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Antifungal Screening of Some Newly Synthesized Cinnamo Hydroxamic Acids

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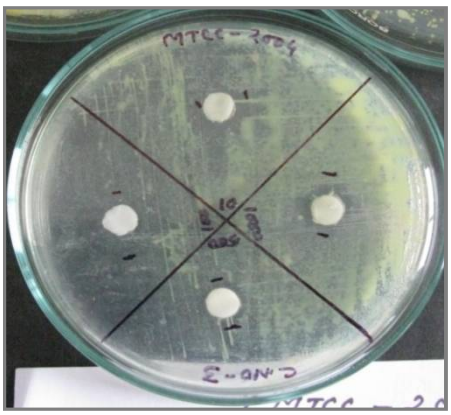
ABSTRACT

Cinnamo hydroxamic acids were synthesized with method followed by the Priya Dharshini and Tondon. Hydroxamic acid and their derivatives fulfill a variety of important role not only in biology and medicinal chemistry but other fields. The promising biology and medicinal application potential of hydroxamic acid and their derivatives prompted us to design antifungal activity of cinnamo hydroxamic acids against two fungal strains Penicillium griseofulvum, Fusarium solani by the paper disc agar plate method. The bacterial cell growth zone of inhibition by these compounds (CHA, MCHA, N-BCHA, p-CH$_3$BCHA, p-ClBCHA) for Penicillium griseofulvumare 23.76 mm, 06.30 mm, 05.00 mm, 09.16 mm, 05.23 mm and for Fusarium solaniare 23.00 mm, 10.20 mm, 09.16 mm, 13.00 mm, 06.23 mm, at 500 ppm respectively. Detailed antifungal testing shown that these compounds are good cell growth of inhibition by the study of antifungal activities against Penicillium griseofulvumand and Fusarium solani two fungal strains.

Graphical Abstract



Antifungal activity of synthesized cinnamo hydroxamic acids
Penicillium griseofulvum (2004)

Keywords: Cinnamo hydroxamic acids, Antifungal, Activity, Medicine, Inhibition.

INTRODUCTION

One survey that literature revealed is two-third of the total population of India is engaged in agricultural activities for cultivation several foods. They are produced major crops here are wheat, rice, maize, banana, apple, sugar cane, papaya, tea, coffee, cotton etc [1]. Now a day the major problem faced by India to maintained this rank for cultivation of agricultural product i.e., most agricultural plants are affected by the fungal disease, fungal infections and pathogens etc [2, 3]. In this way used some antifungal drugs and some pesticides [4] for prevention of plant contamination and killing of these pathogens. Due to this major and important problems not only agriculture fields but medicinal fields also it is necessary to focusing on the biological potential of develop new class of antifungal drug develop [5]. The first hydroxamic acid (Oxalohydroxamic acid) was discovered by Lossen as early as 1869 [6]. Hydroxamic acids refer's to a class of chemical organic compounds having formula RC (=O) NR'OH in which hydroxylamine is inserted in to a carboxylic acids with 'R' as an organic residue (alkyl or aryl group), a CO as a carbonyl group, and a hydroxylamine as NH_2-OH. Hydroxamic acids are commonly synthesized by acylation of hydroxylamine by ester, acids anhydrides or acid chloride (Figure 1) [7].

Figure 1. General structure of a hydroxamic acid.

Last half century the biological activity of hydroxamic acids and their derivatives is investigated not only as potential therapeutic drug butmany fields like –pharmaceutical [8], medicinal biological [9], medical molecular modeling [10], analytical, technical and nuclear chemistry [11], as well as their role as antibacterial [12], antifungal [13], antitumor [14], and anti-inflammatory activities [15]. Because hydroxamic acid and their derivatives having many important characteristics properties for different fields i.e. structurally donor ligands present,their electrophilicity, ability of hydroxamic acids to form complex with metal ions and reactivity of hydroxamic acid and their derivatives [16]. In view of the above application, the present work relates to the screening of antifungal properties of newly synthesized cinnamo hydroxamic acids (CHA), N-methyl cinnamo hydroxamic acid (MCHA), N-benzyl cinnamo hydroxamic acid (N-BCHA), p-methyl benzyl cinnamo hydroxamic acid (p-CH_3BCHA), p-chloro benzyl cinnamo hydroxamic acid (p-ClBCHA), and reports the results of the undertaken antibacterial evaluation against *Penicillium griseofulvum* (2004), *Fusarium solani* (2082).

