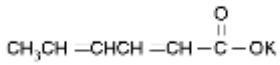
Potassium sorbate

Ingredient synonym names

2,4-Hexadienoic acid, potassium salt
Hexadienoic acid, potassium salt

IDENTIFIER DETAILS

Ingredient chemical structure



CAS Number	FEMA Number	Additive Number	Ingredient EC Number
24634-61-5, 590-00-1	2921	E202	-

CAS Additional Number	FL Number	CoE Number
590-00-1	-	-

Chemical formula C6H7KO2

Ingredient CLP Classification

Ingredient REACH Registration Number

01-2119950315-41

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
0	2	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
2	0	0

SPECIFICATIONS

Melting Point 270°C Boiling Point No data identified

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg) 0-25 (JECFA, 1973)

Acceptable Daily Intake (ADI) comments	-
FDA Status	CFR21 182.3640: Generally recognised as safe as a chemical preservative

CoE limits - Beverages (mg/kg)	No data identified	CoE limits - Food (mg/kg)	No data identified	CoE limits - Exceptions (mg/kg)	No data identified

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Reported found in blueberries [Fenaroli, 2005].

References - Ingredient Natural Occurence

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

Ingredient Reported Uses

Reportedly used (max. levels) in baked goods at 0.72 ppm, fats/oils at 1.44 ppm, milk products at 0.49 ppm, cheese at 2.03 ppm, frozen dairy at 0.10 ppm, fruit juice at 1.02 ppm, fruit ices at 0.70 ppm, fish products at 0.43 ppm, processed vegetables at 0.84 ppm, condiment relish at 0.55 ppm, soft candy at 0.58 ppm, confection frosting at 0.83 ppm, jam and jelly at 0.95 ppm, sweet sauce at 0.67 ppm, gelatin pudding at 5.84 ppm, snack foods at 0.80 ppm, non-alcoholic beverages at 0.36 ppm, alcoholic beverages at 0.26 ppm, gravies at 0.64 ppm and imitation dairy at 0.75 ppm [Fenaroli, 2005].

References - Ingredient Reported Uses

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

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

Species	Test Type	Route	Reported Dose
Rat	LD50	Oral	4920 mg/kg
Mouse	LD50	IP	1300 mg/kg

FAO, (1967).

In Vivo Carcinogenicity/Mutagenicity

A study to assess the chronic toxicity of PS was carried out using six rats, each receiving PS orally in the diet at 0.1 %, with a second group of six animals receiving PS in their drinking water at 0.3 % for 65 weeks. Laparotomy failed to detect hepatic tumours in the animals therefore the study was continued for 100 wks [until the death of all of the experimental rats]. On post mortem examination of all animals [including microscopic evaluation], no tumours were identified in any of the animals [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

Long-term mice and rat carcinogenicity studies with PS administered in the diet [5 %] to six rats revealed no carcinogenic effects in rats. The data from the mouse study was not reported, [no additional data as to the species, number of animals etc. was given] [Food science and techniques, 1996].

A study in which PS was repeatedly administered via subcutaneous injection at the same site in rats [unknown doses] [WHO, 1974].

References - In Vivo Carcinogenicity/Mutagenicity

Final report on the safety assessment of sorbic acid and potassium sorbate. (1988). Journal of the American College of Toxicology. 7(6): 837-880.

Food science and techniques. (1996). Reports of the scientific committee for food, 35th series. European Commission.

WHO (1974). The joint FAO/WHO Expert Committee of Food Additives which met in Geneva, 25th June - 4thJuly. Seventeenth report of the joint FAO/WHO Expert Committee on Food Additives.

Dermal Toxicity

A 35 year-old man who worked as a farmer at a milk transformation suffered from allergic contact dermatitis from PS/sorbic acid. The man was exposed to the PS in a raw powdery form that was then diluted to 0.2 % final concentration. Despite wearing vinyl gloves, exposure occurred via dermal contact on the face and upper limbs. Lesions involved his hands, upper limbs, face, abdomen and thighs [Le Coz & Abensour, 2005].

