Cancer Association of South Africa (CANSA)

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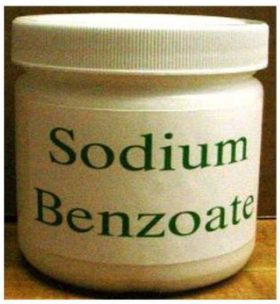
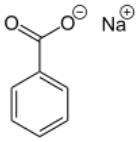
Fact Sheet
and Position Statement
on Sodium Benzoate and Vitamin C

Introduction

Sodium Benzoate has the chemical formula $NaC_7H_5O_2$. It is a widely used food preservative as it helps prevent yeast growth and bacteria formation, with an E Number of E211. It is the sodium salt of benzoic acid and exists in this form when dissolved in water. It can be produced by reacting sodium hydroxide with benzoic acid. Benzoic acid occurs naturally at low levels in cranberries, prunes, greengage plums, cinnamon, ripe cloves and apples.



[Picture Credit: Sodium Benzoate]



Sodium Benzoate preserves food by having anti-fungal properties, protecting foods from invasion by fungi that cause food to spoil and potentially making one sick. Sodium Benzoate works by entering the individual cells in the food and balancing its pH level, increasing the overall acidity of the food. By lowering the intracellular pH of certain foods, Sodium Benzoate creates an environment in which fungi cannot grow and spread.

Sodium benzoate is a preservative, with the E number E211. It is most widely used in acidic foods such as salad dressings (i.e. acetic acid in vinegar), carbonated drinks (carbonic acid), jams and fruit juices (citric acid), pickles (acetic acid), and condiments.

- E number: E211 (preservatives)
- CAS Number: 532-32-1
- RTECS number: DH6650000
- Chemical formula: $C_7H_5NaO_2$

Uses and Sources of Sodium Benzoate

Sodium Benzoate is used in the following:

<u>Industrial uses</u>

- Corrosion inhibitors and anti-scaling agents
- Paint additives and coating additives

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- Plating agents and surface treating agents
- Part of product formulation in solvents

Consumer uses

- Personal care products
- Foods and soft drinks
- Adhesives
- Sealants

[Picture Credit: Soft drinks]

- Agricultural products (non-pesticidal)
- Anti-freeze and de-icing products
- Automotive care products
- Cleaning and furnishing care products
- Laundry and dishwashing products
- Lubricants and greases
- Paints and coatings
- Plastic and rubber products

[Picture Credit: Foods]

Sodium Benzoate is used as a preservative to prevent food from moulding. In this form it is safe, however, scientists have shown that negative side-effects occur when it is mixed with Ascorbic Acid (vitamin C). Their studies indicate that it then turns into Benzene, a known carcinogen and DNA-damager.

Sodium Benzoate and Vitamin C

Claims have been made that when Sodium Benzoate is combined with Vitamin C (as in some soft drinks and other beverages), and exposed to elevated temperatures or light, the IARC Group 1 cancer-causing chemical, benzene, may be formed. The maximum benzene level of the Environmental Protection Agency (EPA) is set at 5 parts per billion (ppb), for drinking water, as a quality standard.
(Drugs.com).

Benzene in Soft Drinks

Several scientific investigations have been undertaken regarding the presence of benzene (a known cancer causing agent) in soft drinks in various countries. Some of the studies are summarised below:

Scientific Investigation 1:

Bonaccorsi, *et al*. (2012), conducted the following study in in Florence (Italy): The aim of this study was to determine the amount of benzene present in soft drinks sold in Florence (Italy). We analyzed 28 different types of soft drinks, by measuring concentrations of benzoic acid, sorbic acid, ascorbic acid (using high performance liquid chromatography with UV detection) and benzene (using gas chromatography and mass spectrometry). Data was analysed by using SPSS 18.0.Traces of benzene were detected in all analyzed beverages, with a mean concentration of 0.45 µg/L (range: 0.15-2.36 µg/L). Statistically significant differences in mean benzene concentrations were found

between beverages according to the type of additive indicated on the drink label, with higher concentrations found in beverages containing both ascorbic acid and sodium benzoate. Two citrus fruit-based drinks were found to have benzene levels above the European limit for benzene in drinking water of 1 µg /L. Sodium benzoate and ascorbic acid were also detected in the two drinks. In conclusion, not all soft drink producers have taken steps to eliminate benzoic acid from their soft drinks and thereby reduce the risk of formation of benzene, as recommended by the European Commission. Furthermore, the presence of benzene in trace amounts in all beverages suggests that migration of constituents of plastic packaging materials or air-borne contamination may be occurring.

Scientific Investigation 2:

The following are the findings of a study by Cao, *et al*. (2007) on the presence of benzene in Soft drinks: An automated, simple, and reproducible method was developed for the determination of benzene in soft drinks, based on isotope dilution headspace gas chromatography/mass spectrometry in the selected-ion monitoring mode. The method was used to assess benzene levels in samples of 124 soft drinks and beverages. Benzene was not detected in 60% of the 124 products. The average benzene levels in 6 products exceeded the Canadian maximum acceptable concentration of 5 microg/L for benzene in drinking water, and 2 of the 6 products had benzene levels above the World Health Organization guideline of 10 microg/L. The highest level of benzene, 23 microg/L, was found in a soft drink product specifically marketed to children.

