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Synthesis, Characterization and Biocidal Studies of Salicylhydroxamic acid and phathalic Salicylhydroxamic acid

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Abstract: The synthesis and characterization of Salicyl hydroxamic acid (SHA) and phathalic Salicyl Hydroxamic acid (PSHA) were done. Elemental analysis IR spectral data of the compounds are discussed and some chemical and physical properties also studied. All the compounds have been tested in vitro against a number of microorganisms in order to assess their antimicrobial properties.

Keywords: Hydroxamic acid, Biocidal Studies**.**

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1. Introduction

The importance of hydroxamic acids and its derivatives has received considerable attention in view of their pharmacological, toxicological and pathological properties, promising biological implications as well as their role as iron chelators and microbial siderophores. However, Hydroxamic acids are a class of organic acids, that have very important role in biological systems. These compounds possess antibacterial and anti-fungal properties and are inhibitors of enzymes (1,2,3). The hydroxamic acids were synthesized by reaction of an alkyl or aryl ester with hydroxylamine in the presence of alkali using adopting Blatt's procedure (4). Many studies were carried out to synthesize of hydroxamic acids from acids or esters with hydroxylamine (4). Hydroxamic acids are used in the synthesis of a wide range of heterocyclic compounds (5,6). Hydroxamic acids, aliphatic or aromatic, are in general prepared by the reaction of an activated acyl or aryl group with hydroxylamine in the presence of an alkali as a catalyst (5,7).

Salicylhydroxamic acid contains two acidic groups, the hydroxamic acid and the phenolic OH groups (8). Salicylhydroxamic acid (SHA) is a drug that is a potent and irreversible inhibitor of bacterial and plant urease usually used for urinary tract infections (9). It is also trypanocidal agent, when administered orally, it is metabolized to salicyamide which exerts analgesic, antipyretic and anti-inflammatory effects (9). Antibacterial, anti-fungal, anti-tumor and anti-inflammatory activities of hydroxamic acids are connected with their ability to inhibit various enzymes (10,11).

Chemicals, Reagents and standard solution:

All reagents and chemicals used is for Analytical uses. NaOH(12%), Hydroxylamine hydrochloride, Methyl salicylate, Sulfuric acid(conc), Phathalic anhydrides and Glacial acetic acid.

Instruments:

All the absorption spectral measurements are made using IR spectra are recorded using spectrometer model (FTIR-8400S, SHIMADSU). Sensitive balance, Melting point, heating mantel.

Experimental:

Preparation of SHA: Hydroxylamine hydrochloride (14 g, 0.2 mole) was added to NaOH(12%, 200 ml) and cooled at room temperature then filtered..Methyl salicylate (15.2 g, 0.1 moles) was added to the filtrate in small portions with vigorous shaking after each addition to ensure complete dissolution. The mixture was allowed to stand for 2 days until

the solution become straw brown, then acidified by sulfuric acid (2M), washed and recrystallized from water containing little acetic acid measuring flask as recommended (11,16).

Preparation of phathalic Salicyl Hydroxamic acid (PSHA): prepared by 1:2 phathalic anhydrides: SHA, then H2SO4 conc added heated until dissolved. washed and recrystallized from water containing little acetic acid.

Test of microorganism:

Bacterial microorganisms: *Bacillus subtilis* NCTC 8236 (Gram + ve bacteria), *Staphylococcus aureus* ATCC 25923(Gram +ve Bacteria), Escherichia coli ATCC 25922(Gram -ve bacteria**),** *Pseudomonas aeruginosa* ATCC 27853 (Gram -ve bacteria)

Fungal microorganisms: Candida albicans ATCC7596

Preparation of bacterial suspensions:

One ml aliquots of a 24 hours' broth culture of the test organisms were aseptically distributed onto nutrient agar slopes and incubated at 37º C for 24 hours. The bacterial growth was harvested and washed off with 100 ml sterile normal saline, to produce a suspension containing about 108-109 C.F.U/ ml. The suspension was stored in the refrigerator at 4° C till used.