PS was administered to the backs [clipped] of 5 male and female NZ rabbits [cream containing 0.15 % PS] for a period of 90 days. The cream covered 10 % of the body surface of each animal in a dose of 6 mg/cm2. The control group consisted of 5 male and female rabbits. At the end of the study, gross and microscopic evaluations revealed average food consumption, along with body and organ weights were normal. Haematology data, clinical chemistry, urinalyses and light microscopic examination of tissue were also normal. Lesions observed in treated rabbits included granulomatous meningoencephalitis and acute colitis. All animals in the first week developed slight to moderate erythema and oedema, which continued throughout the 90 days.
Desquamation was slight to moderate in all treated animals, with 4 animals developing fine line fissures in week 3, one animal showed cutaneous fissures and bleeding on days 46-48. Mild dermatitis was also observed in 8 out of 10 treated animals and characterised by few inflammatory cells in the upper dermis with no erosion or ulceration noted, [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

Clinical irritation studies [using volunteers] for PS produced the following results: [Table modified based on data from, Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].
Results displayed as: Dosage - Test - Group size (n) - Score - Conclusions
0.15% PS cream - Cumulative 23hr occlusive patch. Scoring at 24hr [for 21 days] - 12 - 69/630 [for 10] - Mild cumulative irritation under test conditions.
0.15% PS moisturizer - 23 or 47hr occlusive patches. Scoring 1hr after patch removed [for 20 days] - 12 - 140.83 / 600[For 10] - Slight potential for mild cumulative irritation.
0.15% PS moisturizer - 23 or 48hr occlusive patches. Scoring 1hr after patch removal [for 20 days] - 12 - 43.33 / 600 [For 10] - No evidence of cumulative irritation.
Formulation 0.15% PS - Evaluated for irritation and sensitisation in a Shelanski-Jordan RIPT - 209 to 210 - No score - Not a strong irritant or sensitizer.
Formulation 0.15% PS - Evaluated for irritation and sensitisation in a Shelanski-Jordan RIPT - 199 to 204 - No score - Not a primary irritant or allergic contact sensitizer
Formulation 0.15% PS - Modified Draize Shelanski RIPT = 202 to 205 - No score - Not a primary irritant or allergic contact sensitizer.

Facial scrub 0.1% PS [diluted 1:100 deionised water] - RIPT - 53 - No score - Did not induce dermal irritation or sensitisation.
Facial scrub 0.1% PS [as above] - RIPT - 53 - No score - Did not induce dermal irritation or sensitisation
Facial scrub 0.1% PS [diluted 1:100 in dH20] - RIPT - 56 - No score - Did not induce dermal irritation or sensitisation
Facial scrub 0.1% PS [diluted 1:100 in dH20] - RIPT - 47 - No score - Not a sensitizer

References - Dermal Toxicity

Final report on the safety assessment of sorbic acid and potassium sorbate. (1988). Journal of the American College of Toxicology. 7(6): 837-880.

Le Coz & Abensour (2005). Occupational contact dermatitis from potassium sorbate in milk transformation plant. Contact Dermatitis 53:176-177.

Reproductive/ Developmental Toxicity

The in vitro Hydra assay (a developmental toxicity assay) in which the minimum concentration of test compound needed to interfere with adult hydra and the development of 'hydra artificial embryos' within 92 hrs is assessed, revealed that PS, at 1/10 of the concentration needed to interfere with adult hydra development, interfered with the developing hydra 'embryos'. The authors suggested that PS selectively targeted the embryo relative to the adult [Adult minimum affective concentration, 900 mg/L developmental minimum affective concentration, 90 mg/L]. A previous teratogenicity study using rats and mice was considered to be irrelevant to this study as neither maternal nor foetal toxicity levels were achieved. The study showed that PS was harmless to pregnant animals [and young] at the doses given but they did not report if increasing concentrations would produce developmental effects in the foetus in the absence of maternal toxicity. It should be noted that this particular assay is reported to produce 7 % false positives, and concentrations that produce effects in the Hydra assay may not always be used to predict the levels required to produce an adverse effect in mammals [Newman et al, 1990].

