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Effects of Phenolic Compounds on Environment

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ABSTRACT

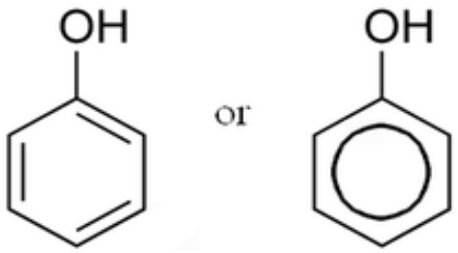
In recent years the natural supply of phenolic substances has been greatly increased due to th release of industrial byproducts into the environment. Phenol is one of the most widely used i the organic compounds in existence and is a basic structural unit for a variety of syntheti organic compounds including agricultural chemicals and pesticides. Among all the toxi compounds, phenol and its substituent phenolic compounds contribute a remarkable adverse impact to the environment. These are major xenobiotics, which are often found in the effluents discharged from the industries such as paper and pulp, textiles, gas and coke, fertilizers, Th US Environmental Protection Agency (EPA, 1979) had classified the phenolic compounds as high priority pollutants due to their extensive impact on the deterioration of the wate environment. In this review paper, we described about plant phenolic compounds, phenoli effects of human exposures, animal exposures, effect on children, reducing the risk of exposur and medical tests to determine concentration of phenol.

Introduction

Phenols and their derivatives commonly exist in the environment. These compounds are used as the components of dyes, polymers, drugs and other organic substances. Synthetic organic chemicals like phenols and their derivatives lead to serious environmental contamination because of their toxicity. Various industries such as pulp and paper mills herbicides and fungicides production etc contribute phenol in their aqueous effluents [1-3]. The growing concern for aquatic contamination in the environment has lead to request for better wastewater treatment methods. Among the available treatments for phenolic in wastewater, micro based degradation of phenols appears to be more promising [4, 5, and 6].Phenol is a colorless or white solid when pure Phenol. Phenol has a distinct odor that is sickeningly sweet and tarry. Most people begin to smell phenol in air at about 40 parts of phenol per billion parts of air (ppb), and begin to smell phenol in water at about 1–8 parts of phenol per million parts of water (1 ppm is 1,000 times more than 1 ppb). These levels are lower than the levels at which adverse health effects have been observed in animals that breathed air containing phenol or drank water containing phenol. Phenol evaporates more slowly than water, and a moderate amount can form a solution with water. Phenol can catch on fire. Phenol is both a manufactured chemical and produced naturally. It is found in nature in some foods and in human and animal wastes and decomposing organic material. Phenol is formed in petroleum products such as coal tar and creosote. Phenol can be released during the combustion of wood, fuel emissions and tobacco. Phenol is naturally formed as a breakdown product of benzene. Phenol and phenolic compounds are ubiquitous pollutants which come to the natural water resources from the effluents of a variety of chemical industrial such as cool refineries, phenol manufacturing, pharmaceuticals and industries of resin paint, dying, textile wood, petrochemical, pulp mill etc. [7-9]

Structure of phenol

The simplest of the class is phenol, which is also called carbolic acid C_6H_5OH. Phenolic compounds are classified as simple phenols or polyphenols based on the number of phenol units in the molecule [Fig 1-3].



General phenol structure 1-methylethylebenzene (cumene)

Phenol - the simplest of the phenols

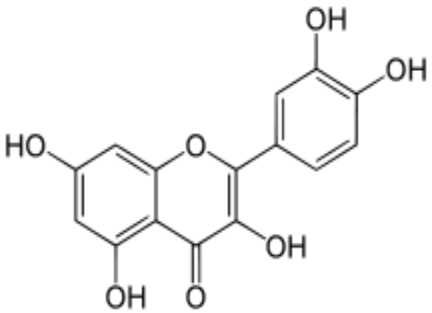


Figure 1, 2 & 3. Chemical structures of phenol

Naturally derived phenol is obtained by fractional distillation of coal tar, mostly phenol is made from 1-methylethylbenzene (cumene), which can be used as an indication of the levels of phenol production. The world annual production of 1-methylethylebenzene is shown in (Figure 2) Phenol can also be made by synthetic processes such as oxidation of toluene, fusion of sodium benzenesulfonate with sodium hydroxide or heating monochlorobenzene with sodium hydroxide under high pressure.

