Acetaldehyde

Group I carcinogen (IARC 2009)

There has been no previous solution to reduce
acetaldehyde exposure

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What is acetaldehyde?

Acetaldehyde is one of the many aldehydes. It is an aldehyde of acetic acid, with chemical formula C2H4O and structural formula CH3CHO. As determined from its older names (ethanal, ethyl aldehyde), acetaldehyde 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/cm3 (water = 1,0 g/cm3). 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, making it easily spreading e.g. along different surfaces (floor, ground) and potentially inflammable also at a distance. Acetaldehyde is extremely harmful for human health, and classified as Group I carcinogen (a substance that causes cancer).

How is acetaldehyde formed and where does it exist?

Acetaldehyde is a widespread substance in nature, and commonly used because of its apple-like odor. In human body, acetaldehyde is derived from three principal sources: 1) in vivo synthesis by the liver, where it is rapidly metabolized into acetic acid and water; 2) in the saliva, acetaldehyde is produced by the microbial flora of the oro-pharynx; 3) acetaldehyde is present in numerous foodstuffs and alcoholic beverages.

Acetaldehyde is manufactured for industry in a large scale. 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 pleasant aroma, acetaldehyde is also used to improve the taste of e.g. yoghurts, candy, sweets, bakery, soft drinks, juices and alcoholic beverages. Another important source of acetaldehyde is tobacco smoke, although far too often neglected in this context.

What are the effects of acetaldehyde in human body?

Some species of the normal microbial flora (yeasts, bacteria) in the gastrointestinal tract comprise the most important source of acetaldehyde production in human body. With saliva, microbes of the normal oral flora are continuously transported into the stomach. In healthy stomach, however, hydrochloric acid is capable of destroying all these microbes. In the subjects with mucosal atrophy (atrophic gastritis), these microbes are capable of multiplying in the stomach mucosa. The same happens among chronic users of acid suppressive medication, i.e., proton pump inhibitors (PPI), to treat dyspeptic symptoms.

These saliva-derived microbes form acetaldehyde from alcohol by oxidation in the stomach, or under specific circumstances, also by fermentation directly from sugars. This colonization of microbes and the consequent increase in acetaldehyde concentration in an acid-free stomach following alcohol or sugar intake has been firmly documented in clinical studies. In contrast to the liver, these microbes in the stomach (or intestines) cannot effectively metabolize acetaldehyde to acetic acid, resulting in accumulation of large quantities of acetaldehyde in the saliva, in acid-free 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 affect alcohol metabolism and the subsequent 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 failure to convert acetaldehyde to acetic acid. In these subjects, high levels of acetaldehyde accumulate in the gastrointestinal tract, and they also have unpleasant sensations while drinking alcohol. In subjects with another (more rare) mutation in alcohol dehydrogenase (ADH) enzyme, alcohol is metabolized more rapidly to acetaldehyde, resulting in high levels of acetaldehyde in the saliva after alcohol intake. Both these mutations expose these people to many of the potentially harmful effects of acetaldehyde in the body.

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 concentration exceeding e.g. that of formaldehyde by 15-fold. Because acetaldehyde is a highly water-soluble substance, its concentration in the saliva increases rapidly while smoking. Thus, the mutagenic levels of acetaldehyde (100 µM; 4,4 mg/l) is exceeded over two-fold by smoking, and with concomitant alcohol intake, this level is exceeded by over 3-fold. Even with these high concentrations in the saliva, however, acetaldehyde is not absorbed directly into the circulation, thus precluding any direct effects on central nervous system.

Whether the same mechanism as found in experimental animals is responsible for acetaldehyde-enhanced nicotine addiction in human smokers remains to be established. In this respect, interesting results were reported in two recently conducted clinical trials (RCT), where elimination of cigarette smoke-derived acetaldehyde in the saliva by Acetium® lozenge proved to be an effective means to stop smoking. As compared with placebo, the likelihood of smoking quit had OR=1.51 (95%CI 1.12-2.02) among those who completed the study per protocol (PP arm). Those who did stop smoking reported that a) sensations of smoking were changed, and b) the level of pleasure obtained from smoking has dropped remarkably.