A teratogenicity study in which approximately 20 pregnant mice [CD-1] and rats [derived from Wistar] were given PS orally as a water suspension [via intubation], on days 6 -15 of gestation, [organogenesis]. Mice received doses of 4.6, 21.4, 99.1 and 460 mg/kg bw and rats received 3.4, 15.8, 73.3 and 340 mg/kg bw PS. No effects were observed on implantation or on maternal or foetal survival in either group of rodents. Abnormalities in soft and skeletal tissues did not differ from the number occurring spontaneously in the vehicle controls [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

Teratogenicity testing using the developing chicken embryo assay [20 or more White leghorn chickens] revealed that PS [solvent: water] administered via air cell injection or via the yolk sac showed no teratogenic effects. The LD50 value was observed to be 2.44 mg/egg at 96 hr [administered via air cell injection], the highest dose of PS tested was 10mg/egg [Verrett et al., 1980].

Similarly no teratogenic effects were observed in mice up to 460mg/kg bw and rats up to 340 mg/kg bw [Food science and techniques, 1996].

References - Reproductive/ Developmental Toxicity

Final report on the safety assessment of sorbic acid and potassium sorbate. (1988). Journal of the American College of Toxicology. 7(6): 837-880.

Food science and techniques. (1996). Reports of the scientific committee for food, 35th series. European Commission.

Newman et al., (1990). Developmental toxicity evaluation of several cosmetic ingredients in the hydra assay.

Journal of the American College of Toxicology. 9(3): 361-365.

Verrett et al., (1980). Toxicity and teratogenicity of food additive chemicals in the developing chick embryo. Toxicology and Applied Pharmacology. 56: 265-273.

Inhalation Toxicity

The preservatives benzalkonium chloride (BZC) and PS are widely used in the formulation of nasal drops and cosmetics. Recently, a number of side effects that resulted from mucosal irritation caused by BZC and PS have been reported. Lebe et al., (2004) investigated the possible clinical and histological alterations induced by in vivo administration of these preservatives to the nasal mucosa of rats. 0.01 % BZC and 0.12 % PS were administered to the nostrils of male rats for 1 or 4 wks. Symptomatic changes such as sneezing and nasal rubbing were observed in almost all groups, starting from the 6th day of administration. Light and electron microscopy showed histological changes and nasal lesions induced by the preservatives. The symptomatic and histological changes were more pronounced with increased duration of administration. Therefore, it has been concluded that in vivo administration of the preservatives BZC and PS may be irritant to the respiratory epithelium of rats (Lebe et al., 2004).

A study in which the surveillance of work-related and occupational respiratory disease in the UK was investigated of the 395 asthma cases reported in 1993 one case was thought to be due to the exposure to PS [classified under, asthma caused by chemicals] [Sallie et al., 1994].

References - Inhalation Toxicity

Lebe et al., (2004). Effects of preservatives in nasal formulations on the mucosal integrity: an electron microscopic study. Pharmacology. 72(2):113-20.

Sallie et al., (1994). SWORD ’93. Surveillance of work-related and occupational respiratory disease in the UK. Occupational Medicine. 44: 177-182.

Cardiac Toxicity

No data identified.

References - Cardiac Toxicity

No data identified.

Addictive Data

No data identified.

References - Addictive Data

No data identified.

Behavioral data

No data identified.

References - Behavioral data

No data identified.

