

HEALTH HAZARDOUS MANIFESTATIONS OF STYRENE IN BIOCHEMICAL PARAMETERS IN NEUROTOXICITY

Priya Das*, Aaheli Basu, Arpita Biswas, Supradip Mandal, Dr. Falguni Patra, Dr. Bankim Nandi, Dr. Khokan Bera, Dr. Dhruvo Jyoti Sen and Dr. Beduin Mahanti

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake Sector, EM-4/1, Sector-V, Kolkata-700091, West Bengal, India.

***Corresponding Author: Priya Das**

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake Sector, EM-4/1, Sector-V, Kolkata-700091, West Bengal, India.

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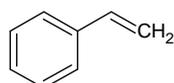
ABSTRACT

Styrene, also known as ethenylbenzene, vinylbenzene, and phenylethene, is an organic compound with the chemical formula $C_6H_5CH=CH_2$. This derivative of benzene is a colorless oily liquid although aged samples can appear yellowish. The compound evaporates easily and has a sweet smell, although high concentrations have a less pleasant odor. Styrene is the precursor to polystyrene and several copolymers. Styrene is a chemical used to make latex, synthetic rubber, and polystyrene resins. These resins are used to make plastic packaging, disposable cups and containers, insulation, and other products. Styrene is also produced naturally in some plants. People may be exposed to styrene by breathing it in the air. Styrene is often detected in urban air. It can be found indoors as a result of operating photocopiers and laser printers, and from cigarette smoke. Small amounts may be eaten when styrene migrates into foods from packaging made of polystyrene. The human health effects from exposure to low environmental levels of styrene are unknown. Workers exposed to large amounts of styrene can develop irritation of the eyes and breathing passages. With long-term and large exposures, workers using styrene have had injury to their *nervous systems*.

KEYWORDS: Styrene, Epoxidation, CYP₄₅₀, Neurotoxicity, Carcinogenicity.

INTRODUCTION

Styrene as IUPAC [Ethenylbenzene], Other names [Vinylbenzene, Phenylethene, Phenylethylene, Cinnamene, Styrol, Diarex HF 77, Styrolene, Styropol]. CAS Number [100-42-5]. Chemical formula [C_8H_8]. Molar mass [104.15 g/mol]. Appearance: colourless oily liquid. Odor: sweet, floral. Density: 0.909 g/cm³. Melting point: -30°C (-22°F; 243K). Boiling point: 145°C (293°F; 418K). Solubility in water: 0.03% (20°C). logP: 2.70. Vapor pressure: 5 mmHg (20°C). Refractive index (nD): 1.5469. Viscosity: 0.762cP at 20°C.



Structure

Dipole moment: 0.13D. Main hazards: flammable, toxic, probably carcinogenic. Styrene is regarded as a "known carcinogen", especially in case of eye contact, but also in case of skin contact, of ingestion and of inhalation, according to several sources. Styrene is largely metabolized into styrene oxide in humans, resulting from oxidation by cytochrome P₄₅₀. Styrene oxide is

considered toxic, mutagenic, and possibly carcinogenic. Styrene oxide is subsequently hydrolyzed *in-vivo* to styrene glycol by the enzyme epoxide hydrolase. The U.S. Environmental Protection Agency (EPA) has described styrene to be "a suspected toxin to the gastrointestinal tract, kidney, and respiratory system, among others".^[1,2] On 10 June 2011, the U.S. National Toxicology Program has described styrene as "reasonably anticipated to be a human carcinogen". However, a STAS author describes a review that was done on scientific literature and concluded that "The available epidemiologic evidence does not support a causal relationship between styrene exposure and any type of human cancer". Despite this claim, work has been done by Danish researchers to investigate the relationship between occupational exposure to styrene and cancer. They concluded, "The findings have to be interpreted with caution, due to the company based exposure assessment, but the possible association between exposures in the reinforced plastics industry, mainly styrene, and degenerative disorders of the nervous system and pancreatic cancer, deserves attention". In 2012 the Danish EPA concluded that the styrene data do not support a cancer concern for styrene. The U.S. EPA does not have a cancer classification for

styrene, but it has been the subject of their Integrated Risk Information System (IRIS) program. The U.S. National Toxicology Program of the U.S. Department of Health and Human Services has determined that styrene is "reasonably anticipated to be a human carcinogen". Various regulatory bodies refer to styrene, in various contexts, as a possible or potential human carcinogen. The International Agency for Research on Cancer considers styrene to be "probably carcinogenic to humans".^[3,4]

