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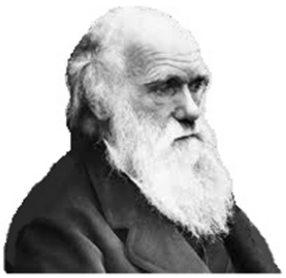

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Investigating the antibacterial and antifungal properties of few organic moieties: a comprehensive analysis

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ABSTRACT

The existing work reveals the novel character of organic compounds like 4-Methoxyphenoxyacetic acid and p-dihydroxybenzene. The compounds were investigated for their antibacterial and antifungal prospective against gram-positive bacteria. At increasing doses of 2-Methoxyphenoxyacetic acid, the zone of inhibition for *Salmonella paratyphi* was (30 mm/ml) at 100 µl and p-dihydroxybenzene is more resistant to bacterial such as *Bacillus subtilis* (38 mm/ml), *Enterococcus faecalis* (40 mm/ml), *Mucor* (42 mm/ml), *Aspergillus niger* (40 mm/ml). The docking investigation was carried out using Auto Dock 4.2.6; interactions between hydrogen atoms and the smallest ligands with macromolecules had the lowest binding energies.

Keywords: 4-Methoxyphenoxyacetic acid, p-dihydroxybenzene, zone of inhibition, biological activity, auto dock, binding energy

1. INTRODUCTION

p-Dihydroxybenzene is a chemical that originates in plant foods as glucose, which is present in foods like pears, drinks, and onions. p-dihydroxybenzene is digested to release benzene and is then absorbed by the intestinal gland (McFadyen et al., 2004). They work well against a few types of bacteria, weeds, pests, and fungi. A few pathogenic bacteria, including *Staphylococcus aureus, Streptococcus pneumonia,* and *Enterococcus faecium*, also exhibit multidrug resistance. Numerous heterocyclic compounds have antitumor (Starcevic et al., 2006)

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analgesic, anti-inflammatory and antiallergic (Katsuura, 1985) properties. The derivatives of phenols oxidation reaction kinetics and its pharmacological activities are reported in the literature (Anbarasu & Ilavenil, 2017) (Anbarasu & Ilavenil, 2018) (Ilavenil et al., 2021) (Ilavenil et al., 2021) (Anbarasu & Ilavenil, 2018) (Ilavenil et al., 2022) (Srinivasan & Ilavenil, 2017) by using various heterocyclic oxidants.

The derivatives of phenol are found to exhibit various insecticidal properties and exhibit toxic nature which pollutes the environment. Various eco-friendly techniques Srinivasan & Ilavenil, 2017) (Ilavenil et al., 2023) (Senthilkumar Vagheesan & Jayaprakash Govindarajulu, 2021) (Karthikeyan et al., 2021) (Senthilkumar Vagheesan & Jayaprakash Govindarajulu, 2019) (Senthilkumar et al., 2015) (Anbarasu & Ilavenil, 2019) are adopted to reduce the toxicity and convert into toxic free compound. The oxidation kinetics of the derivatives are studied using pyrazinium chlorochromate (Senthilkumar & Ilavenil, 2023) and the anti-bacterial assessment is discussed in this paper.

The prepared compounds 4-Methoxyphenoxyacetic acid and p-dihydroxybenzene are tested for their antibacterial and antifungal properties against a small number of bacteria and fungi, including *Streptococcus, Micrococcus, E. coli, Candida albicans, Trichophyton, Fusarium, Enterococcus faecalis, Salmonella typhi, A. niger*, *Mucor,* and *Trichoderma*.

The docking approach is used to anticipate interactions including hydrogen bonds, pi-alkyl bonds, aromaticity, and many ligands.