In Vivo - Other Relevant Studies

[fasted]. No adverse toxicity was reported and weight gain was observed to be normal during a period of 7 days, [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988]. A similar study in which 5 male and female Harlan-Fischer 344 rats, [fasted] were given 13 ml/kg of a bronzer and moisturizer by gavage [0.15 % PS], for 2 wks also showed no signs of adverse toxicity [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

A study in which 1 % PS was placed into the conjuctival sacs of one eye of 3 male and female rats indicated that the ocular irritation score was 0, one day after dose administration. Another study in which 0.1 ml of an unspecified dose of PS was administered to the conjunctival sac [one eye] of 6 New Zealand white rabbits, showed that a Draize scored ranged from 2-11 with an average score of 4.7 [on day 7 after exposure no irritation was observed]. Two rabbits [female] were reported to have conjuctiva bleached white on day 1 of the study, with another rabbits observed to have the same symptoms on day 2; a third female rabbit showed conjuctival petechial haemorrhage on days 1-3, which was absent on day 7 [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

A similar study in which 0.1 ml of a cosmetic containing 0.15 % PS was put into one eye of 6 albino rabbits [observed for seven days]. Conjuctival redness was observed after 1 hr, which cleared within 24 hr [no effect was observed on the cornea and iris] [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

The ocular irritation potential of two cosmetics [bronzer and moisturiser] containing 0.15 % PS was assessed in 6 NZ albino rabbits. 0.1 ml of undiluted formulations were placed into one eye of each rabbit and an irritation score taken at 1, 2, 3 and 7 days. Conjunctival hyperaemia was the only sign of irritation observed 1 hr after treatment with both formulations however, this cleared after 24 hr [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

Rats [unspecified strain and number] were fed 0.25 % or 2 % PS for a 3-month period. At the 0.25 % dosage, an increase in pancreatic juice secretion was observed, this happened in conjunction with an increase in protein content and enzyme activity. At 2 %, increases in bile bilirubin and cholesterol were observed along with a decreased pancreatic chymotrypsin, amylase and lipase activity. The authors stated that ‘the significance of these findings could not be assessed from the data [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

A group of 10 rats [5 M/F] were fed diets containing 0, 1, 2, 5 or 10 % PS for 3 months. Weight loss was observed in females at the 5 and 10 % PS dose. Renal weights were increased in rats fed 10 % PS [smaller increase observed in group fed 5 %], whereas relative hepatic weights remained the same [no high potassium intake controls were described] [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

A 3-month study, in which 8 dogs were fed diets containing 1 and 2 % PS, revealed that any weight gain over the course of the study was comparable to that of the control dogs [group of 4]. No adverse effects were noted after gross examination at necroscopy [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

PS gave an ocular irritation score of 0 [at 24 hr] in a modified Draize ocular irritation test in which 1,5 and 10 % PS [aq. solution] was administered to the eyes of three groups of rabbits [n = 3 per group] [Final report on the safety assessment of sorbic acid and potassium sorbate, 1988].

A case study, in which a patient experienced a ‘burning’ sensation of the oral cavity for three years, indicated that this syndrome was due to an allergy to toothpastes containing nicotinic acid esters and foods preserved with sorbic acid [Haustein, 1988].

References - In Vivo - Other Relevant Studies

Final report on the safety assessment of sorbic acid and potassium sorbate. (1988). Journal of the American

College of Toxicology. 7(6): 837-880.

Haustein (1988). Burning mouth syndrome due to nicotinic acid esters and sorbic acid. Contact dermatitis. 19: 225-226.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

In a study conducted by Mamur et al., (2010) the genotoxic potential of potassium sorbate (PS) was investigated in cultured and isolated human lymphocytes in vitro. Measurements of Chromosomal aberrations (CA), sister-chromatid exchanges (SCEs), micronuclei (MN) and assessment in the comet assay were made. Lymphocytes were treated with four concentrations of PS: 125, 250, 500 and 1000 µg/ml. Results indicated that PS significantly increased CAs (with or without gaps) at the two highest concentrations tested and SCEs at all concentrations tested compared with the vehicle control. However, PS failed to significantly induce micronuclei in the MN assay. The results from the comet assay showed a significantly higher tail intensity than that of the control after 1h in vitro exposure to PS and this effect was concentration dependant. The authors conclude that PS is clearly genotoxic to human peripheral blood lymphocytes in three out of the four assays evaluated.