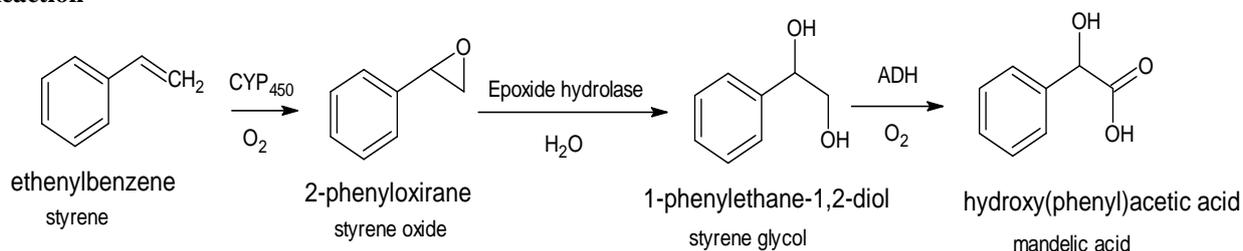
The neurotoxic properties of styrene have also been studied and reported effects include effects on vision (although unable to reproduce in a subsequent study) and on hearing functions. Studies on rats have yielded contradictory results, but epidemiologic studies have

observed a synergistic interaction with noise in causing hearing difficulties.

Industrial accident

On May 7, 2020, a gas, reported to be styrene, leaked from a tank at the LG Chem (LG Polymers India Private Limited) plant at Gopalapatnam on the outskirts of Visakhapatnam, Andhra Pradesh, India. The leak occurred in the early hours of the day, while workers were preparing to reopen the plant which was closed due to the COVID-19 pandemic. Eleven people including a child reportedly died and over 200 people have been admitted to the are hospital. Prime Minister Narendra Modi called for a meeting of the National Disaster Management Authority later that day.

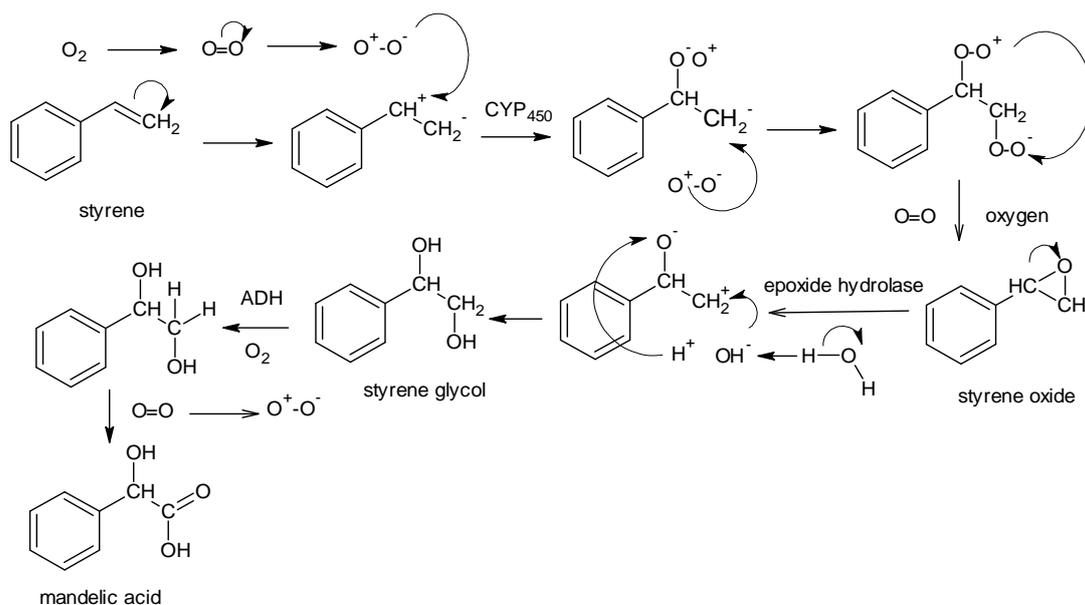
Reaction



Mechanism

Styrene [ethenyl benzene] is aryl alkene having one sigma and one pi bonds attached with one phenyl ring which has resonance property. This moiety when gets reacted with cytochrome P450 oxidase enzyme catalysed in alveolar oxygen of lungs alveoli it reacts *in-vivo* to oxidise double bond of styrene to form epoxide [styrene oxide] which is 2-phenyl oxirane forming three

