Carcinogenic nitrosamines

From malt and cured foodstuffs to balloons and drugs

Definition

Nitrosamines are a class of organic chemical compounds containing an amino group and a nitroso group. The term is used mostly for nitroso-compounds of secondary amines. Most N-nitrosamines are regarded as genotoxic and carcinogenic in animal studies.

Formation and occurrence

Initial products in the formation of nitrosamines are nitrosating compounds such as nitrite and nitrosatable amines (see Figure 1) found in many areas of the human environment. Nitrosamines can be found, for example, in food, tobacco, cosmetics and consumer goods made of latex. Drugs can also contain nitrosamines as impurities. The N-nitrosamines routinely tested at Labor Veritas AG are listed in Table 1.

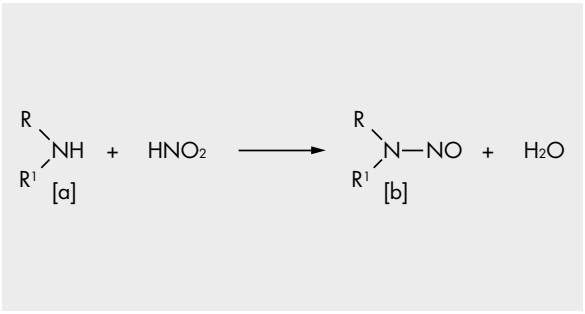

Figure 1: Formation of a nitrosamine [b] from a secondary amine [a]

Name	Short designation	CAS no.	Empirical formula
N-nitrosodibutylamine	NDBA	924-16-3	$C_8H_{18}N_2O$
N-nitrosodiethylamine	NDEA	55-18-5	$C_4H_{10}N_2O$
N-nitrosodiisopropylamine	NDIPA	601-77-4	$C_2H_{14}N_2O$
N-nitrosodimethylamine	NDMA	62-75-9	$C_2H_2N_2O$
N-nitrosodipropylamine	NDPA	621-64-7	$C_6H_{14}N_2O$
N-nitrosomethylethylamine	NMEA	10595-95-6	$C_3H_8N_2O$
N-nitrosomorpholine	NMOR	59-89-2	$C_4H_8H_2O_2$
N-nitrosopiperidine	NPIP	100-75-4	$C_5H_{10}N_2O$
N-nitrosopyrrolidine	NPYR	930-55-2	$C_4H_8N_2O$

Table 1: Nitrosamines routinely tested at Labor Veritas AG

In the 1980s, Switzerland introduced one of the world's most stringent limiting values of 0.5 µg/kg for volatile nitrosamines in beer. The dominant nitrosamine NDMA originates from malt. To comply with the limiting value for beer, NDMA values in malt should not exceed 2 µg/kg. Earlier, beer and malt coffee contained large amounts of nitrosamines. Technical modifications in the production of malt have now made it possible to greatly reduce concentrations. In addition to tobacco smoke, the main sources of nitrosamine today include spices, cured meats and smoked bacon, to which nitrite curing salt is added for the purpose of reddening and preservation. However, not all of these products generally contain nitrosamines.

Nitrosamine formation is also possible in the human organism itself («endogenous» contamination), because the environment as well as food contain nitrosatable amines and nitrosating substances. After transition from the product into human saliva or gastric juice, these substances can be converted into carcinogenic nitrosamines. Of interest in the case of products containing nitrosatable amines is the nitrosamine formation potential which is a measure of the corresponding endogenous contamination. Accordingly, for example, the nitrosation potential of drugs with secondary

amino groups is examined in the scope of regulatory approvals. Nitrosatable amines from elastomer or rubber parts are also endogenous contaminants; appropriate limits on their quantity are therefore imposed on feeding bottle-teats and soothers for infants and young children.

Nitrosamine analysis at Labor Veritas AG

Determination of nitrosamines has a long tradition at Labor Veritas AG. The employed analytical method of measurement has proven itself for a wide range of samples.

In addition to NDMA in foodstuffs and animal feed, requests for determining a release of nitrosamines and nitrosatable substances most frequently deal with bottle teats and soothers, elastomers, rubber (refer to DIN EN 12868) and balloons. Analysis of nitrosamines in water samples is also gaining in importance due to upgrading of wastewater treatment plants by means of an additional cleaning stage (ozonation).

Examination of nitrosamines in drugs and their raw materials is currently at the focus. Several hypotensive drugs containing the active ingredient Valsartan were recently recalled because individual batches were contaminated with the potentially carcinogenic N-nitrosodimethylamine (NDMA).

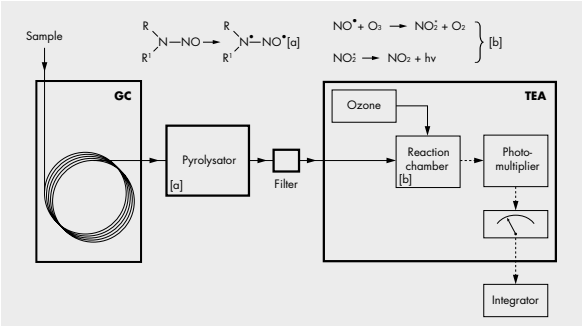

Figure 2: Principle of nitrosamine analysis using GC-TEA

Measuring principle

After sample preparation and extraction, the concentrated eluates are analyzed by means of GC-TEA (Figure 2). This involves separation of substances using gas chromatography, followed by combustion. In this process, nitrosamines form nitrogen radicals which react with ozone and thus emit light. This chemiluminescence is proportional to quantity, and therefore provides direct indications of the initial concentration of the nitrosamines.

Sample material	Determination limit	Required sample quantity
NDMA in malt	0.8 µg/kg	300 g
NDMA in spices and beer	0.2 µg/kg	100 ml
NDMA in animal feed	2 µg/kg	300 g
NDMA in milk powder for infants	2 µg/kg	100 g
N-nitrosamine in water (individual substances)	10 ng/l	1 l
N-nitrosamine in feeding bottle teats and soothers (cumulative)	10 µg/kg	30 g
N-nitrosatable materials in feeding bottle teats and soothers (cumulative)	100 µg/kg	30 g
N-nitrosamine in pharmaceutical products and raw materials	30 µg/kg	10 g

Table 2: Determination limits and sample quantities

Sample shipment

Samples can be shipped by regular mail. For cross-border shipping, a green customs slip CN22 must be affixed to the package, and its contents must be declared as samples of goods. The sample quantities listed in Table 2 are required to achieve the specified determination limits.

The price of analysis depends on the matrix, order volume, sample series and urgency. Labor Veritas AG will gladly submit an offer to you.

Contact persons

Service catalogue

Scan & Go: Download a QR-code reader from the App Store (iOS) or Play Store (Android), scan a code, and discover more.

Labor Veritas AG, Postfach, CH-8027 Zürich
Phone: 044 283 29 30, Fax: 044 201 42 49
admin@laborveritas.ch, www.laborveritas.ch

March 2019