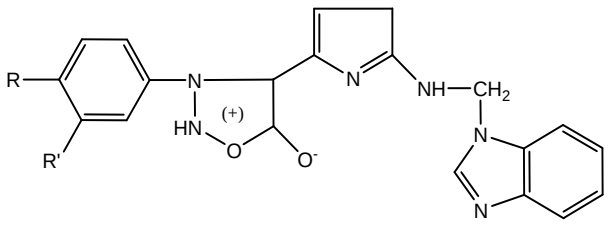
S.P. Singh *et al*., (1978)[4] reported the synthesis of benzimidazoles by the condensation of appropriate 2-hydrazenobenzoles with substituted α-cynoacetophenones. The compounds have reported to have mild anti-inflammatory activities.



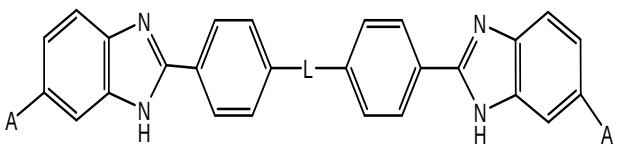
V.M. Reddy *et al*., (2003)[5] reported the synthesis of benzimidazoles from appropriate oxazilinones and ethylenediamine or O–Phenylenediamine by one pot synthesis. The compounds were tested for their anti-inflammatory activity.



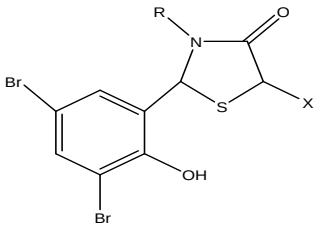
V. Badami *et al*., (2003)[6] reported the synthesis of Mannich base with benzimidazoles in the presence of formaldehyde. The compounds were reported to have anti-fungal activity.



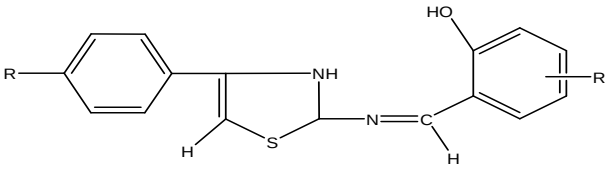
David W. Boykin *et al*., (2004)[7] reported the synthesis of bis-bnzimidazoles and have been evaluated for anti-microbial activity.



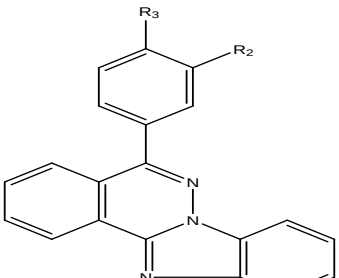
Hansa Parekh *et al*., (2000)[8] reported the synthesis of 4-thiazolidinones by the cyclocondesation of anilines with 2-substituted mercaptoacetic acids and evaluated for anti-microbial activity.



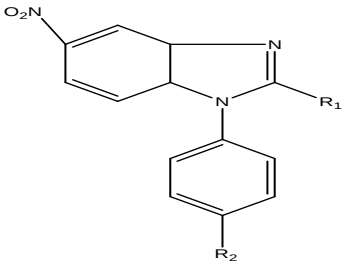
P.G. More *et al*., (2001)[9] reported the synthesis of Schiff base derived from substituted 2-aminothiazole and substituted aldehydes and 2-hydroxy-1-naphthaldehyde.The compounds evaluated for anti-fungal activities.



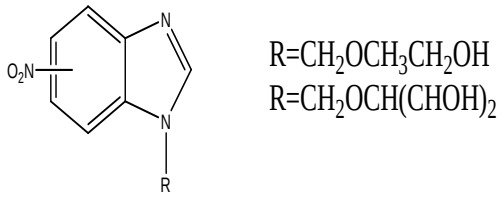
T. Ramalingam *et al*., (1992)[10] reported the synthesis of benzimidazoles by reacting 1-chloro-4-arylpthalazines with 2-aminophenol to afford 1-n-(2-hydroxy-phenyl) amino-4-arylpthalazines followed by their cyclodehydration employing polyphosphoric acid. The compounds have been screened for their anti-inflammatory and anti-hypertensive activities.