MATERIALS AND METHODS

Organisms: *Penicillium griseofulvum* (2004), *Fusarium solani* (2082) microbial type culture collection were used. The mould cultures used were 5-7 days olds.

Glass ware: All the glass wares were cleaned with chromic acids cleaning solution followed by distilled water. These were then sterilized and stored in dust proof cabinets.

Medium: The following standard Potato-dextrose ager medium was used for determination of antifungal activity (Table 1).

Table 1. Ingredients and quantity for standard potato-dextrose ager medium.

S.No.	Ingredients	Quantity
1	Peeled Potato	250 gm
2	Dextrose	20 gm
3	Agar-Agar	20 gm
4	Distilled water	1000 mL

Preparation of culture media: Peeled potato chopped into small pieces and boiled in 500 mL distilled water for one hour filtered and volume made to 1000 mL by distilled water. The medium was auto claved at prior half an hour [**17**]. It is used as culture media for screening of antifungal activities against *Penicillium griseofulvum* (2004) *and Fusarium solani* (2082).

Preparation of bio disc: Preparation of biodisc, multiple layers of Whatman filter paper (no.42) carefully cut in 1cm diameter are used and prepared of the above five synthesized cinnamo hydroxamic acid derivatives in the concentration level of 1000 µg mL^{-1} using chloroform [**18**].

Preparation of standard solution: The antifungal activity of each compound was evaluated at 500 ppm, 100 ppm and 10 ppm concentration. Three solution of different concentration with media (500 ppm, 100 ppmand10 ppm) were prepared with the help of the following equation 1 making use of stock solution [**19**].

$$\text{Desired ppm} = \frac{\text{Stock Solution in ppm x X}}{\text{V}} \qquad \text{Eq. 1}$$

Where, X = Volume of stock solution (in mL added), V= Volume of media

Procedure: Newly prepared compounds were screened for their activity against *Penicillium griseofulvum* and *Fusarium solani*in chloroform by paper disk diffusion method the prepared 50 mL potato dextrose ager medium (PDA) taken in a number of 100 mL conical flask were plugged with cotton autoclaved for half an hour at 20 psi pressure. Normal saline was used to make a suspension of spore of fungal strain was transferred to 30 mL saline to get a suspension of corresponding species. Potato dextrose agar media (20 mL) were powered in to each species. Excess of suspension was decanted and plates were dried by placing in incubation at 72 h at 28±°C in culture room. The testing was repeated three times for each concentration of the compound under investigations, along with affair number of replicates of the control plates [**20**].

RESULTS AND DISCUSSION

Activities of each compound were observed and compared with tetracycline used as standard drugs. The fungal colony (zone of inhibition) diameter was measured at 24, 48 and 72 h in three diameters by millimeter scale. The diameters were marked by pencil for subsequent identification. The inhibition of the fungal growth was determined as the difference in growth between test and control plates (Table 1). The percentage inhibition in colony of the test bacteria was expressed in eq 2. The inhibition of the bacterial growth was displayed in figure 2. The synthesized compounds and the reference drugs were screened under identical conditions and the zone of inhibition was measured in mm.

$$\% \text{ of Inhibition} = \frac{\text{(C-T) x 100}}{\text{C}} \qquad \text{Eq. 2}$$

Where, C=Diameter of fungus colony (mm) in controls plates, T=Diameter of fungus colony (mm) in test plates

Zone of inhibition of Penicillium griseofulvum: The synthesized compounds and the reference drugs were screened under identical conditions and the zone of inhibition was measured in mm. The study of antibacterial activity showed that cinnano hydroxamic acids (CHA) was highly sensitive for *Penicillium griseofulvum* against, p-methyl benzyl cinnamo hydroxamic acid (p-CH_3BCHA), N-methyl cinnamo hydroxamic acid (MCHA), p-chloro benzyl cinnamo hydroxamic acid (p-ClBCHA), N-benzyl cinnamo hydroxamic acid (N-BCHA)derivatives of cinnamo hydroxamic acid (Table 2).

