Acetaldehyde

Group I carcinogen

Previously there has been no medical solution for **acetaldehyde exposure.**

With **Acetium®**, it is now possible to prevent the effects of this carcinogenic substance.

BIOHIT HealthCare

Innovating for Health

What is acetaldehyde?

Acetaldehyde belongs to the large family of aldehydes. It is an aldehyde of acetic acid, with chemical formula C_2H_4O and structural formula CH_3CHO. Acetaldehyde is also known as ethanal, acetic acid aldehyde or ethyl aldehyde. As determined from these older names, acetaldehyde (ethyl aldehyde) is one of the key metabolites of ethanol (ethyl alcohol).

Acetaldehyde has a penetrating odor. It exists as either a gas or a colorless liquid. Its melting point is –123°C, boiling point 20,2°C, and density 0,78 g/cm^3 (water = 1,0 g/cm^3). This substance is highly flammable and its vapor-air mixture is explosive. Acetaldehyde is easily mixed with water, and the relative density of vapor is 1,5, i.e., it is heavier than air (air = 1), making it easily spreading e.g. along different surfaces (floor, ground) and potentially inflammable also at a distance from its origin. When in contact with air, acetaldehyde can form highly explosive peroxides. Acetaldehyde is extremely harmful for human health, and classified as Group I carcinogen (a substance causing cancer).

How is acetaldehyde formed and where does it exist?

Acetaldehyde is a commonly used and (in nature) widespread substance, with an apple-like odor. Acetaldehyde in human body is derived from three principal sources: 1) by in vivo synthesis in the liver, where it is rapidly metabolized into acetic acid and water; 2) acetaldehyde also exists in the saliva, produced by the microbial flora of the oral cavity and pharynx; 3) the third important source of acetaldehyde are numerous foodstuffs and alcoholic beverages.

Acetaldehyde is manufactured for industry several hundreds of thousands tons annually. It is particularly abundant in foodstuffs produced by fermentation, e.g., alcoholic beverages, acetate, dairy products, home-made beer and –cider, soy-based sauces. Because of its nice aroma, acetaldehyde is also used to improve the taste of yoghurts, candy, sweets, bakery, soft drinks, juices and alcoholic beverages among others. Another important source of acetaldehyde is tobacco smoke, which is too often neglected in this context.

What are the effects of acetaldehyde in human body?

Certain members of the normal microbial flora in the gastrointestinal tract (yeasts, bacteria), comprise the most important source of acetaldehyde exposure in human body. During swallow, microbes of the normal oral flora are continuously transported into the stomach, but if the latter is healthy, hydrochloric acid is capable of destroying all these microbes. Instead, among the subjects with mucosal atrophy of the stomach (atrophic gastritis), with disappearance of acid-producing cells, these microbes are capable of multiplying in the stomach mucosa. This situation is similar among subjects with prolonged use of acid suppressors, i.e., proton pump inhibitors (PPI) for dyspeptic symptoms.

These saliva-derived microbes in the stomach form acetaldehyde from alcohol by oxidation, or under specific circumstances, also by fermentation directly from sugars. This multiplication of microbes and the consequent increase in acetaldehyde concentration in an achlorhydric (acid-free) stomach following alcohol or sugar intake has been firmly documented in several clinical studies. In contrast to the liver, these microbes in the stomach and intestinal mucosa cannot adequately metabolize acetaldehyde to acetic acid and water, resulting in accumulation of large quantities of acetaldehyde in saliva, achlorhydric stomach and also in the lower gastrointestinal tract.

Acetaldehyde and alcohol

There is some evidence implicating that acetaldehyde in the brain is possibly involved in regulation of alcohol intake. It is also well established that genetic factors impact on alcohol metabolism and consequently the sensations linked with alcohol intake. Particularly, populations in East Asia are frequent bearers of a specific mutation in the key enzyme involved in aldehyde metabolism, i.e., aldehyde dehydrogenase-2 (ALDH2), resulting in a situation where acetaldehyde formed after alcohol intake is not normally degraded. In these subjects, high levels of acetaldehyde accumulate in the gastrointestinal tract, and they also have unpleasant sensations while drinking alcohol. European populations in turn are bearers of a mutation in alcohol dehydrogenase (ADH) enzyme. As a result of this specific mutation, alcohol is metabolized more rapidly to acetaldehyde, resulting in high levels of acetaldehyde in the saliva after alcohol intake. As will be discussed later, both these mutations also expose these people to many of the harmful effects of acetaldehyde in the body, including also a significantly increased risk of developing cancers.

