A Review on Phenol Toxicity: Environmental and Health Implications

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Abstract: Phenol toxicity: environmental and health implications was reviewed. Phenol is an aromatic compound with a hydroxyl substituent. It is found extensively in the effluents of refinery, coke plant, paint, and textile industries. It is used as: an antiseptic and a raw material for some industries. This review shows that it is toxic, mutagenic and carcinogenic. It may cause endocrine dysfunction, liver dysfunction, intestinal disorder, gene mutation, cancer, reduced growth rate, skin rash, mouth sores and so on. It is also toxic to the aquatic habitat. Phenol persists in water for days and in the sediments for weeks before it is biodegraded.
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1. Introduction

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nations. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities.

Phenol has been found in at least 595 of the 1,678 current or former NPL sites. However, the total number of NPL sites evaluated for this substance is not known, the possibility exists that the number of sites at which phenol is found may increase in the future as more sites are evaluated (ASTDR, 2008).

Phenol has been listed as one of the toxic chemicals in several articles and by several regulatory bodies. Hence, the need to study phenol with respect to its health toxicity and environmental implications. Phenol is an aromatic hydrocarbon with a hydroxyl substituent. It exist as liquid or low melting solid in its simplest form; slightly soluble in water (9g per 100g of water); colorless in its pure form and have a relatively high boiling point because of hydrogen bonding (Morrison, Boyd and Bhattacharjee,2011).

1.1 Natural Sources of Phenol

Phenols are common in nature; examples include tyrosine, one of the standard amino acids found in most proteins; epinephrine (adrenaline), a stimulant hormone produced by the adrenal medulla; serotonin, a neurotransmitter in the brain; andurushiol, an irritant secreted by poison ivy to prevent animals from eating its leaves. Many of the more complex phenols used as flavourings and aromas are obtained from essential oils of plants.

For example, vanillin, the principal flavouring in vanilla, is isolated from vanilla beans, and methyl salicylate, which has a characteristic minty taste and odour, is isolated from wintergreen. It is also one of the chemical compounds found in castoreum.

1.2 Anthropogenic sources of phenols

Industrially, phenol can be got from:

- Coal tar (creosote component)
- Crude oil refineries
- Industries of resin paint
- Textile wood
- Petrochemical (from oxidation of toluene to benzoic acid, which is converted to phenol in the presence of copper salt) and
- Pulp wood, etc.

1.3 Uses of Phenol

Uses of phenols include:

- In household products and as intermediates for industrial synthesis. For example, phenol itself is used (in low concentrations) as a disinfectant in household cleaners and in mouthwash.
- Phenol may have been the first surgical antiseptic. In 1865 the British surgeon Joseph Lister used phenol as an antiseptic to sterilize his operating field. With phenol used in this manner, the mortality rate from surgical amputations fell from 45 to 15 percent in Lister's ward.
- Less-toxic phenols, such as n-hexylresorcinol, have supplanted phenol itself in cough drops and other antiseptic applications.
- Butylated hydroxytoluene (BHT) has a much lower toxicity and is a common antioxidant in foods.
- In industry, phenol is used as a starting material to make plastics, explosives such as picric acid, and drugs such as aspirin. The common phenol hydroquinone is the component of photographic developer that reduces exposed silver bromide crystals to black metallic silver. Other substituted phenols are used in the dye industry to make intensely coloured

azo dyes. Mixtures of phenols (especially the cresols) are used as components in wood preservatives such as creosote.

1.4 Effect of Phenol on Health

Historical information in a case report (Merliss, 1972) indicates that 'carbol marasmus' was a common occupational disorder of physicians and their assistants during the mid19th Century when carbolic acid sprays (1:40 phenol in water) were commonly used for antisepsis in operating rooms.

Among the characteristics of this disorder was anorexia leading to progressive weight loss and excess production of saliva. Similar gastrointestinal effects were observed in one of the author's patients who were involved in the daily distillation of phenol over a 13.5-year period. Exposed both via inhalation of the vapors and dermally from frequent spills, the patient's symptoms included both loss of appetite and weight loss. A cohort mortality study of workers in five phenol-formaldehyde resin manufacturing plants found that exposed workers showed a slight reduction in death rate due to cancers of the digestive system as compared to both non-exposed workers and the general population (Dosemeci et al., 1991).

Several studies carried out on animals, clinical reports and workplace exposure to phenol have shown the effects of phenol exposure on the health quality of the respiratory system. Wilcosky and Tyroler (1983) found a significant increase in mortality from **ischemic heart disease** in phenol exposed workers.

Of the 25 solvents used in the plant, phenol exposure showed the strongest association with mortality from heart disease, greater even than that observed for exposure to carbon disulfide, the only known occupational cause of **atherosclerosis**.