PS reacting with ascorbic acid in the presence of iron salt was reported to be mutagenic and have DNA damaging activity. However PS, sorbic acid and iron salts were inactive when tested separately or with the removal of one component from the mixture [Kitano et al., 2002].

Cell transformation studies in Syrian hamster embryo [SHE] fibroblasts revealed that PS up to 1200 µg/ml did not produce any effects in the SHE fibroblast micronucleus assay and the SHE cell transformation assay [Schiffmann and Schlatter, 1992].

A culture of B. subtilis [strains H17 and M45] when mixed with PS [30 min incubation, 37°C, no dose stated] showed DNA damaging potential. Although PS had given a negative Ames test it was suggested that the liquid B. subtilis assay was a more sensitive assay [Nonaka, 1989 EMS Abstracts].

Mutagenicity studies in which S. typhimurium strains TA1535, 1537 and 1538 was exposed to PS 2.5 % [w/v][in phosphate buffer pH 7.4] was negative for reversions. Results using suspensions of S. typhimurium [as above] and S. cerevisiae [strain D-4] with 2.5 and 5 % PS were negative (+/- S9) [Final report on the safety assessment of Sorbic acid and potassium Sorbate, 1988].

Mutagenicity studies: Ames test S.typhimurium [TA97, 102] (+/- S-9, metabolic activation) gave negative results [0.1-10 mg/plate, solvent water], [Fujita and Sasaki, 1986].

PS at 98 % purity max dose 3mg/plate [solvent: water] gave a negative Ames test [+/- S9] with S.typhimurium strains TA92, 94, 98,100,1535,1537 [Ishidate et al., 1984].

Chromosome aberration test using CHO cells (+/- metabolic activation) at a maximum dose of 4 mg/plate [solvent physiological saline] gave a positive result of 11 % after 48 hrs. Results were considered positive if the incidence of aberrations was more that 10 %. Where a sample was deemed to have a positive result the dose at which structural aberrations [including gaps] were detected in 20 % of the metaphases [D20 mg/ml] was also noted. The TR value was also calculated. This is the frequency of cells with exchange-type aberrations per unit dose [mg/ml]. D20 and TR values for PS were D20, 6.72 mg/ml and TR, 0.25 mg/ml. The highest TR value in this study was 2133, so that the value due to propionic acid seem low in comparison [Ishidate et al., 1984].

The ability of PS [solvent: distilled water] at 5000, 10000, 15000 and 20000 µg/ml to induce chromosomal aberrations, sister chromatid exchange [SCE], and gene mutations in Chinese hamster V-79 cells [v-79/6-

Thioguanine without metabolic activation] was studied. PS induced 28 % chromosomal aberrations with the 20000µg/ml doses but no chromosomal aberrations were observed at the lower concentrations tested. The authors report that the incidence of SCE was limited. The increase in the numbers of SCE was shown to be statistically significant at concentrations ≥ 10000 µg/ml [Hasegawa et al., 1984].

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".

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 [Mohammedzadeh-Aghdash, et al., 2018].

References - In Vitro Carcinogenicity/Mutagenicity

Final report on the safety assessment of sorbic acid and potassium sorbate. (1988). Journal of the American College of Toxicology. 7(6): 837-880.

Fujita and Sasaki (1986). Mutagenicity tests of food additives with Salmonella Typhimurium TA97A and 102. Toritsu Eisei Kenkyusho. 37: 447-452.

Hasegawa et al., (1984). Effects of sorbic acid and its salts on chromosome aberrations, sister chromatid exchanges and gene mutations in cultured Chinese hamster cells. Food & Chemical Toxicology. 22(7): 501-507.

