Naphthalene Mothballs: Emerging and Recurring Issues and their Relevance to Environmental Health

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Abstract

Naphthalene is a polycyclic aromatic hydrocarbon that is commonly encountered in indoor and outdoor environments. There is growing awareness of the environmental health risks associated with inhalation exposure to naphthalene in the indoor environment. While there are numerous potential sources of naphthalene indoors, the use of mothballs can be a significant contributor to ambient concentrations. This review article describes recurring and emerging environmental health issues relating to mothballs containing naphthalene. The toxicology and health effects of naphthalene exposure are reviewed, with discussion of high-risk populations and risk mitigation strategies. Environmental health professionals should be aware of mothball use in the home, and recognize risks associated with accidental exposure and misuse.

Keywords
naphthalene; mothballs; polycyclic aromatic hydrocarbons (PAHs); indoor exposure; public health

Introduction

Naphthalene is a polycyclic aromatic hydrocarbon that is commonly encountered in indoor and outdoor environments. This bicyclic compound exists primarily as a vapor at ambient pressure due to its high vapor pressure. Naphthalene has a strong, characteristic smell with a low odor threshold of approximately 0.44 mg/m³ (0.084 ppm) in air [1]. There are numerous sources of naphthalene in the environment. It is a component of crude oil, and it is also a product of natural combustion. A significant source of non-occupational exposures in residential settings is thought to be from the use of naphthalene-based products, particularly mothballs [2].

Mothballs containing naphthalene are widely available to consumers throughout the world. In the United States, there are nine insect repellent products containing naphthalene that have been registered for use by the U.S. Environmental Protection Agency. These include products intended to kill moths in airtight spaces, and to repel vertebrate pests in attics and wall void spaces. Naphthalene mothballs contain 99.9 percent naphthalene [3], and can range in weight from 0.5 g to 5 g [4]. Accidental exposures and the misuse of naphthalene...
mothballs have previously been associated with incidents of serious morbidity in children and adults [4,5].

The public often misuses mothballs in violation of the pesticide label. In 2006, the National Pesticide Information Center received 769 reports of mothball-related exposure incidents, and 60% of these reports were associated with misapplication of the product [6]. A common manner of misuse is the distribution of mothballs in air ducts or other areas such as crawlspaces, where vapors can enter or be distributed throughout the indoor environment. Once the mothballs are applied in this manner, they can be difficult to retrieve. Another factor that may increase the risk of accidental pediatric exposures to mothballs is the small size and presence of coloring, which may attract attention from toddlers and children [7].

The purpose of this review article is to describe some of the recurring and emerging issues relating to mothballs containing naphthalene. The relative contribution of mothballs to indoor air levels of naphthalene will be discussed, as well as current knowledge of high-risk populations and adverse health impacts from environmental exposure. Emerging issues relating to the intentional misuse of naphthalene mothballs will also be presented, with an emphasis on adverse health impacts and a need for greater awareness among environmental health and medical professionals.

**Exposure to Naphthalene**

The majority of exposure to naphthalene in the environment occurs through inhalation, while other pathways include dermal contact with and ingestion of naphthalene-containing products. Naphthalene can be inhaled after its release into indoor air through smoking cigarettes, wood burning, electric heating systems, cooking, and the use of mothballs or other insect repellents that contain naphthalene [1,8,9]. Naphthalene occurs at lower concentrations in outdoor air. Sources of naphthalene in outdoor air include automobile exhaust, and wood and fossil fuel combustion [1,9].

Dermal exposure can occur from direct contact with mothballs, as well as items stored in enclosed spaces with naphthalene-containing mothballs [1]. Incidents of serious medical outcomes, including acute hemolytic anemia, have been reported in association with dermal exposure in newborns to diapers and blankets that have been stored in mothballs [10,11].

Numerous case reports and case series have been published describing serious morbidity and mortality from accidental and intentional ingestion of mothballs containing naphthalene. One of the consistent findings in these reports is a delay between ingestion and the onset of serious signs and symptoms. A 17 year-old male died 5 days after ingesting an unknown quantity of mothballs [12]. Similarly, a thirty-year old woman died five days after intentionally ingesting mothballs. [13]. Twenty-five mothballs were retrieved from her stomach during autopsy.