The average number of viable organisms per ml of the stock suspension was determined by means of the surface viable counting technique. Serial dilutions of the stock suspension were made in sterile normal saline solution and 0.02 ml volumes of the appropriate dilution were transferred by micro pipette onto the surface of dried nutrient agar plates. The plates were allowed to stand for two hours at room temperature for the drops to dry and then incubated at 37 °C for 24 hours. After incubation, the number of developed colonies in each drop was counted. The average number of colonies per drop (0.02 ml) was multiplied by 50 and by the dilution factor to give the viable count of the stock suspension, expressed as the number of colony forming units per ml suspension. Each time a fresh stock suspension was prepared. All the above experimental conditions were maintained constant so that suspensions with very close viable counts would be obtained.

Preparation of fungal suspension:

The fungal cultures were maintained on Sabouraud dextrose agar, incubated at 25 °C for 4 days. The fungal growth was harvested and washed with sterile normal saline and finally suspension in 100ml of sterile normal saline, and the suspension were stored in the refrigerator until used**.**

Testing of antibacterial susceptibility

Disc diffusion method: The paper disc diffusion method was used to screen the antibacterial activity of plant extracts and performed by using Mueller Hinton agar (MHA). The experiment was carried out according to the National Committee for Clinical Laboratory Standards Guidelines (NCCLS, 1999). Bacterial suspension was diluted with sterile physiological solution to 108cfu/ ml (turbidity = McFarland standard 0.5). One hundred micro-liters of bacterial suspension were swabbed uniformly on surface of MHA and the inoculum was allowed to dry for 5 minutes. Sterilized filter paper discs (Whatman No.1, 6 mm in diameter) were placed on the surface of the MHA and soaked with 20 µl of a solution of each plant extracts. The inoculated plates were incubated at 37 °C for 24 h in the inverted position. The diameters (mm) of the inhibition zones were measured.

Results and discussion:

Infrared spectra The most characteristic bands associated with the hydroxamic acid functional group are due to the O–H and C=O stretching vibrations and these can be assigned rather unambiguously. Hydroxamic acids are characterized in the solid state by the bands between 3200-3150 cm-1 (O–H), a band near 1640 cm-1 (C=O), a band near 1599 cm-1 (C–N–C), a variable intensity band at 1440–1360 cm-1 (C–N), and a strong band near 900 cm-1 (N–O) (10).

SHA: Yield: 76.57%, M P: 167- 168OC, IR spectrum 3288 (O–H), 3132 (N-H), 1618 (C=O), 1577 (C–N–C), 1489 (C–N), 1296, 970 (N–O), 744 cm-1.

PSHA:Yield: 93.1%, MP: 147- 148OC, IR spectrum 3234(O–H), 3049 (N-H ,(1682 (C=O of CONHOH group), 1613, 1583) (C=O), 1531(C–N–C), 1483 (C–N), 974(N–O). cm-1.1739 (C=O of CONHOH group), 1708 (C=O of the COOH group) (12).

Anti-Microbial Activity:

Table (1) Antimicrobial activity of SHA and PSHA

Component	Anti-Bacterial activity					
	conc	Ec	Pc	Sa	Bs	Ca
SHA	100	16	18	17	-	15
PSHA	100	14	16	17	14	25

The all synthesized SHA and SHA complexes have been tested for the in vitro growth inhibitory activity against the bacteria *Enterobacter cloacae*, *Escherichia coli*, *Pseudomonas aeuruginosa*, *Proteus vulgaris*, *Staphylococcus aureus* (coagulase positive and coagulase negative) and the fungi *Candida albicans* by using the disc-diffusion method. From the results (Table 1), it is concluded that out of five bacterial cultures tested, Phathyl Salicyl Hydroxamic Acid (PSHA) exhibited wide spectrum of activity, as they were highly active against all cultures than salicylhydroxamic acid (SHA), as it was also active against four cultures and in active against one.

Concussion:

Salicyl hydroxamic acid and Phathalic Salicyl hydroxamic acid have been prepared and characterized on the basis of Analytical and spectral data. Furthermore, all the compounds were found to be potential bio-active material against the pathogenic microorganism.

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