

## **Formaldehyde: A Review Of Occurrence, Chemical Characteristics, Exposures, Metabolism, Kinetics And Health Effects In Man And Animals**

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### **Abstract**

Formaldehyde is present in man (as a metabolite), food, land, atmosphere, water, clothing, building materials, consumer products (preservatives, tobacco/ cigarettes, shoe care agents, body and hair lotions etc). It is the most common aldehyde in the air. It has high solubility in polar solvents and readily reactive. It is easily photo-oxidized under sunlight. Sources of exposures to man and animal include, inhalation, ingestion and occupational which is the major source of exposure. Formaldehyde is readily metabolized after ingestion. It is absorbed from the respiratory tract on inhalation, but it is poorly absorbed following dermal exposure. Acute inhalation result in irritation and burning of the mucous membranes of the nose, mouth and upper respiratory tract. Arising from occupational exposure, through vapours, a temporary reversible decrease in lung function results. Ocular exposure to formaldehyde could result in permanent alterations to vision or blindness. At concentrations below maternal toxicity, formaldehyde is considered not to be a reproductive or developmental toxicant. Sufficient evidences are now available for the carcinogenicity of formaldehyde in both humans and animals. The International Agency for Research on cancer has classified formaldehyde as a group 1 carcinogen. Scarce information which is not within the reach of the larger population is only available in the developing countries like Nigeria relating to the sources of exposure to formaldehyde and its numerous health hazards. It was against the above background that this review

was initiated to guide the populace in general and those prone to occupational exposure in particular. Additionally, to stimulate research into the unexplored areas relating to formaldehyde so as to generate the data bank on this subject.

**Key words:** Formaldehyde, Occurrence, Chemical characteristics, Exposure, Metabolism, Humans and Animals.

### **Introduction**

Formaldehyde is found generally in the environment and also as a by-product of many natural reactions. For example, it is emitted as gas during biomass combustion (forest and bush burning) [1-3]. Other sources of formaldehyde includes: most living organisms where it is present in low concentrations as a metabolic intermediate [4, 5], anthropogenic sources [6-10]. Formaldehyde is also formed in the troposphere [4, 11].

Exposure sources to humans include: the major source which is from occupational exposure, from finished products like adhesives [12, 4 and 13]; emissions from the combustion of wood, tobacco and automobile emission [12, 4 and 13].

Inhalation of vapour, dermal contact and ingestion are major routes of occupational exposure to formaldehyde [12, 4 and 13]. Apart from being an air pollutant, formaldehyde is a corrosive substance which causes irritation and burns to the skin when in contact [12, 13]. Formaldehyde has been classed as a carcinogenic substance in man and animals [14].

Formaldehyde dehydrogenase is the enzyme that catalyzes the metabolic process of formaldehyde in man to the formation of formate which is excreted as formic acid or exhaled as carbon dioxide [12, 4 and 13]. Though formaldehyde has been classed as a Group 1 carcinogen, it is not considered to be a reproductive or developmental toxicant [4, 13 and 14].

The international group of experts like the United Nations Environment Programme, the international labour organization and the World Health Organization have continuously provided and updated their information/ publications on the management of chemicals in relation to human health and the environment. It was against this background that this review was motivated. To provide an insight on the occurrence, chemical characteristics, exposure, metabolism, toxicity, carcinogenic, health effects and the uses of formaldehyde.

### **Occurrence**

Researchers have identified the various sources of occurrence of formaldehyde which include: the combustion of biomass or organic materials, natural and anthropogenic sources; the atmosphere (air); food; and water etc. The concentration of formaldehyde from the above sources varies [13, 14].

### **Natural sources**

The occurrence of formaldehyde in the natural environment and as product of many natural processes or reactions have been reported. For example, during the combustion of biomass, formaldehyde is released [1, 2]. Beside this source, formaldehyde is also released as a metabolic intermediate at low concentrations in most living organisms [4, 15] and formed by irradiation of humic substances by sunlight [15].

### **Anthropogenic sources**

Several anthropogenic sources of formaldehyde have been detected and reported. These include direct sources such as fuel combustion, industrial on-site uses and off-gassing from building materials and consumer products. For example, combustion of fuels from wood to plastic, furnances, agricultural burns, waste incinerators, cigarette smoking and the cooking of food [7, 8,16-19 and 4].

### **Secondary formation**

Evidences are already available for the formation of formaldehyde in the troposphere by the photochemical oxidation process on many types of organic such as methane [4, 11]. Natural occurring compounds and pollutants from mobile and stationary sources have also served in the production of formaldehyde by the above process [20-27].

### **Drinking water**

Formaldehyde is found in water but at a low concentration level of 0.1mg/litre, except for accidental contamination which could be higher [28].

### **Food**

The occurrence of formaldehyde in natural foods has been detected. Fumigation has also resulted in accidental contamination of foods e.g. grains cooking (as a combustion product) [4].