Why is acetaldehyde so dangerous to human health?

The most severe risk to human health is associated with the potential acetaldehyde-induced 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, in the same class as the well-known carcinogens like tobacco, benzene, asbestos and oncogenic human papillomaviruses.

The evidence on acetaldehyde and increased risk of cancer is based on convincing scientific documentation, derived from both experimental animal studies and large clinical/epidemiological surveys. Malignant tumors associated with acetaldehyde develop in those anatomic sites where acetaldehyde exposure is the most intense, i.e., in the upper gastrointestinal tract (oral mucosa, esophagus, stomach), and upper respiratory tract (acetaldehyde is volatile). 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).

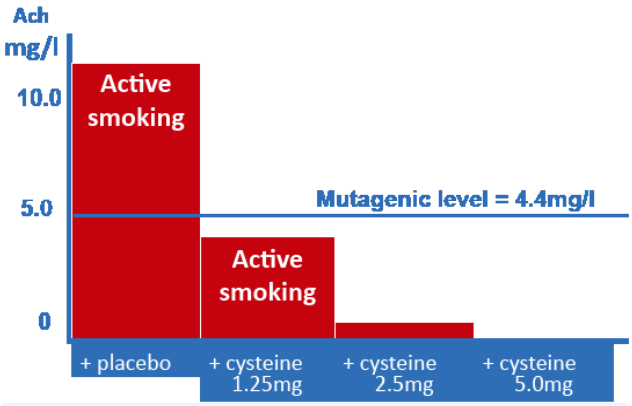
How can we control the health risks of acetaldehyde?

Given that acetaldehyde is a human carcinogen, one should avoid the exposure to it by all available means. In the prevention of any disease, the most optimal 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 to 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 avoid completely even with these measures. Because of this, the only feasible 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 unique formulation.

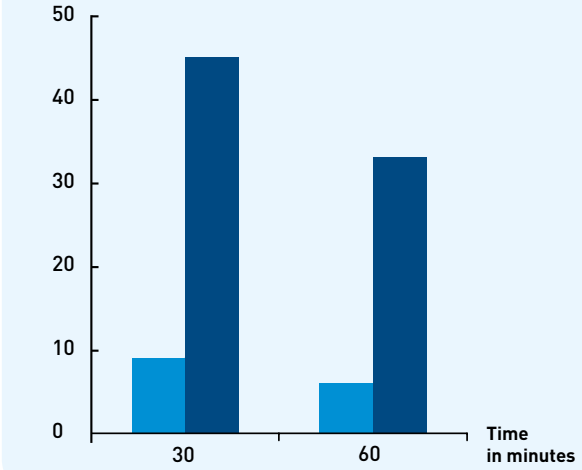
It was shown for some time ago that L-cysteine reacts covalently with acetaldehyde to form a harmless compound, 2-methylthiatsolidne-4-carboxyl acid (MTCA). Using this reaction, it is possible to reduce the concentration of acetaldehyde in the stomach (and in the saliva). L-cysteine is a natural (semi-essential) amino acid, with daily allowance of 1-2 g from an average 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 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. 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 bind acetaldehyde in the 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® containing 3mg of L-cysteine which effectively removes acetaldehyde dissolved into the saliva during smoking (refer to the graphs below).

Acetaldehyde in saliva during smoking



Acetaldehyde in stomach



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

Acetium® Lozenge

HELPS QUIT SMOKING - NICOTINE FREE

Acetium Lozenge can help quit smoking and can be used to alleviate tobacco dependence.

It is easy to use: Take one lozenge every time you smoke a cigarette.

Available in pharmacies and groceries

Acetium® Capsule

PROTECTS STOMACH

Binds acetaldehyde in stomach.

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

CE-marked capsules are available in pharmacies.

Acetium is manufactured in Finland.

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