Benzimidazoles: As Antifungal Drugs

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Abstract:
Benzimidazole is a heterocyclic aromatic organic compound. It is an important pharmacophores and a privileged structure in medicinal chemistry. Benzimidazole shows their antimicrobial activity by inhibiting the bacterial nucleic acid and proteins synthesis. This ability of benzimidazole is due to their structural similarities with the purine. Benzimidazole gives fungicidal activity against fungal species like A.flavus (871), A.fumigatus (2250), C.albidus (2661) and C.albicans (183). Antifungal susceptibility test done using standard method of NCCLS. All the compounds gives comparable activity of all fungal species against standard drug amphotericin-B.

Keywords: *A.flavus (871), A.fumigatus (2250), C.albidus (2661), C.albicans (183), NCCLS, amphotericin-B*

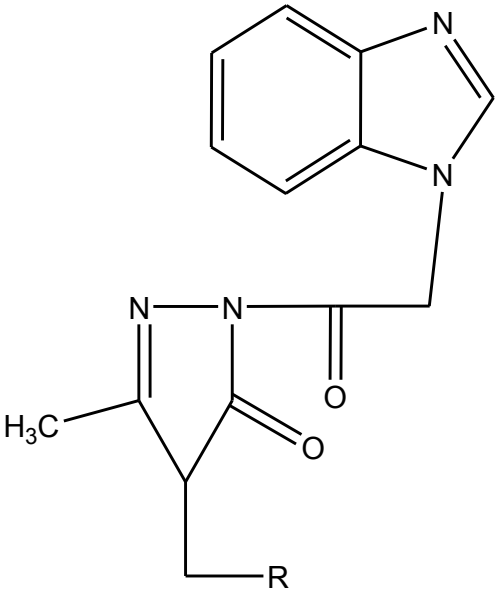
1. Introduction

Drugs are chemicals that prevent disease or assist in restoring health to the diseased individuals as such they play an indispensable role in modern medicine.

Benzimidazole is a heterocyclic aromatic organic compound. It is an important pharmacophores and a privileged structure in medicinal chemistry. This compound is bicyclic in nature which consists of the fusion of benzene and imidazole. Nowadays is a moiety of choice which possesses many pharmacological properties such as antiulcer, antihelminthic, antihypertensive, anticoagulant, antiallergic, analgesic, anti-inflammatory, antimicrobial, antiviral, antiparasitic, antioxidant, antineoplastic etc.

Benzimidazole shows their antimicrobial activity by inhibiting the bacterial nucleic acid and proteins synthesis. This ability of benzimidazole is due to their structural similarities with the purine. Benzimidazole gives fungicidal activity against fungal species like A.flavus (871), A.fumigatus (2250), C.albidus (2661) and C.albicans (183).

2. Benzimidazole Derivatives



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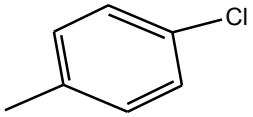
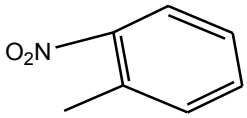
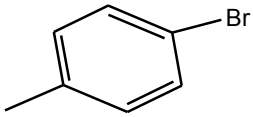
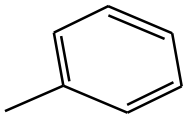
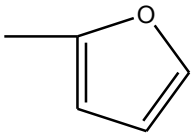
1	
2	
3	
5	
6	

3. Materials and Methods of Antifungal Activity

3.1 Procedure

Antifungal susceptibility test using standard method of NCCLS **(**The National Committee for Clinical Laboratory Standards)

3.1.1 Preparation of broth Medium

10.4 gms of RPMI(Rosewell Park memorial institute)-1640 medium supplemented with glutamine and phenol red, without bicarbonate and 34.53g 3-(N-morpholino) propanesulfonic acid (MOPS) was dissolved in 400 ml of distilled water. pH was adjusted to 7.0 at 25 °C with 1 mol/L sodium hydroxide. The volume was made up to 0.5 L with water and was filtered, sterilized and was stored at 4°C until required.