In nature, formaldehyde is found in a variety of foodstuffs [4, 5]. Several workers have reported on the natural components of formaldehyde in foods. 60mg/kg concentration of formaldehyde has been reported in foods and some fruits [29, 30] and marine fish [31-32]. Although higher concentrations of formaldehyde have been detected in fruits and vegetable juices (800mg.kg) it is not clear if these elevated levels were due to processing [33]. Concentrations of up 267mg/kg have been reported in the outer layer of smoked ham [34]. In a variety of alcoholic beverages concentrations ranging from 0.04 to 1.7mg/litre in Japan [35] and from 0.02 to 3.8mg/litre in Brazil [36] have been reported. In the United States of America, concentration of 3.4 and 4.5kg/kg in brewed coffee and 10 to 16mg/kg in instant coffee have been reported [37].

**Identification and chemical characteristics**

Other names of formaldehyde (CH<sub>2</sub>O) include: methylene oxide, methanol, oxymethylene, methylaldehyde, oxomethane and formic aldehyde [3]. It is a colourless gas with pungent, irritating odour at room temperature. It is highly reactive, readily undergoes polymerization, is highly flammable and can form explosive mixtures in air. It decomposes at temperatures above 150<sup>0</sup>C. It is readily soluble in water, alcohols and other polar solvents. In aqueous solutions, formaldehyde hydrates and polymerizes and can exist in methylene glycol, polyoxymethane, and hemiformals [3]. Solutions with high concentration (> 30%) of formaldehyde become turbid as the polymer precipitates [4]. When formaldehyde is photo-oxidized in sunlight, carbon dioxide results. In the absence of nitrogen dioxide, the half life of formaldehyde is approximately 50 minutes during the daytime; in the presence of nitrogen dioxide, this drops to 35minutes [4].

**Consumer products**

Various concentrations of formaldehyde and its derivatives have been detected in a wide variety of consumer products meant to protect them as preservative [38]. Reports from researchers have implicated some preservatives as formaldehyde releasers [39]. The release of formaldehyde from such product is dependent on temperature and pH when they decomposed.

Tobacco products contain formaldehyde in their smoke both mainstream and side stream, which have been determined by several workers based on cigarettes from several countries [40]. Further investigation by other workers indicated that side stream smoke contain higher levels of formaldehyde than the mainstream smoke [41].

Household products like cleaning agents, dish washing liquids, fabric softeners, shoe care agents, car shampoos and waxes, carpet cleaning agents etc and cosmetics have been reported to contain different levels of concentrations of formaldehyde [4, 42] being part of the components in their industrial preparations. Additionally, formaldehyde serves as an antimicrobial agent in several products like, hair lotions (e.g. suntan lotion and dry skin lotion) makeup and mouthwashes, hand cream, bath products, mascara and eye makeup, cuticle softeners, nail creams, vaginal deodorants and shaving cream [4, 12].

**Clothing and fabrics**

Clothing and fabrics have been identified to contain varied concentrations of formaldehyde. For example, reports by workers have indicated that approximately 100 – 200µg free formaldehyde/g are contained by textiles made in the USA [43]. Moist baby toilet tissues also contain formaldehyde [44].

**Building materials**

Majority of building materials e.g. pressed wood products (particle board, medium-density fireboard, and hardwood) have been identified as one of the positive sources

of indoor emission of formaldehyde and sources of residential contamination [45, 46]. It has been recognized that the release of formaldehyde is highest from newly made wood products. Thus, the emission would decrease over time, to very low rates, after some years [45]. Additionally, it has been identified that the concentrations of formaldehyde released from pressed wood materials is greater in mobile homes compared to conventional houses. These observations resulted from the fact that mobile homes have minimal ventilation, minimally insulated and are often situated in exposed sites subjected to temperature extremes [47].

### **Kinetics and metabolism in laboratory animal and man**

In vivo, formaldehyde is formed during the metabolism of amino acids and Xenobiotic, as a metabolite, which may be bound (reversibly) to macromolecules. In short, this results during the oxidative DE methylation of xenobiotic and can be detected in the liver [5]. Due to the spontaneous reaction of formaldehyde with primary and secondary amines, thiols, hydroxyls and amides, methyl derivate are formed. When formaldehyde is absorbed it is oxidized to formate in the presence of formaldehyde dehydrogenase, along three different pathways, and it could be exhaled as carbon dioxide, or incorporated into biological macromolecules via tetrahydrofolate – dependent one-carbon biosynthetic pathways [5]. Evidences have been provided showing that the exposure of humans, monkeys or rats to formaldehyde by inhalation does not alter the concentration of endogenous formaldehyde in the blood, which is about 2-3mg/litre for each of the three species [5]. Arising from the reactivity of formaldehyde with biological macromolecules, when it is inhaled it is deposited and absorbed around the upper respiratory tract with which the substance first come into contact [48-50]. Additionally, at the point of contact and on absorption it has been recognized that formaldehyde produces intra and intermolecular crosslinks within proteins and nucleic acids [51]. Several enzymes that are widely distributed are involved in the rapid metabolism of formaldehyde to formate. The most important of these cellular enzymes is the  $\text{NAD}^+$  - dependent formaldehyde dehydrogenase. Formate, which is one of the products of metabolism of formaldehyde, is excreted through the urine [52, 48 and 53-56].

