

A Review Article on Derivative's and Toxicity of Phenols

Mr.Sarthak R . Gawali, Ms. Dipali M.pagire
Pratibhatai Pawar college of pharmacy, Wadala Mahadev, Shirampur

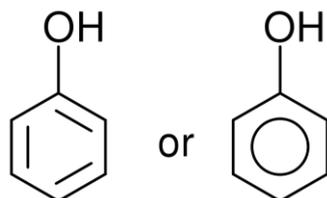
Abstract

In the environment, phenols and their derivatives are frequently found. These chemicals find application as constituents of dyes, polymers, pharmaceuticals, and other organic compounds. The manufacturing and deterioration of various pesticides as well as the creation of industrial and municipal sewages are associated with the existence of phenols in ecosystems. Additionally, certain phenols are produced by natural processes. These chemicals can be nitrated, methylated, alkylated, or replaced with chlorine atoms. Catechols and phenols are both dangerous ecotoxins. These substances' unidentified toxicity is caused by their hydrophobicity, which also produces reactive oxygen species and organic radicals. Catechols and phenols exhibit peroxidative potential, cause mutagenesis and carcinogenesis in humans and other living things, and are hematotoxic and hepatotoxic.

Keywords: Phenols, catechol, natural origin of phenols, anthropogenic sources of phenols, toxicity of phenols

Introduction :

The presence of anthropogenic phenols in the environment can be attributed to the operations of the chemical, petroleum, tinctoral, and pharmaceutical sectors. When industrial or municipal sewage drains into surface water, the chemicals seep into ecosystems [1]. Phenoxyherbicides such as 2,4-dichlorophenoxyacetic acid (2,4-d) [2] or 4-chloro-2-methylphenoxyacetic acid (mcpa) as well as phenolic biocides like pentachlorophenol (pcp) [3], dinoseb, or diarylether pesticides [4] are specifically responsible for the presence of phenols in the environment. Certain phenols can be produced naturally, for example, when organic matter decomposes and produces phenol and p-cresol, or when fungus and plants produce chlorinated phenols [5]. There are two primary mechanisms associated with phenol toxicity: Unidentified toxicity associated with the compound's hydrophobicity and the production of free radicals [6].the localization of the substituent is another factor contributing to the compound's potent poisonous effect. For example, adding a chlorine atom to the ortho position of a phenol molecule reduces its toxicity, while adding a chlorine atom to the meta position increases the compound's poisonous effect. After entering the cell, phenols actively change, mostly with the help of oxidases found in cytochrome p450. Sometimes the creation of electrophilic metabolites—which have the potential to bind to and harm dna or enzymes—during transformation processes increases the toxicity of the individual chemicals. Phenols and their derivatives have deleterious effects on histopathological alterations, mutagenicity, carcinogenicity, and acute toxicity. The review's constituents are the most prevalent phenols found in both the environment and humans conditions that have a harmful impact on all living things, including humans.[7]

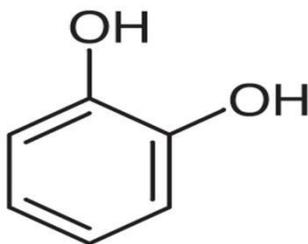
Natural source of phenol :**Phenol****Structure :**

Phenol (hydroxybenzene) is a colourless, crystalline substance of characteristic odour, soluble in water and organic solvents. Phenol was one of the first compounds inscribed into the list of priority pollutants by the us environmental protection agency (us epa). Phenol is synthesized on an industrial scale by extraction from coal tar as it is formed by transformation of high quantities of cumene present in plants that were used for tar production. Phenol is also obtained in a reaction between chlorobenzene and sodium hydroxide, toluene oxidation and synthesis from benzene and propylene. It is commonly used in different branches of industry including chemical – production of alkylphenols, cresols, xlenols, phenolic resins, aniline and other compounds [8]in the united states, there are approximately 580,000 individuals who are occupationally exposed to phenol influence [9]. Phenol not only enters the environment through vehicle exhaust but is also utilized as a disinfectant and reagent in chemical analysis. phenol is additionally produced through chemical reactions

Taking place in the atmosphere within condensed water vapor, which eventually forms clouds. Hydroxybenzene is also generated through natural processes such as biosynthesis by plants or the decomposition of organic matter [10].

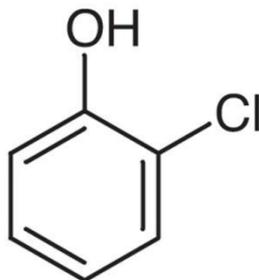
This compound is also produced through the reaction of amino acids found in plants' hemicelluloses when exposed to uv irradiation (sunlight) [11], as well as the conversion of tyrosine in the digestive tract of mammals, including humans [12]. The levels of phenol in surface water vary. In natural bodies of water, its concentrations range from 0.01 to 2.0 $\mu\text{g/l}$ [13]. Due to its relatively rapid degradation, the concentration of phenol in waters exposed to significant anthropogenic pollution can be comparable. In the surface water of the netherlands, the concentration of phenol ranged from 2.6 to 5.6 $\mu\text{g/l}$. River water contaminated with sewage from petroleum processing plants contained phenol concentrations exceeding 40 mg/l [9].