In a cohort-mortality study of workers from five phenol-formaldehyde resin plants, Dosemeci *et al*. (1991) found a slight reduction in mortality due to heart disease. These investigators hypothesized a protective effect of phenol exposures; however, these results clearly conflict with those of Wilcosky and Tyroler (1983).

In a report on the clinical treatment of phenol poisoning, Langford et al. (1998) provide a summary of a case report in which a woman accidentally consumed an ounce of 89% phenol that had mistakenly been given to her in preparation for an in-office procedure.

Her immediate reaction upon consuming the phenol was to clutch her throat and collapse, and within 30 minutes, she was comatose and had gone into respiratory arrest. Treatment was initiated with an endotracheal intubation. Ventilation with a bag and mask led to the detection of a lamp oil odor. Within an hour, she developed ventricular tachycardia, which responded to cardioversion; however, she subsequently developed (in the first 24 hours) supraventricular and ventricular dysrhythmias, metabolicacidosis, and experienced a grand mal seizure.

Serum markers of liver effects: bilirubin, glucose, cholesterol, and AST activity were not affected in 39 persons exposed to phenol in the drinking water at an estimated dose of 0.14–3.4 mg/kg/day for several weeks (Baker et al., 1978).

Because these examinations were completed 7 months after the spill, this study does not provide conclusive evidence that there was no reversible liver damage. Autopsy of a fatal case of ingestion of phenol revealed substantial toxic changes in the liver including extension of sinusoid lumens and an increase in centrilobular increase of cytoplasmiceosinophility (Tanaka *et al.*, 1998).

Serum markers of liver effects (lactic dehydrogenase, alkaline phosphatase, ALT, bilirubin) and histopathological changes in the liver were observed in rats given single gavage doses of 224 mg/kg or14 daily gavage doses of 40 mg phenol/kg in water (Berman et al., 1995).

1.5 Effect of Phenol on Aquatic Lives

Static renewal bioassay was experimentally conducted to evaluate the toxic effects of phenol on the African catfish *C. gariepinus*. Ninety-six-hour acute toxicity tests revealed that the median lethal concentration of phenol (LC50) is 35 mg/L by immersion.

Four experimental fish groups were assigned for 3 weeks exposure test; three were exposed 20%, 50% and 70% LC_{50}, the fourth control fish group received a vehicle of dechlorinated water. Abnormal signs observed were cessation of feeding, nervous manifestations; skin expressed perfuses mucous, black patches with skin erosion and ulcerations in the later stages.

All observations were correlated to the time and dose of exposure. Post mortem examination revealed adhesion of the internal organs. For tissue alterations; Skin, gills, brain, liver and kidney showed variable degrees of degenerative changes and necrosis.

Muscle residues shown in mean ± SE were 4.3 ± 0.05 and 6.65 ± 0.05 ppm in groups that received 20 and 50% LD_{50}, respectively. Infection with *Aeromonas hydrophila* resulted in high percent of mortalities with a non-significant difference between the challenged fish groups. The study cleared that phenol is toxic to *C. gariepinus* under experimental conditions (Ibrahem, 2012).

Also, Gad and Saad (2008) investigated the effect of three sublethalconcentrations (0.7, 1.4 and 2.8 mg/L representing 1/40,1/20 and 1/10 LC50. respectively) of phenol on some physiological

parameters of *Oreochromis niloticus* after long term exposure (16 weeks).

Results showed that serum tri-iodothyronine (T3) and thyroxin (T4) hormones decreased significantly, serumtotal cholesterol and lipids content significantly increased, genotoxic potential was observed through theincrease in number of micronuclei production. Also decrease in growth performance and accumulation ofphenol in fish tissues (liver, muscles and gills) were detected.

It was concluded that phenol causes a lot of harmful effects to fish and of public health concern. Recommendation: Industrial drainage water must be treated before entering the water resources. In a similar study, Sannadugappa et al (2011) carried out a similar study using *Oreochromis Messambians.*

In their study, they determined the acute toxicity of phenol to be 35.0mg/l the fish. The fish was exposed to two sublethal concentrations of phenol (2.3 and 3.5mg/l) for 30days. The effects of exposure were studied on the bioaccumulation and elimination of phenol from the kidney and muscle at intervals of 10, 20 and 30days.

A statistically significant increase in phenol concentration was noted in tissues from all treated fish groups. Bioaccumulation and biochemical changes were dose and duration dependent. Recovery in fish after post exposure were observed after transferring the fish to normal tap water for 30days.

Elimination of phenol was noted, however, the concentration of phenol was significantly higher than the control after 30days of the experiment. Total protein, total carbohydrate and total lipid in the tissues of the liver, gill and muscle of the fish greatly reduced. It was also observed that longer exposure gave rise to greater percentage reduction of organic matter in the treated fish.

