Biotech Health Sci. 2016 August; 3(3):e35084. doi: 10.17795/bhs-35084.

Published online 2016 May 25. **Review Article**

An Overview on the Effects of Sodium Benzoate as a Preservative in Food Products

Mojtaba Shahmohammadi,[1] Maryam Javadi,[1,2] and Marjan Nassiri-Asl[3,*]

[1]Department of Nutrition, School of Health, Qazvin University of Medical Sciences, Qazvin, IR Iran
[2]Children Growth Research Center, Qazvin University of Medical Sciences, Qazvin, IR Iran
[3]Department of Pharmacology, Qazvin University of Medical Sciences, Qazvin, IR Iran

[*]*Corresponding author*: Marjan Nassiri-Asl, Department of Pharmacology, Qazvin University of Medical Sciences, Qazvin, IR Iran. Tel: +98-2833336001, Fax: +98-2833324970, E-mail: mnassiriasl@qums.ac.ir

Received 2015 December 15; **Revised** 2016 February 02; **Accepted** 2016 February 24.

Abstract

Context: Food spoilage has been a common problem throughout history, and much of the spoilage is caused the activity of microorganisms or enzymatic reactions during the storage of food. Thus, using chemical substances could prevent or delay food spoilage and this has led to the great success of these compounds in the treatment of human diseases. Sodium benzoate is one of the synthetic additives that are widely used in the food industry.

Evidence Acquisition: In this review we summarized the history and role of benzoate sodium in the food industry, its limited value in different food, other uses, pharmacokinetics, and its toxicity in animal studies. A literature search was carried out using MEDLINE, Scopus, Science Direct, and Scientific Information Databases (SID).

Results: Sodium benzoate is used in different industries as well as the food industry and it has adverse effects similar to other food additives.

Conclusions: Studies on natural ingredients in foods to find compounds with similar effects as benzoate with less adverse effects is necessary.

Keywords: Sodium Benzoate, Preservative, Food Safety, Spoilage

1. Context

The availability and consumption of safe food, which supplies the body's needs is essential for the human. Food and its active constituents have a significant effect on human health and nutrition. Food safety is not a new concept in the modern world and is deeply rooted in the history of human civilization. In developed countries, the issue was raised after world war II. Food spoilage has been a common problem throughout history, and much of the spoilage is due to the activity of microorganisms or enzymatic reactions during the storage of food. Using food preservation methods has been common both naturally and chemically since the past 1000 to 8,000 years (1, 2). It has been estimated that approximately one third of the population of developed countries suffer from diseases transmitted through food. More than 250 microbial, physical and chemical factors are responsible for these diseases. In 2011, the Center of disease control in America estimated that 128 thousand people are hospitalized due to diseases transmitted through food and three thousand die annually (3).

Using chemical substances to prevent or delay food spoilage is partly due to the great success of these compounds in the treatment of diseases in humans, animals and plants. Although a large number of chemical compounds are effective food preservatives, yet because of strict laws on food safety that have been adopted by the FDA and to a lower extent due to the fact that, in vitro, all compounds show antimicrobial effects, adding these compounds to some food products has no effect and only a few of them are permitted for use in food products (1, 3).

Nowadays, processed foods make up 75 percent of the diet of western societies (4). Sodium benzoate is one of the synthetic additives that are widely used in the food industry and is generally recognized as safe (GRAS). Sodium benzoate is a salt of benzoic acid, which is used as an important preservative in the food industry against bacteria, fungi and yeast with the natural pH of 4.5. Also, this substance can be used in pharmaceutical and cosmetics industries (5, 6).

Although sodium benzoic is in the category of safe additives, yet the disadvantages of synthetic preservatives such as sodium benzoate on human health has been pre-

viously indicated (7, 8). In the recent decades, the use of additives has increased, so that it has been estimated that each individual consumes about 8 - 10 lbs of food additives annually (3, 4, 8).

The increasing use of synthetic additives in food and consumers' desire to consume fast and processed foods on one hand and the adverse effects of many of these chemical additives on the other hand, indicate the need to focus on their benefit and adverse effects. Thus, the aim of this study was to summarize the important pharmacological, toxic effects, application, and pharmacokinetic of sodium benzoate as an important additive in the food industry.