3.1.2. Preparation of Inocula

Fungal strains were sub-cultured on to their respective growth medium and incubated for 48 hrs at 25-30°c. From these plates, several colonies were transferred to 5 ml of sterile distilled water.

The suspensions were mixed for 15 s to ensure homogeneity and were subsequently diluted to match the turbidity of a 0.5 McFarland standard (i.e. OD = 0.12–0.15 at k = 530 nm, corresponding to 1–5* 10^6CFU/ml). Then the working suspensions were prepared by a 1 in 30 further dilution of the stock suspension in sterile distilled water to yield 1–5 * 10^3 CFU/ml. 0.1ml sterilized solution of resazurin (20 mg/ml in water) was supplemented to the working suspension.

3.1.3 Preparation of Samples

Stock solutions of the synthesis compounds and the positive control drug amphotericin B were prepared in dimethyl sulphoxide (DMSO) at the concentrations of 1000000 nM/ml. Further it was diluted to 1:50 in broth.

3.1.4 Preparation of Plates

Microdilution susceptibility testing was performed in flat-bottom 96-well clear plates containing broth medium in each well. Sample solutions were subsequently serially diluted two-fold in the plates with the broth, starting with the final concentration. The working inoculum suspension was added to give a final inoculum concentratio. Amphotericin B was used as the standard antifungal drug. Sterility and growth controls in the presence of DMSO were also included. The plates were then incubated at 37 °C for 48 h. The amount of growth was measured using plate reader.

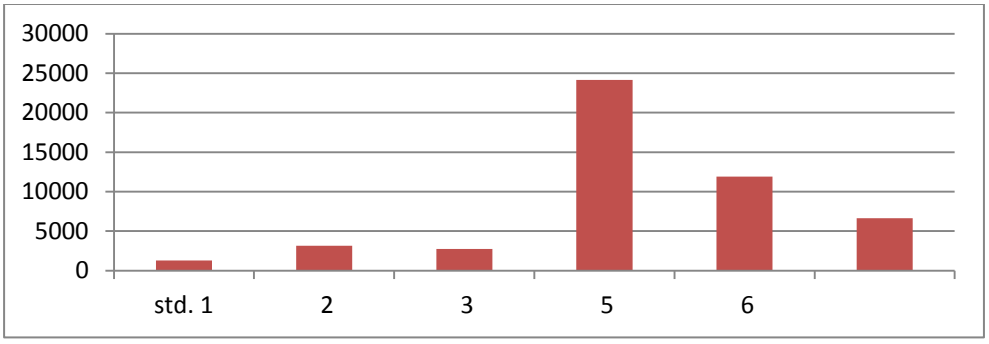
4. Results and Discussion

4.1 IC 50 (nm/ml) of all Synthesis Compounds

Table 1

Comp. no.	A.flavus (871)	A.fumigatus (2250)	C.albidus (2661)	C.albicans (183)
Std.	1274	584.2	4118	882.1
1	3167	5200	15552	516.4
2	2736	4482	4182	7751
3	24148	16020	5999	3471
5	11911	7096	11697	8571
6	6648	2988	2026	6730

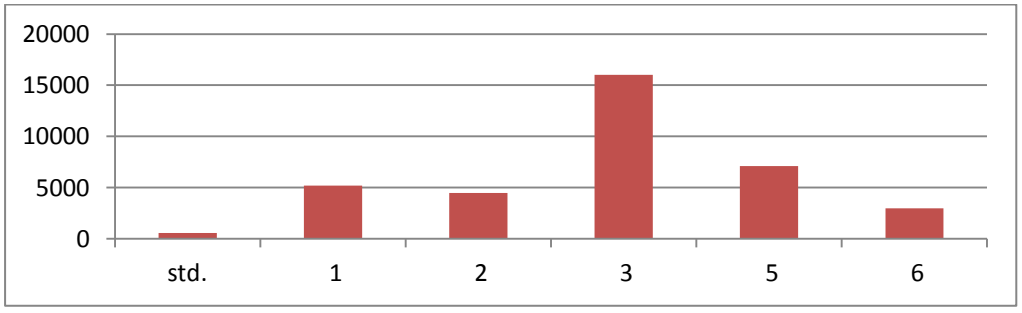
4.1 Graph for the IC50 of all compounds against A. flavus (871)