Acetaldehyde and smoking

One important source of acetaldehyde is the tobacco smoke. In fact, acetaldehyde is the single most abundant carcinogenic substance in tobacco smoke, its concentrations exceeding those of formaldehyde by 15-fold. Acetaldehyde is a highly water-soluble substance, and because of this, also its concentrations in the saliva increase dramatically during the smoking. The cut-off for mutagenic levels of acetaldehyde is 100 µM (4,4 mg/l), and this is exceeded over two-fold by smoking. In case of concomitant alcohol intake, acetaldehyde concentration in the saliva will exceed this mutagenic level by over 3-fold. Even with these high concentrations in the saliva, acetaldehyde is not absorbed directly into the circulation, thus precluding the direct effects on central nervous system, in contrast to nicotine.

During smoking, nicotine is transported from the lung via circulation directly into the brains within 10 seconds. Brains do synthesize dopamine, an important neurotransmitter that impacts on our mood and desires. Thanks to this up-regulated dopamine, brains start expecting a regular dose of nicotine, and withdrawal symptoms develop if this usual nicotine dose remains undelivered. There is some recent evidence suggesting that acetaldehyde derived from tobacco smoke could worsen tobacco (nicotine) addiction, by indirectly reinforcing the effects of nicotine in the central nervous system. Acetaldehyde from tobacco smoke is known to form with biogenic amines, condensation products known as harmans. These are rapidly absorbed into blood circulation and transported into the brains, where they inhibit MAO (monoamine oxidase)-enzyme. The latter is needed to degrade dopamine, and as a consequence of MAO-inhibition by harmans, dopamine is not degraded, resulting in aggravation of nicotine addiction.

Why is acetaldehyde so dangerous to human health?

The most severe risk to human health is associated with acetaldehyde's capacity to induce malignant transformation of human cells, i.e., acetaldehyde is a carcinogenic substance. International Agency for Research on Cancer (IARC) declared in October 2009, that acetaldehyde present in alcoholic beverages or derived thereof in vivo is classified as Group I carcinogen, i.e., in the same class as the well known carcinogens like tobacco, benzene and asbestos.

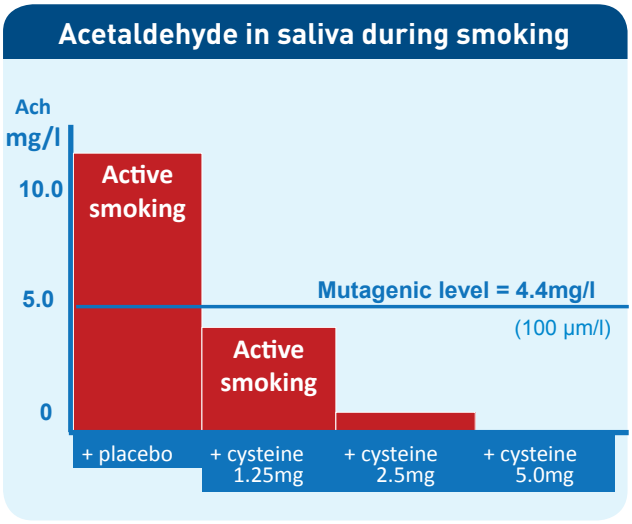
The associations of acetaldehyde with an increased risk of cancer are based on extensive scientific documentation, derived from both experimental (animal) studies and large clinical-epidemiological surveys on humans. Malignant tumors associated with acetaldehyde develop in those anatomic sites where acetaldehyde exposure is the most intense, i.e., in the upper gastrointestinal tract, upper respiratory tract (acetaldehyde is volatile) as well as in the esophagus and stomach. In addition to alcohol, the risk of upper gastrointestinal tract cancer is increased by smoking, poor oral hygiene, as well as the genetic factors affecting the alcohol and aldehyde metabolism (mutations in ALDH2 and ADH-enzymes). It is estimated that acetaldehyde exposure is associated with approximately 4 million new cancer cases annually worldwide, representing almost 40% of all cancers.