Phenol was also found in domestic water supply in the usa at a level of 1 $\mu\text{g/l}$. Background levels of phenol in air are expected to be low, at about 1 ng/m^3 [14]. In high concentrations phenol is determined near factories that impregnate wood and its value reaches 9.7 $\mu\text{g/m}^3$ [15]. Phenol is also present in food. Moderate quantities of this compound (5 $\mu\text{g/kg}$) were determined in honey [16], also in coffee, in which is formed from ferulic acid. In this process ferulic acid it the natural compound present in corn-undergoes conversion to vinyl-guaiacol, guaiacol and finally to phenol [17]. Phenol concentration in processed food may reach alarming concentrations. For example, in grilled sausage an pork the content of phenol was 7 and 28.6 $\mu\text{g/kg}$, respectively [18]. Other authors have found phenol in the outer layer of smoked meat in concentrations of 37-70 mg/kg . The exposure data are inadequate to determine the degree of exposure of the general population to phenol. However, persons exposed to phenol through inhalation of air from strongly industrialized areas or with frequent consumption of smoked food with high phenol content may accept toxic doses of phenol about 4 mg and 2 mg per day, respectively. It also has been estimated that 0.3–0.4 mg of phenol per cigarette is released during its burning. Exposure to phenol may also be accidental. Delfino and dube described the case of contamination of ground water with phenol that was then used for drinking purposes. The authors evaluated the daily exposure to be 10-240 mg of phenol per person. The result was statistically significant increases of diarrhoea, mouth sores, dark urine and burning pain in mouth [19]

Catechol and chlorocatechols :**Structure :**

Chlorocatechols are more commonly found in polluted water due to anthropogenic activities. The analysis of water samples taken from the polluted river in central Poland revealed significant amounts of chlorocatechols, including the highly toxic tetrachlorocatechol, at a concentration of 2 µg/l. The concentrations of chlorocatechols in municipal raw sewage that contaminated the river exceeded 5 µg/l [1]. In water of natural origin, chlorocatechols may be absent or present in low concentrations. A yearly investigation in the drainage of the Dzierżyna river in central Poland showed no presence of chlorocatechols in the studied ecosystems [14]. In the drinking water of major cities in Poland, low concentrations of chlorocatechols, specifically 4-chlorocatechol and 3,4,5-trichlorocatechol, were detected [20]. Catechol is an aromatic alcohol with hydroxyl residues on the first and second carbon positions. It is soluble in both water and organic solvents. On an industrial scale, catechol is produced through the catalytic hydrolysis of 2-chlorophenol at high temperatures. It is also formed through the hydroxylation process of phenol and benzoic acid. Catechol finds applications in photography, rubber and synthetic material production, as well as drug synthesis [21].

It is also used in cosmetic, dye and insecticide production [22]. Catechols are also employed in production of 4-tert-butylcatechol, the compound that inhibits the polymerization process of synthetic materials [23]. Chlorinated derivatives of catechol are used in dichloroaniline and chlorinated biphenyls production [24]. Catechol and chlorocatechols are the main products of phenol and chlorophenols environmental transformation. The processes are mainly performed by microbes that hydroxylate phenols at the second carbon position [25]. For example, the transformation of pentachlorophenol leads to tetrachlorocatechol formation that may be further degraded to chlorinated catechols of lower number of chlorine atoms. It was also noted that microbiological transformations of chlorobenzenes, chlorinated phenoxyacetates and chlorobiphenyls result in chlorocatechols formation [26].

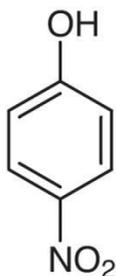
Chlorophenol :**Structure :**

Chlorophenols, which are the largest and most widespread group of phenols, are formed in the environment through the chlorination of mono and polyaromatic compounds found in soil and water. The synthesis of chlorophenols involves the participation of chloroperoxidases present in plants and microorganisms, along with

hydrogen peroxide and inorganic chlorine [27]. For example, fungi from the *hypholoma* genera are capable of synthesizing chlorinated phenols [5, 28]. The concentrations of chlorophenols in oceanic waters range from 5-10 ng/l, while river waters exhibit higher concentrations ranging from 2-2000 µg/l. Chlorophenols can also be found in drinking water due to the substitution of organic matter and low molecular weight compounds with chlorine atoms derived from inorganic chlorine oxidants. Studies conducted on drinking water in warsaw and łódź (poland) revealed the presence of 2,4,5-trichlorophenol and tetrachlorophenol in concentrations of 0.2 – 0.3 µg/l [29]. Industrial sewages contain the highest concentrations of phenols, with levels reaching 0.1-10 mg/l for pentachlorophenol. Atmospheric concentrations of chlorinated phenols are typically low, ranging from 0.25 to 7.8 ng/m³. However, in urbanized areas of holland, the concentration can even reach 1 µg/m³ [30]. Chlorophenol concentrations in soils that are not exposed to anthropogenic pollution are generally low. However, soil samples from the former site of a pesticide plant in richmond (british columbia) contained 2 mg of tcep and 0.18 mg of tcp per kg of soil, as reported by garrett. Soils located within sawmills are typically heavily contaminated with chlorophenols. Kitunen and his colleagues determined the concentrations of chlorophenols in these soils. the concentration of chlorophenols in the vicinity of preservation facilities at four distinct sawmills ranged from 500 to 3500 µg/kg [31].

