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A REVIEW ON TOXIC EFFECT OF FORMALIN ON HUMANS

Lirin Mary M. K.*[1], Nipu Sam P. George[2] and Kavya R.[3]

[1]Assistant Professor, Department of Pharmaceutical Chemistry, K V M College of Pharmacy, Cherthala.
[2]Assistant Professor, Department of Pharmaceutics, K V M College of Pharmacy, Cherthala.
[3]Student, K V M College of Pharmacy, Cherthala.

***Corresponding Author: Prof. Lirin Mary M. K.**

Assistant Professor, Department of Pharmaceutical Chemistry, K V M College of Pharmacy, Cherthala.

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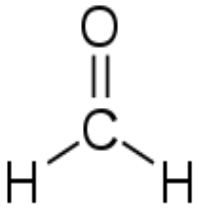
ABSTRACT

Formaldehyde is colourless, highly flammable gas which is commercially available as 30-50% aqueous solution. It is highly reactive; readily under goes polymerization and other self-oxidation reactions. They are soluble in water, alcohols and other polar solvents. According to International Agency for Research on Cancer they classify formaldehyde as a carcinogen in humans. Formaldehyde is a good preserving agent. So they may be used in different consumer products and food products to prevent spoilage by microbial contamination. Increased concentration of formaldehyde in consumer products and food products like fish may affects the human body and causes serious health problems like cough, nose and eye irritation, headache irreversibly changes to brain cancer. And also they produce genetic effects in buccal or nasal mucosal cells and in lymphocytes peripheral. In order to decrease the consumption of formalin adulterated fish we can use formalin detection kit. The main advantage of formalin detection kit is the simple and economical, and can be performed by consumers itself, detects the contaminants within few minutes. Formaldehyde adulterated fish can be noticed by its physical appearance blackened gills, eyes become whitish or opaque and the muscles lost their tenderness.

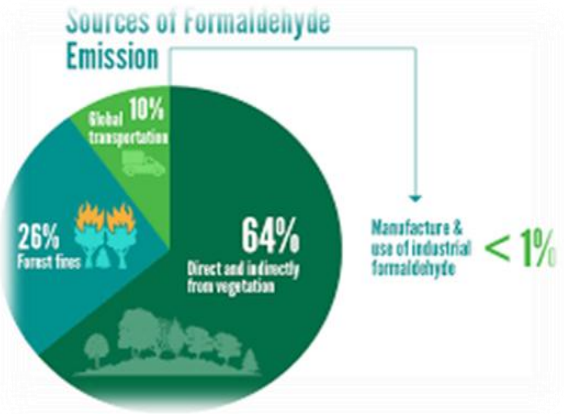
KEYWORDS: Formaldehyde, Fish, Consumer products, Formalin detection kit.

INTRODUCTION

Formaldehyde is a colourless, highly flammable gas that is sold commercially as 30–50% (by weight) aqueous solutions. Formaldehyde enters the environment from natural sources (including forest fires) and from direct human sources, such as auto-motive and other fuel combustion and industrial onsite uses.



Secondary formation also occurs, by oxidation of natural and anthropogenic organic compounds present in air. The highest concentrations measured in the environment occur near anthropogenic sources; these are of prime concern for the exposure of humans and other biota. Releases from industrial processes are considerably less. Industrial uses of formaldehyde include the production of resins and fertilizers. When formaldehyde is released to or formed in air, most of it degrades, and a very small amount moves into water. When formaldehyde is released into water, it does not move into other media but is broken down.