### **Health effects**

The effects on man depend on the duration of exposure and amount of concentration. Evidences from studies are available to show that formaldehyde is toxic by inhalation and ingestion. The general toxicity of the chemical indicates that it is a severe irritant to skin, eyes, skin, mouth, nose and upper respiratory tract [12, 4 and 13-14]. Case reports and clinical studies have shown that deaths following acute inhalation exposures to formaldehyde were not identified [3]. However, ulceration and damage along the aerodigestive tract, including oral and gastrointestinal mucosa have been recognized where formaldehyde had been ingested [57, 58 and 4]. Several workers have reported on cases of systemic (e.g. Anaphylaxis) and contact dermatitis (localized) allergic reactions arising from formaldehyde (or resins which contain

formaldehyde) used for household and personal care and dental products, clothing and textiles, bank note paper and medical treatments and devices [59- 64]. Additionally, other clinical studies/reports have indicated generally mild to moderate sensory eye, nose and throat irritation as exemplified by the exposure of volunteers to 0.25ppm (0.030mg/m<sup>3</sup>) formaldehyde [65]. In the cases of sufferers from asthma and in health individuals that were exposed to concentrations of formaldehyde up to 3.0ppm (3.6mg/m<sup>3</sup>) no significant clinical detrimental effect upon lung function was observed [65].

Genotoxicity, carcinogenicity and dermal/ocular effects of formaldehyde on man have been reported by several workers. Skin irritation or allergic contact dermatitis has been observed during repeated or prolonged dermal exposure to splashes of solutions containing formaldehyde [4]. Evidences are available which suggest that formaldehyde may be genotoxic in humans. Increased DNA-Protein cross-links have been observed in occupational workers who were exposed to formaldehyde, while this effect was absent in non exposed subjects [12, 14]. Significant increases in chromosomal aberrations and chromosomal breakage were observed in another group of workers exposed to formaldehyde compared to the unexposed controlled group. However there were no evidences to show any differences between the sister chromalid exchange and scheduled DNA synthesis and repair in the same study [12]. Sufficient evidence for the carcinogenicity of formaldehyde in humans has been evaluated and reported by the International Agency for Research on Cancer (IAPC) and thus classified the substance as a group 1 carcinogen [14]. For example, nasopharyngeal cancers caused by formaldehyde have been reported [14].

However, limited evidences are available to support the fact that formaldehyde causes sinonasal cancer in humans based on epidemiological studies [14]. Currently there are limited and/or scarce studies on the reproductive and developmental toxicity of formaldehyde. However, one of the few studies have revealed an increased incidence of menstrual disorders, anaemia, toxemia and low birth weight of offspring in female workers to urea-formaldehyde [4]. On the other hand, another report has indicated that formaldehyde is not expected to cause reproductive or developmental toxicity at exposure below maternally toxic doses [14].

### **Animal and in-vitro studies**

The effects of formaldehyde on some species of animals have been reported by numerous authors and World Bodies. In studies involving the exposure of mice to high concentrations of formaldehyde by inhalation, a marked reduction in body weight, labored breathing, listlessness, hunched posture and loss of coordination were observed [13].

Male and female Wister rats showed a significant reduction in body weight compared to the controls when exposed to formaldehyde in drinking water. The reduction in body weight resulted from the drop or reduction in food in-take [12, 13].

Epidermal hyperplasia and cutaneous ulcers were observed in hairless mice dermally exposed to 0.2ml (100%) formaldehyde, 2times per week for a period of

60weeks. The genotoxicity of formaldehyde in animals have been reported [4, 13-14 and 69]. Based on the genotoxic potentials of formaldehyde as evident from results of both in-vitro and in-vivo studies, formaldehyde is regarded as mutagenic at the site of contact [13-14].

The Carcinogenicity of formaldehyde has been demonstrated in several studies involving rats by inhalation [14]. Additionally, the carcinogenicity of formaldehyde has also been observed in rats exposed to formaldehyde in drinking water [14]. Currently, sufficient evidences are available to conclude that formaldehyde is carcinogenic in experimental animals [14].

Evidences from the application of does below those causing significant maternal toxicity have indicated that formaldehyde is not reproductive or developmental toxicant [4, 13-14].

### **Conclusion**

Formaldehyde is found in the total environment (air, soil and water) food, man (as a metabolite), and consumer products etc. It is highly soluble in polar solvents. Sources of exposure include by contact, inhalation and ingestion. On inhalation, it is readily absorbed from the respiratory tract and from the gastrointestinal tract during ingestion. Formaldehyde is poorly absorbed following dermal exposure. Various effects and disorders results on exposure to formaldehyde, depending on time and concentration of exposure. Formaldehyde has been classified as a human carcinogen. Formaldehyde is mutagenic at the site of contact. Additionally, formaldehyde is not a reproductive or developmental toxicant. It has varieties of uses in science, industry and medicine. Researches are underway to determine and generate data for formaldehyde in harvested rain waters in parts of the country and consumable products due to scarce literature on this subject.

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