Nitrophenol :

Structure :



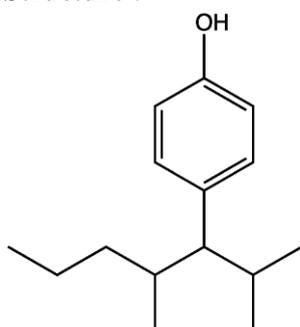
The occurrence of nitrophenols in the environment can be attributed to both natural processes and human activities. Nitrophenols, specifically 2-nitrophenol and 4-nitrophenol, are produced when phenol reacts with nitrite ions in water. These reactions occur under the influence of uv irradiation (sunlight) and within a wide range of ph values [32, 33]. Nitrophenols are also formed in the atmosphere through environmental reactions. The reaction between phenol, nitrite ions, and hydroxyl radicals results in the formation of 2-nitrophenol and other nitrated compounds [34]. Enzymes present in plant tissues, such as peroxidases and lipoxygenases, facilitate the nitration of phenols substituted primarily in the ortho and para positions. This nitration process occurs in the presence of nitric ions and hydrogen peroxide, and it contributes to the presence of nitrophenols in the soil environment [35]. In the atmosphere, nitrophenols are typically found in low concentrations of a few ng/dm³. However, significant air pollution caused by industrial emissions can lead to increased concentrations of nitrophenols, reaching up to 320 ng/dm³ [36]. In water, nitrophenols are present in concentrations that rarely exceed a few µg/l. An analysis of the ebro river in spain revealed the presence of 2-nitrophenol, 4-nitrophenol, and 2,4-dinitrophenol within the range of 0.1 – 5.0 µg/l for each individual compound. In japan, 2-nitrophenol and 4-nitrophenol were detected in 177 samples of river water, with concentrations ranging from 0.04 to 10 µg/l. Rainwater and snow contain levels of 2-nitrophenol between 0.03 to 5.7 µg/l. Nitrophenols are produced by humans during the manufacturing and degradation of pesticides like 2-buthyl-4,6-dinitrophenol (dinoseb) and 4,6-dinitro-2-methylphenol (dnoc). These compounds are also utilized as components and precursors in the production of polymers and drugs [37]. in addition to being used as photographic developers and preservatives, nitrated phenols have various other applications. They are utilized in the production of dyes, solvents, plastics, and explosives [38]. These compounds are formed as a result of industrial

activities in the fields of electricity, electronics, and metallurgy. Mononitrophenols, specifically 3-methyl-4-nitrophenol and 4-nitro-3-phenylphenol, are released into the environment through vehicular emissions [39].

In the united states, exposure to nitrophenols has been linked to the excessive and illegal use of methylparathion, a pesticide. This has resulted in the accumulation of the main metabolite of methylparathion, 4-nitrophenol, in the tissues of individuals. An analysis of samples collected from 16,000 people revealed an increased concentration of 4-nitrophenol, which was found to be correlated with the quantity and frequency of methylparathion usage in households [40].the general population is primarily exposed to nitrophenol isomers through ambient air and drinking water. The estimated daily intake of nitrophenols through inhalation is approximately 0.06 $\mu\text{g}/\text{kg}$ per body weight. The intake through drinking water for 2- and 4-nitrophenols is calculated to be around 0.02 $\mu\text{g}/\text{kg}$ body weight [41].

Alkylphenols :

Structure :