2. Evidence Acquisition

Data was collected from well-known databases including MEDLINE, Scopus, Science Direct, and Scientific Information Databases (SID). The keywords for the search were: sodium benzoate and benzoic acid. A total of 46 articles (from 80 articles) and two books were selected for this review. There was no limitation in the selection of the year of publication.

3. Results

3.1. Effects of Sodium Benzoate

Sodium benzoate is salt of benzoic acid found with the chemical formula $C_7H_5NaO_2$, and is a white salt, odorless in crystalline, and found as powder or grain. This compound is dissolved easily in water but is hardly dissolved in ethanol. Its molecular weight is 114.11 and its solubility is enhanced by increasing water temperature. Ninety-nine percent of this compound is dry and the amount of benzoic acid is 84.7% and is specified in food products by E-211. Its harmlessness was confirmed first in 1909 by the department of agriculture in America, during three separate investigations; a summary report entitled No. 88 was published (1-3, 9). This study reported that benzoate has no adverse effect on health and also has no destructive effect on the quality or nutritional value of food products (10).

Benzoic acid is found in small quantities in plums, tomatoes, cinnamon, cloves and apple. Benzoic acid is formed in fermented dairy products by lactic acid bacteria, although anaerobic processes such as metabolism of phenol can interfere in the formation of benzoic acid in cheese (4). Although benzoic acid is the most effective preservative, yet salt is used in it to dissolve easily in water, as it does not dissolve well in water. Sodium benzoate was the first preservative allowed by the FDA for use in food products. Antimicrobial activity of benzoate is related to pH, so that most of its activity occurs at low pH. Its antimicrobial activity is due to the intact molecule. These compounds are ineffective in neutral pH. The pKa of benzoate is equivalent to 4.2 and at pH of 4, where 60% of this compound has not been separated, while at pH equal to 6 only 1.5% is not separated. For this reason, the use of benzoic acid and its sodium salt is not limited to products with high-acidity; this acidity is usually enough to prevent the growth of bacteria in food products. However, some mold and yeast are grown in acidic environments, and benzoate acts as an effective deterrent force against mold and yeast. Note that inhibition of this substance, if added at the beginning of the production process can stop the enzyme activity. The use of sodium benzoate is not recommended in foods that are corrupting (10).

In food products such as fruit juice, benzoate at concentrations up to 1% causes undesirable flavor, this taste is called pepperoni or hot (1, 11, 12). Sodium benzoate is used orally (eating and drinking food and beverages) and through skin (use of benzoate in cosmetics, sanitary and pharmaceutical) of the consumer's body (13).

The world's production of benzoic acid is 638,000 tons annually and the available sodium benzoate around the globe is 100,000 tons. Seventy percent of this amount of sodium benzoate can be used as a preservative (5, 14). The joint committee of the world health organization and food and agriculture organization of the United Nations on food additives (JECFA) reported a limit on the amount of sodium benzoate, which was 0 - 5 mg/kg (15, 16). In Europe, this amount is 0.015 to 0.5% and in America and Iran this amount is 0.1% (17, 18).

Sodium benzoate is used mainly as a preservative in margarine, salad dressings, marinades, cider, soft drinks, pickles, fruit salad, wafers, bakery products, jams, jellies, juices, biscuits, cakes and muffins, tomato paste and soy sauce (1, 2, 4, 5, 10, 12, 16, 19-22). Sodium benzoate has been reported to be used in various cheeses and in some caviar (14, 22). There are also reports on the use this substance in wine and beer (23, 24) and olives (25). Sodium benzoate is detectable in foods in the laboratory by a spectrophotometer at a wavelength of 224 nm (25-27).

Sodium benzoate is used in the pharmaceutical industry in syrups, in containers used for preparation of liquids, to prepare tablets, and at 0.2 to 0.4% to make tablets transparent and smooth and to allow rapid decomposition of the tablets. The maximum concentration of sodium benzoate used in the pharmaceutical industry is 5% and is also used in cosmetics products (1, 21, 28).

3.2. Pharmacokinetics of Sodium Benzoate

Metabolizing this compound by living organisms can ultimately make an active compound that reacts with DNA,

changes the genetic structure of cells and has adverse effects on cell division (21, 23, 29, 30). Sodium benzoate in the mitochondria of liver cells is metabolized by binding to the amino acid glycine and excreted as hippuric acid from the urine. Natural excretion of hippuric acid in urine is approximately 1 - 2 mL and 400 - 800 mg of glycine is excreted as hippuric acid in the urine, daily (23, 31).

