ASSESSMENT OF SOME GONADAL AND PULMONARY TOXIC EFFECTS OF TOLUENE INHALATION IN ADULT ALBINO RATS

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INTRODUCTION

Toluene is a clear, colorless volatile liquid with a distinctive smell . It occurs naturally in crude oil and in the tolu tree ; and is produced in the process of making gasoline and other fuels ***(Wade , 2003)*** .

Toluene is a good solvent ; it is used in the manufacture of paints, paint thinners, fingernail polish, lacquers, adhesives, rubber and in some printing and leather tanning processes ***(Vural and Ogel ; 2006)*** .

Exposure to toluene occurs by inhalation , oral or dermal routes. General population can be subjected to toluene inhalation in streets from automobile exhaust . In workplaces , people who work with gasoline, kerosene, heating oil, paints, printers and lacquers are at the greatest risk of exposure ***(Martin , 2006)***.

Deliberate or intentional toluene inhalation occurs during glue sniffing or solvent abuse to get a sensation of euphoria . It became a widespread social and public health problem especially among young poeple (children and adolescents) as toluene is readily available and inexpensive ***(Gelazonia et al ., 2006).***

The health hazards of toluene exposure vary greatly according to dose , route of exposure (inhalation , oral or dermal) and duration of exposure . Researches proved that toluene has many toxic effects on various systems of the body . They include neurological , respiratory , cardiovascular, hematological, musculoskeletal , hepatic , renal , endocrine , ocular , auditory , immunological , reproductive , developmental and genotoxic effects ***(Goldfrank's et al ., 2006)*** .

The federal agencies developed regulations and recommendations for toxic substances to protect public health from the possible toxic health effects of toluene in the environment . They include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA) ***(Roberts et al., 2003)*** .

AIM OF THE WORK

The aim of the present study is to assess some ***gonadal*** and ***pulmonary*** toxic effects of subchronic toluene inhalation in adult albino rats .

The importance of this study arises from the fact that toluene as a volatile organic solvent is contained in hundreds of household , industrial and consumer products ; therefore , accidental or intentional inhalation of toluene vapors and fumes occurs frequently at home , street and workplaces .

The easy availability and low prices of glue and other toluene containing products make it a common solvent for abuse by especially by teenagers .

Toluene Review

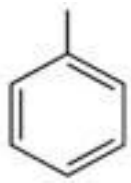
History:

The name toluene was derived from the older name *toluol* that refers to tolu balsam, an aromatic extract from the tropical Colombian tree *Myroxylon balsamum*, from which it was first isolated. It was originally named by Jöns Jakob Berzelius ***(March , 1992) .***

Preparation:

Toluene occurs naturally at low levels in crude oil and is usually produced in the processes of making gasoline via a catalytic reformer, in an ethylene cracker or making coke from coal. Final separation takes place either via distillation or solvent extraction ***(Matar and Hatch , 2001) .***

Toluene is known as **methylbenzene**, **toluol** or **phenylmethane**. It is a clear, water-insoluble volatile liquid with a distinctive smell typical of paint thinners, similar to the sweet smell of the related compound benzene. It is an aromatic hydrocarbon that is widely used in industry and as a solvent ***(Flanagan , 2005) .***



Molecular formula : C_7H_8 ($C_6H_5CH_3$)

Physical properties:

Table 1 : Toluene physical properties in ***(Flanagan , 2005)*** :

Molecular formula	C_7H_8 ($C_6H_5CH_3$)
Molar mass	92.14 g/mol
Appearance	Clear colorless, liquid
Density	0.8669 g/mL, liquid
Melting point	−93 °C
Boiling point	110.6 °C
Solubility in water	0.053 g/100 mL (20-25°C)
Viscosity	0.590 cP at 20°C
Main hazards	highly flammable
Related aromatic hydrocarbon	benzene xylene naphthalene

Chemical properties:

Toluene reacts as an aromatic hydrocarbon towards electrophilic aromatic substitution . The methyl group makes it around 25 times more reactive than benzene in such reactions. It undergoes smooth sulfonation to give p-toluenesulfonic acid, and chlorination by Cl2 in the presence of FeCl3 to give ortho and para isomers of chlorotoluene . It undergoes nitration to give ortho and para nitrotoluene isomers, but if heated it can give dinitrotoluene and ultimately the explosive trinitrotoluene TNT ***(Chang and Chen , 2008) .***

With other reagents the methyl side chain in toluene may react, undergoing oxidation. Reaction with potassium permanganate leads to benzoic acid, whereas reaction with chromyl chloride leads to benzaldehyde (Étard reaction) ***(Wade , 2003) .***

Uses:

Toluene is a common solvent , it is also a main constituent of many consumer products such as : paints, paint thinners, many chemical reactants, rubber, printing ink, adhesives (glues), lacquers, leather tanners, and disinfectants ***(Zeliger , 2008) .***

Industrial uses of toluene include dealkylation to benzene and disproportionation to a mixture of benzene and xylene. When oxidized it yields benzaldehyde and benzoic acid, two important intermediates in chemistry. Toluene can be used to break open red blood cells in order to extract hemoglobin in biochemistry experiments ***(Goldfrank's et al., 2006) .***

Methods of exposure to toluene:

Exposure to toluene can occur from accidental or deliberate inhalation of fumes as well as by ingestion or dermal absorption ***(Dodson et al., 2007) .***

The principal source of toluene exposure for the general population is gasoline, which contains 5% to 7% toluene by weight . Toluene is released to the atmosphere during the production, transport, and combustion of gasoline. Therefore , toluene concentrations are highest in areas of heavy traffic where air is saturated with automobile exhaust , also near gasoline filling stations and refineries ***(Churchill et al., 2001) .***