Scientific Investigation 3:

During 2008 Nyman, *et al*., conducted a survey on the presence of benzene in soft drinks and reported as follows: Benzene, a carcinogen that can cause cancer in humans, may form at nanogram per gram levels in some beverages containing both benzoate salts and ascorbic or erythorbic acids. Through a series of reactions, a hydroxyl radical forms that can decarboxylate benzoate to form benzene. Elevated temperatures and light stimulate these reactions, while sugar and ethylenediaminetetraacetic acid (EDTA) can inhibit them. A headspace gas chromatography/mass spectrometry method for the determination of benzene in beverages was developed and validated. The method was used to conduct a survey of 199soft drinks and other beverages. The vast majority of beverages sampled contained either no detectable benzene or levels below the U.S. Environmental Protection Agency's drinking water limit of 5 ng/g. Beverages found to contain 5 ng/g benzene or more were reformulated by the manufacturers. The amount of benzene found in the reformulated beverages ranged from none detected to 1.1 ng/g.

Scientific Investigation 4:

A study by Van Poucke, *et al*., in 2008, provided the following: Whenever benzoic acid is combined with ascorbic acid in acidic beverages such as soft drinks, benzene can be formed. To determine the current situation on the Belgian market, a headspace gas chromatographic-mass spectrometric method was developed, which needs little to no sample preparation. This method was then used to analyze 134 soft drinks sampled on the Belgian market by the Federal Agency for the Safety of the Food Chain. Thirty-three percent of the samples contained no detectable benzene, whereas the majority of the samples (47%) contained trace amounts below the limit of quantification of the method (0.3 microg L (-1)). Ten samples were above the European limit for benzene in drinking water of 1 microg L (-1), and one sample had a concentration of 10.98 microg L (-1), thereby exceeding the action limit for benzene in soft drinks of 10 microg L (-1) discussed at the Standing Committee on the Food Chain and Animal Health of the European Commission. Statistical analyses revealed that besides

benzoic acid, ascorbic acid, and acidity regulators, the packing may also play an important role in benzene formation.

Side Effects of Sodium Benzoate

Sodium Benzoate can cause side effects. If any of the following side effects occur while taking or immediately after taking something which contains sodium benzoate / sodium phenylacetate, one should consult with one's doctor or nurse immediately:

More common side effects

- abdominal or stomach pain or cramps
- blurred vision
- decreased urine output
- dry mouth
- fatigue
- flushed, dry skin
- fruit-like breath odour
- increased hunger
- increased thirst
- increased urination
- irregular heartbeat
- loss of appetite
- muscle pain or cramps
- nausea or vomiting
- numbness or tingling in the hands, feet, or lips
- seizures
- shortness of breath
- sweating
- troubled breathing
- unusual tiredness or weakness

Less common side effects

- agitation
- anxiety
- bleeding, blistering, burning, coldness, discoloration of the skin, feeling of pressure, hives, infection, inflammation, itching, lumps, numbness, pain, rash, redness, scarring, soreness, stinging, swelling, tenderness, tingling, ulceration, or warmth at the injection site
- bloody or cloudy urine
- bloody, black, or tarry stools
- confusion
- coughing that sometimes produces a pink frothy sputum
- depression
- dizziness, faintness, or lightheadedness when getting up suddenly from a lying or sitting position
- drowsiness

- feeling, seeing, or hearing things that are not there
- headache
- muscle tremors
- nightmares or unusually vivid dreams
- rapid, deep breathing
- restlessness
- sleepiness or unusual drowsiness
- trouble with breathing when moving or walking
- unusual bleeding or bruising

Some Sodium Benzoate / Sodium Phenylacetate side effects may not need any medical attention. One's health care professional may be able to help prevent or reduce these side effects, but do check with them if any of the above side effects continue, or if there are concerns about them.

Lennerz, B., Vafai, S.B., Delaney, N.F., Clish, C.B., Deik, A.A., Pierce, K.A., Ludwig, D.S. & Mootha, V.K. 2015.
"Sodium benzoate is a widely used preservative found in many foods and soft drinks. It is metabolized within mitochondria to produce hippurate, which is then cleared by the kidneys. We previously reported that ingestion of sodium benzoate at the generally regarded as safe (GRAS) dose leads to a robust excursion in the plasma hippurate level [1]. Since previous reports demonstrated adverse effects of benzoate and hippurate on glucose homeostasis in cells and in animal models, we hypothesized that benzoate might represent a widespread and underappreciated diabetogenic dietary exposure in humans. Here, we evaluated whether acute exposure to GRAS levels of sodium benzoate alters insulin and glucose homeostasis through a randomized, controlled, cross-over study of 14 overweight subjects. Serial blood samples were collected following an oral glucose challenge, in the presence or absence of sodium benzoate. Outcome measurements included glucose, insulin, glucagon, as well as temporal mass spectrometry-based metabolic profiles. We did not find a statistically significant effect of an acute oral exposure to sodium benzoate on glucose homeostasis. Of the 146 metabolites targeted, four changed significantly in response to benzoate, including the expected rise in benzoate and hippurate. In addition, anthranilic acid, a tryptophan metabolite, exhibited a robust rise, while acetylglycine dropped. Although our study shows that GRAS doses of benzoate do not have an acute, adverse effect on glucose homeostasis, future studies will be necessary to explore the metabolic impact of chronic benzoate exposure."