Food consumption containing sodium benzoate increases this amount (32, 33). Glycine excretion from the body indicates impaired function of the liver in metabolic processes in which glycine is essential. In addition, low glycine levels in the body can reduce creatinine levels, glutamine, urea and uric acid in the urine and increases the levels of these substances in the blood. Hydrogen and hydrophobic bonds are vital in binding sodium benzoate to the amino acid glycine and it should be noted that the limited sodium benzoate in foods is enough for this bond (34-37). In a study conducted during year 2012 on 3083 Belgian consumers, it was concluded that these people use 1.25 mg/kg of sodium benzoate daily and this amount is 0.25% of the acceptable daily limit and is enough to bind with 50 mg of glycine and excreted as hippuric acid (23).

After entrance of sodium benzoate to the body, the intestinal cycle occurs, and sodium benzoate binds to trypsin and can increase the activity and result in the restructure of trypsin. Trypsin is released from the pancreas and has an important role in the digestion of food products. However, this has not been fully proven and requires further studies and research (38).

3.3. Toxicity

Although sodium benzoate is accepted as a safe substance, but short-term exposure can cause irritation of eyes, skin and respiratory tract, yet prolonged or repeated contact may cause high skin sensitization (39). Using high doses causes release of histamine and prostaglandin, ulcers and gastric mucus secretion changes (40, 41).

In a study conducted during year 2007, sodium benzoate increased blood pressure, eventually tearing the vessels in the blood cells of the rat (42). Damage to the hepatocyte cell membrane and crista losses in mitochondria, connection to outer shell of vacuole mitochondria in the cytoplasm and liver and kidney dysfunction are other adverse effects of consuming sodium benzoate (43). Research has also shown the formation of benzene in the reaction between benzoic acid and ascorbic acid in the presence of metal catalysts in soft drinks and fruit juices (44).

In a study by Afshar et al. on mice, 560 mg/kg concentration of sodium benzoate reduced weight and crown-rump length of the fetus when compared with the control group and fetal absorption rate was statistically significant at concentrations of 280 and 560 mg (21). In a study by Sohrabi et al. on mice, sodium benzoate at a concentration of 560 mg/kg reduced the weight of the ovaries and FSH and LH hormones compared to the control group and decreased progesterone hormone at a concentration of 280 mg compared with the control group (19).

Another study showed that sodium benzoate at concentration of 200 mg/kg can decrease weight in mice and increase creatinine, urea and uric acid in the isolated serum from mice (36). Fujitani et al. in a study on rats and mice showed that at a concentration of 2.4%, the average weight of the rats was reduced compared to the control group; weight gain in kidney and liver occurred at a concentration of 2.4% in rats and liver and kidney weight increased when compared with the control group at 3% concentration in the mice (22).

Taheri et al. investigated the effect of sodium benzoate, at concentrations of 9.3 and 18.6 mM/kg, on the fetus of pregnant rats and found that, both concentrations can cause a significant reduction in weight and height and also reduce the weight and diameter of placenta in the fetus compared to the control group (45). Eberechukwu et al. investigated the effect of benzoate sodium in rats and concluded that sodium benzoate could reduce white blood cells at concentrations of 60 and 120 mg/kg and the amount of hemoglobin at all concentrations compared to the control group and this decrease make their white blood cells more susceptible to infection (42).

Yilmaz et al. investigated the effect of benzoate sodium on human cell lymphocytes at concentrations of 200 and 500 μg/mL. Benzoic acid increased indices of sister chromatid exchanges (SCEs), chromosomal aberration (CA), and Micronucleus (MN) and at a concentration of 500 μg/mL decreased the mitotic division index (Mitotic index) (46). Hu et al. studied lymph node cells isolated from mice treated with different concentrations of sodium benzoate compared to control cells and found that sodium benzoate can change the structure of lymphocytes and damage the cell membrane. Higher concentration and time exposure to this substance increases the adverse effects (47).