The massive use of antibiotics led to the destruction of a group of organisms and an amplified number of resistant organisms (Senthilkumaran, & Pavithra, 2014) Numerous microbes have gained resistance towards antimicrobial drugs including *Streptococcus pneumoniae, Haemophilus* sp., *Trichophyton, Pseudomonas aeruginosa, Staphylococcus aureus,* and *Candida albicans*. Owing to the diverse functionalities, derivatives of $C_8H_8O_3$ bestow biological measures like anti-inflammatory (Kunsch et al., 2005), antibacterial (Yar et al., 2007), platelet aggregation inhibition (Menawell et al., 1993), 2-(4-chloro-3,5-dimethylphenoxy) acetic acid derivatives are potential towards bacteria, fungi and possess anthelmintic property. The antipyretic, herbicidal, antinociceptive, and analgesic activity resulted in phenoxy ester and amide derivatives (Ilavenil & Dhamodharan, 2016) (Bhavana et al., 2014) (Turan-Zitouni et al., 2015).

2. EXPERIMENTAL

2. 1. Materials and Methods

Para-dihydroxybenzene, an organic chemical, was bought from Sigma Aldrich in AnalaR grade (Figure 1) and 4-Methoxyphenoxyacetic acid (Koelsch, 1931) ($C_9H_{10}O_4$) was prepared by the (Figure 2) standard method. The Eumic Analytical Laboratory and Research Institute in Tiruchirappalli provided the bacteria and fungus. The bacterial strains were supported using the Hi media nutrient agar slant at 4 °C.

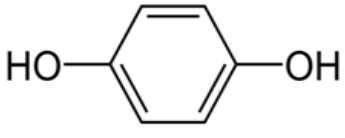

Figure 1. Structure of p-dihydroxybenzene

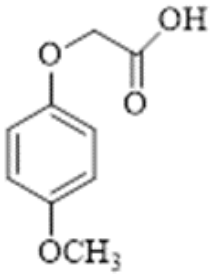

Figure 2. 4-Methoxyphenoxyacetic acid

2. 2. Selection of Ligand and Macromolecules

The protein data bank resource's website was used to find the structures of the large protein molecules. For the purpose of researching the biological interactions between protein molecules and ligands, the proteins with the IDs 7BRA and 5AF1 were gathered. The ligands were molecules of the chemical p-dihydroxybenzene. Using open bable software, the molecule in the SDF mode was transformed into charged PDBQT form and stored for docking after the ligand structures were retrieved from the NCBI-Pub Chem database.

2. 3. Anti-bacterial Assay

The anti-bacterial test used the conventional agar well diffusion method. A diluted inoculum of the test organism was spread over 0.5 ml (105 CFU/ml) of Nutrient agar plates. Agar media was perforated into a well (8 mm in diameter), which was then filled with various amounts of plant extracts and incubated at 37 °C. For evaluating the antibacterial activity, the zone of inhibition against the test organism was employed. The findings of measuring and contrasting the diameter of the zone of inhibition with the typical antibiotics are then interpreted. Peptone (5 g/l), beef extract (3 g/l), agar (15 g/l), sodium chloride (5 g/l), yeast extract (1.5 g/l), and pH 7 neutral are the substances needed to prepare the culture medium.

2. 4. Auto docking Investigation

Using AUTO DOCK 4.2.6 models, the extensive structure and activity of the ligands, such as p-dihydroxybenzene auto docking, were carried out for the chosen bacteria (*E. coli and Candida albicans*) macromolecules in the binding sites. For docking, a single folder included all the required extension files, such as autogrid.exe, auto dock.exe, AD4-parameter file, and AD 4.1 bound data files. Using a Kollman United atom and Gasteiger charges, the polar hydrogen and the charges were added. To develop an auxiliary program, use the AUTOGRID. The information pertaining to the macromolecule, ligand, and grid size was saved in text files. It assessed how well the ligand and receptor form a strong hydrogen connection. The interactions are immediate, stiff, and constant, as shown by the least binding energy.