There are various classification schemes. A commonly used scheme is based on the number of carbons and was devised by Jeffrey Harborne and Simmonds in 1964 and published in 1980 [10].

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Major uses and Sources of phenol.(HSDB, 1995) [11]

Phenols and their derivatives commonly exist in the environment. These compounds are used as the components of dyes, polymers, drugs and other organic substances. The presence of phenols in the ecosystems is also related with production and degradation of numerous pesticides and the generation of industrial and municipal sewages. Some phenols are also formed during natural processes. These compounds may be substituted with chlorine atoms, may be nitrated, methylated or alkylated. Both phenols and catechols are harmful ecotoxins. Toxic action of these compounds stems from unspecified toxicity related to hydrophobocity and also to the generation of organic radicals and reactive oxygen species. Phenols and catechols reveal peroxidative capacity, they are hematotoxic and hepatotoxic, provoke mutagenesis and carcinogenesistoward humans and other living organisms.

Phenol is obtained from coal tar and is widely used as a disinfectant for industrial and medical applications. It also serves as a chemical intermediate for manufacture of nylon 6 and other man-made fibers and for manufacture of epoxy and other phenolic resins and as a solvent for petroleum refining. Approximately half of the U.S. consumption is directly related to the housing and construction industries, in applications such as germicidal paints and slimicides. Phenol is present in the atmosphere as an emission from motor vehicles and as a photo oxidation product of benzene. The annual statewide industrial emissions from facilities reporting under the Air Toxics Hot Spots Act in California, based on the most recent inventory, were estimated to be 234,348 pounds of phenol (CARB, 1999)[12].Table -1 shows the levels of phenol reported in industrial waste water.

Table 1. Levels of Phenol Reported in Industrial Wastewaters (Metcalf and Eddy, 2003)[13]

Industrial Source Phenol Concentration	mg/L
Petroleum refineries	40 - 185
Petrochemical	200 - 1220
Textile	100 - 150
Leather	4.4 - 5.5
Coke ovens (without dephenolization)	600 - 3900
Coal conversion	1700 - 7000
Ferrous industry	5.6 - 9.1
Rubber industry	3 – 10
Pulp and paper industry	22
Wood preserving industry	50 – 953
Phenolic resin production	1600
Phenolic resin	1270 – 1345
Fiberglass manufacturing	40 – 2564
Paint manufacturing	1.1

Phenol Exposure to environment

The mostly likely source of exposure to phenol is at manufacturing and hazardous waste sites; therefore, people living near landfills, hazardous waste sites, or plants manufacturing phenol are the most likely populations to be exposed. Other possible direct exposure may occur through use of consumer products containing phenol. Phenol is present in a number of consumer products that are swallowed, rubbed on, or applied to various parts of the body. These include throat lozenges, mouthwashes, gargles, and antiseptic lotions. Phenol has been found in drinking water, tobacco smoke, air, and certain foods, including smoked summer sausage, fried chicken, mountain cheese, and some species of fish. The magnitude, frequency, and likelihood of exposure and the relative contribution of each exposure route and source to total phenol exposure cannot be estimated using information currently available. Nonetheless, for persons not exposed to phenol in the workplace, possible routes of exposure include: breathing industrially contaminated air; smoking or inhaling ETS polluted air; drinking water from contaminated surface water or groundwater supplies; swallowing products containing phenol; and coming into contact with contaminated water and products containing phenol through bathing or skin application. Populations residing near phenol spills, waste disposal sites, or landfill sites may be at risk for higher exposure to phenol than other populations. If phenol is present at a waste site near homes that have wells as a source of water, it is possible that the well water could be contaminated.

If phenol is spilled at a waste site, it is possible for a person, such as a child playing in dirt containing phenol, to have skin contact or to swallow soil or water contaminated with phenol. Skin contact with phenol or swallowing products containing phenol may lead to increased exposure. This type of exposure is expected to occur infrequently and generally occurs over a short time period. At the workplace, exposure to phenol can occur from breathing contaminated air. However, skin contact with phenol during its manufacture and use is considered the major route of exposure in the workplace. It has been estimated that about 584,000 people in the United States are exposed to phenol at work. Total exposure at the workplace is potentially higher than in non-workplace settings. Phenol is a product of combustion of coal, wood, and municipal solid waste; therefore, residents near coal and petroleum fueled facilities as well as residents near municipal waste incinerators may have increased exposure to phenol. Phenol is also a product of auto exhaust, and therefore, areas of high traffic likely contain increased levels of phenol.