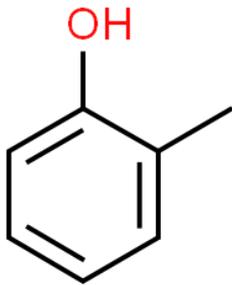


Low molecular weight alkylphenols are commonly found in rock-oil and shale oils. These compounds, particularly those substituted in the para position, are sourced from geochemical processes such as methylation, butylation, and alkylation that occur in geological structures. Additionally, certain technological processes also contribute to the production of these compounds. For instance, nonylphenols are derived from nonylphenol ethoxylates, which are surfactants manufactured for industrial and agricultural purposes. Nonylphenols serve as emulsifiers, wetting agents, and dispersing agents. They find applications in various sectors including textile processing, pulp and paper processing, paints, resins, oil production, and steel manufacturing. Alkylphenols can also be formed as a result of pesticide degradation, as well as agricultural and industrial sewage production. An analysis of drinking water purified by plants located near textile and wood processing factories in quebec, canada, revealed the presence of alkylphenols with mean concentrations ranging from 0.02 to 2.8 $\mu\text{g}/\text{l}$, with the highest concentration recorded at 43.3 $\mu\text{g}/\text{l}$. Similarly, an analysis of rainwater collected in germany and belgium demonstrated the common occurrence of 4-nonylphenol, with concentrations ranging from 0.253 to 0.534 $\mu\text{g}/\text{l}$.the concentrations of alkylphenols in surface water vary, ranging from 0.7 to 21,000 $\mu\text{g}/\text{l}$. However, the most common compounds are found in low concentrations. Analysis of representative sites in the usa indicates that nonylphenol levels in rivers are less than 0.1 to 0.6 $\mu\text{g}/\text{l}$, and in sediments, they range from 0.003 to 3.0 $\mu\text{g}/\text{g}$. In canadian rivers, nonylphenol levels were found to be insignificant, ranging from 0.01 to 0.9 $\mu\text{g}/\text{l}$. Water samples obtained from the elba river in germany showed concentrations between 0.028 to 1.22 $\mu\text{g}/\text{l}$. The concentration of nonylphenol in soil can be high, as observed in a field where municipal sewage sludge was applied, with a concentration of 2.7 mg/kg of soil for 4-nonylphenol. Alkylphenols and alkylphenol ethoxylates have the ability to accumulate in the tissues of living organisms. Analysis of fish tissue collected from the kalamazoo river in michigan, usa, revealed the presence of alkylphenol with the highest concentration of 3.4 $\mu\text{g}/\text{l}$ of body weight. Similar investigations conducted in rivers of germany and the baltic sea showed significant concentrations of nonylphenol up to 112 $\mu\text{g}/\text{kg}$ of body weight in molluscs such as dreissena polymorpha and mytilus edulius, along with lower concentrations of octylphenol at

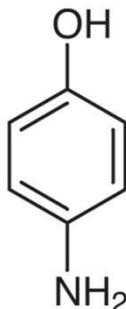
5.5 $\mu\text{g}/\text{kg}$. The presence of p-butylphenol and p-octylphenol was also detected in rubber products that come into contact with food. The range of high concentrations of octylphenol in these products was found to be between 2.6 to 513 $\mu\text{g}/\text{kg}$ [42].

Methylphenol :

Structure :



Methylphenols are commonly found in the environment, often in significant concentrations. In the hayashida river in tatsuno town, japan, which is polluted by industrial effluents, a high level of 4-methylphenol at 204 $\mu\text{g}/\text{l}$ was observed. The highest concentrations of methylphenols are typically found in water sources near coal tar (creosote) production plants, with groundwater exceeding 2 mg/l of 4-methylphenol. There have been reports on the atmospheric concentrations of methylated phenols as well. Air samples collected from eleven areas in california, each with varying levels of industrial emissions, showed concentrations of methylphenols ranging from 0.07 to 4.6 $\mu\text{g}/\text{m}^3$. The median air concentration of cresols, another type of methylphenol, was 1.58 $\mu\text{g}/\text{m}^3$ across 32 source sites in the usa. Rainwater concentrations of o-cresol were determined to be between 0.24 and 2.8 $\mu\text{g}/\text{l}$. These findings suggest that methylphenols may exist in higher amounts in the air compared to other phenolic compounds. Additionally, the degradation of pesticides can lead to the formation of xenobiotics, such as 2-methylphenol, in the environment. methylphenols are present in high concentrations (up to several grams per kilogram) in coal tar, which is utilized for asphalt production and wood impregnation. The widespread use of creosote leads to significant release of methylphenols, particularly 4-methylphenol, into the natural environment. Cresols, which are representatives of methylphenols, exist in three isomeric forms - ortho, meta, and para-cresol. The chlorinated and nitrated form of o-cresol is employed as a compound with herbicide and pesticide properties. Additionally, it finds application in the production of epoxy-resins, dyes, and drugs. Both cresols, dimethylphenol, and 2,4,6-trimethylphenol are generated during the combustion of coal and gasoline. The presence of p-cresol is also associated with sewage production by the petrochemical industry. The occurrence of m-cresol in the environment is primarily linked to its use in cosmetic, fragrance, disinfectant, explosive, and pesticide production [43].

Aminophenols :**Structure :**

Para-aminophenol finds application in various industries such as oil, lubricants, and photography as a developer. When acetylated, it serves as the primary component of paracetamol, a drug known for its anti-inflammatory and analgesic properties [44]. 3-aminophenol is utilized as a marker in the analysis of antibacterial drugs, specifically sulphonamides [45]. On the other hand, 2-aminophenol acts as a precursor for the synthesis of indoles. All isomers of aminophenols and 2,4-diaminophenol are employed in hair dyes for coloring purposes [46]. The presence of p-aminophenol in urine serves as an indicator of the influence of paracetamol and aniline on the human body. Individuals with the highest occupational exposure to aniline are those working in rubber production and processing [47].