**Naphthalene in Outdoor and Indoor Air**

As a product of combustion, naphthalene is commonly detectable in outdoor air. The median naphthalene concentration was 0.94 μg/m³ (0.0002 ppm) in urban and suburban air samples collected from 11 U.S. cities [1]. Higher concentrations have been measured in proximity to industrial sources [1,14]. Average naphthalene concentrations in the air in locations surrounding a wood treatment facility ranged from 0.4 to 12.9 μg/m³ (0.00008 to 0.00246 ppm) during a 24-hour period [15]. Concentrations as high as 25.6 μg/m³ (0.00488 ppm) were measured in short-term (1-3 hours) samples collected in this study.
In the indoor environment, tobacco use, cooking, heating, and use of mothball and other consumer products are predominant sources of naphthalene [1]. In one investigation, the mean concentration of naphthalene in non-smoking urban homes was 0.851 μg/m^3 (0.00016 ppm) and mothball storage was identified as a significant emission factor [8]. Higher concentrations of naphthalene (2.190 – 2.3 μg/m^3, or 0.00042-0.00044 ppm) have been measured in homes with smokers [16,17]. It has been estimated that a single box of mothballs containing 396 g of naphthalene, released within an indoor residential environment, is capable of raising the indoor air concentration to an average of approximately 200 μg/m^3 for a period of one year [3]. A recent study conducted in China reported data assessing the relative contribution of naphthalene mothballs to indoor air concentrations in smoking and non-smoking residences [18]. In this investigation, naphthalene was the PAH found at highest concentrations (ranging from 0.258 to 35.4 μg/m^3), and it accounted for the majority of the total PAHs that were measured. The results of a multiple regression analysis found that mothball emissions accounted for 71.5% of the total PAHs that were measured in indoor air of nonsmoking residences.

The Agency for Toxic Substances and Diseases Registry (ATSDR) has established a minimum risk level (MRL) of 0.0007 parts per million (ppm), or 0.004 mg/m^3 for chronic inhalation exposure to naphthalene [1]. The Occupational Safety and Health Administration (OSHA) in the United States has established a permissible exposure limit (PEL) of 10 ppm for naphthalene. The National Institute of Occupational Safety and Health (NIOSH) established an immediately dangerous to life or health (IDLH) value of 250 ppm for naphthalene.

**Naphthalene Toxicology and Health Effects**

Naphthalene undergoes hepatic metabolism, and is oxidized to alpha-naphthol and other metabolites. It has recently been reported that certain cytochrome P450 enzymes that are highly expressed in the human respiratory tract (2A13) are also capable of catalyzing these metabolic transformation reactions [19]. The metabolites of naphthalene produce oxidative stress, leading to the formation of methemoglobinemia and the oxidation of hemoglobin [20]. Oxidized hemoglobin can become denatured, resulting in the formation of visible Heinz bodies and increased susceptibility of the red blood cell (RBC) to hemolysis. Hemolysis of the red blood cells can occur following exposure to naphthalene by all routes of exposure.

When hemolysis or methemoglobinemia occur, the onset of related signs and symptoms usually occurs 1-2 days after exposure because of the slow rate of metabolism of naphthalene to its oxidative metabolites. The anemia from hemolysis of red blood cells often takes 3-5 days after exposure to reach its peak. Signs and symptoms of hemolysis and methemoglobinemia include weakness, tachycardia, shortness of breath, and altered mental status. Methemoglobinemia produces cyanosis, while hemolysis results in jaundice and pallor [20].