Ishidate et al., (1984). Primary mutagenicity screening of food additives currently used in Japan. Food &Chemical Toxicology. 22(8): 623-36.

Kitano et al., (2002). Mutagenicity and DNA-damaging activity caused by decomposed products of potassium sorbate reacting with ascorbic acid in the presence of Fe salt. Food & Chemical Toxicology. 40(11): 1589-94.

Mamur et al., (2010). Does potassium sorbate induce genotoxic or mutagenic effects in lymphocytes? Toxicology in Vitro 24:790-794.

Mpountoukas et al., (2008). Cytogenetic study in cultured human lymphocytes treated with three commonly used preservatives. Food & Chemical Toxicology. 46(7): 2390-3.

Nonaka (1989). EMS Abstracts. DNA repair and food additives. Environmental &. Molecular Mutagenicity. 14(15):143.

Schiffmann & Schlatter (1992). Genotoxicity and cell transformation studies with sorbates in Syrian hamster embryo fibroblasts. Food & Chemical Toxicology. 30(8): 669-672.

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

In vitro toxicity testing of tobacco ingredients in burnt form (Internal document R-020.

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

Rabbit tracheal ciliated cell culture was established and ciliary beat frequency (CBF) was determined using high-speed digital imaging methods. The effects of preservatives at different concentrations on CBF were observed over a 10-min exposure period. A low concentration of potassium sorbate (PS) (0.12 %) only resulted in a mild decrease in CBF during a 10-min exposure. Application of 0.24, 0.48 and 0.96 % of PS to rabbit tracheal cells resulted in an increase in CBF, with an increase of 105 ± 9.8, 107.6 ± 4.0, and 117.1 ± 9.5 % relative to baseline CBF after 10 min of exposure, respectively. PS could be considered as a safer and more promising preservative for use in topical formulations [Wang et al., 2012].

The in vitro effects of preservatives on human nasal epithelial cells including PS present in nasal sprays were assessed following reports of side effects resulting from mucosal damage. Primary human nasal epithelial cells were exposed to different concentrations of PS and phosphate buffered saline (PBS) as the control group for 15 min. No significant cell damage was observed by measuring cell viability and morphology compared to the control group, even at levels higher than concentrations clinically used. PS appears to be relatively safe for use in nasal sprays and drops when tested under in vitro conditions (Ho et al., 2008).

Pentadiene is a metabolite of PS produced by yeast strains belonging to the species Zygosaccharomyces rouxii and Debaryomyces hansenii (Casas et al., 2004).

PS caused no effect (at any concentration) on ciliary beat frequency in human nasal mucosal cultured ciliated cells (removed via endoscopy and cultured for 10 days to produce ciliated cells). It was concluded by the author that potassium sorbate was harmless to cell motility in vitro (Hofmann et al., 2004).

PS is used as an antimicrobial agent against pathogenic bacteria such as E.coli O157:H7, L.monocytogenes or S.aureus on fresh beef. PS alone or combined with 0.5 % cetylpyridinium chloride or 0.12 % acidified NaCl was not as effective as cetylpyridinium chloride or acidified NaCl alone. To effectively reduce E.coli O157:H7, L.monocytogenes or S.aureus concentrations of PS higher than (> 0.1 %) were required (Lim & Mustapha, 2004).

Investigations into the safety of combined usage of PS and nitrates have indicated that under normal conditions of use 'there is no hazard to human health' [Food and science techniques, 1996].

PS [2.5 mg/ml] gave negative test results for genotoxicity tests using cultured V79 Chinese hamster cells and somatic cells of Drosophila melanogaster [wing spot test]-up to 3.75 mg/ml. PS solutions stored for 28 days were observed to be cytotoxic [Schlatter et al., 1992].

References - In Vitro - Other Relevant Studies

Casas et al., (2004). Pentadiene production from potassium sorbate by osmotolerant yeasts. International Journal of Food Microbiology. 94(1): 93-96.