Indoors, the principal sources of toluene in air are common household products and cigarette smoke ***(Zeliger , 2008)***. Toluene-containing consumer products include household aerosols,

paints, paint thinners, varnishes, adhesives, glues, cosmetic nail polishes and solvent-based cleaning agents ***(Linde , 2005)*** . Cigarette smokers absorb about 80 to 100 micrograms (μg) of toluene per cigarette ***(Tarrant et al., 2009) .***

Industrial use of toluene as a solvent makes workers at increased risk of exposure in contaminated work places. Workers at greatest risk include automobile mechanics; gasoline manufacturers; dye and ink makers; and painters, adhesives and coatings manufacturers, coke-oven workers, printing workers and shoe manufacturers ***(Heuser et al., 2007).***

Toluene is occasionally detected in drinking water supplies. Water contamination occurs from spill of solvents, industrial effluents and petroleum wastes ***(Fan et al ., 2009) .***

Many volatile organic solvents, including toluene have an addictive potential. Volatile solvent abuse is the deliberate inhalation of fumes contained in hundreds of household and industrial products for their sedative and mind – altering effects ***(Vale , 2007) .*** Studies indicate that volatile-solvent sniffers are typically teenagers between the ages of 10 and 15 years of age who might concurrently use or later develop an alcohol, marijuana, or opiate habit ***(Roberts et al., 2003)*** .

The Occupational Safety and Health Administration (OSHA) has determined the acceptable level of occupational exposure to toluene for people in the workplace. Toluene levels of 100 ppm are considered safe for workers. Levels of 150 ppm are acceptable for short periods (<8 h). Toluene levels of 2000 ppm are considered dangerous to life and health. However, some people may be more sensitive to the effects of inhaled solvents than others ***(Anundi et al ., 2000) .***

Occupational asthma has occurred in some workers exposed to toluene levels considered safe in the workplace. For such people, protective equipment should be used and provided by employers, even when toluene levels are in the acceptable range ***(Dykewicz , 2009) .***

Toxicokinetics of Toluene:

Absorption:

Inhalation is the primary route of toluene exposure; however, toluene can be absorbed through ingestion and dermal contact. Peak blood concentrations occur 15 to 30 minutes after inhalation. The amount of toluene absorbed by inhalation depends on the respiratory minute volume; thus, exercise affects the absorption

rate of toluene. At rest, the lungs absorb about 50% of an inhaled dose ***(Bowen et al., 2007) .***

After oral intake , the rate of absorption is slower than after inhalation. Nevertheless, gastrointestinal absorption is nearly complete, and blood toluene levels reach peak 1 to 2 hours after ingestion. Percutaneous absorption is slow through intact skin and rarely produces toxicity ***(Lammers et al., 2005).***

Distribution:

Toluene is lipophilic and has little water solubility. It is distributed quickly to highly perfused tissues such as brain, liver, and kidney. It passes readily through cellular membranes and accumulates primarily in adipose and other tissues with high fat content ***(Darracq et al., 2009) .***

In the body, the half-life of toluene ranges from several minutes in highly vascular organs to slightly over 1 hour in fatty tissue. Toluene's affinity for the lipid-rich structures of nervous tissue results in CNS toxic effects within minutes ***(Gerasimov et al., 2002) .***

Metabolism and Excretion:

The toxicity of toluene can be explained mostly by its metabolism. About 80 % of absorbed toluene is oxidized in the liver. The methyl group of toluene is more easily oxidized by cytochrome P450 enzyme than the benzene ring. Therefore, in the metabolism of toluene, 95% is oxidized to become benzyl alcohol. The toxic metabolites are created by the remaining 5% that are oxidized to benzaldehyde and cresols. Most of the reactive products are detoxified by conjugation to glutathione but the remainder may severely damage cells ***(Campo et al., 2006) .***

Toluene is mainly excreted in urine as benzoic acid and hippuric acid , both formed by further metabolic oxidation of benzyl alcohol. A small amount (7 - 20 %) is eliminated as free toluene in the expired air. Less than 2 % of total toluene metabolites are excreted in bile ***(Bolt et al., 2003) .***

Toxic effects of Toluene:

The toxic effects of toluene depend on the concentration, duration and route of exposure (inhalation, ingestion or dermal) ***(Brouette and Anton , 2001) .*** These toxic effects include neurological, respiratory, cardiovascular, hepatic, renal, immune,

endocrinal, reproductive and developmental effects. By far, the nervous system appears to be most sensitive to its toxic effects ***(Waldner and Clark , 2009) .***

Central Nervous System Effects:

The central nervous system is the main target organ in cases of toluene-induced toxicity; therefore dysfunction of the central nervous system is a critical human health effect following acute, subchronic or chronic exposure to toluene ***(Kang et al., 2005) .***

Toluene's anesthetic action can result in rapid CNS depression and narcosis at high concentrations. Volatilization after ingestion and hypoxia after aspiration can contribute to CNS toxicity, and aromatic impurities in commercial toluene-containing products can have additive neurotoxic effects ***(Lubman et al., 2008)*** .

Several studies have examined the neuropsychiatric effects of acute exposure to toluene vapors; cerebellar and CNS integrative dysfunction predominate. Manifestations include euphoria, dizziness, headache, confusion, hallucinations, ataxia, tinnitus, peripheral neuropathy, optic neuropathy, stupor and coma ***(Win-Shwe et al., 2007) .***