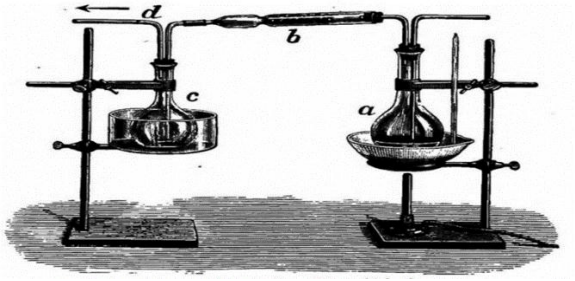


Formaldehyde does not persist in the environment, but its continuous release and formation result in long-term exposure near sources of release and formation. Based on available data, the highest concentration of formaldehyde occurring naturally in foods are in some fruits and marine fish. Formaldehyde may also be present in food due to its use as a bacteriostatic agent in production and its addition to animal feed to improve handling characteristics. Formaldehyde and formaldehyde

derivatives are also present in a wide variety of consumer products to protect the products from spoilage by microbial contamination. Since formaldehyde (also a product of intermediary metabolism) is water soluble, highly reactive with biological macro-molecules, and rapidly metabolized, adverse effects resulting from exposure are observed primarily in those tissues or organs with which formaldehyde first comes into contact (i.e., and aerodigestive tract, including oral and gastrointestinal mucosa, following inhalation or ingestion respectively). Dermal exposure to concentrations of formaldehyde, in solution, in the vicinity of 1–2% (10,000–20,000 mg/litre) is likely to cause skin irritation; however, in hypersensitive individuals, contact dermatitis can occur following exposure to formaldehyde at concentrations as low as 0.003% (30 mg/litre). Following inhalation in laboratory animals, formaldehyde causes degenerative, non-neoplastic effects in mice and monkeys and nasal tumours in rats.[1]

SYNTHESIS OF FORMALDEHYDE

A flask **(a)** which contains about 50ml of methyl alcohol is stoppered with two holes stopper. Through one hole a glass tube reaches the bottom of the flask with methanol and through the second a bent glass tube connects the flask with the short cm combustion tube ***(b)***.



Combustion tube ***(b)*** contains in the centre a loose plug of platinized asbestos, which is kept in position by a short roll of copper gauze (how to prepared catalyst is already described in the post – preparation of platinized asbestos). The open end of combustion tube ***(b)*** is attached, by a bent tube dipping to the bottom of the flask ***(c)***, which is cooled in ice-water. A second tube ***(d)***, which terminates below the stopper, is joined to a water-jet aspirator. The flask ***(a)***, containing methanol, is warmed to about 40°C, and a rapid current of air aspirated through the apparatus. The platinized asbestos is then heated until it begins to glow, after which the glowing will continue so long as the air current is sufficiently rapid for the oxidation of methanol to formaldehyde. The liquid which condenses in the flask ***(c)*** is a strong solution of formaldehyde in methanol.

IDENTITY AND PHYSICAL/CHEMICAL PROPERTIES

Formaldehyde (CH_2O) is also known as methanal, methylene oxide, oxy methylene, methyl aldehyde, oxomethane and formic aldehyde. At room temperature, formaldehyde is a colourless gas with a pungent, irritating odour. It is highly reactive, readily under goes polymerization, is highly flammable and at temperatures above 150°C. Formaldehyde is readily soluble in water, alcohols, and other polar solvents. In aqueous solutions, formaldehyde hydrates and polymerizes and can exist as methylene glycol, poly oxymethylene, and hemi-formals. Solutions with high concentrations of formaldehyde become turbid as the polymer precipitates. As a reactive aldehyde, formaldehyde can undergo a number of self-association reactions, and it can associate with water to form a variety of chemical species with properties different from those of the pure monomolecular substance. These associations tend to be most prevalent at high concentrations of formaldehyde; hence, data on properties at high concentrations are not relevant to dilute conditions.[2]

PROPERTY	RANGE OF REPORTED VALUES
Relative molecular mass	30.03
Melting point (°C)	118 -92
Boiling point (°C, at 101.3 kPa)	121 – 19
Vapour pressure ((calculated) (Pa, at 25 °C)	516 000
Water solubility (mg/litre, at 25 °C)[c]	400 000 to 550 000
Henry's law constant (Pam3/mol, at 25 °C)	2.2 × 10–2 to 3.4 × 10–2
Log octanol/water partition coefficient (log K_{ow}	!0.75 - 0.35
Log organic carbon / water partition coefficient (log K_{oc})	0.75 - 1.57
Conversion factor	1 ppm = 1.2 mg/m3

ANALYTICAL METHODS

The most widely used methods for the detection of formaldehyde are based on spectrophotometry, but other methods, such as colorimetry, fluorimetry, high-performance liquid chromatography, polarography gas chromatography, infrared detection, and gas detector tubes, are also used. Organic and inorganic chemicals, such as sulphur dioxide and other aldehydes and amines, can interfere with these methods of detection.