Effects of Human Exposures

- You may be exposed to phenol if you live near landfills or hazardous waste sites that contain phenol or near facilities manufacturing phenol.
- You may be exposed to very low levels in your home because it is found in a number of consumer products, including mouthwashes and throat lozenges.
- You may be exposed to phenol if you undergo “chemical peels” to remove skin lesions with phenol-containing products or are treated for chronic pain or spasticity with injections of phenol.
- Low levels of phenol are found in some foods, including smoked summer sausage, fried chicken, mountain cheese, and some species of fish.
- Smoking or inhaling second hand smoke will expose you to phenol.• Low levels of phenol can be present in air and drinking water.

The information that is available on the health effects of phenol exposure to humans is almost exclusively limited to case reports of acute effects of oral exposure (Bruce *et al*., 1987)[14], dermal exposure (Griffiths, 1973)[15], or occupational exposures, including some exposure by inhalation (Dosemeci*et al*., 1991; Ohtsuji and Ikeda, 1972;[16-17] Connecticut Bureau of Industrial Hygiene, undated).

Severe chronic poisoning manifests in systemic disorders such as digestive disturbances including vomiting, difficulty swallowing, ptyalism (excess secretion of saliva), diarrhea, and anorexia (Bruce *et al*.,1987; [14]Baker *et al*., 1978)[18].

Phenol poisoning is associated with headache, fainting, vertigo, and mental disturbances (Bruce *et al*., 1987[14]; Gosselin *et al*. 1984)[19] which are likely symptoms of neurological effects well documented in animal studies. Ochronosis, or discoloration of the skin, and other dermatological disorders may result from dermal phenol

exposure (Deichmann and Keplinger, 1962[20]; Bruce *et al*., 1987[14]).

Several investigators (Truppman and Ellenby, 1979; [21] Warner and Harper, 1985) [22]have reported that the use of phenol in the surgical procedure of skin peeling can produce cardiac arrhythmias although specifics of dose received were not determined and would be expected to be high.

Merliss (1972)[23] described muscle pain and weakness of unknown etiology, enlarged liver, and elevated serum enzymes (LDH, GOT, and GPT) characteristic of liver damage in an individual with intermittent inhalation and dermal exposures to phenol, cresol and xylenol.

Bruze (1986)[24] noted that a number of phenol-formaldehyde based resins are dermal irritants and contact sensitizers.

Johnson *et al*. (1985) [25]examined 78 iron and steel foundry workers with multiple chemical and aerosol exposures that included phenol and found more respiratory symptoms in the phenol exposed group. However, multiple exposures to diphenyl methane diisocyanate, formaldehyde, and silica containing aerosols prevented determination of the effects of phenol.

Baj *etal*. (1994)[26] examined twenty-two office workers exposed for six months via inhalation to a commercial product containing formaldehyde, phenol and chlorohydrocarbons. At the end of the six month period the indoor air of the workers contained 1,300 $\mu g/m^3$ of formaldehyde and 800 $\mu g/m^3$ of phenol. The eight workers with the highest concentrations of phenol in their urine had decreased erythrocyte and T-helper lymphocyte numbers and increased numbers of eosinophils and monocytes compared to controls. The multiple chemical exposure of this study prevents concluding that these effects are attributable to phenol exposure.

In a study of hospital workers Apol and Cone (1983) [27] documented dermal effects in workers exposed to a number of chemicals including phenols contained in disinfectants. This study however could not document any differences in urinary levels of phenol metabolites between control populations and exposed populations and could not assign any of the dermal effects seen to phenol or other substances in the work environment.

Dosemeci*et al*. (1991)[16] conducted a follow-up study to evaluate mortality in 14,861 workers in five manufacturing facilities producing or using phenol and formaldehyde. Arteriosclerotic heart disease, emphysema, disease of the digestive system, and cirrhosis of the liver were inversely related to the extent of phenol exposure. Due to multiple chemical exposures the effects of phenol alone could not be identified with any certainty.

Baker *et al*. (1978)[18] completed a study of 39 individuals exposed to drinking water contaminated with phenol for a period of 4-8 weeks. Doses of phenol were estimated to range between 10 mg/day and 240 mg/day. Effects that are seen included increased incidence of diarrhea, mouth sores and irritation of the oral cavity.