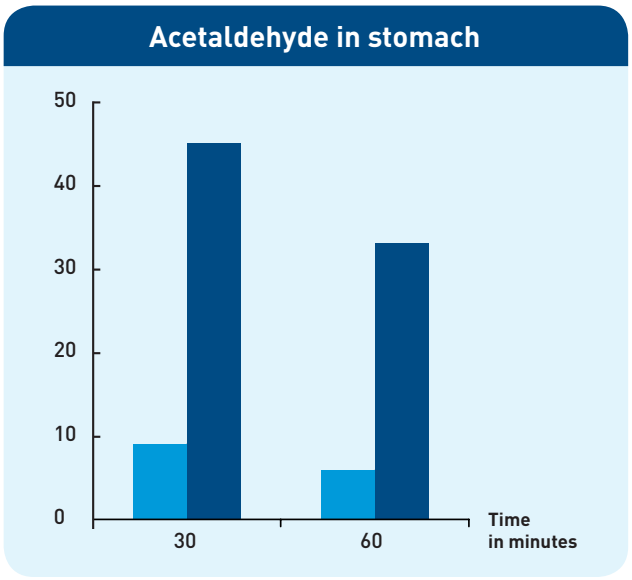
How can we reduce the health risks of acetaldehyde?

Given that acetaldehyde is a human carcinogen, one should avoid the exposure to it by all available means. In the prevention of any disease (or harm), the best option is the primary prevention, i.e., complete avoidance or marked reduction of exposure to the causative agent. At the level of an individual, a significant step toward this direction would be made by quitting alcohol intake and refrain from smoking. Because acetaldehyde is ubiquitous, however, and present is numerous foodstuffs, the exposure to it is impossible to completely avoid even with these measures. Because of this, the only realistic option is to reduce acetaldehyde exposure to the absolute minimum. Fortunately, a very simple and inexpensive means for this is currently available, which, in addition, is based on the exploitation of the characteristics of a natural amino acid (L-cysteine) using a completely novel approach.

It has been known for some decades that L-cysteine reacts covalently with acetaldehyde to form an inert and harmless compound, 2-methylthiatsolidne-4-carboxyl acid (MTCA) and by so doing reduces the concentration of acetaldehyde in the stomach (and in the saliva). L-cysteine is a natural (semi-essential) amino acid, and 1-2 g of it is obtained from the proteins of an average daily diet. It is also commonly used as a food additive (E920), approved by both EFSA (Europe) and FDA (US) as a GRS (Generally Regarded as Safe) compound.

Biohit Oyj has obtained extensive patents to cover various applications of L-cysteine for elimination of acetaldehyde in the stomach and in the saliva. The first-line product in this category is Acetium capsule, containing as an active substance, 100 mg of L-cysteine. In contrast to L-cysteine derived from the daily diet, L-cysteine in Acetium capsules is released at controlled speed into the stomach contents, and as free amino acid, L-cysteine is capable of binding acetaldehyde locally in the stomach. The crucial difference is that the diet-derived L-cysteine does not reduce acetaldehyde concentration in achlorhydric stomach, simply because the amino acids derived from the dietary proteins are liberated by the pancreatic enzymes only in the small intestines (duodenum) and rapidly absorbed into systemic circulation without any local effects in the stomach.
Second product is Acetium Lozenge which with help of L-cysteine effectively removes acetaldehyde dissolved into saliva during smoking. (please see the picture below)





Reference: Väkeväinen et al., ScandJGastroenterol 2002
Linderborg et al. 2009, http://research.med.helsinki.fi/esbra2009/Book of Abstracts (adapted)

Acetium® Lozenge
FOR SMOKERS

Effectively removes acetaldehyde from the saliva during smoking

Dosage: Let 1-2 tablets dissolve in the mouth during smoking.

Acetium® capsule
PROTECTS YOUR STOMACH

Acetium binds carcinogenic acetaldehyde in the stomach, if you have anacidic stomach, use anti-acid medication or have chronic *helicobacter pylori* infection

Dosage: 1-2 capsules just before every meal or drinking alcohol.

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