The most sensitive of these methods is flow-injection, which has a detection limit of 9 ppm (0.011µg/m3).

Another commonly used method is high-performance liquid chromatography, which offers a detection limit of 0.0017 ppm (0.002 mg/m3) Gas detector tubes and infrared analysers are often used for monitoring workplace atmospheres and have a sensitivity of about 0.33–0.42 ppm (0.4–0.5mg/m3).[3]

GENERAL IDENTIFICATION TEST FOR FORMALDEHYDE

1. PYROGALLOL TEST

When an aqueous solution of formaldehyde is added to a freshly prepared solution of pyrogallol containing excess of concentrated HCL, white precipitate turning to pink is produced.

2. REMINI TEST

About 1ml of 1 percentage of phenylhydrazine and 1ml of freshly prepared solution of sodium nitroprusside are added to 5ml of dilute solution of formaldehyde are making the volume alkaline by adding excess of sodium hydroxide ,a indigo blue changes to green brown and finally red is produced.

3. SCHRYER TEST

To a dilute solution of formaldehyde is added 1ml of 1 percentage phenylhydrazine HCL and 1ml of 5 percentage potassium ferrocynate solution, followed by 5ml of concentrated HCL, pink to red colour is obtained.[4]

METHODS FOR THE ANALYSIS OF FORMALDEHYDE IN FOOD

1. Chromotropic Acid Test

Distil sample; add 1, 8-dihydroxynaphthalene-3, 6-disulphonic acid in sulphuric acid; purple colour indicates presence of formaldehyde.

2. Hehner – Fulton Test

Distil sample; add to cold sulphuric acid; add aldehyde free milk; add bromine hydrate solution; purplish-pink colour indicates presence of formaldehyde.[3]

ENVIRONMENTAL TRANSPORT AND DISTRIBUTION

Water

In water, formaldehyde is rapidly hydrated to form a glycol. Equilibrium favours the glycol less than 0.04% by weight of unhydrated formaldehyde is found in highly Concentrated solution.[5][6] In surface of water or ground water, formaldehyde can be bio-degraded. Incorporated into atmospheric water, formaldehyde or its hydrate can be oxidized.[7]

Food

Available data suggest that the highest concentrations of formaldehyde naturally occurring in foods are in some fruits and in marine fish.[8] While formaldehyde may be formed during the deterioration of fish flesh, high levels do not accumulate in the fish tissues, due to subsequent conversion of the formaldehyde formed to other chemical compounds.[9] However, formaldehyde accumulates during the frozen storage of some fish species, including cod, Pollack, and haddock.[10] Formaldehyde formed in fish reacts with protein and subsequently causes muscle toughness, which suggests that fish containing the highest levels of formaldehyde, may not be considered palatable as a human food source.[11]

Consumer Products

Formaldehyde and formaldehyde derivatives are present in a wide variety of consumer product to protect the products from spoilage by microbial contamination. Formaldehyde is used as a preservative in household cleaning agents, dishwashing liquids, fabric softener shoe care agents, car shampoos and waxes, carpet cleaning agents, etc. Formaldehyde industry in three principal areas: preservation of cosmetic products and raw materials against microbial contamination. Formaldehyde is used as antimicrobial agent in hair preparations, hand creams and lotions.[12]

EFFECTS ON LABORATORY MAMMALS AND *IN- VITRO* TEST SYSTEMS

Single Exposure

Reported LC_{50}s in rodents for the inhalation of formaldehyde ranges from 414 ppm to 820 ppm. For rats and guinea-pigs, oral LD_{50}s of 800 and 260 mg/kg body weight have been reported. Acute exposure of animals to elevated concentrations of inhaled formaldehyde produces dyspnoea, vomiting, hyper salivation, muscle spasms, and death.[13]

