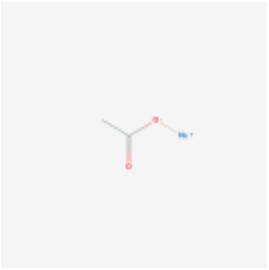
Sodium acetate

Ingredient synonym names

Acetic acid, sodium salt, trihydrated
Acetic acid, sodium salt
Anhydrous sodium acetate
Trihydrated sodium acetate

IDENTIFIER DETAILS

Ingredient chemical structure



CAS Number	FEMA Number	Additive Number	Ingredient EC Number
127-09-3	3024	E262	204-823-8

CAS Additional Number	FL Number	CoE Number
6131-90-4, 325477-99-4 883902-29-2	-	-

Chemical formula: $C_2H_3NaO_2 \cdot nH_2O$ (n=0, or 3 for trihydrated)

Ingredient CLP Classification

Ingredient REACH Registration Number: 01-2119485123-42

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
0	0	0
Acute Dermal Toxicity	**Respiratory Sensitisation**	**Reproductive Toxicity**
0	0	0
Acute Inhalation Toxicity	**Skin Sensitisation**	**Aspiration Toxicity**
0	0	0
Skin Corrosive/Irritant	**Mutagenicity/ Genotoxicity**	**Specific Target Organ Toxicity**
0	0	0

SPECIFICATIONS

Melting Point	Boiling Point
58°C (Trihydrate -136º C)	120°C (Trihydrate - 253ºC)

Sodium acetate

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	Not limited (JECFA, 1997)
Acceptable Daily Intake (ADI) comments	No comments (JECFA, 1997)
FDA Status	CFR21 184.1721: FDA GRAS

CoE limits - Beverages (mg/kg)	-	CoE limits - Food (mg/kg)	-	CoE limits - Exceptions (mg/kg)	-

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Sodium acetate (SA) is the sodium salt of acetic acid and occurs naturally in plants and animals. Sodium acetate may occur in either the anhydrous or trihydrated form. (FDA 184.1721).

Acetic acid or acetates are present in most plant and animal tissues in small, but detectable amounts (Fenaroli, 2005).

References - Ingredient Natural Occurence

Fenaroli's Handbook of Flavor Ingredients (2005). Fifth Edition. CRC Press. ISBN: 0-8493-3034-3.

Food & Drug Administration. CFR 21 170.3, CFR 21 182.70 & CFR 21 582.1721. U.S National Archives and Records Administration's Electronic Code of Federal Regulations.

Ingredient Reported Uses

SA meets the Food Chemical Codex (1981) and FDA regulations as a flavouring agent and adjuvant and a pH control agent (CFR 21 170.3) at levels, which do not exceed FDA status 184.1721. Also used as a food additive in animal feeds and drugs, GRAS when used in association with good manufacturing procedures (CFR 21 582.1721). Used to purify glucose and as a hydrate as a meat preservative. In the food industry SA has been shown to extend the shelf life of whole shrimps by 3 days and peeled shrimps by 17 days, extending the microbial lag phase and generation time from 15.8 hours in the control to 38.7 hours (Al-Dagal & Bazaraa, 1999).

Reportedly used (maximum levels) in breakfast cereals at 0.01 ppm, in fats & oils at 5.0 ppm, in meat products at 1.0 ppm, in other grains at 6.0 ppm, in snack foods at 0.76 ppm, in soft candy at 0.91 ppm, in soups at 0.5 ppm, in sweet source at 0.32 ppm (Fenaroli, 2005).

Approved drug product CFR 21 505 and 507, and approved for use in dry food packaging (CFR 21 182.70). Used as a buffer to eliminate the use of strong acids in photography, a catalyst for dyes and polyester resins in the textile industry (Kirk-Othmer, 1978).

At concentrations < 2g/kg soil sodium acetate / sodium formate (1:1) can fertilize soil promoting biomass yield (Bang & Johnston, 1998).

References - Ingredient Reported Uses

Al-Dagal M.M & Bazaraa W.W (1999). Extension of shelf life of whole and peeled shrimp with organic acid salts and bifidobacteria. Journal of Food Protein. 62(1): 1-6.

Bang S.S & Johnston D (1998). Environmental effects of sodium acetate/ formate de-icer, ice sheartrade mark. Archives of Environmental Contamination & Toxicology. 35(4): 580-587.

Fenaroli's Handbook of Flavor Ingredients (2005). Fifth Edition. CRC Press. ISBN: 0-8493-3034-3.

