

Review on toxic effect of naphthalene

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Abstract

Naphthalene is a toxic substance. Naphthalene, also known as naphthalin, is a crystalline, aromatic, white, solid hydrocarbon (PAH: Polycyclic Aromatic Hydrocarbon) with formula C₁₀H₈ and the structure of two fused benzene rings. It is best known as the traditional, primary ingredient of moth balls. Repeated naphthalene exposure has also been found to potentially cause airway epithelial damage, aberrant repair, and inflammation. Greater numbers of peribronchial Mac-3-positive macrophages and CD3-positive T-cells were observed throughout the airways which displays acute inflammation within the airways. The effects of naphthalene poisoning are particularly severe in infants and young children. Toxic effects vary from individual to individual. This article gives a brief review about the toxic effect of naphthalene.

Keywords: Naphthalene, toxicity effect

Introduction

Naphthalene is a white solid substance with a strong smell. The principal route of exposure for naphthalene is by inhalation of vapours due to its uses in industry and its release as a product of the combustion of organic materials. Ingestion of naphthalene is not a common route of exposure, although it may occur in some cases. Naphthalene is readily absorbed into the systemic circulation following either inhalation or ingestion and may result in systemic toxicity. Systemic absorption of naphthalene can also occur following dermal contact.

Kinetics and metabolism

- Naphthalene is readily absorbed into the systemic circulation following inhalation, ingestion or dermal exposure
- Naphthalene is initially metabolised into a number of reactive epoxide and quinone metabolites by cytochrome P450 oxidation

- Metabolites of naphthalene are excreted in the urine as mercapturic acids, methylthio derivatives and glucuronide conjugates •
- Glutathione and cysteine conjugates are excreted in the bile •
- Following ingestion the urinary excretion of naphthalene metabolites is prolonged due to delayed absorption from the gastrointestinal tract

Clinical features:

- An acute inhalation exposure to naphthalene can cause signs and symptoms such as nausea, vomiting, abdominal pain, diarrhoea, headache, confusion, profuse sweating, fever, tachycardia, tachypnoea and agitation.
- In some cases this may lead to convulsions and coma.
- The most characteristic sign of naphthalene toxicity is acute intravascular haemolysis, particularly in individuals with a deficiency of glucose 6-phosphate dehydrogenase (G6-PD) which can cause anaemia, leukocytosis, fever, haematuria, jaundice and liver and kidney dysfunction.
- Acute dermal exposure to naphthalene will give rise to mild irritation and in some sensitive individuals may cause dermatitis. Dermal exposure to sufficient amounts of naphthalene may result in dermal absorption, thus causing systemic toxicity similar to that observed following inhalation or ingestion.
- Ocular exposure may cause eye irritation, corneal damage and can lead to the formation of lens opacities and

in some cases can result in the formation of cataracts.

- Chronic inhalation exposure to naphthalene may give rise to similar effects as observed following acute exposure, including nausea, headache, malaise and haemolytic anaemia and its related hepatic and renal effects.

Toxic effect:

- Naphthalene is the poisonous ingredient. Poisoning from naphthalene destroys or changes red blood cells so they cannot carry oxygen. This can cause organ damage.
- Due to the adverse health effects of acute exposure, chronic exposure to amounts sufficient to cause significant toxicity is relatively uncommon.
- There is some limited evidence that naphthalene may cause developmental toxicity as it may cross the placenta giving rise to neonatal haemolytic anaemia. However, the dose required to produce developmental toxicity is also likely to cause significant maternal toxicity.
- There is insufficient data available regarding the carcinogenicity of naphthalene in humans. The International Agency for Research on Cancer (IARC) classified naphthalene as possibly carcinogenic to humans (group 2B) based on the evidence of carcinogenicity in animals. The EU system classifies naphthalene as a category 3 carcinogen, meaning that it has limited evidence of a carcinogenic effect. Naphthalene is not mutagenic in animals and the carcinogenicity is due to a non-genotoxic mechanism.

Animal and In-Vitro Data

- **Inhalation** The nose and lungs are the principal target for naphthalene toxicity following inhalation in rats and mice. Chronic inhalation exposure to naphthalene resulted in an increased incidence of neoplastic and non-neoplastic lesions in the nose and lungs of rats. In mice, an increase in non-neoplastic lesions was seen in the nose, whilst the incidence of both neoplastic and non-neoplastic lesions were increased in the lungs. The non-neoplastic lesions observed in the nasal cavity of rats and mice included hyperplasia, atrophy, chronic inflammation and hyaline degeneration of the olfactory epithelium and hyperplasia, metaplasia or degeneration of the respiratory epithelium. Neoplastic lesions include respiratory epithelial adenoma and olfactory epithelial neuroblastoma.
- **Ingestion** Chronic oral exposure of naphthalene to rats and rabbits has been shown to increase ocular lens density followed by the formation of cataracts after approximately 4 weeks exposure to 500 and 1000 mg kg⁻¹ day⁻¹ [1, 2]. Pregnant female rats that were orally exposed to naphthalene at 50, 150 and 450 mg kg⁻¹ day⁻¹ during organogenesis exhibited lethargy, slow respiration, had periods of apnoea, appeared to be dazed and were unable to move following exposure. The rats administered 50 mg kg⁻¹ day⁻¹ was seen to acclimatise quickly, with symptoms only apparent during the first 2 days of dosing. A significant reduction in body weight gain was also observed in the animals treated with either 150 or 450 mg kg⁻¹ day⁻¹. These effects were not observed in

non-pregnant rats or mice, suggesting that pregnant animals are more susceptible to naphthalene toxicity.

- **Genotoxicity** Naphthalene has consistently given negative results in the well established Salmonella assay for gene mutation in bacteria. There is some evidence that naphthalene is clastogenic invitro, but negative results were obtained in the bone marrow assay for clastogenicity in-vivo in mice. Negative results were also obtained in an in-vivo assay for DNA damage in the liver of rats in an unscheduled DNA synthesis (UDS) study. A number of expert groups have concluded that on-balance naphthalene is not an in-vivo genotoxin [7-10].
- **Carcinogenicity** The carcinogenicity of naphthalene has been studied in rats and mice following inhalation exposure. Neuroblastomas of the olfactory epithelium and adenomas of the nasal respiratory epithelium were induced in both male and female rats exposed to naphthalene. In mice exposed to naphthalene by inhalation there was an increased incidence of bronchiolaralveolar adenomas in females, but this was not seen in males [2-4]. The International Agency for Research on Cancer (IARC) has evaluated that there is sufficient evidence for the carcinogenicity of naphthalene in experimental animals

Conclusions

- Adverse effects following chronic inhalation of naphthalene are similar to those seen following acute exposure, such as nausea, headache, malaise and haemolytic anaemia and its related hepatic and renal effects.

- In cases of human exposure to naphthalene vapours, the dose and duration of exposure is often unknown and as such it is difficult to assess the effect of chronic naphthalene exposure. Also, due to the adverse health effects of acute exposure to naphthalene, chronic exposure to amounts sufficient to cause significant toxicity is relatively uncommon
- There is some evidence of developmental toxicity in rats and mice exposed to naphthalene by oral ingestion. However, this was observed only at levels which produced significant maternal toxicity.

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