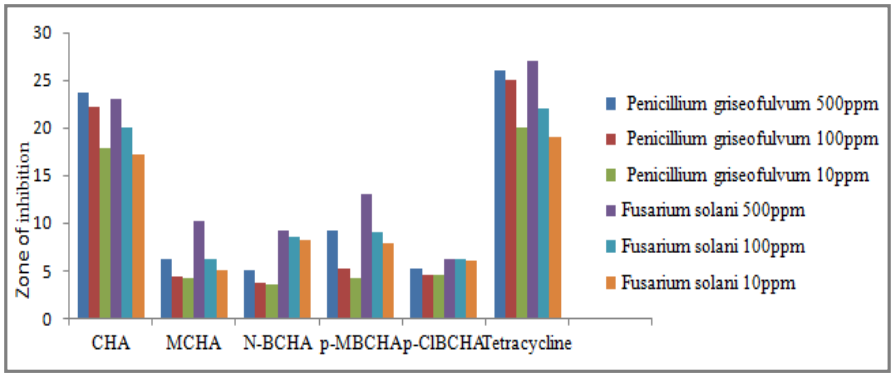


Figure 2. Graph represented antifungal activity of all five newly synthesized cinnamo hydroxamic acid derivatives.

Table 2. All five newly synthesized compounds have been evaluated for their antifungal activities.

S.No.	Name of Compound	Average percentage inhibition *Penicillium griseofulvum*			Average percentage inhibition *Fusarium solani*		
		500 ppm	100 ppm	10 ppm	500 ppm	100 ppm	10 ppm
1	CHA	23.76	22.26	17.90	23.00	20.00	17.26
2	MCHA	06.30	4.43	4.23	10.20	6.16	05.00
3	N-BCHA	05.00	03.80	3.56	09.16	08.50	08.23
4	p-CH_3BCHA	09.16	05.30	04.23	13.00	09.10	07.83
5	p-ClBCHA	05.23	04.56	04.50	06.23	06.15	05.99
6	Tetracycline (standard)	26.00	25.08	20.00	27.06	22.04	19.07

Zone of inhibition of Fusarium solani: The synthesized compounds and the reference drugs were screened under identical conditions and the zone of inhibition was measured in mm. The study of antibacterial activity showed that cinnano hydroxamic acids (CHA) was highly sensitive for *Fusarium solani* against N-methyl cinnamo hydroxamic acid (MCHA), cinnamo hydroxamic acids (CHA), p-methyl benzyl cinnamo hydroxamic acid (p-CH_3BCHA), N-benzyl cinnamo hydroxamic acid (N-BCHA) derivatives of cinnamo hydroxamic acid (Table 2).