membered heterocyclic ring. This moiety reacts with epoxide hydrolase catalysed by water (H₂O) molecule present in lungs capillary to form styrene glycol [1-phenylethane-1,2-diol] and finally it reacts with ADH [anti diuretic hormone] which oxidises -CH₂OH terminal primary alcoholic group into mandelic acid [hydroxy phenyl acetic acid]



Health hazards of styrene

Styrene is a colorless liquid that evaporates easily. In its pure form, styrene has a sweet smell. Manufactured

styrene may contain aldehydes, which give it a sharp, unpleasant odor. Large amounts of styrene are produced in the United States. Small amounts are produced

naturally by plants, bacteria, and fungi. Styrene is also present in combustion products such as cigarette smoke and automobile exhaust. Styrene is widely used to make plastics and rubber. Consumer products containing styrene include: packaging materials, insulation for electrical uses (i.e., wiring and appliances), insulation for homes and other buildings, fiberglass, plastic pipes, automobile parts, drinking cups and other "food-use" items, carpet backing. These products mainly contain styrene linked together in long chains (polystyrene). However, most of these products also contain a small amount of unlinked styrene. Styrene can be found in air, soil, and water after release from the manufacture, use, and disposal of styrene-based products.^[5,6]

Air: Styrene is quickly broken down in the air, usually within 1-2 days by air oxidation. The primary way you can be exposed to styrene is by breathing air containing it. Releases of styrene into the air occur from: industries using or manufacturing styrene, automobile exhaust, cigarette smoke, and use of photocopiers. Rural or suburban air generally contains lower concentrations of styrene than urban air. Indoor air often contains higher levels of styrene than outdoor air. 0.06-4.6 parts per billion (ppb) in outdoor air and 0.07-11.5 ppb in indoor air. Styrene is occasionally detected in groundwater, drinking water, or soil samples. Drinking water containing styrene or bathing in water containing styrene may expose you to low levels of this chemical.

Workplace air: A large number of workers are potentially exposed to styrene. The highest potential exposure occurs in the reinforced-plastics industry, where workers may be exposed to high air concentrations and also have dermal exposure to liquid styrene or resins. Workers involved in styrene polymerization, rubber manufacturing, and styrene-polyester resin facilities and workers at photocopy centers may also be exposed to styrene.

Water and soil: Styrene evaporates from shallow soils and surface water. Styrene that remains in soil or water may be broken down by bacteria or other microorganisms.

Food: Low levels of styrene occur naturally in a variety of foods, such as fruits, vegetables, nuts, beverages, and meats. Small amounts of styrene can be transferred to food from styrene-based packaging material.

Inhalation: When you breathe air containing styrene, most of the styrene will rapidly enter your body through your lungs. The most common health problems in workers exposed to styrene involve the nervous system. These health effects include changes in color vision, tiredness, feeling drunk, slowed reaction time, concentration problems, and balance problems. The styrene concentrations that cause these effects are more than 1,000 times higher than the levels normally found in the environment. Hearing loss has been observed in animals exposed to very high concentrations of styrene.^[7,8]



Figure-1: Styrene gas outbreak.

Animal studies have shown that inhalation of styrene can result in changes in the lining of the nose and damage to the liver. However, animals may be more sensitive than humans to the nose and liver effects.

Ingestion: Styrene in food or water may also rapidly enter your body through the digestive tract.

Dermal contact: A very small amount may enter through your skin when you come into contact with liquids containing styrene. Once in your body, styrene is broken down into other chemicals. Most of these other chemicals leave your body in the urine within few days. How can styrene affect my health?

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.

Oral: Impaired learning has been observed in rats exposed to high doses of styrene. Sperm damage has also been observed in rats exposed to high doses of styrene.

Cancer: The Department of Health and Human Services (DHHS), National Toxicology Program (NTP) listed styrene as "reasonably anticipated to be a human carcinogen" in the Report on Carcinogens, Twelfth Edition, released on June 10, 2011. The International Agency for Research on Cancer (IARC) has determined that styrene is a possible carcinogen.