4. Conclusions

Sodium benzoate, as a synthetic additive, is widely used in food, pharmaceutical and cosmetics industries. The disadvantages of sodium benzoate have been approved on human health, which include cell damage. In the recent years, many studies have been done on the use of natural ingredients with different goals in foods and have achieved some success, but there is still a need to study and research in the food industry.

Footnote

Authors' Contribution: Mojtaba Shahmohammadi and Marjan Nassiri-Asl wrote the paper. Marjan Nassiri-Asl and Maryam Javadi designed the manuscript. Supervision of the study was done by Marjan Nassiri-Asl and Maryam Javadi.

References

1. Jay JM, Loessner MJ, Golden DA. Modern food microbiology. New York: Springer Science; 2005.
2. Turkoglu S. Genotoxicity of five food preservatives tested on root tips of Allium cepa L. *Mutat Res.* 2007;**626**(1-2):4–14. doi: 10.1016/j.mrgentox.2006.07.006. [PubMed: 17005441].
3. Makwana S, Choudhary R, Dogra N, Kohli P, Haddock J. Nanoencapsulation and immobilization of cinnamaldehyde for developing antimicrobial food packaging material. *LWT-Food Sci Technol.* 2014;**57**(2):470–6. doi: 10.1016/j.lwt.2014.01.043.
4. Zengin N, Yuzbasioglu D, Unal F, Yilmaz S, Aksoy H. The evaluation of the genotoxicity of two food preservatives: sodium benzoate and potassium benzoate. *Food Chem Toxicol.* 2011;**49**(4):763–9. doi: 10.1016/j.fct.2010.11.040. [PubMed: 21130826].
5. Hong H, Liang X, Liu D. Assessment of benzoic acid levels in milk in china. *Food Control.* 2009;**20**(4):414–8. doi: 10.1016/j.foodcont.2008.07.013.
6. Williams RE, Lock EA. Sodium benzoate attenuates D-serine induced nephrotoxicity in the rat. *Toxicology.* 2005;**207**(1):35–48. doi: 10.1016/j.tox.2004.08.008. [PubMed: 15590120].
7. Yolmeh M, Najafi MBH, Farhoosh R, Salehi F. Modeling of antibacterial activity of annatto dye on escherichia coli in mayonnaise. *Food Biosci.* 2014;**8**:8–13. doi: 10.1016/j.fbio.2014.09.001.
8. Mamur S, Yuzbasioglu D, Unal F, Yilmaz S. Does potassium sorbate induce genotoxic or mutagenic effects in lymphocytes?. *Toxicol In Vitro.* 2010;**24**(3):790–4. doi: 10.1016/j.tiv.2009.12.021. [PubMed: 20036729].
9. Nair B. Final report on the safety assessment of Benzyl Alcohol, Benzoic Acid, and Sodium Benzoate. *Int J Toxicol.* 2001;**20 Suppl 3**:23–50. [PubMed: 11766131].
10. Stanojevic D, Comic L, Stefanovic O, Solujic-Sukdolak S. Antimicrobial effects of sodium benzoate, sodium nitrite and potassium sorbate and their synergistic action in vitro. *Bulg J Agric Sci J.* 2009;**15**(4):307–11.
11. Khayatzadeh J, Afshar M, Moallem SA, Shahsavan M, Naseh GH. Effect of potassium benzoate on BALB/c mice placenta: A histopathological study. *J Gorgan Uni Med Sci.* 2011;**13**(1):8–15.
12. Safari R, Saeidi AM. The effect of nisin A and sodium benzoate on behavior of listeria monosytogenes and some microbial and chemical parameters in silver carp (hypophtalmichtys molitrix) fillet stored at 4 ° c. *J Food Hygiene.* 2011;**1**(3):9–13.
13. Mirshekari S, Moeini S, Bahri A, Safari R, Saeidi Asl M. Effect of Bacteriocine Z And Sodium Benzoate on Shelf-Life of Caspian Roach (Rutilus Frisii Kutum) Fillet. *J Food Sci Technol.* 2010;**2**(1):19–27.
14. European Commission . Scientific Committee on Consumer Products (SCCP): Opinion on benzoic acid and Sodium Benzoate. European Commission; 2005.
15. Mpountoukas P, Vantarakis A, Sivridis E, Lialiaris T. Cytogenetic study in cultured human lymphocytes treated with three commonly used preservatives. *Food Chem Toxicol.* 2008;**46**(7):2390–3. doi: 10.1016/j.fct.2008.03.021. [PubMed: 18467014].
16. Zhang G, Ma Y. Spectroscopic studies on the interaction of sodium benzoate, a food preservative, with calf thymus DNA. *Food Chem.* 2013;**141**(1):41–7. doi: 10.1016/j.foodchem.2013.02.122. [PubMed: 23768324].
