Benzotriazoles and microbial infections: a review supporting for microbial control

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ABSTRACT

The triazole-based therapeutic medications are more widely used in clinical practise for their various pharmacological activities. This will promote to develop new structural triazole derivatives which can be used extensively in clinicals. Benzotriazole is a fused heterocyclic having a triazole ring fused with a benzene ring and exhibit antioxidative, antiparasitic, antiviral, antibacterial, antifungal, antitubercular, anticancer activities. This present study gave sight on a latest and outstanding developments of benzotriazole compounds. Which will help to design the new benzotriazole-based medications with high bioactivity and low toxicity.

KEYWORDS

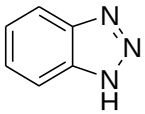
Benzotriazole, antioxidative, antiparasitic, antiviral, antibacterial, antifungal, antitubercular, anticancer

INTRODUCTION

Microbial infections in humans has become one of the most serious public health concerns across the world. The recurrence of death-defying diseases has increased worldwide due to pathogenic microorganisms (Chowdhury et al., 2011). Therefore, the advancement of new and distinctive antimicrobial agents has become a significant step due to unsuitable results from these medications like, side reactions, and the resistance in microorganisms for the existing drugs. Regardless of a various attempt to get the new basic structural feature in the quest for powerful antimicrobials, benzotriazole still stay as one of the most flexible class of compounds against microorganisms (Yadav, Chauhan, Sharma, & Singhal, 2010).

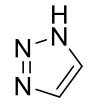
1*H*-Benzotriazoles **(1)** are considered as significant because of their diverse biological activities such as antibacterial (Asati, Srivastava, & Srivastava, 2006; Toraskar, Kadam, & Kulkarni, 2009), antifungal (Asati et al., 2006; Cui et al., 2012), anthelmintic (Pawar, Gorde, & Kakde, 2010), antihistaminic (Boido, Boido, & Sparatore, 2001), DNA cleavage (Pućkowska, Bartulewicz, & Midura-Nowaczek, 2005), antitubercular (Augustynowicz-Kopec, Zwolska, Orzeszko, & Kazimierczuk, 2008), anticancer (Srivastava et al., 2006), antiulcer (Srinivasulu, Satyanarayana, Reddy, Hegde, & Chakrabarti, 2006), anti-nociceptive (Aiyalu Rajasekaran & Rajagopal, 2009), anti-inflammatory (Akhter et al., 2011; Aiyalu Rajasekaran & Rajagopal, 2009), anticonvulsant (A. Rajasekaran, Murugesan, & AnandaRajagopal, 2006), protein kinase inhibitors (Ruzzene, Penzo, & Pinna, 2002) and respiratory syndrome protease inactivators, analgesic (Aiyalu Rajasekaran & Rajagopal, 2009), antiviral (Carta et al., 2006) etc.

Several triazole derivatives shows high oral bioavailability, low toxicity and broad-spectrum activity (Sharma, Samadhiya, Srivastava, & Srivastava, 2011; Wan, Lv, Tian, & Zhu, 2010). From this study we can conclude that this is the prominent class of heterocycle and became the most rapidly expanding group of antibacterial compounds.

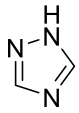


(1)

Due to various activities, the triazole derivatives have a unique position in heterocyclic chemistry. A triazole five-membered ring heterocyclic compound, having molecular formula $C_2H_3N_3$. There are one pair of isomeric chemical compound that differ only in the relative positions of the all nitrogen atoms (Singhal, Sharma, Dudhe, & Kumar, 2011).



1H-1,2,3-triazole



1H-1,2,4-triazole

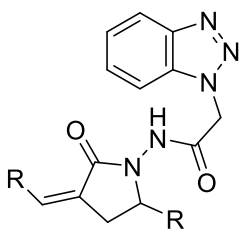
(2) **(3)**

1,2,3-Triazoles are known for their multiple applications, one of them is used as synthetic intermediates for pharmaceuticals. Some other important therapeutic activities include antimicrobial compounds, β_3-selective adrenergic receptor agonists, anti-HIV agents, kinase inhibitors and other enzyme inhibitors (Klein, Krainz, Redwan, Diner, & Grotli, 2009).

The conventional synthetic techniques for the synthesis of benzotriazole derivatives have several drawbacks including drastic conditions, longer reaction times, toxic solvents, low yields of products, etc and is inefficient and harmful to environment. Therefore, some alternative methods are also suggested like Microwave irradiation. Microwave irradiation have more importance is due to reduction in the amounts of hazardous substance like solvents required, short reaction time and the operational simplicity and also reduces the formation of the byproducts obtained from conventional techniques. We have also included some 1,2,3-benzotriazoles which are synthesized by microwave technique (Muvvala, Sugreevu, & Rao, 2011; Sen & Shukla, 2011).