4.2 Conclusion of A.flavus (871) Result

From the graph we conclude that compound 2 and compound 1 gives better activity against A.flavus (871). whereas compound 2 gives better activity then compound 1 because it contain nitro group which is more electronegative then compound 1 contain chlorine group.

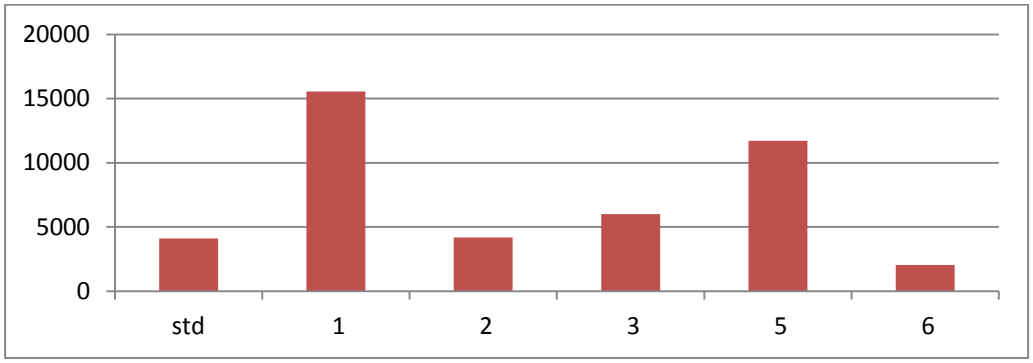
4.2 Graph for the IC50 of all compound against A. fumigatus (2250)



4.3 Conclusion of A.fumigatus (2250) Result

From the graph we conclude that compound 2 and compound 6 gives better activity against A.fumigatus (2250). Whereas compound 6 gives better activity then compound 2 because it contain furan moiety were compound 2 contain o-nitro benzene.

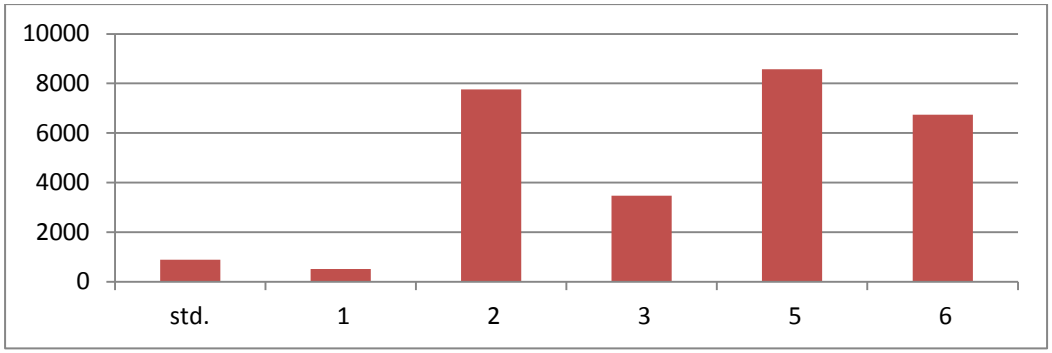
4.4 Graph for the IC50 of all compounds against C.albidus (2661)



4.4 Conclusion of C.albidus (2661) Result

From the graph we conclude that compound 2 and compound 6 gives better activity against C.albicans (2661). Whereas compound 6 gives better activity then compound 2 because it contain furan moiety were compound 2 contain o-nitro benzene.

4.4 Graph for the IC50 of all compounds against C.albicans (183)



4.5 Conclusion of C.albicans (183) Results

From the graph we conclude that compound 1 gives better activity against C.albicans (183). Compound 1 contains p-chloro benzene with stable structure.

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