Long-Term Exposure and Carcinogenicity

The principal non-neoplastic effects in animals exposed to formaldehyde by inhalation are histopathological changes (e.g., squamous metaplasia, basal hyperplasia, and rhinitis) within the nasal cavity and upper respiratory tract. Most chronic inhalation toxicity studies have been conducted in rats, with the development of histopathological effects in the nasal cavity being observed at concentrations of formaldehyde of 2 ppm and higher.[14] The principal non-neoplastic effect in animals exposed orally to formaldehyde is the development of histopathological changes within the fore stomach and glandular stomach, with effects in rats at 82 mg/5kg body weight per day and above.[15]

Genotoxicity

A wide variety of end points have been assessed in *in vitro* assays of the genotoxicity of formaldehyde. Generally, the results of these studies have indicated that formaldehyde is genotoxic in both bacterial and mammalian cells *in vitro* (inducing both point and large-scale mutations). Formaldehyde induces mutations in *Salmonella typhimurium* and in *Escherichia coli*, with positive results obtained in the presence or absence of meta- bioactivation system.

EFFECTS ON HUMANS

1. Case Reports and Clinical Studies

Ulceration and Damage along the aerodigestive tract, including oral and gastrointestinal mucosa, have been observed in cases where formaldehyde had been ingested.[16] There are frequent reports on cases of systemic (e.g., anaphylaxis) or more often localized (e.g., contact dermatitis) allergic reactions attributed to the formaldehyde (or formaldehyde containing resins) present in house hold and personal care (and dental) products, clothing and textiles, and medical treatments and device. In a number of clinical studies, generally mild to moderate sensory eye, nose, and throat irritation was experienced by volunteers.[17]

2. EPIDEMIOLOGICAL STUDIES

Carcinogenicity

In most epidemiological studies, the potential association between exposure to formaldehyde and cancer of the respiratory tract has been examined. However, in some case control and cohort studies, increased risks of various non-respiratory tract cancers (e.g., multiple myeloma, non-Hodgkin's lymphoma, ocular melanoma, brain, connective tissue, pancreatic, leukemic, and lymphoid and haematopoietic, colon have occasionally been observed).

Genotoxicity

An increased incidence of micro nucleated buccal or nasal mucosal cells has been reported in some surveys of individuals occupationally exposed to formaldehyde. Evidence of genetic effects in peripheral lymphocytes from individuals exposed to formaldehyde vapour has also been reported in some studies, but not others.[18]

USE OF FORMALDEHYDE

Health Care Applications

Formaldehyde has a long history of safe use in the manufacture of vaccines, anti-infective drugs and hard gel capsules. For example, formaldehyde is used to inactivate viruses so they don't cause disease, such as the influenza virus in making the influenza vaccine.

Personal Care and Consumer Products

Formaldehyde-based chemistry is essential in the production of man and consumer items. These products may contain formaldehyde-releasing ingredients, which act as a preservative to kill microorganisms and prevent growth of bacteria and other pathogens, extending product shelf life.

Industrial Applications

Formaldehyde is a common precursor to more complex compounds and materials. In approximate order of decreasing consumption, products generated from formaldehyde include urea formaldehyde resin, melamine resin, phenol formaldehyde resin, poly-oxymethylene plastics, 1,4-butanediol, and methylene diphenyl diisocyanate.

The textile industry uses formaldehyde - based resins as finishers to make fabrics crease- resistant. Formaldehyde - based materials are keys to the manufacture of automobiles, and used to make components for the transmission, electrical system, engine block, door panels, axles and brake shoes. Formaldehyde is also a precursor to poly functional alcohols such as pentaerythritol, which is used to make paints and explosives.