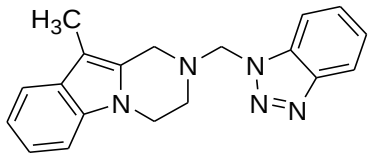
LITERATURE REVIEW

In 2006, some "5-Arylidene-2-aryl-benzotriazoloacetamidyl-1,3-thiazolidin-4-ones" derivatives were synthesized and analysed for their antibacterial activity (Asati et al., 2006).



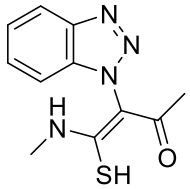
(4a-4j)

Tiwari *et al*. (2006) reported synthesis of substituted "1,2,3,4-Tetrahydropyrazino [1,2-a] indole" and tested against various strains of bacteria *S. aureus, S. typhi, P. aeruginosa* and *E. coli* and was found inactive against *E. coli* (Tiwari et al., 2006).



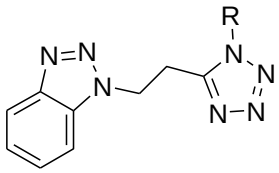
(5)

Awadi *et al.* (2008) synthesized a new series of Cu^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+} complexes of "3-(*1H*-benzo[d][1,2,3]triazol-1-yl)-4-mercapto-4-(methylamino)but-3-en-2-one" (9) and screened for their antimicrobial activities (Al-Awadi et al., 2008).



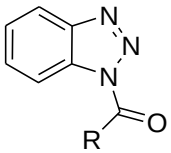
(6)

Rajasekaran *et al*. (2006) reported synthesis of novel "1-[2-(1*H*-Tetrazole-5-yl) ethyl]-1*H*-benzotriazoles" and evaluated for antibacterial and antifungal activity. The compound 10f found to have maximum activity against *B. subtilis* and *C. albicans* with zone of inhibition of 16mm and 15mm (A. Rajasekaran et al., 2006).



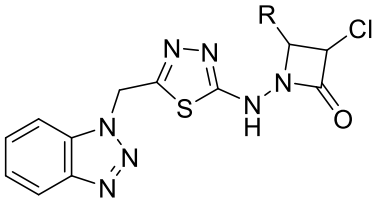
(7a-7h)

Rauf *et al*. (2008) reported synthesis of "*N*-Acyl-1*H*-1,2,3-benzotriazoles" and were analyzed for antimicrobial activity. All compounds showed good antifungal activity except 8d (Rauf & Gangal, 2008).



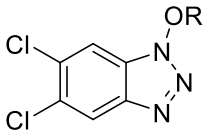
(8a-8d)

Shukla *et al*. (2008) synthesized several new "5-[2-((1,2,3-Benzotriazole)-1-yl-methyl)-1'-(4'-substituted aryl-3'-chloro-2'-oxoazetidine] amino-1,3,4-thiadiazoles" and evaluated for their antifungal and antibacterial activity (Shukla & Srivastava, 2008).



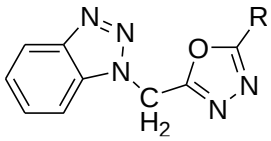
(9a-9n)

Kopec *et al*. (2008) prepared a series of 1-(nitrobenzyloxy)benzo-triazoles and were tested against *Mycobacterium* strains using isoniazid as standard. Out of that "5,6-dichloro-1-(3,5-dinitrobenzyloxy)-1*H*-benzotriazole" was found to be more potent among them (Augustynowicz-Kopec et al., 2008).



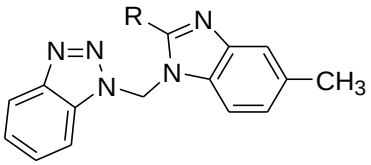
(10a-10e)

Patel *et al*. (2009) carried out synthesis of "Ethyl-2-(1*H*-Benzotriazole-1-yl) acetate and 2*H*-(Benzotriazole-1-yl)acetohydrazine" and evaluated for the antimicrobial activity on *S. aureus* and *E. coli* (J. S. Patel, Garg, & Sen, 2012).



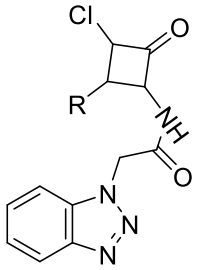
(11a-11e)

Singh *et al*. (2009) synthesized "1,2,3-Benzotriazoles" and were evaluated for their antifungal activity against *A. nigar, T. rubrum, P. oryzae, C. albicans and B. cinereal* (Singh, 2009).



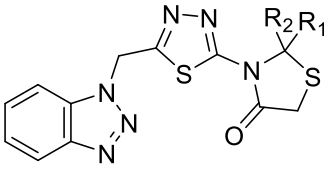
(12a-12e)

Toraskar *et al*. (2009) synthesized "*N*-substituted-2-azetidinones" (16a-16j) and were tested in vitro against *C.albicans*. All the compounds were active and out of them 16g and 16h were the most active (Toraskar et al., 2009).