Food science and techniques. (1996). Reports of the scientific committee for food, 35th series. European Commission.

Ho et al., (2008). In vitro effects of preservatives in nasal sprays on human nasal epithelial cells. American Journal of Rhinology. 22(2):125-9.

Hofmann et al., (2004). Influence of preservatives and topical steroids on ciliary beat frequency in vitro. Archives of Otolaryngology – Head & Neck Surgery. 130(4): 440-445.

Kitano et al., (2002). Mutagenicity and DNA-damaging activity caused by decomposed products of potassium sorbate reacting with ascorbic acid in the presence of Fe salt. Food & Chemical Toxicology. 40(11): 1589-94.

Lim & Mustapha (2004). Effects of cetylpyridinium chloride, acidified sodium chlorite, and potassium sorbate on populations of E.coli O157, L.monocytogenes and S.aureus on fresh beef. Journal of Food Protection. 67(2): 310-315.

Schlatter et al., (1992). The potential genotoxicity of sorbates: Effects on cell cycle in vitro in V79 cells and somatic mutations in Drosophila. Food & Chemistry and Toxicology. 30: 843-851.

Wang et al., (2012) Effects of benzalkonium chloride and potassium sorbate on airway ciliary activity. ORL J Otorhinolaryngol Relat Spec. 74(3):149-53

Emissions and Associated Toxicity Data

Gaworski et al. (2008), assessed the toxicological effects of PS added to cigarette tobacco as a mould growth inhibitor or as a preservative in flavouring systems or paper adhesives. The effect of PS added to cigarettes was assessed in neat material pyrolysis studies, on smoke chemistry and on biological activity studies (including bacterial mutagenicity, cytotoxicity, in vivo micronucleus, and 90-day nose-only rat inhalation) with mainstream smoke (MS), or MS preparations from cigarettes containing various levels of PS (0 %, 0.15 %, 1.6 %, and 3.7 %). At burning temperatures up to 10000C, neat PS completely pyrolysed to form chemicals including benzene, toluene, naphthalene, and substituted forms. Under (FTC/ISO) smoking machine conditions high levels of PS altered the burning characteristics of the cigarette causing decreased puff count, total particulate matter, CO, hydrogen cyanide, 2-nitropropane, and tobacco specific nitrosamines yields in smoke. An increase in the yield of nicotine, 1,3-butadiene, isoprene, and some PAHs were also observed. In addition there were no relevant differences in the genotoxic / cytotoxic potential of MS from cigarettes (+/- PS) and rats exposed to MS developed respiratory tract changes consistent with those seen in other smoke inhalation studies (no relevant histopathological differences). In summary high levels of PS can alter the burn rate of the tobacco leading to an alteration in the smoke chemistry profile. However, overall PS added to cigarette tobacco produced little relevant changes in the overall toxicity profile of smoke [Gaworski et al (2008)].

Renne et al., (2006) evaluated the effects of tobacco flavouring and casing ingredients on both mutagenicity, and a number of physiological parameters in Sprague-Dawley (SD) rats. Test cigarettes containing a mixture of either 165 low-uses or eight high-use flavouring ingredients which included PS at 39 ppm, were compared to a typical commercial tobacco blend without flavouring ingredients. The Ames assay (TA 98, 100,102, 1535 and 1537 ±S9) did not show any increase in Mutagenicity from “low” or “high” cigarette smoke condensate compared to the control. SD rats were exposed by nose-only inhalation for 1h/day, 5 days/wk for 13 wks to smoke at concentrations of 0.06, 0.2 or 0.8mg/L from the test or reference cigarettes, or to air only. Plasma nicotine, COHb and respiratory parameters were measured periodically. Rats were necropsied after 13wk of exposure or following 13 wk of recovery from smoke exposure. Biological endpoints assessed included; clinical appearance, bw weight, organ weights, and lesions (both gross and microscopic). The results of these studies did not indicate any consistent differences in toxicological effects between smoke from cigarettes containing the flavouring or casing ingredients and reference cigarettes.