DISCUSSION

Formalin in fish trading: an inefficient practice for sustaining fish quality

Storage period	Treated fish	Control fish
0 d	12.197 } 0.814a	0b
8 d	8.095 } 0.077a	0.067b
12 d	8.153 } 0.296a	0.070b
14 d	8.003 } 0.063a	0.066b

Mrigel carp, Cirrhinus mrigala, Hamilton, weighing between 50 to 55g (1.4 kg in total) were purchased. The fish were then separated in two different lots for analysis, i.e., ice stored fish with (treated) or without (control) formalin treatment. Fish from the treated group were treated with a 5% formalin solution for 30 min before ice storage. The fish specimens from the two lots were kept in separate ice boxes surrounded by crushed ice at a 1:1 fish to ice ratio. The boxes were stored in a refrigerator at 4°C. When required, the ice was renewed. Control and treated fish samples were taken for analysis on days 0, 8, 12, and 14 of ice storage.

The formalin content of the fish samples was determined with the spectrophotometric method, that is, fish muscle is extracted with TCA and absorbance was measured at 415 nm, and the formalin content was calculated from a standard curve.

In the control fish, the formalin concentration was almost negligible. The assessment of the organoleptic characteristics of the treated fish revealed that the gills had blackened, the eyes had become whitish a opaque, the muscles had lost tenderness, and the fish had stiffened. The quality assessment score of the control batch was significantly higher than that of the treated batch. The microbes in the fish were still lower than the amount specified for fish spoilage.

The study clearly shows that once added, formaldehyde content decreased but could not be fully removed from the samples. Nevertheless, the continuous ingestion of formaldehyde, even in low doses, in fish could be hazardous to the human body.[19]

Formalin treated fish marketing and its impact on public health

At first, the samples were washed with small quantity of water. Three drops washed-out water was taken in a test-tube using a dropper. Formalin detection kit in food developed by Bangladesh Council of Scientific and

Industrial Research (BCSIR) was used in this experiment. The kit contains three solutions (No. 1-3). Added 15 drops from solution No.1 in the test tube containing washed out water. After well stirring, the solution was allowed to wait for 30 seconds. Then 15 drops from solution No.2 were added in the same test-tube containing solution. After well stirring, the solution was also allowed to wait for 30 seconds. After then 15 drops from solution No.3 were added in the same test tube containing solution. After adding No.3 solution, if the colour of the solution changes into pink or red colour, the presence of formalin was ensured. On the other hand, if the colour of the solution remains unchanged, there is no formalin in the sample.

Findings revealed that majority of the consumers buy all types of fishes from open market place on 2days/weekly without checking out the presence of formalin before buying fishes. Consumers are not so concerned about checking out the presence of formalin. However, they observed absence of fly on displayed fish sample as well as freshness of eye and overall body appearance to avoid buying formalin treated fishes. Among the tested 180 fish samples, 25% were contaminated with formalin. Cough, bronchitis and headache were major perceived health hazards being suffered by the consumers.[20]

Toxic Effects of Formaldehyde on the Nervous System

Various animal experiments have conclusively shown FA to be a carcinogen in rats. In humans, FA exposure has been associated with cancers of the lung, nasopharynx and oropharynx, and nasal passages. Also prolonged or repeated exposure to FA may result in respiratory impairment. Rats exposed to FA at 2ppm developed benign nasal tumours and changes of the cell structure in the nose as well as inflamated mucous membrane of the nose. Structural changes in the epithelial cells in the human nose have also been observed.

Some persons have developed asthma or bronchitis following exposure to FA, most often as the result of an accidental spill involving a single exposure to a high concentration of FA. It is found in the environment as a result of natural processes and from man-made sources and it is widely used in industries and medical settings. Several symptoms might be manifested related to formaldehyde – exposure among which lethargy, decrease in motor activity, and loss of appetite is common. Formaldehyde resulted in minor headache to irreversible neurotoxicity and brain cancer. The neurotoxic effects produced by formaldehyde exposure are dependent on the concentration of formaldehyde and duration of exposure which is more pronounced in concentrated and increased duration of exposure. Acute exposure to low concentrations it leads to stimulation while in higher concentrations it acts as central nervous system depression.[21]