3. RESULTS AND DISCUSSION

3. 1. Zone of Inhibition of p-dihydroxybenzene

The Table1 displays the antibacterial and antifungal effects of organic compounds dissolved in Dimethyl Sulphoxide $(CH_3)_2SO$ extract on diverse species. All bacteria and fungi

are effective in resisting the antibiotic Gentamicin, according to the study. The diameter of the decrease zone that develops around each well, which gauges the level of inhibition, serves as a proxy for the activity. According to the information in Table 1, there are species-specific differences in the level of inhibition. With respect to each species, it was found that the inhibitory zone width generated by the DMSO extract was lower, greater, or comparable to that produced by conventional antibiotics.

The concentrations of the substances 4-Methoxyphenoxyacetic acid and p-dihydroxybenzene were compared to the standard in Figure 1-4 at 25 µl, 50 µl, 70 µl, and 100 µl, respectively. At four different dilutions, the actions of the gram-positive bacteria *Bacillus subtillis, Streptococcus, Salmonella paratyphi,* gram-negative *E. coli, fungi Candida albicans,* and *A. niger* are compared.

Table 1. Inhibition zone of the organic compounds

	$(CH_3)_2SO$ Extract 100 µl added and Zone of inhibition (mm/ml)					
4-Methoxyphenoxyacetic acid	Microorganisms	25 µl	50 µl	75 µl	100 µl	Control Gentamicin antibiotic disc
	Streptococcus	15	18	22	26	20
	E. coli	17	21	24	27	20
	Bacillus subtilis	16	20	25	28	22
	Salmonella para typhi	18	22	27	30	22
	Candida albicans	14	16	18	20	20
	A.niger	12	14	16	18	20
p-Dihydroxybenzene	*Bacillus subtilis*	25	30	34	38	20
	Enterococcus faecalis	28	34	36	40	18
	E. coli	25	30	34	38	18
	Salmonella typhi	20	22	24	26	20
	Candida albicans	30	34	37	40	20
	A. niger	30	34	36	40	20
	Mucor	30	35	38	42	20
	Trichoderma	20	22	25	28	20

The compound p-dihydroxybenzene was tested against several species, and it was shown to be effective against *Bacillus subtilis* (38 mm/ml), *E. coli* (38 mm/ml), *Salmonella typhi* (26 mm/ml), *Candida albicans* (40 mm/ml), *A. niger* (40 mm/ml), *Mucor* (42 mm/ml), and *Trichoderma* (28 mm/ml).