17. Heydaryinia A, Veissi M, Sadadi A. A comparative study of the effects of the two preservatives, sodium benzoate and potassium sorbate on aspergillus niger and penicillium notatum. *Jundishapur J Microbiol.* 2011;**4**(4):301–7.
18. Lennerz BS, Vafai SB, Delaney NF, Clish CB, Deik AA, Pierce KA, et al. Effects of sodium benzoate, a widely used food preservative, on glucose homeostasis and metabolic profiles in humans. *Mol Genet Metab.* 2015;**114**(1):73–9. doi: 10.1016/j.ymgme.2014.11.010. [PubMed: 25497115].
19. Sohrabi D, Rahnama M, Shams AM, Fakheri F. The effects of sodium benzoate (c6h5coona) on ovaries and its hormones and gonadotropins on female balb/c mice. *J Shahrekord Univ Med Sci.* 2007;**9**(3):67–70.
20. Yılmaz S, Unal F, Aksoy H, Yuzbasıoglu D, Celik M. Cytogenetic effects of citric acid and benzoic acid on allium chromosomes. *Fresen Environ Bull.* 2008;**17**:1029–37.
21. Afshar M, Moallem SA, Taheri MH, Shahsavan M, Sukhtanloo F, Salehi F. Effect of long term consumption of sodium benzoat before and during pregnancy on growth indexes of fetal balb/c mice. *Mod Care J.* 2013;**9**(3):173–80.
22. Fujitani T. Short-term effect of sodium benzoate in F344 rats and B6C3F1 mice. *Toxicol Lett.* 1993;**69**(2):171–9. [PubMed: 8212059].
23. Beyoglu D, Idle JR. The glycine deportation system and its pharmacological consequences. *Pharmacol Ther.* 2012;**135**(2):151–67. doi: 10.1016/j.pharmthera.2012.05.003. [PubMed: 22584143].
24. Vernole P, Caporossi D, Tedeschi B, Porfirio B, Melino G, Bonmassar E, et al. Cytogenetic effects of 1-p-(3-methyltriazeno) benzoic acid potassium salt on human lymphocytes in vitro. *Mutat Res Genet Toxicol.* 1987;**189**(3):349–56.
25. El-Ziney MG. GC-MS analysis of benzoate and sorbate in saudi dairy and food products with estimation of daily exposure. *J Food Technol.* 2009;**7**(4):127–34.
26. Huang X, Wang Y, Hou H, Zhang Z, Liu W. [Determination of caffeine and sodium benzoate contents in caffeine and sodium benzoate injection by P-matrix method]. *Guang Pu Xue Yu Guang Pu Fen Xi.* 1997;**17**(2):119–22. [PubMed: 15810401].
27. Somya KV, Ravishankar K, Basha DP, Kiranmayi GVN. Estimation of caffeine and sodiun benzoate in caffeine and sodium benzoate injection by isoabsorption method (isobestic method). *Int J Pharm Chem Biol Sci.* 2011;**1**(1):26–31.
28. Tsay HJ, Wang YH, Chen WL, Huang MY, Chen YH. Treatment with sodium benzoate leads to malformation of zebrafish larvae. *Neurotoxicol Teratol.* 2007;**29**(5):562–9. doi: 10.1016/j.ntt.2007.05.001. [PubMed: 17644306].
29. Toth B. Lack of tumorigenicity of sodium benzoate in mice. *Fundam Appl Toxicol.* 1984;**4**(3 Pt 1):494–6. [PubMed: 6745539].
30. Oyanagi K, Kuniya Y, Nagao M, Tsuchiyama A, Nakao T. Cytotoxicities of sodium benzoate in primary culture of hepatocytes from adult rat liver. *Tohoku J Exp Med.* 1987;**152**(1):47–51. [PubMed: 2887046].
31. Gonzalez KC, Sagebin FR, Oliveira PG, Glock L, Thiesen FV. [A retrospective study analysis of urinary hippuric acid levels in occupational toxicology exams]. *Cien Saude Colet.* 2010;**15 Suppl 1**:1637–41. [PubMed: 20640325].
32. Ogawa M, Suzuki Y, Endo Y, Kawamoto T, Kayama F. Influence of coffee intake on urinary hippuric acid concentration. *Ind Health.* 2011;**49**(2):195–202. [PubMed: 21173531].
33. Penner N, Ramanathan R, Zgoda-Pols J, Chowdhury S. Quantitative determination of hippuric and benzoic acids in urine by LC-MS/MS using surrogate standards. *J Pharm Biomed Anal.* 2010;**52**(4):534–43. doi: 10.1016/j.jpba.2010.01.016. [PubMed: 20149566].
34. Oyewole OI, Dere FA, Okoro OE. Sodium benzoate mediated hepatorenal toxicity in wistar rat: Modulatory effects of azadirachta indica (neem) leaf. *Eur J Med Plant.* 2012;**2**(1):11.
35. de Mendonça AJG, Vaz MIPM, de Mendonca DIMD. Activity coefficients in the evaluation of food preservatives. *Innov Food Sci Emerg Technol.* 2001;**2**(3):175–9. doi: 10.1016/s1466-8564(01)00037-6.
36. Lu N, Shen M. Research on mutagenicity of sodium benzoate in born marrow cells. *J Jilin Agri Univ.* 2006;**28**(4):466–8.