Phenol pollution :

Environmental pollution is a global issue that both developing and developed nations have been grappling with for many years [48]. Phenol, a widely used chemical, is produced at a staggering rate of approximately 3 billion pounds annually in the United States and 6 billion pounds worldwide. In the United States, phenol ranks among the top 50 chemicals produced each year, primarily due to its extensive use in the housing and construction industries [49]. The main source of phenol pollution in the environment is human activities, particularly in soil, where its movement is limited compared to aqueous environments due to its strong adsorption onto solid surfaces [49, 36]. Sawmill areas, in particular, tend to have high levels of phenolic compound contamination in the soil, as these compounds are commonly used in wood preservatives [50]. Phenol has been utilized in various industries since the 1860s, initially in the production of basic plastic resin and later in the manufacturing of dyes, chemical intermediates, and even aspirin during the early 19th century. Phenol is primarily utilized in the manufacturing of phenolic resins, which are synthetic polymers widely used in the construction, automotive, and appliance industries. It is also commonly used in the production of bisphenol A, a key component in plastics manufacturing, as well as caprolactam for synthetic fibers and nylon. In the medical field, phenol finds application in the production of general antiseptics, slimicides, lotions, ointments, mouthwashes, and salves. Additionally, it has minor applications in the production of paint, tanning dyes, lacquers, perfumes, and ink.[51]

Toxicity of phenol and phenolic compound :

Phenol is regarded as the primary pollutant of concern due to its harmful and toxic effects, and its ability to accumulate in living organisms. In response to this concern, international regulations have imposed limits on the levels of phenol in drinking water and wastewater. Various profitable and non-profitable agencies, such as the EPA and WHO, have been established by each country to address this issue. Exposure to phenol, whether through direct contact or accidental means, can disrupt the metabolic system in microorganisms, humans, and animals. Additionally, a small amount of phenol is produced during the breakdown of proteins in the intestines by bacterial interactions and is excreted independently. Phenol can enter living organisms through three different routes: Dermal contact, ingestion, and inhalation [52]. Microorganisms, which are abundant in the environment, are often exposed

to phenolic pollution. This has led to numerous studies aimed at identifying species that can adapt, utilize, and develop mechanisms to convert phenolic pollution into non-harmful substances. Microorganisms play a crucial role in aquatic ecosystems as producers, contributing to the maintenance of food chains and nutrient cycles on earth. Over the past few decades, researchers have recognized the need for phenol-tolerant organisms to ensure the availability of non-polluted water sources. As a result, various types of microorganisms, such as yeast, fungus, and bacteria, have been isolated for their ability to degrade phenol in the environment. The metabolic processes of microorganisms and other organisms can be negatively affected by phenol, potentially leading to death if they are unable to adapt. The toxicity of phenol to humans and animals further emphasizes the importance of removing phenol and phenolic compounds from the environment. Table 2 provides an overview of different types of bacteria that have been found to degrade phenol. It is evident from table 2 that phenol pollution has been a significant concern over the past decade, with *pseudomonas sp* being the primary organism capable of utilizing phenol as a sole carbon source [53] numerous approaches have been suggested for the degradation of phenol or phenol derivative compounds, either through biological or chemical means. However, the biological method has gained popularity among researchers due to its cost-effectiveness and environmentally friendly characteristics. Recent studies conducted by researchers indicate that the utilization of a bacterial culture mixture exhibits a greater potential for achieving higher degradation rates in the removal of phenol from heavily polluted areas [54].

1.Acute toxicity :-

Phenol induces skin irritation and leads to necrosis, resulting in harm to the kidneys, liver, muscles, and eyes. The skin damage occurs due to the coagulation process triggered by the interaction between phenol and the amino acids present in the keratin of the epidermis, as well as the collagen in the deeper layers of the skin [55].administering a 1 g dose of phenol can be fatal for an adult male, although some individuals may have a high tolerance for this substance. There have been reports indicating that a person can survive even after being given 30 g of phenol (equivalent to 60 ml of a 50% solution). It is worth noting that due to its rapid absorption through the skin (between 60% and 90%), even coming into contact with a phenol solution using the hand or forearm can result in death [56].phenol-induced acute poisoning is distinguished by the sensation of dryness in the throat and mouth, the presence of dark-colored urine, and intense irritation of the mucous membranes. Extensive investigations have revealed that prolonged administration of phenol to animals results in pathological alterations in various organs including the skin, esophagus, lungs, liver, kidneys, and urogenital tract. These observed changes primarily arise from the process of lipid peroxidation, which is accountable for the damage and eventual degradation of cellular membranes. Prolonged exposure of workers to phenol vapors leads to symptoms such as loss of appetite, weight loss, weakness, headaches, muscle pain, and jaundice [57]phenol primarily accumulates in the brain, kidneys, liver, and muscles. Within two days of phenol administration, it is primarily excreted in its original form and also conjugated with sulphates and glucuronides. Catechol is also recognized as a potent toxin. Doses ranging from 50 to 500 mg/kg of body weight typically result in fatality. In the case of mice, the ld_{50} after oral administration of catechol is 260 mg/kg of body weight. The highest occupational exposure is observed with methylphenols. It has been estimated that approximately 600 to 1,200 thousand workers worldwide are exposed to 4-methylphenol. This primarily pertains to individuals involved in the production of antioxidants, disinfectants, dyes, plastics, explosives, epoxy-resins, coal tar, and steel. Acute poisoning with methylphenols leads to symptoms such as burning pain in the mouth and throat, abdominal pain, headache, weak and irregular pulse, hypotension, decrease in body temperature, stentorous breathing, dark-colored urine, shock, paralysis of the nervous system, coma, and death. An incident involving the intentional administration of 140 ml of a 50% solution of 4-methylphenol by a man resulted in an elevation of plasma aminotransferase activity and subsequent degradation of hepatocytes. Despite intensive detoxification efforts, the individual succumbed to the poisoning after 14 days [57].