The effect of phenol (hydroxybenzene) and phenols on marine fish was also studied by Roche and Boge (2000). In the study, Sea bass (*Dicentrarchus labrax*) were injected intraperitoneally once (single dose) or three times (fractionated dose) with phenol or OH-phenols (hydroquinone, resorcinol, and pyrocatechol). On the basis of the lethal doses, OH-phenols were more toxic than phenol, and pyrocatechol was the most powerful compound.

Hematological, metabolic and antioxidant blood parameters were measured 3 days after the end of the treatment. Metabolic variations as specific effects on erythrocytes were revealed and differences between single and fractionated doses were observed.

OH-phenols-treated fish showed disorders in the metabolic toxicity indicators as hypoglycemia, low blood urea nitrogen level (BUN) and decrease of alkaline phosphatase activity (ALP). In addition, quantitative structure-activity relationships were developed using the n-octanol: water partition coefficient (log K_{ow}). Positive correlations were found with ALP, plasma glucose and hemoglobin.

1.6 Effect of phenol on plant germination, growth and Development

Reigosa *et al*. (1999) investigated the effect of phenolic compounds on the germination of six weeds species. They tested the allelopathic effect of six phenolic compounds (ferulic acid, gallic acid, p-coumaric acid, p-hydroxylbenzoic acid, vanillic acid and p-vanillin) at the final concentration of 10, 1, 0.1 and 0-01mM on germination of *Chenopodium album* L., *Plantago lanceolata, Amaranthus retroflexus* L, *Solanum nigrum* L, *Cirsium sp.* and *Rumex crispus* Leaves.

The highest concentration of the compounds inhibited the germination of all these weeds but lower concentrations had no effect or were stimulatory. Wallstedt et al. (2001) also studied the effect of Batatasin-III on the uptake of ammonium ion. In the study, Excised birch roots were exposed tobatatasin-III during brief periods in *15* NH*4* + solutions, and then analyzed for labeled N.

Batatasin-III inhibited N-NH*4*+ uptake by 28, 89 and 95% compared with the control, when roots were treated with 0.1, 1.0 and 2.8 m*M* of batatasin-III, respectively. The effect of 1.0-m*M* batatasin-III was greater at pH 4.2 than at pH 6.8. In addition, the inhibition of N-NH*4*+ uptake by batatasin-III was not reversed after rinsing the roots in water and transferring them to a batatasin-III free solution.

Furthermore, birch seedlings immersed in a 1.0-m*M* batatasin-III solution for 2 h, and then replanted in pots with soil, had decreased growth, such that 10 weeks after treatment, the dry mass of both shoots and roots was reduced by 74 and 73%, respectively, compared with control seedlings. This suggests that a brief exposure to batatasin-III may have a long-term inhibitory effect on whole plant growth.

1.7 Bioaccumulation of Phenol

Buttle, Willig and Zauke (1987) carried a research on the bioaccumulation of phenols in Zebrafish determined by a Dynamic Flow through Test. In his study, the bioaccumulation test No. 305E (OECD), a dynamic flow-through test, was applied to 13 phenols: phenol, 4-cyanophenol, 3-nitrophenol, 2-methylphenol, 3-chlorophenol, 4-bromophenol, 2,4-dinitro-6-methylphenol, 3,5-dibromo-4- cyanophenol, 4-tert-butylphenol, 2,4,6-tribromophenol, 2,4-dinitro-6-sec- butylphenol, 2,4-dinitro-6-tert-butylphenol, and pentachlorophenol.

Biocon- centration factors (BCFs) for zebrafish (*Brachydanio rerio*) were calculated from the kinetics of the uptake and clearance phases. BCFs ranged from 1.4 for 2,4-dinitro-6-methylphenol to 980 for pentachlorophenol. They were correlated to the

physico-chemical properties of the phenols (i.e., lipophilicity constants), derived from reversed phase chromatography (HPLC), dissociation constants (pK_As), as well as an indicator parameter, representing the structure element "2, 4-dinitro-substitution" (IN).

For the 10 phenols not bearing a 2, 4-dinitro-group only the lipophilicity was correlated to the BCFs (log BCF = 0.116 + 0.575 log P). For all 13 phenols, no significant correlation of the BCFs on lipophilicity and pK_As was found. However, the regression equation obtained for the 10 phenols was also valid for the 2,4- dinitro-substituted phenols subtracting a constant factor decreasing the bioaccumulation of these compounds (log BCF = 0.189 + 0.548log P−1.59 IN).

In another study by Samadurgappa and Aladakatti (2011) on effect of oxygen consumption and bioaccummulation in different tissues of freshwater *Cyprinus carpio*, he observed that the longer the time phenol was exposed to the tissues, the greater the percentage reduction of organic matter (total protein, total carbohydrate and total lipids) of the fish.