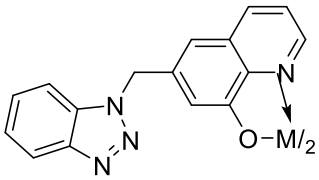
(13a-13j)

Namdeo *et al*. (2009) reported the "2-substituted-5-[(*N*-Benzotriazolo methyl)-1,3,4-thiadiazolyl]-4-thiazolidinone" synthesis and evaluated against *C.albicans, A.flavus* and *A.niger* (Namdeo, Singh, & Prajapati, 2009).



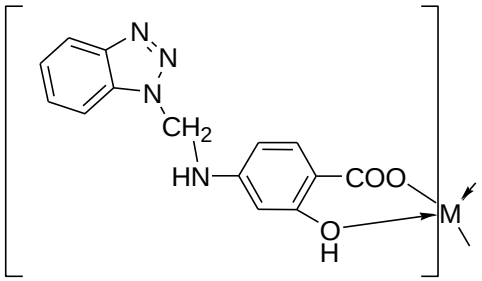
(14a-14f)

Patel *et al*. (2009) synthesized "5-(1*H*-Benzotriazole methylene)-8-quinolinol (BTMQ)" and the transition metal chelates of BTMQ and were screened for antifungal activity. All the compounds show good antifungal agents (H. Patel & Oza, 2009).



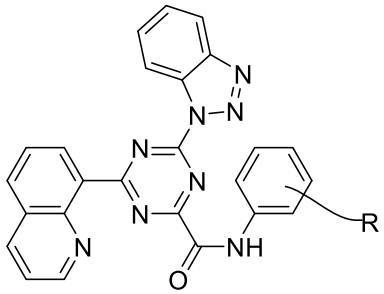
(15)

Patel *et al*. (2009) synthesized as "1-(4-Carboxy-3-hydroxy-4-phenyl amino methyl) benzotriazole" and its transition metal complexes and evaluated for antimicrobial activity (P. Patel & Dpatel, 2009).



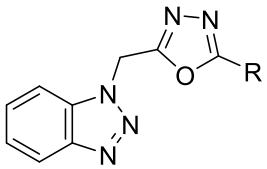
(16)

Vora *et al*. (2009) synthesized the series of *s*-triazines derived with quinolines and characterized by conventional and instrumental methods. Antibacterial evaluation was done with Ampicillin as standard. Out of these compounds 17b, 17f, 17j were found to be equal active as standard (Vora et al., 2009).



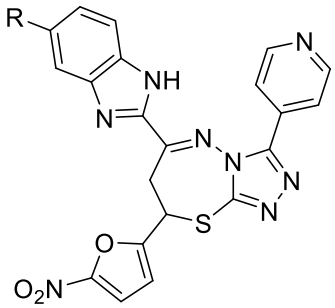
(17a-17j)

Saini *et al*. (2010) synthesized of "Ethyl-2-(1*H*-benzotriazol-1-yl) acetate and 2*H*-(benzotriazole-1-yl)acetohydrazine" and was evaluated for anti-fungal activity. All the synthesized compounds were active (Rakesh, Saurabh, Kesari, & Swatrantra, 2010).



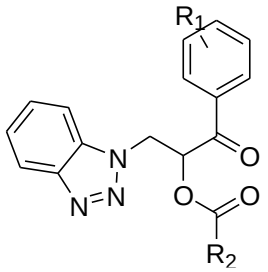
(18a-18e)

Reddy *et al*. (2010) reported the "6-(1*H*-Benz[*d*]imidazol-2-yl)-8-(5-nitro-2-furyl)-3-(4-pyridyl)-7,8-dihydro[1,2,4]triazolo[3,4-*b*] [1,3,4] thiadiazepines" series and were analyzed for antibacterial activity (Reddy & Reddy, 2010).



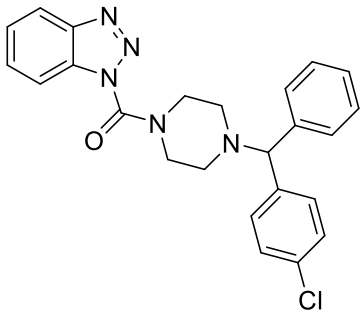
(19a-19e)

Wan *et al*. (2010) reported the synthesis of benzotriazole derivatives (compounds **20a-20z$_1$**) and were analyzed for antibacterial activities against *B. subtilis*, *P. aeruginosa*, *S. faecalis*, *S. aureus*, *E. coli*, and *E. cloacae*. Out of all compounds 23s showed the most favorable antibacterial activity (Wan et al., 2010).