2. Mutagenicity :

The mutagenic activity of phenol was discovered during investigations of hamster fibroblasts. Additionally, this compound hindered the synthesis and replication of dna in hela cells [108]. Furthermore, phenol impeded the repair of dna in diploid human fibroblasts. Hydroquinone (1,4-dihydroxyphenol) induced chromosome damage in human lymphocytes, resulting in an increased deletion ratio in chromosome 7. This could potentially lead to the development of leukemia [109]. In a separate experiment, phenol, catechol, and hydroquinone caused morphological changes in cells of hamster embryos. Catechol and hydroquinone also inhibited the activity of ribonucleotide reductase, an enzyme involved in dna synthesis, thereby halting the activation and proliferation of t lymphocytes. These compounds also hindered the proliferation cycle of lymphocytes in the g1 phase . Catechol, in the presence of nadph and cu²⁺, was capable of modifying guanine and thymine residues, leading to gene mutations and chromosome aberrations. Catechol and hydroquinone damaged chromatides and induced incorrect dna synthesis. Similar changes were observed with pyrogallol, which caused the most significant chromosome aberrations among hydroxybenzenes. Pyrogallol and hydroquinone exhibited their toxicity by generating reactive oxygen species, including a hydroxy radical that caused deprotonation of the substrates and subsequently degraded deoxyribose [58].

Nitrophenols and nitrated aminophenols were found to have mutagenic effects. In a test conducted using salmonella typhimurium, mutagenic activity was observed for 2,3-dinitrophenol, 2,5-dinitrophenol, 3,4-dinitrophenol, 2,4,6-trinitrophenol, and 2-nitro-5-aminophenol. Another experiment involving salmonella typhimurium and escherichia coli also showed mutagenic activity for bisphenol f. This particular compound increased the frequency of sister chromatid exchange and decreased the number of micronuclei in human lymphocytes [114]. Additionally, 4-aminophenol was found to interact with genetic material in the presence of fe³⁺ and cause damage to dna in both mouse and human lymphocytes. This process was attributed to the action of free radicals formed through the reaction of iron ions and hydrogen peroxide [59].

Reference :

1. Jaromir m., ożadowicz r., duda w. Analysis of chlorophenols, chlorocatechols, chlorinated methoxyphenols and monoterpenes in communal sewage of łódź and in the ner river in 1999-2000. 16, 205, 2005.
2. Rózański l. The transformations of pesticides in living organisms and the environment, agra-enviro lab. Poznań. 1998. [in polish]
3. Laine m., jorgensen k. Straw compost and bioremediated soil as inocula for the bioremediation of chlorophenol – contaminated soil. Appl. Environ. Microbiol. 54, 1507, 1996.
4. Schmidt s. Biodegradation of diaryl ether pesticides, from: Biodegradation of dioxins and furans, chapter 8, 229- 281. 1998.
5. Swarts m., verhagen f., field j., wijnberg j. Trichlorinated phenols from hypholoma elongatum. Phytochem. 49, 203, 1998.
6. Hansch c., mccarns s., smith c., dodittle d. Comparative qsar evidence for a free-radical mechanism of phenol-induced toxicity. Chem. Biol. Interact. 127, 61, 2000
7. Boyd e., killham k., meharg a. Toxicity of mono-, di- and tri-chlorophenols to lux marked terrestrial bacteria burkholderia species rasc c2 and pseudomonas fluorescens. Microbiol. Let. 43, 157, 2001.
8. Bobrański b. Organic chemistry, pwn. Warszawa. 1973.
9. Bruce r., santodonato j., neal m. Summary review of the health effects associated with phenol. Toxicol. Indust. Health. 3, 535, 1987.
10. Us. Epa. Ambient water quality criteria doc: Phenol, us epa-440/5-80-066 (pb 81-117772), pp. 1100-1156, 1980.