Kirk-Othmer (1978 - 1984). Encyclopaedia of Chemical Technology 3rd Edition John Whiley & Sons, New York. Volume 1. 142

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

Data displayed as: Test - Dose reported - Species - Route of Administration - Source
LD50 - 3.5-5.6g/kg - Rat - Oral - [EPA, 1991]
LD50 - 4.96g/kg - Mouse - Oral - [Kirk-Othmer, 1981]

References
EPA (1991). Registration eligibility document (RED). Sodium Diacetate. US Environmental Protection Agency.

Kirk-Othmer (1978 - 1984). Encyclopaedia of Chemical Technology 3rd Edition John Whiley & Sons, New York. Volume 1. 142

In Vivo Carcinogenicity/Mutagenicity

No data identified.

References - In Vivo Carcinogenicity/Mutagenicity

No data identified.

Dermal Toxicity

An in vivo eye irritation assay assessing 34 chemicals in the rabbit including SA applied 0.1ml of 10% aqueous SA to a sample of six rabbits. No irritation, i.e. erythema, oedema, corneal opacity and corneal swelling was observed [Jacobs & Martens, 1989]. Continuous exposure to 0.1M aqueous SA (pH 7) for 3 hours also caused no corneal effects in the rabbit [Grant, 1986].

SA has the potential to increase the aqueous humour/plasma concentration ratio of timolol (a vasoconstrictive agent), 20-fold when used as a buffer for polymer matrices composed of PVM-MA matrices (monoisopropyl poly (vinyl methyl ether-maleic anhydride) compared to an alternatives such as disodium phosphate. The authors concluded that SA improves the ocular/systemic absorption ratio of timolol by decreasing the systemic but not ocular absorption of timolol in rabbit's eyes [Finne et al., 1991].

No evidence of skin irritancy occurred in rabbits exposed to 50% SA [EPA, 1991].

References - Dermal Toxicity

EPA (1991). Registration eligibility document (RED). Sodium Diacetate. US Environmental Protection Agency.

Finne U, Salivirta J & Urtti A (1991). Sodium acetate improves the ocular/systemic absorption ratio of timolol applied ocularly in monoisopropyl PVM-MA matrices. International Journal of Pharmacology. 75: 1-4.

Grant W.M (1986). Toxicology of the Eye. 3rd Edition. Charles C Thomas Publisher.

Jacobs G.A & Martins M.A (1989). An objective method for the evaluation of eye irritation in vivo. Food & Chemical Toxicology. 27: 255.

Reproductive/ Developmental Toxicity

The teratogencity of SA was assessed using the Chernoff/Kavlock teratogenicity in vivo screen, which uses postnatal growth and viability of prenatally exposed offspring as a measure of developmental toxicity (Chernoff & Kavlock, 1982). SA was assessed in a group of 46 chemicals. Thirty pregnant CD-1 mice were treated with 1000mg/kg/day, known to cause slight maternal toxicity, on days 8-12 of gestation by oral gavage. No observable teratogenic effects were detected compared to a control group of 40 mice in the dams or their offspring (Kavlock et al., 1987).

Male rats exposed to 3.6g/kg bw SA via a stomach tube showed no significant changes in sperm production or change in testes weight, 24hrs after treatment (Mebus et al., 1989).

Sodium acetate when administered daily during pro-oestrous through to gestation at concentrations 1mg in mice (pro-oestrous for 7 days), 10-20mg in rabbits and 200mg in hamsters and 50mg in guinea pigs (from day 1-10 of gestation) had a anti-fertility action causing termination of pregnancy with no apparent side effect. The degree of termination in female rats varied. A maximum of 70% was achieved when exposed to up to 500mg/rat (Dutta & Fernando, 1972).

References - Reproductive/ Developmental Toxicity

Dutta N.K. & Fernando G.R (1972). Anti-fertility action of sodium acetate in animals. Indian Journal of Medical Research. 69: 48-53.

Kavlock R.J, Short R.D & Chernoff N (1987). Further evaluation of an in vivo teratology screen. Teratogen, Carcinogen, Mutagen. (1): 7-16.

Mebus C.A, Welsch F & Working P.K (1989). Attenuation of 2-methoxyethanol-induced testicular toxicity in the rat by simple physiological compounds. Toxicology & Applied Pharmacology. 99(1): 110-21.

Inhalation Toxicity

No data identified.

References - Inhalation Toxicity

No data identified.

Cardiac Toxicity

No data identified.