Pongsayee, M. 2015**.**
"Sodium benzoate is food preservative that inhibits microbial growth. The effects of sodium benzoate preservative on micronucleus induction, chromosome break, and Ala40Thr superoxide dismutase gene mutation in lymphocytes were studied. Sodium benzoate concentrations of 0.5, 1.0, 1.5, and 2.0 mg/mL were treated in lymphocyte cell line for 24 and 48 hrs, respectively. Micronucleus test, standard chromosome culture technique, PCR, and automated sequencing technique were done to detect micronucleus, chromosome break, and gene mutation. The results showed that, at 24- and 48-hour. incubation time, sodium benzoate concentrations of 1.0, 1.5, and 2.0 mg/mL increased micronucleus formation when comparing with the control group ($P < 0.05$). At 24- and 48-hour. incubation time, sodium benzoate concentrations of 2.0 mg/mL increased chromosome break when comparing with the control group ($P < 0.05$). Sodium benzoate did not cause Ala40Thr (GCG→ACG) in superoxide dismutase gene. Sodium benzoate had the mutagenic and cytotoxic toxicity in lymphocytes caused by micronucleus formation and chromosome break."

Benzene
Benzene has been classified as a carcinogen (Group 1) by the International Agency for Research on Cancer (IARC) and is a "known" human carcinogen by all routes of exposure.

Human exposure to benzene has been associated with a range of acute and long-term adverse health effects and diseases, including cancer and aplastic anaemia. Benzene causes acute myeloid leukaemia (acute non-lymphocytic leukaemia), and there is limited evidence that benzene may also cause acute and chronic lymphocytic leukaemia, non-Hodgkin's lymphoma and multiple myeloma. Exposure can occur occupationally and domestically as a result of the ubiquitous use of benzene-containing petroleum products, including motor fuels and solvents. Active and passive exposure to tobacco smoke is also a significant source of exposure. Public health actions are needed to reduce the exposure of both workers and the general population to benzene.
(World Health Organization).

World Health Organization (WHO) Benzene Guidelines

Drinking-water
0.1mg/l (guideline values corresponding to the upper 95% confidence limit of modelled excess lifetime cancer risks of 10−4, 10−5 and 10−6 are 0.1, 0.01 and 0.001 mg/l, respectively).
An excess lifetime cancer risk of 10−4, 10−5 or 10−6 means the risk of one new cancer case above background levels per 10 000, 100 000 or 1 million people, respectively.

Air
No specific guideline value has been developed for air. Benzene is carcinogenic to humans, and no safe level of exposure can be recommended. For general guidance, the concentrations of airborne benzene associated with an excess lifetime risk of leukaemia of 10−4 , 10−5 and 10−6 are 17, 1.7 and 0.17 $\mu g/m^3$, respectively.
(World Health Organization; Environmental Protection Agency).

Sodium Benzoate and Vitamin C in South African Soft Drinks
CANSA is aware that Sodium Benzoate is ubiquitous and that it is used in a variety of settings including a variety of foods, soft drinks and personal care products. Exposure to Sodium Benzoate may, therefore, be difficult to control.

CANSA resolved to test Vitamin C containing soft drinks that are available in South Africa which also contains the preservative 'Sodium Benzoate' to determine whether any benzene could be isolated from them. Soft drinks (all brands) which, according to their labels, contained citrus (Vitamin C) and Sodium Benzoate were bought at different stores in Gauteng. The samples were all subjected to testing at an independent reputable chemical laboratory in the Western Cape.

Every single sample tested negative for benzene. CANSA can, therefore, confirm that all citrus drinks (those potentially containing Vitamin C) and the preservative Sodium Benzoate which were tested were found to be safe for consumption.

CANSA, however, wishes to confirm that:

- The labels of all products should be checked to ensure that cognisance is taken of the possible inclusion of the preservative, Sodium Benzoate, in the formulation so that informed decisions can be taken
- Because of the many varied side effects of Sodium Benzoate, children should be minimally exposed to it
- Any adverse reaction or side effect following the ingestion of Sodium Benzoate should be reported immediately to one's health care professional

Medical Disclaimer

This Fact Sheet and Position Statement is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet and Position Statement. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet and Position Statement.

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