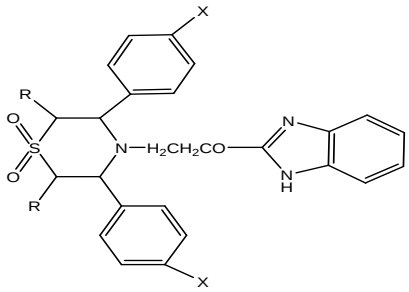
Satyavan Sharma *et al*., (1981)[11] reported the synthesis of disubstituted benzimidazoles and reported to have anti-helminithic, anti-bacterial, anti-fungal activities.



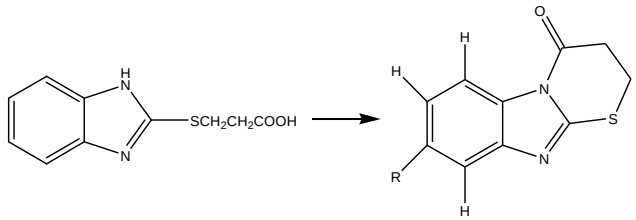
Mashooda Hasan *et al*., (2000)[12] reported the synthesis of 5-nitrobenzimidazole.The synthesized compound exhibits anti-inflammatory and antiviral activity.



V. Sundari *et al.*, (2004)[13] reported the synthesis of some thiazine substituted benzimidazoles and reported to have anti-bacterial and anti-fungal activity.

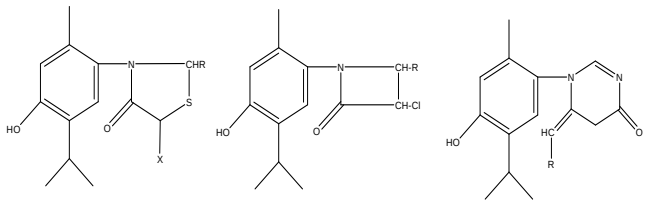


Jagmohan *et al.*, (1992)[14] reported the cyclization of β-(5- indobenzimidazole-2- thio)-propionic acid(2B) with acetic anhydride/pyridine gave regioselectively 2H-8-iodo(1,3)-thiazino(3,2-a) benzimidazole-4(3H)-one(4b). The compound showed antibacterial and antifungal activity against, Staphylococcus aureus, E-coli, Pseudomonas aeruginosa and candida albicans.



A=B=R=H
A=B=R=I

V.H. Shan *et al.*, (1995)[15] reported the synthesis of 4-thiazolidinones, 2-azetidiononones, and 4-imidazolinone derivatives and reported the synthesized compound exhibits good antimicrobial and anti-tubercular activity.

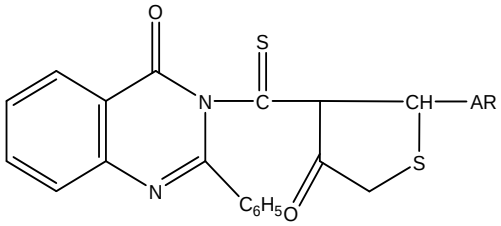


X=H/CH3/CH2COOH X=CH3/C6H5

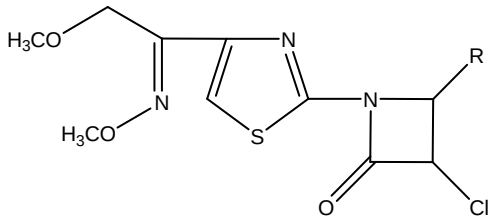
V.V. Mulwad *et al.*, (2002)[16] reported the synthesis of Schiff bases, 4-thiazolidinones, and 2-azetidinones.The synthesized compounds exhibits anti-tubercular activity against $H_{37}RV$.

Virgil I. Stenberg *et al.*, (1981)[17] reported the synthesis of 4-thiazolidinone by various methodology. The synthesized compounds exhibits anticonvulsant, hypnotic, respiratory, anti-inflammatory, antiproteolytic, antihemolytic, antitubercular, antihelmitic, cardiovascular, antibacterial, antifungal, insecticidal, antiviral, herbicidal activity.