Two occupational studies are of note since they reported NOAELs. Workers exposed continuously for an unspecified period of time to an average air concentration of 4 ppm phenol experienced no respiratory irritation (Connecticut Bureau of Industrial Hygiene, undated). No adverse effects were reported among workers in a Bakelite factory who were exposed to levels of phenol up to 12.5 mg/m^3 (3.3 ppm) (Ohtsuji and Ikeda, 1972)[17]. In this study urinary phenol levels were measured and were observed to return to preexposure levels within 16 hours after exposure indicating a relatively rapid clearance of phenol from the body that was confirmed in a study by Piotrowski (1971)[28]. Ohtsuji and Ikeda (1972)[18] did not clearly indicate the number of workers sampled or the duration of exposure.

Effect of Animal exposure

Deichmann*et al*. (1944)[29] exposed guinea pigs, rats, and rabbits to concentrations of phenol between 26 and 52 ppm for 28-88 days depending on species. Guinea pigs exposed for 7 hours per day, five days per week, for four weeks, displayed signs of respiratory difficulty and paralysis primarily of the hind quarters, indicating neurological effects. Five of twelve animals exposed at this concentration died at 28 days. At necropsy, extensive myocardial necrosis, lobular pneumonia, fatty degeneration of the liver, and centrilobular hepatocellular necrosis were observed in all animals exposed at this level. Guinea pigs that were necropsied at 41 days also exhibited pulmonary inflammation, pneumonia, bronchitis, endothelial hyperplasia, and capillary thrombosis. Rabbits exposed at these same concentrations did not exhibit any signs of discomfort, but showed similar findings at necropsy at 88 days. Rats were less sensitive in this study with an apparent NOAEL of 26 ppm phenol for these effects. In this study, guinea pigs were the most sensitive species. Limitations of the Deichmann study include the range of exposure concentrations and the lack of a control group.

Sandage (1961)[30] exposed Sprague-Dawley rats, mice and rhesus monkeys for 90 days continuously to 5 ppm phenol. Sandage found no effects on pulmonary, cardiovascular, hematological, hepatic, or renal systems, thus defining free-standing NOAELs for these systemic effects in these species. Limitations of this study include absence of guinea pigs (previously identified as the most sensitive species in the Deichmann study) and lack of a demonstrated dose response to the effects of phenol.

Dalin and Kristofferson (1974)[31] examined the effects of phenol on the nervous system in rats exposed continuously for 15 days to a concentration of 26 ppm phenol and found muscle tremors, twitching and disturbances in walking rhythm and posture after 3-5 days exposure. After 15 days exposure, severe neurological impairment as measured by decreased performance on tilting plane test was found. The Dalin and Kristofferson (1974)[31] study also documented elevated serum concentrations of LDH, GOT, GPT, and GDH indicative of liver damage in animals exposed to 26 ppm phenol continuously for 15 days.

The NCI (1980)[32] study of the carcinogenicity of phenol is the most complete chronic study using the oral route of exposure. Mice and rats were exposed for 103 weeks to concentrations of phenol in their drinking water of 100, 2500, 5000, and 10,000 ppm. NOAELs in the mouse of 523 mg/kg/day (5000 ppm in drinking water) and NOAELs in the rat of 630 mg/kg/day (5000 ppm in drinking water) were observed for effects on the respiratory system, cardiovascular system, gastrointestinal system, hepatic system, renal system, and the brain based on histological examination of tissues. Male rats exposed to the 5000 ppm had a higher incidence of kidney inflammation (94%) than controls (74%). No tests of kidney function were performed in this study.

Boutwell and Bosch (1959)[33] reported on the results of a chronic study in mice involving skin painting of 1.2 mg phenol or 2.5 mg phenol for a 52 week period. A NOAEL of 1.2 mg/animal for a 52 week exposure for dermal effects was found.

Jones-Price *et al*. (1983a)[34] reported that pregnant rats dosed orally with 0, 30, 60, and 120 mg/kg/day on gestation days 6-15 exhibited reduced fetal weight in a dose-related manner. However, no teratogenic effects or fetal deaths were observed. In a following study Jones-Price *et al*. (1983b)[35]reported that pregnant mice dosed orally with 0, 70, 140, and 280 mg/kg/day on gestation days 615 exhibited decreased maternal weight gain, tremors, and increased maternal mortality at the 280 mg/kg/day dose. In the fetus reduced growth, decreased viability, and increased incidence of cleft palate were seen at the 280 mg/kg/day dose.