37. Cameron JS, Greger R. In: Oxford textbook of clinical nephrology. Davison AM, Cameron JS, Grunfeld JP, editors. 1. Oxford: Oxford University Press; 1998. pp. 39–69.Renal function and testing of function.
38. Mu Y, Lin J, Liu R. Interaction of sodium benzoate with trypsin by spectroscopic techniques. *Spectrochim Acta A Mol Biomol Spectrosc.* 2011;**83**(1):130–5. doi: 10.1016/j.saa.2011.07.092. [PubMed: 21890401].
39. do Nascimento Filho I, Schossler P, Santos Freitas L, Melecchi MI, Rodrigues Vale MG, Bastos Caramao E. Selective extraction of benzoic acid from landfill leachate by solid-phase extraction and ion-exchange chromatography. *J Chromatogr A.* 2004;**1027**(1-2):167–70. [PubMed: 14971499].
40. Kreindler JJ, Slutsky J, Haddad ZH. The effect of food colors and sodium benzoate on rat peritoneal mast cells. *Ann Allergy.* 1980;**44**(2):76–81. [PubMed: 6153872].
41. Schaubschlager W, Becker W-M, Schade U, Zabel P, Schlaak M. Release of mediators from human gastric mucosa and blood in adverse reactions to benzoate. *Int Arch Allergy Immunol.* 1991;**96**(2):97–101.
42. Eberechukwu S, Amadikwa A, Okechukwu M. Effect of oral intake of sodium benzoate on some haematological parameters of wistar albino rats. *Sci Res Essays.* 2007;**2**(1):6–9.
43. Bakar E, Aktac T. Effects of sodium benzoate and citric acid on serum, liver and kidney tissue total sialic acid levels: An ultrastructural study. *J Appl Biol Sci.* 2014;**8**(2):9–15.
44. Gardner LK, Lawrence GD. Benzene production from decarboxylation of benzoic acid in the presence of ascorbic acid and a transition-metal catalyst. *J Agric Food Chem.* 1993;**41**(5):693–5. doi: 10.1021/jf00029a001.
45. Taheri SSD. Teratogenic effects of Sodium Benzoate on rat embryos. *J Zanjan Univ Med Sci.* 2002;**10**(39):1–4.
46. Yilmaz S, Unal F, Yuzbasioglu D. The in vitro genotoxicity of benzoic acid in human peripheral blood lymphocytes. *Cytotechnology.* 2009;**60**(1-3):55. doi: 10.1007/s10616-009-9214-z. [PubMed: 19642007].
47. Hu M, Wang J, Cai J, Wu Y, Wang X. [Analysis of sodium benzoate biotoxicity by atomic force microscope]. *Sheng Wu Gong Cheng Xue Bao.* 2008;**24**(8):1428–32. [PubMed: 18998546].