References - Cardiac Toxicity

No data identified.

Addictive Data

No data identified.

References - Addictive Data

No data identified.

Behavioral data

The activity of adult BK: W-mice was monitored using ultrasound over a 24 hour period when exposed to 0.025 SA from conception compared to a distilled water control. A lower level of activity was detected initially. However, during the later sages of the 24-hour period this level was similar to that of control mice [Donald et al., 1988].

SA is commonly used as a control in lead acetate toxicity studies [Donald et al., 1988; Bunn & Deitert, 2001]. However, it has been reported that SA may not be appropriate as a control in behavioural studies as it also affects mice activity, which could mask the effects of lead acetate [Donald et al., 1988].

References - Behavioral data

Donald J.M, Bradley M, O'Grady J.E, Cutler M.G & Moore M.R (1988). Effects of low levels of lead exposure on 24hour activity patterns in the mouse. Toxicology Letters. 42(2): 137-147.

In Vivo - Other Relevant Studies

Over sized Sprague-Dawley rats exposed to 8mg/kg of SA for 20 days via intraperitoneal injection had impaired weight and length increment compared to normal sized Sprague-Dawley rats exposed to 1mg/kg [Luthman et al., 1992].

SA effects adenine nucleotide concentrations in isolated rat liver hepatocytes in situ. Total adenine nucleotide concentrations remained constant. However, a significant threefold increase in AMP concentrations and a small but significant decrease in ATP concentrations, 15 minutes after intraperitoneal injection occurred (Zydowo et al., 1993). This caused a decline in the ATP/AMP ratio from the control value of 14 to 3, similar to rats injected with SA (Zydowo et al., 1993).

Hypertension caused by increase vascular response was investigated in tail arteries of Wistar rats exposed to drinking water containing 100ppm SA for 7 months, stimulated with vasoactive agents such as norepinephrine-bitartrate, methoxamine-hydrochloride or a methoxy verapamil derivative. The systolic blood pressure of rats exposed to lead acetate was significantly higher than those exposed to SA and no alteration in contractile response or electrical stimulation to SA was observed (Webb et al., 1981).

The toxicity of a SA / sodium formate (SF) (1:1) alternative de-icer (Ice Sheartrade) has been assessed in relation to its environmental impact. Results demonstrated low toxicity to aquatic animals such as rainbow trout (96h LC50 – 16.1g/L) and minimal toxicity to vegetation including herbaceous and woody plants (Bang & Johnston, 1998).

Tomino et al., (2004) described a new maintenance fluid containing sodium acetate as the base component and electrolytes (Veen 3G, test preparation) for a maximum of 24 h, was infused to 15 patients hospitalized for renal biopsies and requiring intravenous supplements of water, electrolytes and energy because oral or enteric ingestion was impossible or inadequate. A physical examination, blood chemistry tests and urinalysis were performed, and the global improvement rating was obtained by scoring the effects on a) maintenance of cardiovascular hemodynamics (systolic blood pressure), b) blood glucose control (blood glucose level), c) utilization of sugar (free fatty acids, total ketone bodies), d) maintenance of serum electrolytes, e) amount of sugar excreted in the

urine and f) maintenance of urinary volume. Tomino et al., (2004) reported that the results were excellent or good in all of the 15 patients analyzed. The test agent was not the direct cause of any adverse events or abnormal changes in laboratory findings, and no safety-related problems were observed in any of the patients. They concluded that the test preparation used in the study was clinically useful and a highly safe fluid agent [Tomino et al., 2004].

In a study conducted in 2007, eight healthy volunteers took part in two separate trials, 7 days apart in a single-blind, randomized, cross-over design. On each occasion, volunteers were given a drink containing either sodium acetate or sodium bicarbonate at a dose of 2 mmol/kg body mass. Before and during 180 min following consumption of a drink, respiratory gas and arterialized venous blood samples were taken. Both sodium salts induced a mild metabolic alkalosis and increased energy expenditure to a similar magnitude. However, sodium bicarbonate ingestion increased fat oxidation but sodium acetate did not, despite the fact that both sodium salts induced a similar increase in energy expenditure and shift in acid-base balance. The authors determined that 80.1 +/- 2.3 % of an exogenous source of acetate is oxidized in humans at rest [Smith et al., 2007].

Within the body the acetate ion of SA is metabolised rapidly producing sodium bicarbonate [Osol et al., 1975]

References - In Vivo - Other Relevant Studies

Bang S.S & Johnston D (1998). Environmental effects of sodium acetate/ formate de-icer, ice sheartrade mark. Archives of Environmental Contamination & Toxicology. 35(4): 580-587.