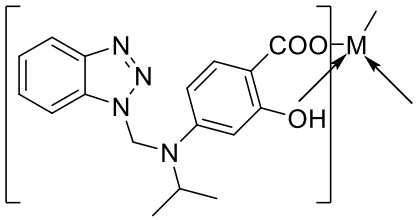
(20a-20z$_1$)

Gan *et al*. (2010) synthesized an azole containing piperazine derivative "Benzotriazol-1-yl-[4-((4-chlorophenyl)phenylmethyl)piperazin-1-yl]methanone" and investigated *in-vitro* for its antibacterial activitiy. The compound exhibited antibacterial activity with MIC value less then 400µg/mL (Gan, Fang, & Zhou, 2010).



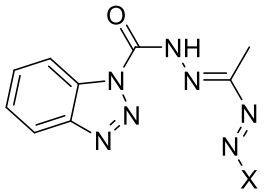
(21)

Patel *et al.* (2010) reported the synthesis of "1-(4-Carboxy-3-hydroxy-*N*-isopropylphenyl aminomethyl)benzotriazole" and it's complexes with metals which were evaluated for their antimicrobial activity (P. K. Patel & Patel, 2010).



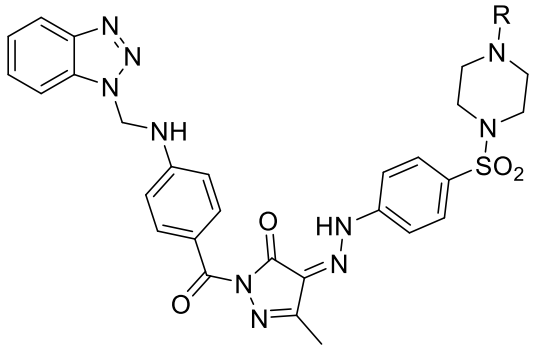
(22)

Muvvala *et al*. (2011) synthesized 1,2,3-Benzotriazole derivatives under microwave irradiation and characterized by melting points and spectral studies (Muvvala et al., 2011).



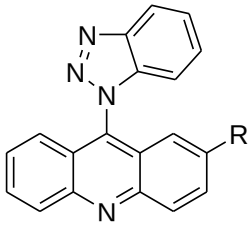
(23a-23h)

Shah *et al*. (2011) synthesized "1-[4-((1*H*-Benzotriazol-1-yl)methyl amino)benzoyl]-3-methyl-4-[2-(4-(4-alkylpiperazin-1-ylsulfonyl)phenyl)hydrazono]-1*H*-pyrazol-4*H*-ones". All these compounds showed significant antimicrobial activity (Shah, Patel, & Patel, 2013).



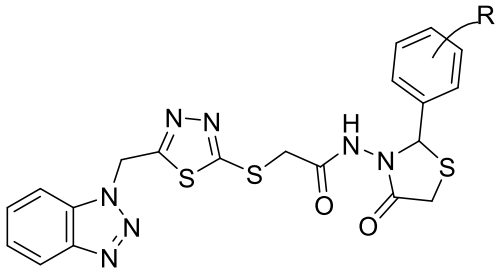
(24a-24h)

Singh *et al*. (2011) reported the synthesis of benzotriazole substituted acridine derivatives and evaluated for antibacterial activity against *E.coli, S.aureus* and *B.subtilis* (Singh, 2009).



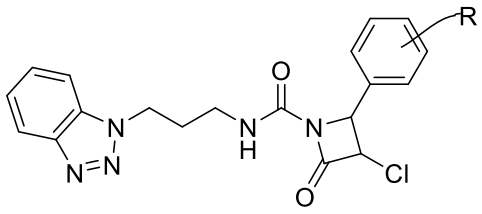
(25a-25b)

Sen *et al*. (2011) synthesized "5-[(2'"substituted Aryl-1'",3'"-thiazolidine-4"-ones)-1"-(iminothioacetyl)-1-(methylene)-1,'3'4'-thiadiazoles]-1,2,3-benzotriazoles". The synthesized products were analyzed as antibacterials (Sen & Shukla, 2011).



(26a-26k)

Sharma *et al*. (2011) synthesized "*N*-(3-(1*H*-1,2,3-Benzotriazol-1-yl) propyl)-2-(4-substituted phenyl)-3-chloro-4-oxo-1-azetidinecarboxamide" and were analyzed as antibacterial. All the compounds show good activity (Sharma et al., 2011).



(27a-27s)

DISCUSSION

In this discussion we conclude the various aspects of the pharmacological properties of triazoles. It is obvious that in certain areas the activities are overlapped, on the basis of that we conclude that the ring structure is the chief parameter which determines the activity against various microorganisms. In the structure, it is also important that the substitution on different positions and also affects the degree of activity. Out of all the nitro group on the ring seems to be essential for activity against bacteria, fungi and viruses.

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