While the classical effects of naphthalene on hemolysis and methemoglobinemia have been well-studied, recent experimental investigations in animals have provided important information about other potentially important targets of toxicity including the upper and lower respiratory tract. Considerable inter-species differences have been observed in the susceptibility to the effects of naphthalene on the respiratory tract, with observed effects being more pronounced in certain rodent models in comparison with humans [21]. An experimental study of rhesus macaques demonstrated that P450-dependent metabolism of naphthalene in the lung results in the generation of reactive metabolites that covalently bind...
to proteins, an effect which correlated with epithelial cell injury in the airways [22]. Other investigators have observed airway injury in the nasal epithelium and olfactory mucosa in rats with short-term inhalation exposure to naphthalene at levels below the current OSHA standard (10 ppm, 8 h) [23]. These experimental findings are of interest given the observation that serum levels of naphthalene have been reported to be significantly higher among asthmatic children in comparison to non-asthmatics [24]. Recent biomonitoring studies have confirmed that the metabolites of naphthalene (including 1-hydroxynaphthalene and 2-hydroxynaphthalene) are commonly detectable in urine samples obtained from adults and children in the United States and in Europe [25,26].

Naphthalene and Cancer

The potential for environmental exposure to naphthalene to result in cancer is poorly understood. Despite the widespread use and occurrence of naphthalene, few epidemiological studies exist and numerous challenges remain in the interpretation of animal bioassays. Currently, naphthalene is classified as a rodent carcinogen that is “reasonably anticipated” to be a human carcinogen by the International Agency for Research on Cancer [27] and as a possible carcinogen by EPA [28].

In 1992 and 2000, the National Toxicology Program conducted whole animal bioassays to elucidate the role of naphthalene in tumor formation [29,30]. Recently, these studies were reviewed for their relevance to human effects [31]. Benign pulmonary alveolar/bronchiolar adenomas were detected at doses that were likely induced by cytotoxic effects, a suggestion supported by others that infer a cytotoxic mechanism for naphthalene [32, 33]. The observed cytotoxic effects occurred at doses that are orders of magnitude higher than anticipated from chronic inhalation of ambient indoor levels of naphthalene. Differences in the anatomy, physiology and sensitivity of the nasal cavity among rodent species, and between rodents and humans, are challenges in assessing the external validity of these data to human cancer.

Naphthalene Toxicology: High Risk Populations

There are genetic and developmental factors that can increase an individual’s susceptibility to the effects of naphthalene. Under normal circumstances, there are multiple mechanisms within the RBC to prevent toxicity from oxidative stress. The most important protective effect is via the generation of reduced nicotine adenine dinucleotide phosphate (NADPH) from the hexose monophosphate shunt. The NADPH is used to maintain adequate stores of reduced glutathione to prevent hemolysis from oxidative stress.

Individuals who have glucose-6-phosphate deficiency (G6PD) do not produce as much NADPH. Such individuals have lower levels of glutathione and are subsequently at much higher risk of hemolysis and methemoglobinemia after exposure to naphthalene [34,35]. As the gene coding for G6PD is X-linked, males are more commonly affected than females. The prevalence of G6PD is highest among individuals of African, Asian, Mediterranean, and Middle Eastern descent [36]. In a retrospective review of 24 African-American children with G6PD who were hospitalized with acute hemolytic anemia, 14 were reported to have had exposure to naphthalene-containing mothballs [35]. It is of interest that this case series observed that naphthalene mothballs had frequently been used in these environments for the fresh scent, and not for repellent purposes in a manner consistent with their labeling instructions.

Neonates are more susceptible to the effects of oxidative stress from naphthalene, as they have thinner skin and decreased stores of reduced glutathione [4,10]. There is also evidence that naphthalene and its metabolites are capable of crossing the placenta resulting in perinatal toxicity. A case report described an African American female with
methemoglobinemia and hemolytic anemia of unknown origin who gave birth to an infant with fetal distress and cyanosis [37]. Methemoglobinemia and hemolysis was observed in the newborn, who recovered after exchange transfusion. In this incident, an entire box of moth flakes containing naphthalene had been spilled into a heating vent at home during the week prior to delivery. *In utero* exposure to naphthalene is also of relevance given reports of maternal pica and chronic ingestion of mothballs during pregnancy [38].