Luthman J, Oskarsson A, Olson L & Hoffer B (1992). Postnatal lead exposure affects motor skills and exploratory behaviour in rats. Environmental Research 58(2): 236-252.

Osol, A. and J.E. Hoover, et al. (eds.). Remington's Pharmaceutical Sciences. 15th ed. Easton, Pennsylvania: Mack Publishing Co., 1975., p. 772

Smith G. I., Jeukendrup A. E., Ball D. (2007). Sodium acetate induces a metabolic alkalosis but not the increase in fatty acid oxidation observed following bicarbonate ingestion in humans. American Society for Nutrition J. Nutr. 137: 1750-1756

Tomino Y et al., (2004) Effects of a new maintenance fluid containing sodium acetate as the base component and electrolytes during renal biopsies in patients with chronic glomerulonephritis. Arzneimittelforschung ;54(9): 538-44.

Webb R.C, Winquist R.J, Victery W & Vander A.J (1981). In vivo and in vitro effects of lead on vascular reactivity in rats. American Journal of Physiology. 241: H211-H216.

Zydowo M.M, Smolenski R.T, Swierczynski J (1993). Acetate induced changes of adenine nucleotide levels in rat liver. Metabolism. 42(5): 644-648.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

No sister chromatid exchanges were observed in human lymphocytes exposed to SA in vitro [Latt et al., 1981].

SA has been found to be slightly mutagenic for E.coli (Demdec et al., 1951). SA appears to have no carcinogenic effects (no further data provided) [Tracor-Jitco Incorporated, 1974].

Additional information concerning the in vitro mutagenicity and genotoxicity of this material may be found in “An

Interim report on data originating from Imperial Tobacco Limited's Genotoxicity testing programme September 2003" or "An updated report on data originating from Imperial Tobacco Limited's external Genotoxicity testing programme – Round 2 August 2007".

The present study examined the impacts of sodium acetate (SA), sodium acid pyrophosphate (SAPP), and citric acid (CA) on the viability, proliferation, and DNA damage of isolated lymphocytes in vitro. 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) and lactate dehydrogenase (LDH) release assays were adopted to evaluate cell viability, while comet assay was employed to assess the genotoxic effects. The cells were incubated with different levels of SA (50, 100, and 200 mM), SAPP (25, 50, and 100 mM/L), or CA (100, 200, and 300 μg/mL). The lymphocytes treated with the tested food additives showed concentration-dependent decreases in both cell viability and proliferation. A concentration-dependent increase in LDH release was also observed. The comet assay results indicated that SA, SAPP, and CA increased DNA damage percentage, tail DNA percentage, tail length, and tail moment in a concentration-dependent manner. The current results showed that SA, SAPP, and CA are cytotoxic and genotoxic to isolated lymphocytes in vitro [Abd-Elhakim, et al., 2018].

Cytotoxicity and genotoxicity of sodium acetate (SA), sodium diacetate (SDA), and potassium sorbate (PS) was tested on Human Umbilical Vein Endothelial Cells (HUVEC). Cytotoxicity was investigated by MTT assay and flow cytometry analysis, while genotoxicity was evaluated using DNA fragmentation and DAPI staining assays. The growth of treated HUVECs with various concentrations of SA, SDA and PS decreased in a dose-and time-dependent manner. The IC50 of 487.71, 485.82 and 659.96 μM after 24 h and IC50 of 232.05, 190.19 and 123.95 μM after 48 h of treatment were attained for SA, SDA and PS, respectively. Flow cytometry analysis showed that early and late apoptosis percentage in treated cells was not considerable. Also neither considerable DNA fragmentation nor DNA smear was observed using DAPI staining and DNA ladder assays. Overall, it can be concluded that the aforementioned food additives can be used as safe additives at low concentration in food industry [Mohammadzadeh-Aghdash, et al., 2018].

References - In Vitro Carcinogenicity/Mutagenicity

Buchanan R.L Jr & Ayrs J.C (1976). Effect of sodium acetate on growth and aflatoxin production by Aspergillus parasiticus NRRL 2999. Journal of Food Science. 41(1): 128-132.

Demdec M, Bertani G and Flint J (1951). A survey of chemicals for mutagenic activity on E.coli. American Nature. 85(821): 119-136.

Latt S.A, Allen J, Bloom S.E, Carrano A, Falke E, Kram D, Schneider Schreck R, Tice R, Whitfield B & Wolff S (1981). Sister-chromatid exchanges: a report of the GENE-TOX program. Mutation Research. 87(1): 17-62.