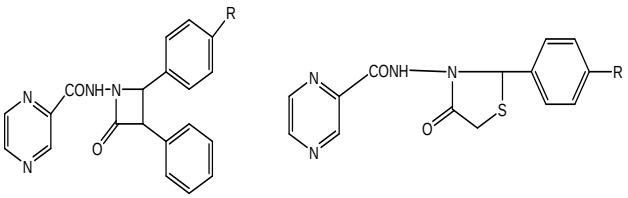
V.P. Trivedi *et al.*, (2004)[18] reported the synthesis and biological activity of some new 4-thiazolidinone derivatives. The compound found to have anti bacterial and antitubercular activity.



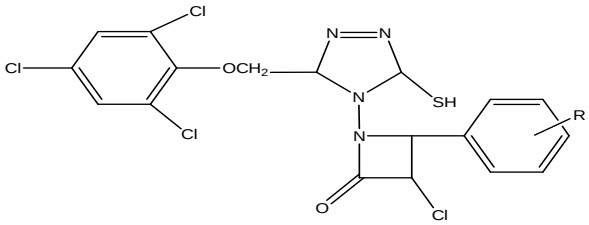
Khyati A. Parikh *et al.*, (2000)[19] synthesized Schiff bases by the condensation reaction 2-amino-4(2-sustituted)thiazole and aromatic aldehydes, which on treatment with Chloroacetyl chloride in the presence of Triethylamine as basic catalyst affords 2-azetidinones. The synthesized compounds have been tested for their antimicrobial activity against mycobacterium tuberculosis $H_{37}R_{V.}$



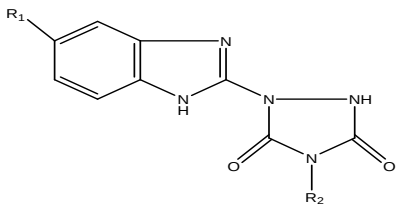
R. Govindarajan *et al.*, (2003)[20] synthesized a series of azetidinones and thiazolidinones of pyrazonic acid studied for their vitro anti-tubercular, anti-fungal and antibacterial activity.



K.D. Patel *et al.*, (2003)[21] synthesized some new azetidinones from their Schiff bases reacting with Chloroacetyl chloride, to form 4-aryl-1-[3-2, 4, 6-trichlorophenoxymethyl-4(mercapto1, 2, 4-triazol-4) yl], 3-chloro-2 azetidinones.The compound were screened for antibacterial and anti-mycobacterial activity.

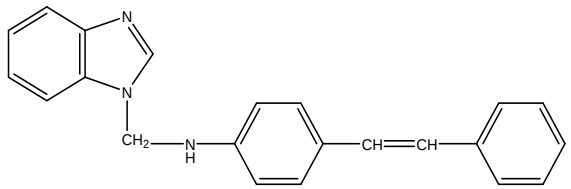


Magdum Chandrakanth *et al*., (2000)[22] reported the synthesis of new 4-aryl/alkyl-1[substituted benzimidazole-2yl]-5-thio-1, 2, 4-thiazolidine 3-ones and reported to have significant anticancer activity.

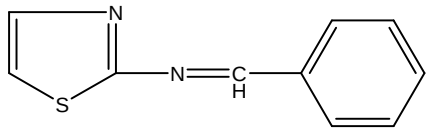


R_1	R_2
H	CH_3
H	CH_3
H	CH_3

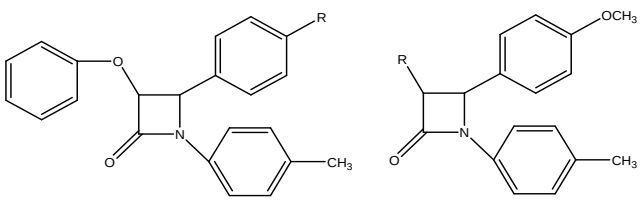
R.S. Varman *et al*., (2004)[23] reported the 5 membered nitrogen and sulphur heterocyclic compound such as benzimidazole, benzimidazolin-2-thione have been prepared and subjected to amino methylation reaction in presence of formaldehyde and amines. Secondary as well as primary aromatic amine bearing different substitutes have been successfully utilized in the amino methylation reaction. The amino methylated products have been rested for antibacterial and anti-filarial activity.