11. Davidson r. The photodegradation of some naturally occurring polymers. *J. Photochem. Photobiol. B: Biol.* 33, 3, 1996.
12. Tsuruta y., watanabe s., inoue h. Fluorometric determination of phenol and p-cresol in urine by precolumn high-performance liquid chromatography using 4-(n-phthalimidyl)benzenesulfonyl chloride, *analyt. Biochem.* 243, 86, 1996.
13. Michałowicz j., duda w. Chlorophenols and their derivatives in waters of the drainage of the dzierzazna river. State and anthropogenic changes of the quality of waters in poland, tom iii, ed. Burchard j. Hydrological committee of polish geographical society, university of łódź, łódź, 2004. [in polish]
14. Rivm [criteria document: Phenol]. Bilthoven, the netherlands, national institute of public health and environmental protection (document no. 738513002). 1986.
15. Allen s., allen c. Phenol concentrations in air and water samples collected near a wood preserving facility. *Bull. Environ. Contam. Toxicol.* 59, 702, 1997.
16. Gyroik m., herpai z., szecsenyi i., varga u., szigeti j. Rapid and sensitive determination of phenol in honey by high performance liquid chromatography with fluorescence detection. *J. Agric. Food chem.* 51, 5222, 2003.
17. Dorfner r., ferge t., kettrup a., zimmermann r., yeretzian c. Real time monitoring of 4-vinylguaiacol, guaiacol and phenol during coffee roasting by resonant laser ionization time-of-flight mass spectrometry. *J. Agric. Food chem.* 51, 5768, 2003.
18. Us epa. Treatability manual, 1:1.8.6-1 to i.8.6-5, us epa 600/8-80-042, 1980.
19. Delfino f., dube d. Persistent contamination of ground water by phenol. *J. Environ. Sci. Health.* 43, 345, 1976.
20. Niedan v., pavasars j. Oberg g. Chloroperoxidasemediated chlorination of aromatic groups in fulvic acid. *Chemosphere.* 41, 779, 2000.
21. Schweigert n., alexander j., zehnder j., eggen r. Chemical properties of catechols and their molecular modes of toxic action in cells from microorganisms to mammals. *Environ. Microbiol.* 3, 81, 2001.
22. Arc., Iarc monographs on the evaluation of carcinogenic risks to humans: Catechol. 71, 433, 1999.
23. Chae h., yoo y. Mathematical modelling and simulation of catechol production from benzoate using resting cells of *pseudomonas putida*. *Proc. Biochem.* 32, 423, 1997.
24. Lin p., sangaiah r., ranasinghe a., ball l., swenberg j., gold a. Synthesis of chlorinated and nono-chlorinated biphenyl-2.3-and 3.4-catechols and their [h-2(3)]-isotopomers. *Organ. Biomol. Chem.* 2, 2624, 2004
25. Moiseva o., solyamikowa j., kaschabek s. Groning j., thiel m., golovleva l., schomann m. A new modified ortho cleavage pathway of 3-chlorocatechol degradation by *rhodococcus opacus* 1cp: *Gen. Biochem. Evid. J. Biotechnol.* 184, 5282, 2002.
26. Sauret-ignazi g., gagnon j., beguin c., barelle m., markowicz y., pelmont j., toussaint t. Characterization of a chromosomally encoded catechol 1.2-dioksygenase [e.c. 1.13.11.1.] from *alicagenes eutrophus* ch34. *Arch. Microbiol.* 166, 42, 19
27. Niedan v., pavasars j. Oberg g. Chloroperoxidasemediated chlorination of aromatic groups in fulvic acid. *Chemosphere.* 41, 779, 2000.
28. Verhagen f., swarts m., wijnberg j., field j. Biotransformation of the major fungal metabolite 3.5-dichloro-p-anisyl alcohol under anaerobic conditions and its role in formation of bis (3.5-dichloro-4-hydroxyphenyl) methane. *Appl. Environ. Microbiol.* 64, 3225, 1998.
29. Michałowicz j. The occurrence of chlorophenols, chlorocatechols and chlorinated methoxyphenols in drinking water of the largest cities of poland, polish j. *Environ. Sci.* 14, 143, 2005
30. Czaplicka m. Sources and transformation of chlorophenols in the natural environment. *Sci. Total environ.* 322, 21, 2004.
31. Delfino f., dube d. Persistent contamination of ground water by phenol. *J. Environ. Sci. Health.* 43, 345, 1976.