1.8 Persistence of Phenol in the Ecosystem

Liber, Kruth and Stay (2009) carried out an integrated evaluation of the persistence and effects of 4-nonylphenol in an experimental littoral ecosystem. His studycreated a 20-d application period which was followed by a three to fourteen month observation period, depending on the endpoint measured.

Mean ± SD NP concentrations in the water column measured 2 h after each application averaged 5 ± 4, 23 ± 11, 76 ± 21, and 243 ± 41 µg/L at nominal treatments of 3, 30, 100, and 300 µg/L, respectively. Persistence in the water column was relatively short, with a dissipation half-life estimated at ≤1.2 d. Persistence of NP in sediment and on macrophytes was substantially longer, with estimated half-lives of 28 to 104 d and 8to 13 d, respectively.

1.9 Conclusion/Recommendations

This study has shown that phenol is toxic, mutagenic and carcinogenic. It may cause endocrine dysfunction, liver dysfunction, gene mutation, cancer, reduced growth rate, skin rash, mouth sores and even persists in water for days and more in the sediments. Therefore, for public health reasons, the industrial drainage should be treated before entering the water bodies.

Workers, researchers, laboratory scientists and students that handle phenol should put on complete personal protective equipment (PPE) during work. Research opportunities exist in the area of effect of phenol in the absorption of nutrients.

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References

1. ASTDR (2008). Toxicological profile for phenol. United State Department for Health and Human Services. Atlanta.
2. Berman E, Schlicht M, Moser V.C. (1995). A multidisciplinary approach to toxicological screening: I. Systemic toxicity. *J Toxicol Environ Health*, 45:127-143.
3. Buttle, W., Willig, A. and Zauke G. P. (1987). Bioaccumulation of Phenols in Zebrafish determined by a dynamic flow through test. *QSAR in Environmental Toxicology*, 11, 43-53. doi: 10.10071978-94-009-3937-0_4.
4. Deichmann WB, Keplinger ML. (1981). Phenols and phenolic compounds. In: Clayton GD, Clayton FE, eds. Patty's industrial hygiene and toxicology, 3rd ed. New York, NY: John Wiley and Sons, Inc., 25672627.
5. Dosemeci M, Blair A, Stewart PA, et al. (1991). Mortality among Industrial workers exposed to phenol. *Epidemiology*, 2:188-193.
6. Gad, S. N. and Saad, S. A. (2008). Effect of environmental pollution by phenol on some physiological parameters of Oreochromis niloticus. *Global Veterinaria*, 2(6): 312-319.
7. Ibrahem, D. M. (2012). Experimental exposure of African Catfish Clarias Garepinus (Burchell, 1822) to phenol: Clinical evaluation, tissue alterations and residue assessment. Journal of Advance *Research*, 3(2), 177-183. Doi: 10.1016/j.jare. 2011.07.002.
8. Langford, C. P., Bartlett R, Haddad LM. (1998). Phenol and related agents. In: Haddad LM, Shannon MW, Winchester JF, eds. Clinical management of poisoning and drug overdose. Philadelphia, PA: Saunders, 956-960.
9. Liber, K., Kruth, M. L. and Stay, F. S. (2009). An integrated evaluation of the persistence and effects of 4-nonylphenol in an experimental littoral ecosystem. *Environmental toxicology and chemistry*, 18(3), 357-362.
10. Lo Dico C, Caplan YH, Levine B, et al. (1989). Phenol: Tissue distribution in a fatality. *J Forensic Sci*, 34:1013-1015.
11. Merliss, R. R (1972). Phenol marasmus. *Occup Med*, 14:55-56.

12. Morrison, R.T, Boyd, R.N. and Bhattacharjee, S.K (2011). Pearson Organic Chemistry. 7th Edition. Prentice Hall, Delhi.
13. Reigosa, M. J., Souto, X. C., and González, L. (1999). Effect of phenolic compounds on the germination of six weeds species. *Plant Growth Reg*., 28:83–89.
14. Roche, H. and Boge, G. (1999). In vivo effects of phenolic compounds on blood parameters of a marine fish (Dicentrarchuslabax). Comparative Biochemistry and Physiology Partc: Pharmacology, *Toxicology and Endocrinology*, 125(3): 345-353.
15. Samadurgarpa, D. and Aladakatti, R.H. (2011). Effects of Phenol on Oxygen consumption and bioaccumulation in different tissues of fresh water Cyprinuscarpio. *Journal of Basic and clinical Physiology and Pharmacology*, 21(1), 1-14. Doi: 10.1515/ JB.
16. Tanaka S, Choe N, Kita T, et al. (1998). Distribution of phenol in a fatal poisoning case determined by gas chromatography/mass spectrometry. *J Forensic Sci,* 43(5):1086-1088.
17. Wilcosky TC, Tyroler HA. (1983). Mortality from heart disease among workers exposed to solvents. *J Occup Med*, 25:879-885.

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