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

Effects in children: There are no studies evaluating the effects of styrene exposure on children or immature animals. It is likely that children would have the same health effects as adults. We do not know whether children would be more sensitive than adults to the effects of styrene.

Birth defects: Studies in workers have examined whether styrene can cause birth defects or low birth weight; however, the results are inconclusive. No birth defects were observed in animal studies.

Breast milk: Nursing infants can be exposed to styrene from breast milk.

Tobacco smoke: Styrene is a component of tobacco smoke. Avoid smoking in enclosed spaces like inside the home or car in order to limit exposure to children and other family members.

Copier: Styrene is released during the use of home copiers. Families should use a copier only when needed

and turn it off when finished. It is also important to keep the room with the copier well ventilated.

Detecting exposure: Styrene can be measured in blood, urine, and body tissues for a short time following

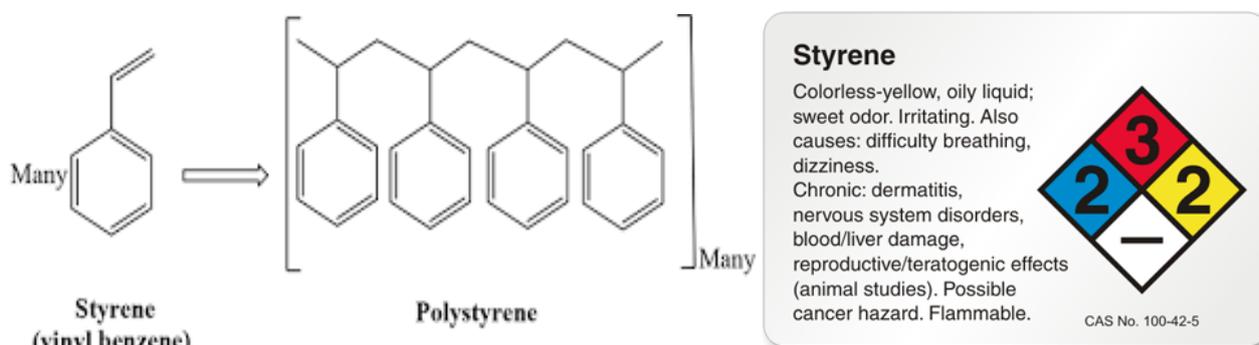


Figure 2: Styrene catabolism & Hazards.

Measuring exposure: The presence of styrene breakdown products (metabolites) in urine might indicate that you were exposed to styrene; however, these metabolites can also form when you are exposed to other substances. Measuring styrene metabolites in urine within 1 day of exposure allows medical personnel to estimate actual exposure level. The detection of these metabolites in your urine cannot be used to predict the kind of health effects that might develop from that exposure.

Government regulations: The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. The EPA, the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) are some federal agencies that develop regulations for toxic substances. Recommendations provide valuable guidelines to protect public health, but cannot be enforced by law. The Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH) are two federal organizations that develop recommendations for toxic substances. Regulations and recommendations can be expressed as "not-to-exceed" levels. These are levels of a toxic substance in air, water, soil, or food that do not exceed a critical value. This critical value is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or other factors. Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that provides it. Some regulations and recommendations for styrene include the following: Drinking water. The EPA (Environmental Protection Agency) has determined that exposure to styrene in drinking water at concentrations of 20 mg/L for 1 day or 2 mg/L for 10 days is not expected to cause any adverse effects in a child. The

exposure to moderate-to-high levels. This should be done within a few hours after exposure occurs because these metabolites leave the body very quickly.

EPA has determined that lifetime exposure to 0.1 mg/L styrene in drinking water is not expected to cause any adverse effects.^[9,10]

Bottled water: The FDA has determined that the styrene concentration in bottled drinking water should not exceed 0.1 mg/L.

Workplace air: OSHA set a legal limit of 100 ppm styrene in air averaged over an 8-hour work day.