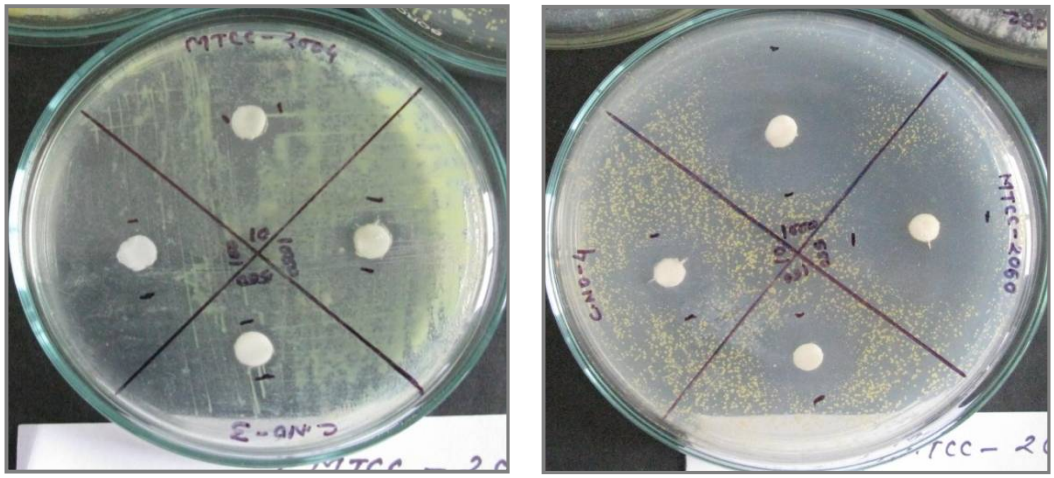
APPLICATION

The method used for the synthesis of final compounds in the manuscript is very useful in various field of analytical, pharmaceutical, medical molecular modeling, docking and nuclear chemistry. The compounds are very big antibacterial and antifungal, antimalarial and analgesic activities and are selective inhibitors of various enzymes. The final compounds are having very good anticancer (Histone Deacetylase Inhibition) and antitumor's properties. The compounds are having selective inhibitors of various enzymes, inhibitors of matrix metalloproteinase inhibition, urease, peroxidase, lipoxygenase inhibitory activity etc. The most important properties of hydroxamic acid derivatives are antimelanogenic agents. The final compounds are having very good iron uptake by siderophores.

CONCLUSION

The compounds are shown very good antifungal activity (Figure 3) and are selective inhibitors of various enzymes. The antifungal investigation data showed a moderate to good activity at higher concentration but zone of inhibition decreases considerably upon dilution. CHA are more toxic to *Penicillium griseofulvum*. The sequence of antifungal activity of all five newly synthesized compounds for *Penicillium griseofulvum* are CHA > p-CH_3BCHA >MCHA >p-ClBCHA >N-BCHA. Also CHA is more toxic to*Fusarium solani*. The sequence of antifungal activity of all five newly synthesized compounds for *Fusarium solani* are CHA > p-CH_3BCHA > MCHA >N-BCHA > p-

CH_3BCHA at higher concentration 500 ppm respectively (Figure 2). The entired results we cocluded that CHA is more toxic for both fungal strains i.e. *Penicillium griseofulvum* and *Fusarium solani.*



(a) (b)

Figure 3. Antifungal activity of synthesized cinnamo hydroxamic acids
(a) *Penicillium griseofulvum* (2004) (b) *Fusarium solani* (2060).