Tracor-Jitco Incorporation (1974). Scientific literature reviews on generally recognised as safe (GRAS) food ingredients. Acetic acid and its acetates. Food and Drug Administration. Pages 1-136.

An Interim report on data originating from Imperial Tobacco Limited's Genotoxicity testing programme September 2003 – internal document.

An updated report on data originating from Imperial Tobacco Limited's external Genotoxicity testing programme – Round 2 August 2007 – internal document.

Abd-Elhakim, Y. M., Anwar, A., Hashem, M. M., Moustafa, G. G., & Abo-El-Sooud, K. (2018). Sodium acetate, sodium acid pyrophosphate, and citric acid impacts on isolated peripheral lymphocyte viability, proliferation, and DNA damage. Journal of biochemical and molecular toxicology, 32(8), e22171.

Mohammadzadeh-Aghdash, H., Sohrabi, Y., Mohammadi, A., Shanehbandi, D., Dehghan, P., & Dolatabadi, J. E.

N. (2018). Safety assessment of sodium acetate, sodium diacetate and potassium sorbate food additives. Food chemistry, 257, 211-215.

In Vitro - Other Relevant Studies

Human gastric adenocarcinoma epithelial cells incubated with sodium acetate (up to 12.5 mM) for 72 hours exhibited increased cell viability and proliferation in a dose-dependent manner. After 24 hour incubation, there were increases in the levels of pro-inflammatory cytokines, IL-1beta, IL-8, and TNF-alpha (protein & mRNA). The highest concentration tested (100 mM) resulted in increased expression of pro-inflammatory cytokines which may be cytotoxic above a critical level [Sun et al, 2005].

Concentrations of 1-5 and 20mM of SA significantly inhibit cellular proliferation, bone nodule formation and mineralisation in rat osteoprogenitor cells in vitro, resulting in a significant inhibition of bone deposition. In comparison a concentration of 10mM causes no effect [Visconti et al., 1998].

High concentrations of SA and acetic acid found in industrial waste water (25-800mg) can cause failure of BPR from waste water systems during biological nutrient removal [Randall & Chapin, 1997].

SA has the potential to completely inhibit the growth of aflatoxin production by Aspergillus parasitius NRRL 2999 in modified Adye and Mateles (AM) medium containing 2% yeast extract (pH 4.5) [Buchanan & Ayres, 1976] at concentrations greater or equal than 1g/100ml. SA also has the potential to inhibit the growth of Staphylococcs aureus and Escherichia coli [Frech et al., 1979].

References - In Vitro - Other Relevant Studies

Frech G, Allen LV, Stiles M & Levinson R.S (1979). Sodium acetate as a preservative in protein hydrolysate solutions. American Journal of Hospital Pharmacology. 36: 1672-1675.

Randall C.W & Chapin R.W (1997). Acetic acid inhibition of biological phosphorus removal. Water Environment Research. 69(5): 955-960.

Sun J et al (2005). Effect of sodium acetate on cell proliferation and induction of proinflammatory cytokines: a preliminary evaluation. Food Chem Toxicol 43(12):1773-80.

Visconti L.A, Yen E.H & Johnson R.B (1998) Effects of sodium acetate on rat bone-nodule formation and mineralisation in vitro. Archives of Oral Biology. 43(9): 729-733.

Emissions and Associated Toxicity Data

The addition of sodium acetate at 12 ppm to reference cigarettes, used in a 90 day-sub-chronic inhalation exposure in rats, led to a series of pathological changes to smoke exposure that were indistinguishable from those changes caused by the control cigarettes. This indicated that addition of sodium acetate to a reference cigarette had no discernable effect upon the type or severity of the treatment related pathological changes associated with tobacco smoke exposure [Baker et al., 2004].

Baker et al., [2004]; examined the effects of the addition of 482 tobacco ingredients upon the biological activity and chemistry of mainstream smoke. The ingredients, essentially different groups of flavourings and casings, were added in different combinations to reference cigarettes. The addition of sodium acetate at 12 ppm was determined not to have affected the mutagenicity of the total particulate matter (TPM) of the smoke in either the Ames, in vitro micronucleus assay or the neutral red assay when compared with that of the control cigarettes [Baker et al., 2004].

References - Emissions and Associated Toxicity Data

Baker RR, et al., (2004) An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. Food Chem Toxicol. 42 Suppl: S53-83.