Safety measures and treatments: After you come in contact with Styrene gas, there is only one way to treat the effects of the gas. You have to wash your skin and eyes with water properly and provide breathing support in case of ingestion. The local administration in Vizag has advised people to use wet cloth as a mask to cover nose and mouth to prevent inhalation of the gas. Corona discharge and ultraviolet (UV) radiation treatments have been used as environmentally friendly alternatives to the common surface treatment of halogenation for a styrene-butadiene-styrene (S6) rubber. The corona energy and the length of treatment under UV radiation of the S6 rubber have been studied and the surface modifications produced have been assessed by contact angle measurements, ATR-IR spectroscopy, XPS and SEM. Adhesion properties were obtained from T-peel tests of surface treated S6 rubber/polyurethane adhesive/leather joints. Corona discharge and UV radiation treatments modified the S6 rubber surface by creating C–O, C=O and COO– moieties that improved wettability. The extent of the surface modifications of S6 rubber was different by treatment with UV radiation or corona discharge. The higher the corona discharge energy or the higher the length of the UV radiation treatment, the more marked modifications were achieved on the S6 rubber surface. On the other hand, corona discharge and UV radiation treatment produced different morphologies on the S6 rubber surface. The poor adhesion obtained with the corona discharge treatment has been ascribed to a lack of surface roughness and/or the creation of weak boundary layer on the S6 rubber. On the contrary, UV radiation treatment produced cracks on the S6 rubber surface that favoured the mechanical adhesion. The modifications produced by both treatments were

compared to those produced by the solvent-based halogenation treatment. Few easy ways to avoid and stay safe:

- If you smoke, quit. Avoid second hand smoke.
- Routinely test your well water for styrene.
- If your well water contains styrene levels above EPA's drinking water advisory levels:

- Contact your local or state health agency or the Centers for Disease Control and Prevention (CDC) for information on how to reduce your exposure.
- Consider using bottled water for drinking and cooking or install an activated carbon filtration system or reverse osmosis system.



Figure 3: Precautionary measures in drinking water.

- Limit your time near idling cars, trucks, or buses.
- Use a home copy machine only when needed and turn it off when finished.
- Keep the room with the copier well ventilated. The regulation for styrene became effective in 1992. Between 1993 and 1995, EPA required your water supplier to collect water samples every 3 months for one year and analyze them to find out if styrene is present above 0.5ppb. If it is present above this level, the system must continue to monitor this contaminant. Doubts on, Styrene being present in drinking water. If contaminant levels are found to be consistently above the MCL (maximum contaminant level), your water supplier must take steps to reduce the amount of styrene so that it is consistently below that level. The following treatment methods have been approved by EPA for removing styrene: Granular activated charcoal in combination with Packed Tower Aeration.

CONCLUSION

Long-term exposure to styrene can cause: 1. Central nervous system and kidney effects. 2. Headaches. 3. Depression. 4. Fatigue and weakness. 5. Hearing loss. 6. Balance and concentration problems. 6. Cancer.

Styrene is a flammable liquid that is used to make polystyrene plastics, fiberglass, rubber, and latex. It occurs naturally in some fruits, vegetables, meats, nuts, and beverages.

Styrene is used to make: Insulation, Pipes, Automobile parts, Printing cartridges and copy machine toner, Food containers, Packaging, Carpet backing, Luggage, Shoes, Toys, Floor waxes and polishes, Cigarette smoke and vehicle exhaust contain styrene.

Where is Styrene found?

Consumer products – cigarettes, and many packaging, household, and building products

Air – emissions from styrene-based products, cigarettes, vehicle exhaust, and copy machines

Food and water – containing styrene from naturally occurring sources or contamination

How can I be exposed to Styrene?

Styrene commonly enter(s) the body through: Eating, Ingestion (swallowing), Swallowing food or water contaminated with styrene. Styrene may leach from polystyrene containers used for food, but the levels are low, Inhalation, Inhalation (breathing), Smoking cigarettes, or breathing cigarette smoke, second hand smoke, or emissions from vehicles, copy machines, or building materials, Touching, Skin contact, Touching products made with styrene

What happens when I am exposed to Styrene?

Short-term: Exposure to styrene can cause: Irritation to the eyes, skin, and nose. Gastrointestinal effects. Respiratory effects

Long-term: Long-term exposure to styrene can cause: Central nervous system and kidney effects. Headaches. Depression. Fatigue and weakness. Hearing loss. Balance and concentration problems. Cancer.

Who is at risk for exposure to Styrene?

Consumers: Some food, packaging materials, and consumer and building products contain styrene. Cigarette smokers: Cigarette smoke and second hand smoke contain styrene.

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