Plant phenolic compounds

Phenolic compounds in plant leaves are involved in several physiological mechanisms. They are well known as UV protecting agents in plant tissues (Takeda et al., 1994)[36] and are often involved in plant–pathogen interactions, both constitutively and as newly induced compounds (Cle´rivet et al., 1996)[37]. The composition of these phenols in plant tissues is markedly influenced by such environmental conditions as UV-light (Markham et al., 1998a,b)[38,39], temperature (Rivero et al., 2001)[40] and nutrition (Ruehmann et al., 2002)[41]. Leaf phenolics were used as a chemotaxonomic method to distinguish various species and interspecific hybrids of the genus Pyrus(Challice and Westwood, 1973)[42]. Within species having distinct cultivars, recent work has evaluated the qualitative composition of pear fruits (Spanos and Wrolstad, 1990, 1992; Amiot et al., 1993; Schieber et al., 2001)[43-46] and the flavonoids in Pyrus bark (Musacchi et al., 2000)[47]. However, little is known of the variability of phenolic compounds in the leaves of pear cultivars despite the fact that a thorough understanding of the variability in leaf phenolic composition is considered a prerequisite for understanding their role in defence mechanisms (Hildebrand et al., 1969)[48].

How can phenols effect on health?

Most of the phenol that you may inhale or ingest will enter the bloodstream; less will enter if there is contact with the skin. Short-term exposure to phenol in the air can cause respiratory irritation, headaches, and burning eyes. People who had skin exposure to high amounts of phenol had skin burns, liver damage, dark urine, irregular heartbeat, and some died. Ingestion of high concentrations of phenol has resulted in internal burns and death. In animals, breathing air with high levels of phenol resulted in irritation of the lungs. Repeated exposures induced muscle tremors and loss of coordination. Exposure to high concentrations of phenol in the air for several weeks caused paralysis and severe injury to the heart, liver, kidneys, and lungs, and in some cases, death. Some animals that drank water with very high concentrations of phenol suffered from muscle tremors and loss of coordination. Phenol can have beneficial effects when used medically as an antiseptic or anesthetic.

The International Agency for Research on Cancer (IARC) and the EPA have determined that phenol is not classifiable as to its carcinogenicity to humans.

Scientists use many tests to protect the public from harmful effects of toxic chemicals and to find ways for treating persons who have been harmed.

One way to learn whether a chemical will harm people is to determine how the body absorbs, uses, and releases the chemical. For some chemicals, animal testing may be necessary. Animal testing may also help identify health effects such as cancer or birth defects. Without laboratory animals, scientists would lose a basic method for getting information needed to make wise decisions that protect public health. Scientists have the responsibility to treat research animals with care and compassion. Scientists must comply with strict animal care guidelines because laws today protect the welfare of research animals.

It is not known if phenol causes cancer in humans. However, cancer has been shown to occur in mice when phenol was applied to the skin several times each week during the whole lifetime of the animal. When it is applied in combination with certain cancer-causing chemicals, a higher rate of cancer occurs than when the carcinogens are applied alone. Phenol did not cause cancer in mice or rats when they drank water containing phenol for 2 years. The International Agency for Research on Cancer (IARC) considers phenol not classifiable as to its carcinogenicity in humans. The EPA determined that phenol is not classifiable as to human carcinogenicity. Under updated guidelines, the EPA information available on the carcinogenicity of phenol is inadequate for an assessment of the potential for phenol to cause cancer in humans.

Phenol can have beneficial effects when used for medical reasons. It is an antiseptic (kills germs) when applied to the skin in small amounts and may have antiseptic properties when gargled as a mouthwash. It is an anesthetic (relieves pain) and is a component of certain sore-throat lozenges and throat sprays or gargles. Small amounts of phenol in water have been injected into nerve tissue to lessen pain associated with certain nerve disorders. Phenol destroys the outer layers of skin if allowed to remain in contact with skin, and small amounts of concentrated solutions of phenol are sometimes applied to the skin to remove warts and to treat other skin blemishes and disorders.

Effect on children

This section discusses potential health effects in humans from exposures during the period from conception to maturity at 18 years of age.