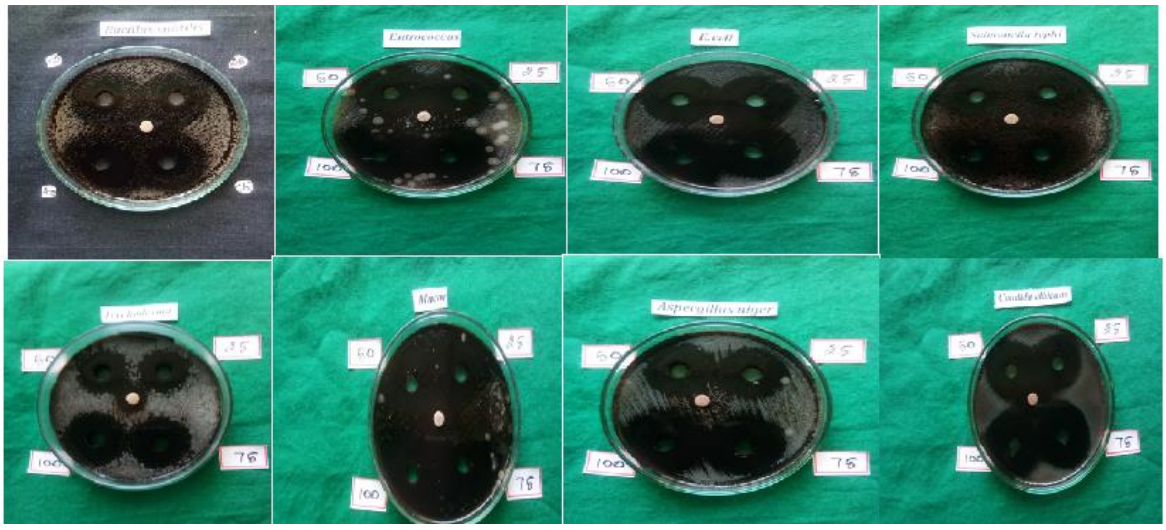

Figure 3. Inhibition of p-dihydroxybenzene

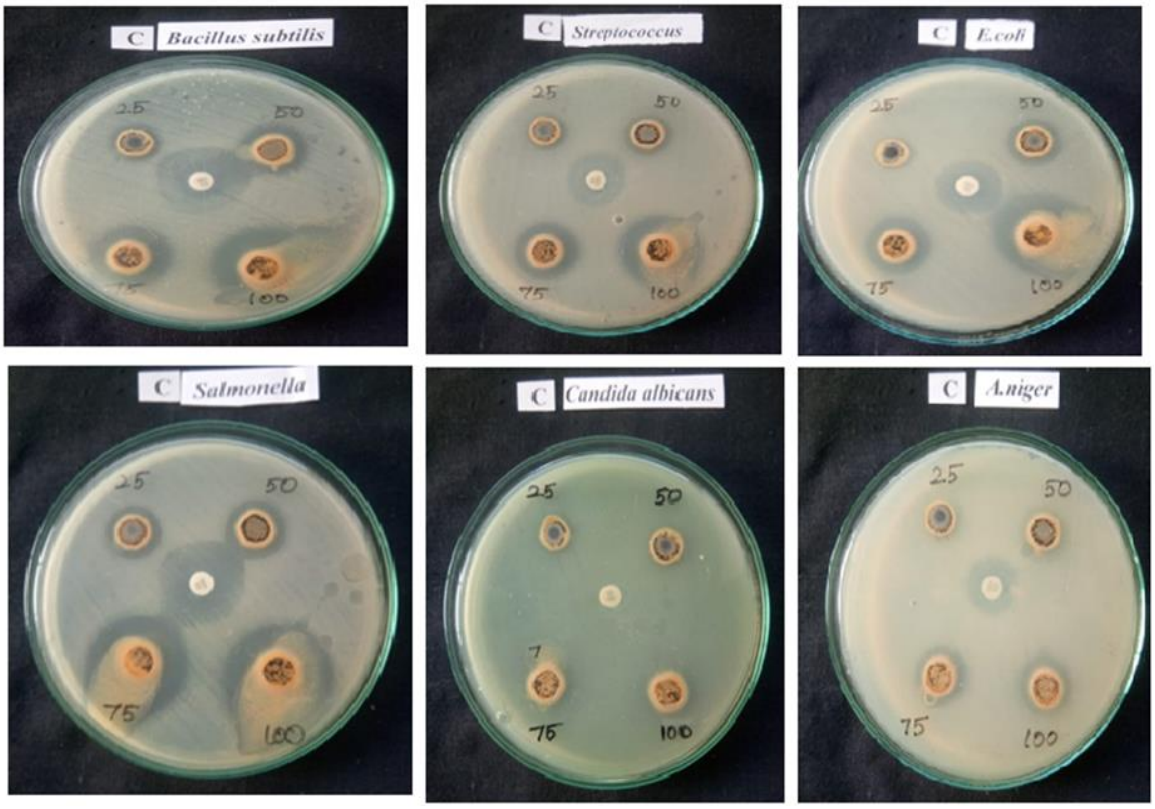

Figure 4. Inhibition of para-methoxyphenoxy acetic acid

The hydroxyl group (-OCH_3) in the molecule itself has a character that makes it resistant to bacteria and fungi. For the species, *Bacillus subtillis* (28 mm/ml), *Streptococcus* (26 mm/ml), *E. coli* (27 mm/ml), *Salmonella para typhi* (30 mm/ml), *Candida albicans* (20 mm/ml), and *A. niger* (18 mm/ml), the lethal zone is greater than the reference medication used for the test. Lipoprotein, lipid bilayer, and lipopolysaccharide make up the exterior membrane of gram-negative bacteria's cell walls. The lipid and cell membranes are similar (bilayer). Additionally, gram-negative bacteria have periplasmic space, which is home to many enzymes including protease, nuclease, and detoxifying enzymes. These enzymes are all crucial for bacterial antidrug resistance. The chemical substances proved more effective in stopping the growth of the microbes and hence more resistant.