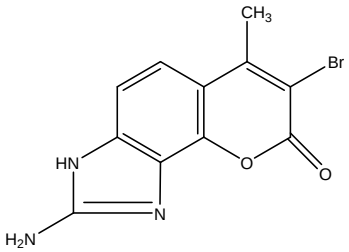
A.K.D. Mazumdar *et al*., (1979)[24] reported the synthesis of Schiff bases and evaluated for anti-cancer activity.



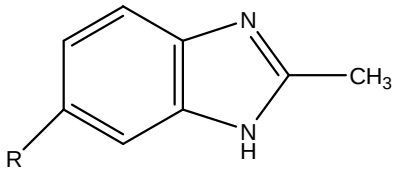
M. S. Manhas *et al*., (1979)[25] synthesized various substituted β-lactams carrying a bis (2-chloroethyl) amino group and some of the compounds shown mild anti-tumour activity and low toxicity.



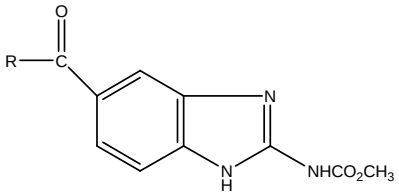
Z. M. Nofal *et al*.,(1998)[26] reported the synthesis of benzimidazoles by reacting coumarin derivatives with thiourea and evaluated for antimicrobial activity.



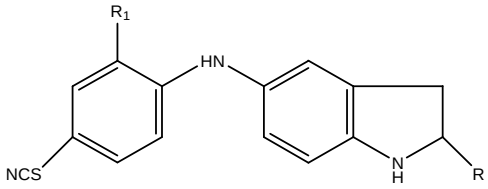
Arturo Navaro-Ocafia *et al*., (2001)[27] reported the synthesis of benzimidazoles by the reduction of 4-substituted 2-nitro acetanilide by baker yeast in acid media effected cyclization and evaluated for analgesic and anti-inflammatory activity.



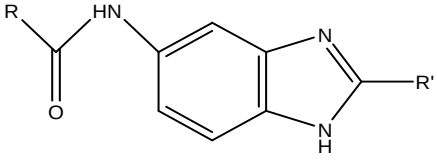
Satyavan Sharma *et al*., (1988)[28] reported the synthesis of 2-substituted benzimidazoles by starting from 4-amino-3-nitrobenzoic acid. The compounds were reported to have anti-helminthic activity.



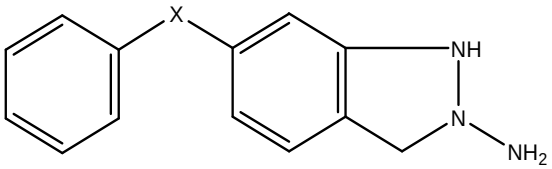
Satyavan Sharma *et al*., (1980)[29] reported the synthesis of 2-substituted benzimidazoles and reported to have anti-helminthic activity.



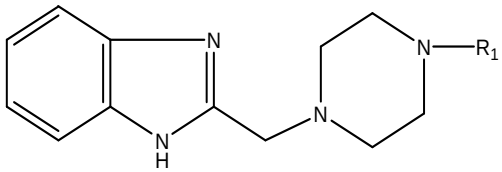
S. N. Sawhney *et al*., (1989)[30] reported the synthesis of benzimidazoles & evaluated for their anti-helminthic activity.



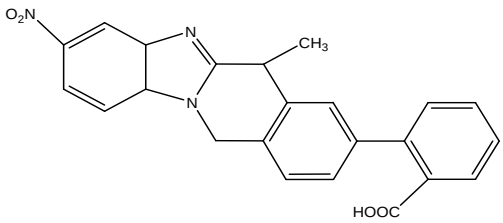
Satyavan Sharma *et al*., (1989)[31] reported the synthesis of substituted benzimidazoles and evaluated for their anti-helminthic activity.