The exposure of children to phenol is likely to occur by most of the same routes experienced by adults, the major exception being that children are unlikely to be exposed due to their parents' occupations. There are no unique routes of exposure for children. However, there is evidence that children are at greater risk of accidental ingestion of certain products than adults. In the case of one product, a disinfectant containing 26% phenol, children under the age of 5 represented 60 of 80 (75%) of the poisoning cases associated with this product reported to a major poison control center between 1987 and 1991. Oral exposure was the predominant route of exposure, underscoring the need for parents to keep cleaning or disinfectant products out of the reach of children. Vomiting and lethargy were the main signs of toxicity that were observed.

Information on the toxic effects of phenol in infants and children also comes from the use of phenol in medical treatments. Phenol was once used as an antiseptic in wound dressing products and there are several reports of deaths in children and infants following overzealous application of such products to burns or open wounds. All of these cases occurred decades ago, however, and there is little indication that such products, which contained relatively high levels of phenol, are still in use.

Other phenol-containing products are used as "chemical peels" to remove skin lesions, and in the treatment of chronic pain or spasticity. These uses have occasionally been associated with adverse outcomes, like cardiac arrhythmias, that have been seen in both adults and children. These effects do not appear to occur more frequently in children than adults; however, the information on such effects in children is very limited. It is

unknown whether infants or children are more susceptible than adults to the adverse effects of phenol.

The effects of exposure to phenol on reproduction and the developing human fetus are unclear. Several studies in animals have not shown phenol to be active in developmental toxicity. In general, adverse developmental effects, such as low birth weights and minor birth defects, have occurred at exposure levels that also were toxic to the pregnant mothers. It seems likely that any adverse developmental effects would require much higher doses than would normally be encountered at hazardous waste sites.

How to effect on human and animal metabolisam

Phenols were a substance which was adsorbed by all exposure routes. Phenol absorption mainly conjugates with mixture of sulfonic and gluconic acids. And the formation of hydroquinone and catechol from hydroxylates. A shift rate of urinary excretion of phenol urinary excretion elimination to glucurodination was observed the phenol dose. The liver, and the lung are sites of sulfation phenol metabolism. The relative role played by these tissues depends on phenol. In vivo and invitro studies have administration metabolites demonstrated to tissue and of in rats after proteins. The most important some increasing and dose also bind to plasma route protein is the major route in animals and gastrointestinal mucosa humans. The varies with dose, route of administration, and species. A minor part is excreted in faeces and expired air.

Reducing the risk of exposure

If your doctor finds that you have been exposed to substantial amounts of phenol, ask whether your children might also have been exposed. Your doctor might need to ask your state health department to investigate.

Since ETS contains phenol, reducing the amount of smoking indoors will reduce phenol exposures. Household products and over-the-counter medications containing phenol should be stored out of reach of young children to prevent accidental poisonings and skin burns. It is always better to store household chemicals in their original labeled containers. Never store household chemicals in containers that children would find attractive to eat or drink from, such as old soda bottles. Keep your Poison Control Center's number next to the phone. Communities can find out if phenol is a contaminant in nearby landfills or polluting facilities and petition for cleanup.

Medical tests

Urine can be tested for the presence of phenol. This test can be used to determine if the urine has a higher than normal concentration of phenol, thus suggesting recent exposure to phenol or to substances that are converted to phenol in the body (e.g., benzene). There is no test available that will tell if a person has been exposed only to phenol, since many substances are converted to phenol in the body. Because most of the phenol that enters the body is excreted in the urine within 24 hours, this test can only detect exposures that have occurred within 1 or 2 days prior to the test. The test results cannot be used to predict what health effects might result from exposure to phenol. Measure-ment of phenol in urine requires special laboratory equipment and techniques that are not routinely available in most hospitals or clinics. However, urine samples can be taken at a doctor's office and can be sent to specialized laboratories for analysis.

Conclusion

Phenols and phenolic compounds are of environmental concern due to their toxicity and being as ubiquitous contaminants in the environment. Studies related to toxicity should be more concerned with sublethal effects and sublethal studies have been forced due to there is urgent need to find the safe concentration of the pollutants. Human exposure studies in which populations were exposed to phenol over longer periods of time (subchronic and chronic) are limited and have serious deficiencies including multiple chemical exposures, in many cases small size of exposed populations, and lack of information on dose received. The major strength of the key study is the observation of a NOAEL from a continuous exposure study involving exposure of several different species. The primary uncertainties are the lack of adequate human health effects data, the lack of multiple concentration inhalation exposure studies demonstrating a dose response relationship, the lack of animal studies longer than 90 days, and the lack of studies with guinea pigs, which have previously been identified as a sensitive species for phenol.

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