The addition of PS at 6000 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 PS 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 PS at 6000 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].

Carmines (2002), Rustemeier et al., (2002), Roemer et al., (2002) and Vanscheeuwijck et al., (2002) reported on a testing program designed to evaluate the potential effects of 333 ingredients added to typical commercial blended test cigarettes on selected biological and chemical endpoints. The studies performed included a bacterial mutagenicity screen [Ames assay] a mammalian cell cytotoxicity assay [neutral red uptake], determination of smoke chemical constituents and a 90-day rat inhalation study. Based on the findings of these studies, the authors concluded that the addition of the combined ingredients, including potassium sorbate (PS) at levels up to 837 ppm, "did not increase the overall toxicity of cigarette smoke" [Carmines, 2002].

A recent study investigated the effect of cigarettes, containing various additives in three combinations, in a 90-day nose-only smoke inhalation study in rats. These ingredients included PS at 837 ppm, a level described as a multiple of its typical use in a US cigarette. The data from this study, along with that from a number of other biological and chemical studies indicate that the addition of the combined ingredients "did not increase the inhalation toxicity of the smoke, even at the exaggerated levels used" [Vanscheeuwijck et al., 2002].

Roemer et al., (2002) reported on a study in which cigarettes containing various additives in three different combinations were produced. Smoke condensates prepared from these cigarettes were then tested in two different in vitro assays. The mutagenicity of the smoke condensate was assayed in the Salmonella plate incorporation [Ames] assay with tester strains TA98, 100, 102, 1535 and 1537 (+/- S9). The cytotoxicity of the gas/vapour phase and the particulate phase was determined in the neutral red uptake assay with mouse embryo BALB/c 3T3 cells. The authors concluded that the in vitro mutagenicity and cytotoxicity of the cigarette smoke was not increased by the addition of the ingredients which included PS at levels up to 837 ppm [a multiple of its typical use in a US cigarette] [Roemer et al., 2002].

A mouse skin painting study investigated the carcinogenicity of condensate prepared from cigarettes containing a number of additives in combination, including PS at 0.1 ppm. The authors concluded that the study "did not indicate any substantive effect of these ingredients on the tumorigenicity of cigarette smoke condensate" [Gaworski et al., 1999]. [It should be noted that the cigarettes contained a typical American blend humectant and sugar component (i.e. glycerine ≈ 20,000 ppm, propylene glycol at ≈ 24,000 ppm, and brown invert sugar at ≈ 24,000 ppm)].

When tested at 0.1 ppm in cigarettes, in a 13-wk inhalation study, the presence of PS "…had no discernible effect on the character of extent of the biologic responses normally associated with inhalation of mainstream cigarette smoke in rats"[Gaworski et al., 1998]. [However, it should be noted that the cigarettes had been spiked with a number of flavour ingredients in combination prior to smoking, and they contained a typical American blend humectant and sugar component (i.e. glycerine ≈ 20,000 ppm, propylene glycol at ≈ 24,000 ppm, and brown invert sugar at ≈ 24,000 ppm)].

The mutagenicity of the smoke condensate was assayed in the Salmonella plate incorporation [Ames] assay with the tester strain TA98 in the presence of an S9 metabolic activation system. The cytotoxicity of the cigarette condensate was determined in the neutral red uptake assay and the (3-(4,5-dimethylthiazol-2-yl)-5-(3-

carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H tetrazolium, inner salt assay (MTS assay) with the human hepatocellular liver carcinoma cell line, HEP-G2. It was concluded that the in vitro mutagenicity and cytotoxicity of the cigarette smoke was not increased by the addition of the ingredients, which included potassium sorbate at levels up to 2 ppm [In vitro toxicity testing of tobacco ingredients in burnt form (Internal document R-020)].

References - Emissions and Associated Toxicity Data

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