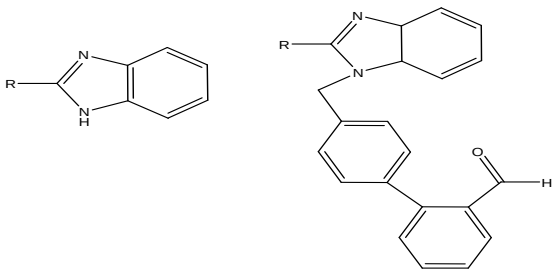
Satyavan Sharma *et al*., (1979)[32] reported the synthesis of benzimidazoles by the nucleophillic reaction of the corresponding amines with dibenzimidazo [1, 2-α: 1', 2'-d] tetrahydropyrazin-6, 13-diones.The compounds were to have anti-helminthic activity.



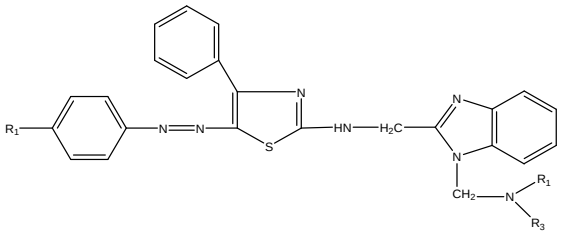
Vipin Kumar *et al*., (2002)[33] reported the synthesis of benzimidazoles via coupling of substituted benzimidazoles with substituted benzimidazoles with substituted biphenyl and reported to have anti-hypertensive activity.



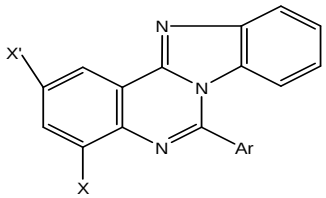
K. Verma *et al*., (1988)[34] reported the synthesis of 2-substituted-1-[(2'-carboxyl biphenyl-4-yl) methyl] benzimidazoles. The synthesized compounds are reported to have modest binding affinity for both AT_1 and AT_2 receptors.



S. K. Bajpai *et al*., (1993)[35] reported the synthesis of 1-(N-substituted)-amino-methyl-2-N-2-(4-phenyl-5-substituted-diazo)-thiazolo-amino-methyl benzimidazoles and reported it exhibits antiviral activity against Ranikhet disease virus (RDV).

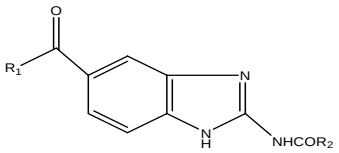


A. Raghuram Rao *et al*., (1999)[36] reported the synthesis of 6-aryl-benzimidazole (1, 2-C) Quinozolines as possible bronchodilators in which benzimidazole nucleus is widely accepted for its antiallergic and its antihistaminic activity.



6-aryl-benzimidazole (1, 2-C) Quinozolines

D. S. Bhakuni *et al*., (1993)[37] reported the synthesis of 5-aryl-2-acylamino-1H-benzimidazoles.The compounds have been screened for their macrofilaricidal and chemo sterilizing activity.



R_1=H/CH_3/CH_2COOH R_2=CH_3/C_6H_5

CONCLUSION

The plethora of research subscribed in this review indicates a wide spectrum of pharmacological activities exhibited by 2-substituted benzimidazole Schiff's bases derivatives. The biological profiles of these new generations of 2-substituted benzimidazole Schiff's bases would represent a fruitful matrix for further development of better medicinal agents.

ACKNOWLEDGEMENT

The authors are thankful to **Department of Chemistry, Magadh University, Bodh Gaya, Bihar, India,** Spectrum Institute of Pharmaceutical Sciences and Research, Greater Noida, India and Department of Chemistry, Maharaja College, Ara, Bihar, India for providing work platform, encouragement and to our friends those who helped us to complete this review.

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