32. Patnaik p., khoury j. Reaction of phenol with nitrite ion: Pathways of formation of nitrophenols in environmental waters. *Water. Res.* 38, 206, 2004.
33. Vione d., maurino v., pelizzeti z., minero c. Phenol photonitration and photonitrosation upon nitrite photolysis in basic solution. *Internat. J. Environ. Analyt. Chem.* 84, 493, 2004.
34. Harrison m., bara s., borghesi d., vione d., arsene c., olariu r. Nitrated phenols in the atmosphere: A review. *Atmospher. Environ.* 39, 231, 2005.
35. Budde ch., beyer a., mumir i., dorick., khmelinsky y. Enzymatic nitration of phenols. *J. Mol. Catal. B: Enzym.* 15, 123, 2001.
36. Flox c., garrido j., rodriguez r., centellas f., cabot p-l., arias c., brillas e. Degradation of 4.6-dinitro-cresol from water by anodic oxidation with a boro-doped diamond electrode. *Electrochim. Acta.* 50, 3685, 2005.
37. Pocurull e., marce r., borull b. Determination of phenolic compounds in natural waters by liquid chromatography with ultraviolet and electrochemical detection after on-line trace enrichment. *J. Chromat. A.* 738, 1, 1996.
38. Furuta c., suzuki ak., tanaeda s., kamata k., hayashi h., mori y., li cm., watanabe g., taya k. Estrogenic activities of nitrophenols in diesel exhaust particles. *Biol. Reproduct.* 70, 1527, 2004.
39. Bravo r., driske w., patterson d., hill r., needham l., pirkle j., sampson e. Measurement of p-nitrophenol in the urine of residents whose homes were contaminated with methyl parathion. *Environ. Health perspect.* 110, 1085, 2002.
40. Pruppacher, h., klett, j. *Microphysics of clouds and precipitation.* Dordrecht/boston/london. D. Reidel publishing co. 1978.
41. Masselter s., zemann a. & bobleter o. Separation of cresols using coelectroosmotic capillary electrophoresis. *Electrophoresis.* 14, 36, 1993
42. J. Michałowicz*, w. Duda ,phenols – sources and toxicity,issue:December 18, 2006, page no:
43. Re-poppi n., santiago-silva m. Identification of polycyclic aromatic hydrocarbons and methoxylated phenols in wood smoke emitted during production of charcoal. *Chromat.*
44. Nagaraja p., yathirajan h., raju c., vasantha r., nagendra p., kumar m. 3-aminophenol as a novel coupling agent for the spectrophotometric determination of sulfonamide derivatives. *Il farmaco,* 58, 1295, 2003.
45. La vecchia c., tavani a. Epidemiologic evidence on hair dyes and the risk of cancer in humans. *Eur. J. Cancer prev.* 4, 31, 1995.
46. Chen j., jiang j., zhang f., yu h., zhang j. Cytotoxic environmentally relevant chlorophenols on 1929 cells and their mechanisms. *Cell biol toxicol.* 20, 183, 2004.
47. Nikonorow m. *Pesticides in the light of environmental toxicology., agricultural and forest national publishing.* Warszawa, 1979. [in polish]
48. [35] suza w, harris r, and lorence a. Hairy roots: From high value metabolite production to phytoremediation. *Elec. J. Integrat. Biosci.* 2008; 3: 57– 65.
49. [32] barlow j, johnson jap, belcher sm, and fenton se. Early life exposure to phenols and breast cancer risk in later years: Fact sheet on phenols. *Breast cancer and the environment research centre community outreach and translation cores.* 2007; 1–20
50. [27] boudet am. Evolution and current status of research in phenolic compoun
51. Tuan nn, hsieh hc, lin yw, and huang sl. Analysis of bacterial degradation pathways for long-chain alkylphenols involving phenol hydroxylase, alkylphenol monooxygenase and catechol dioxygenase genes. *Bioresour. Technol.* 2011; 102: 4232–4240.
52. Agency for toxic substances and disease registry (atsdr), 2008. Toxicological profile for phenol. Division of toxicology and environmental medicine/applied toxicology branch us department of health and human services. Georgia, united states. 2008; 1–20

53. Yang cf, and lee cm. Enrichment, isolation, and characterisation of phenol-degrading pseudomonas resinovorans strain p-1 and brevibacillus sp. Strain p-6. Intern. Biodeterior. Biodegrad. 2007; 59: 206–210
54. Al-khalid t, and el-naas mh. Aerobic biodegradation of phenols: A comprehensive review. Environ. Sci. Technol. 2012; 42: 1631–1690.
55. . Clayton g.d., clayton f.e. Patty's industrial hygiene and toxicology. 4th ed.; john wiley & sons inc: New york, vol. 2a, pp.132, 1994.
56. Ford m.d., delany k.a., ling l.j., erickson. Clinical toxicology. W. B. Saunders company: Philadelphia, pp.753, 2001.
57. Kamijo y., soma., kokuto m., ohbu m., fuke c., ohwada t. Hepatocellular injury with hyperaminotransferasemia after cresol ingestion, arch. Pathol. Lab. Med. 127, 364, 2003.
58. Silva m.d., gaspar j., silva i.d., leao d., rueff j. Induction of chromosomal aberrations by phenolic compounds: Possible role of reactive oxygen species. Mut. Res. – gen. Toxicol. Environ. Mutagen. 540, 29, 2003
59. Yoshida r., oikawa s., ogawa y., miyakoshi y., oida m., asanuma k., shimizu h. Mutagenicity of paminophenol in e. Coli wp2uvra/pkm101 and its revelance to oxidative dna damage. Mutat. Res. 415, 139, 1998.