3. 2. Molecular Docking

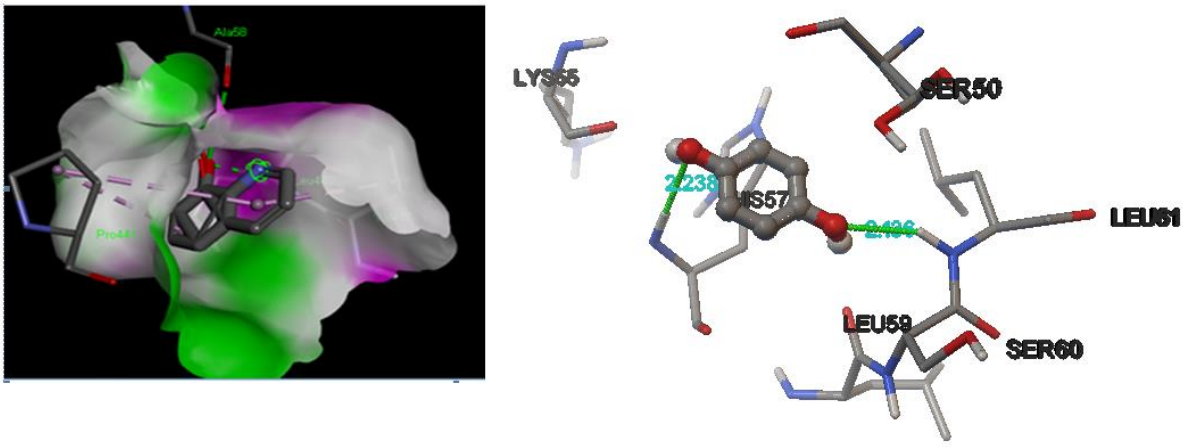

Figure 5. Two Hydrogen atom bonds for the 5AF1 macro molecule

Through the residues HIS57, LEU61, and SER60, the ligand p-dihydroxybenzene forms bonds with the macromolecule 5AF1 that contains two hydrogen atoms (Figure 7). The binding energy, intermolecular energy, and torsional energy are all -5.16, -5.78, and 0.7 Kcal/mol, respectively. The protein 7BRA displays a hydrogen bond with the residues GLN347 and SER345; the binding energy is -6.32 Kcal/mol, the intermolecular and internal energies are -6.91 Kcal/mol and 0.42 Kcal/mol, respectively, and the torsional energy is 0.42. The target macromolecules 1CUS and 5VG3 were docked and the interaction between the target and the 2-Methoxyphenoxyacetic acid was improved by the inclusion of the methoxyl group. The Fusarium solani cutinase protein 1CUS showed interaction with the ready ligand 2-Methoxyphenoxyacetic acid. A minimum of -5.11 kcal/mol was required for the receptor and ligand to bind.

4. CONCLUSIONS

The present study offers a foundation for employing p-dihydroxybenzene and 4-Methoxyphenoxyacetic acid to treat pathogenic bacteria. They have a higher potential for Gram-positive, Gram-negative, and a few fungi because of their hydroxyl groups and

heterocyclic nitrogen atoms. In the compound 4-Methoxyphenoxyacetic acid at temperature (297.14K), the inhibition constant (Ki) was discovered to be 73.86 uM for TYR77 and ARG78, and there was evidence of a hydrogen bond between the amino acid chains. The hydrogen bond, pi-pi interactions, and binding energy were found to be in excellent agreement when the tiny ligand was docked with the microorganism's protein.

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