The Health Risk of Formaldehyde to Human Beings

Human studies have shown that chronic inhalation exposure to formaldehyde is associated with respiratory symptoms and eye, nose and throat irritation. On the other hand, the oral exposure to formaldehyde related to the induction of gastrointestinal tract ulcer.[16] There are also cases of systemic or localized allergic reaction attributed to the formaldehyde has been reported in clothing and textiles, medical treatment and household and personal care.[17,18] In clinical studies, eye, nose and throat irritation was experienced in volunteers that exposed to formaldehyde ranging from 0.25-3.0 ppm, eye, nose and throat irritation was experienced. Mucociliary clearance in the nasal cavity has been found to be reduced following exposure to 0.25 ppm formaldehyde in volunteers. In healthy volunteers as well as asthma patients, there was no clinical effect on lung function after exposure to formaldehyde up to 3.0 ppm for up to 3hrs. In genotoxicity studies, formaldehyde is considered to be a weak genetic toxicant at the first contact. Studies of genetic effects in buccal or nasal mucosal cells and in lymphocytes peripheral have been observed in individuals occupationally exposed to formaldehyde but in some studies, genetic effects of formaldehyde were not observed in lymphocytes peripheral. In some studies shows that formalin is carcinogenic in nature ie, formaldehyde was long considered as a potential human carcinogen based on experimental animal studies and limited evidence of human carcinogenicity. However, formaldehyde was classified as a human carcinogen (Group 1) by the *International Agency for Research on Cancer* (IARC) in June 2004 based on "sufficient epidemiological evidence that formaldehyde causes nasopharyngeal cancer in humans.[22]

Toxicity of Formalin and its Management

Formaldehyde is a physiological intermediary metabolite taking part of many biological processes on the body. It is constituent of many items of daily use, including foods. A number of reports have documented the toxic effect of FA exposure through different routes because it is absorbed from all surfaces of the body. An animal study shows that the FA is both carcinogenic and mutagenic in experimental study .Formalin is irritating, corrosive and absorbed from all surfaces of the body. Ingestion can lead to dangerous effect in body including GI tract, CVS, CNS and hepato-renal system causing GI haemorrhage, CV collapse, unconsciousness or convulsions. No specific antidote is available. Treatment of toxicity is supportive care of the various organ systems. Multidisciplinary approach is required for proper management.

Several studies reported that the formalin is toxic to humans. Presence of hazardous chemicals like formalin in fish may cause serious health problems to humans. Formaldehyde is a highly flammable, colourless gas with pungent and irritating odour and commercially available as 37% known as formalin which is used as disinfectant and preservatives in household products. Formalin has an ability to produce serious health hazards like cancers of the lung, eye irritation, bronchitis and cough to the population.

The concentrations of formaldehyde greater than 6.0 ppm (7.2 mg/m^3) can cause cancer. And also cause dangerous effect in body including GI tract, CVS, CNS and hepato-renal system causing GI haemorrhage, CV collapse, unconsciousness or convulsions.

CONCLUSION

India's domestic fish market is reported to be selling formaldehyde adulterated fishes, for long term preservation especially in markets located far away from landing centres or production sites. Such fishes when consumed are very harmful to human health and lead to health hazard. Cheaply available over the counter substances have attracted traders to use hazard chemicals like formaldehyde & formalin that are also added as preservatives for enhancing the shelf life. These can enter human body on ingestion or exposure while handling and cause serious health problems. On exposure it can cause eye irritation, respiratory tract irritation, larynx constraint, skin allergies, worsening of asthma. Now a day, to decrease the consumption of formalin containing fish we have to use Formaldehyde detection kit.

FORMALDEHYDE DETECTION KIT

- It is non destructive, simple and economical
- Saves time and fast interpretation
- Does not require huge quantity of toxic chemicals

FEATURES

- Can be performed by consumers and general public
- Simple, reliable and rapid
- Detects the contaminants within few minutes
- Visual Interpretation by colour change
- Visual –Test Kit for detection of formaldehyde on skin and dermal

layers of fish, shell fish and other seafoods.

HIMEDIA'S HIRAPID FORMAL TEST KIT (K137)

Step 1: Prepare Reagent before the test (Reagent should be used within 20 days of preparation).
Step 2: Take out the strip and rub on fish surface/ cut surface to wet the paper strip.
Step 3: Add one drop of Reagent F-2 on swabbed paper strip.
Step 4: Check for colour development within 2 minutes.

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