### An Emerging Issue: Mothballs and Inhalant Abuse

Inhalant abuse of volatile chemicals is an important, but probably under recognized, source of significant morbidity and mortality among school-aged and adolescent children [39]. In the past 10 years, several case reports have described the intentional misuse of mothballs as inhalants. Feuillet et al. reported twin 18-year old sisters who had been “bagging” (inhaling mothball fumes) daily for four to six months [40]. They had been encouraged by classmates to use mothballs as a recreational drug.

Another case report described a 26-year old female with a history of polysubstance abuse, who admitted to chronic inhalation of mothball vapors on a daily basis for several years [41]. She was anemic, and had abnormal liver function tests. The authors concluded that her clinical presentation was consistent with toxicity from chronic inhalation of naphthalene mothballs. Others have reported chronic inhalant and ingestion abuse of mothballs in a 54-year old woman over a period spanning four decades, with serious medical complications including anemia and chronic renal failure [42]. These case reports suggest that adults as well as children are at risk of complications from inhalant abuse of mothballs, and that greater recognition of this is needed from health care professionals.

### Naphthalene: Incident Trends in the United States

Human exposures to mothballs containing naphthalene are frequently reported to Poison Control Centers. In 2008, 1445 human exposure incidents to naphthalene repellents were reported to the National Poison Data System (NPDS) in the United States [43]. The number of incidents is relatively consistent with what was reported in 2007 and 2008 (1504 and 1617 incidents, respectively) [44,45].

A review of the NPDS reports on human exposures to naphthalene during 2006-2008 reveals that the majority of exposure incidents occurred among children under the age of six. Approximately 20% of these exposure incidents resulted in the victim receiving medical care. There were no deaths or major medical outcomes reported during 2008 associated with naphthalene incidents. In the two preceding years, no deaths were reported but two exposures resulted in major medical outcomes.

As part of the reregistration review of naphthalene repellents, the U.S. EPA reviewed human exposure incidents that occurred during 1993 – 2005 [46]. The results of the analysis showed that human exposure incidents involving naphthalene were disproportionately high when compared to exposures to other pesticide active ingredients during that time period. The majority of naphthalene exposures resulted from indoor use products. When compared to other types of pesticides, there was a significant proportion of pediatric exposure incidents, most of which occurred through ingesting mothballs.

### Risk Mitigation Measures

Naphthalene has been categorized in the highest priority for indoor air pollutants in the European Union [47]. A long-term exposure limit guideline value of 10 micrograms/m³ has been recommended for naphthalene in indoor air based upon the data supporting health
endpoints of airway irritation, inflammation, and hyperplasia. A management option that has been suggested is the restriction of mothball products containing naphthalene [47].

The U.S. EPA required several new restrictions based upon their recent reregistration review of the naphthalene repellents [46]. The risk mitigation strategies included new packaging requirements and precautionary labeling to protect toddlers and children from mothball ingestion. Acceptable packaging includes tear- and moisture-resistant sachets, and plastic containers that allow volatilization but no direct contact with the naphthalene. These packaging measures must be implemented by the year 2013. Label language required since 2009 includes warnings to consumers of the possible ingestion risk to children, and to keep the products out of the reach of children. Some States have enacted more restrictive regulations, including cancellations of the use of naphthalene as a pesticide. California has not allowed the registration of naphthalene as an active ingredient since 1992.

Conclusions

While there are numerous sources of exposure to naphthalene in the environment, a review of the recent literature has demonstrated that mothball products can be a significant contributor to ambient levels in the indoor environment. The toxicological effects of naphthalene on erythrocytes are well understood, and recent investigations have shed additional insight on mechanisms of injury to the respiratory tract. As certain subpopulations are more susceptible to the effects of naphthalene, environmental health professionals should be aware of mothball use in the home. Particular attention should be paid to the assessment of proper use (in a manner consistent with the product labeling), and reducing the risks of accidental pediatric exposures. More recent reports of intentional inhalation abuse of mothballs raise additional concerns about the safety of these consumer products, and potential for misuse. Several different risk mitigation strategies have been recently proposed and enacted to reduce the environmental health risks associated with naphthalene. There are several sources of exposure incident data, including the NPDS, which should be utilized to assess the impact of these interventions on human exposures.

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