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REFERENCES

[1]. G. Gruere and D. Sengupta, Bt Cotton and Farmer Suicides in India: An Evidence-based Assessment, J. Develop Studies, **2011**, 47, 316-337.
[2]. P. S. Wharton, P. Tumbalam, W. W. Kirk, First Report of Potato Tuber Sprout Rot Caused by Fusarium sambucinum in Michigan, *Plant Disease*, **2006**, 90, 1460-11464.
[3]. H. Saremi, S. M. Okhovvat, S. J. Ashrafi, Fusarium diseases as the main soil borne fungal pathogen on plants and their control management with soil solarization in Iran, *Afri. J. Biote*., **2011**, 10, 18391-18398.
[4]. M. W. Aktar, D. Sengupta, A. Chowdhury, Impact of Pesticides Use in Agriculture: Their Benefits and Hazards, *Interdiscip Toxicol*, **2009**, 2(1), 1-12.
[5]. M. D. J. Haron, H. Jahangirian, M. H. S.Ismail, R. Rafiee-Moghaddam, M. Rezayi, K. Shameli, Y. Gharayebi, Y. Abdollahi, M. Peyda and B. Mahdavi, Antifungal Properties of Phenyl Fatty Hydroxamic Acids and Their Copper Complexes Synthesized Based on Canola and Palm Kernel Oils, *Asian J. Chem*., **2013**, 25, 4183-4188.
[6]. H. Lossen, Ueber die Oxalohydroxamsäure, *Liebigs Ann*, **1869**, 150, 314-322.
[7]. U. Priyadarshini, S. G. Tandon, Preparation and properties of some N-aryl hydroxamic acids, *J Chem Engg Data*, **1967**, 12, 143-144.
[8]. S. K. Rajput, A. Patel and K. N. Bapat, Antibacterial Screening Of Newly Synthesized Cinnamo Hydroxamic Acid, *Chem and Mate Res*, **2017**, 9(2), 14-17.
[9]. M. B.Plewe, S. L.Butler, K. R.Dress,Q. Hu, T. W.Johnson, J. E. Kuehler, A. Kuki, H. Lam, W. Liu, D. Nowlin, Q. Peng, et al, Azaindole hydroxamic acids are potent HIV-1 integrase inhibitors, *J. Med Chem.*, **2009**, 52(22), 7211-7219.

[10]. M. Miethke, and M. Marahiel, Siderophore-Based Iron Acquisition and Pathogen Control, *J. Microbio and Mole Biolo Rev*, **2007**, 71(3), 413-451.
[11]. S.Minucci, P. G. Pelicci, Dimethyl sulfoxide to vorinostat: development of this histone deacetylase inhibitor as an anticancer drug, *Nat Biotechnol*, **2007**, 25(17), 84-90.
[12]. S. K.Rajput, A.Patel, K. N. Bapat, Syntheisis, Characterization and Antifungal Activity of p-CH_3 Benzyl and p-Cl Benzyl Cinnamo Hydroxamic Acid, *Interna . J Green and Herbal Chem*., **2018**, 7(3), 489-499.
[13]. D. M. Vashi, B. V. Devani, H. K. Bhagatwala and K. B. Kurmi, Synthesis and antimicrobial activity of some 4-morpholino-6- trifluoromethyl pyrimidine derivatives based on Schiff base, *J. Applicable Chem*., **2019**, 8(5), 2098-2106.
[14]. P. A. Marks, Discovery and development of SAHA as an anticancer agent. *Oncogene*, **2007**, 26(9), 1351-1356.
[15]. I. B. McInnes, G. S. Chett, Cytokines in the pathogenesis of rheumatoid arthritis, *Nat Rev. Immunol*, **2007**, 7, 429-442.
[16]. C. Indiani, E. Santoni,M. Becucci, A. Boff, K. Fukuyama, G. S.Mulevich, New Insight into the Peroxidase−Hydroxamic Acid Interaction Revealed by the Combination of Spectroscopic and Crystallographic Studies, *J. Biochem*, **2003**, 47, 14066-14074**.**
[17]. M. Seitz, K. N. Raymond, Efficient Route to Highly Water-Soluble Aromatic Cyclic Hydroxamic Acid Ligands, *Europian J. Org Chem*, **2008**, 16, 2697-2700.
[18]. S. K. Rajput, A. Patel, K. N. Bapat, Antibacterial activity of some Cinnamo hydroxamic Acid, *International Journal of Green and Herbal Chemistry*, **2018**, 7(2), 355-360.
[19]. S. K. Rajput, A. Patel, K. N. Bapat, Antibacterial Screening Of Some Newly Synthesized Cinnamo Hydroxamic Acid, *Chem. Material. Res*., **2017**, 9(2), 14-17
[20]. H. M. Naveenakumari, Manjunath Hariharamathada, Mahesh Kumar and K. M. Basavaraja, Synthesis, Characterization, Biological Screening of 5-BromoBenzofuranyl Aryl Ureas and Carbamates, *J. Applicable Chem*., **2019**, 8(5), 2067-2073.