

Cinnamic acid

Botanical Source

Synonyms	PHENYL-2-PROPENOIC ACID(trans-3-)
IUPAC Name	3-phenylprop-2-enoic acid
CAS Reference	621-82-9
E Number	

Food Legislation

Council of Europe (CoE)

Number	Comment
22	Listed by the Council of Europe as acceptable for use in food at up to 40 ppm.

US Food and Drug Administration

Number	Comment
172.515	Approved by the US FDA. FDA 21 CFR 172.515

Joint FAO/WHO Expert Committee on Food Additives (JECFA)

Number	ADI	Comment
657	No Safety concern @ intake	No safety concern at current levels of intake when used as a flavouring agent.

FEMA

FEMA No.	Comment
2288	

Natural Occurrence and Use in Food

Found in beer, blackberry, capers, cherry, grape, guava, malt, mango, mushroom, passion fruit, strawberry; used in soft candy.

Estimated Intake From Food and Drink

Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
40	93.436

Tobacco Legislation

Tobacco Ingredients

Cinnamic acid

Country	Cigarettes	RYO	Cigars	Pipe
Afghanistan				
Algeria				
Argentina				
Australia				
Brazil				
Burundi				
Canada				
Comoros				
Djibouti				
EEC				
Egypt				
Eritrea				
EU TPD2				
Fiji				
France	Y	Y	Y	Y
GCC (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, UAE)				
Germany	Y	Y	Y	Y
Hong Kong				
Hungary	Y	Y	Y	Y
Iceland				
Iran				
Iraq				
Jordan				
Kazakhstan				
Lebanon				
Libya				
Macedonia				
Madagascar				
Malaysia				
Maldives				
Mexico				
Moldova				
Montenegro				

Cinnamic acid

New Zealand				
Nigeria				
Norway				
Pakistan				
Palestine				
Papua New Guinea				
Rwanda				
Samoa				
Serbia				
Solomon Island				
Somalia				
Somaliland				
South Sudan				
Sri Lanka				
Sweden				
Switzerland	Y	Y	Y	Y
Syria				
Tunisia				
Turkey				
UK	0.15	0.15	0.15	0.5
United Arab Emirates				
Vietnam				

Y=Permitted for use in tobacco products. If use is limited, the maximum permitted level is given.

Cinnamic acid

Tobacco Product related Chemical and Biological Studies for Ingredients Added in a Mixture

Smoke Chemistry

Published Source	Level Tested %	Comment
Philip Morris	0.00010	An overall assessment of the data suggests that this ingredient did not add to the toxicity of smoke.
BAT	0.00100	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.

Ames Activity

Published Source	Level Tested %	Comment
BAT	0.00100	Within the sensitivity and specificity of the system the Ames activity of the cigarette smoke condensate was not increased by the addition of the ingredient.
Philip Morris	0.00010	Within the sensitivity and specificity of the system the Ames activity of the cigarette smoke was not increased by the addition of the ingredient.

Micronucleus

Published Source	Level Tested %	Comment
BAT	0.00100	Within the sensitivity of the in vitro micronucleus assay the activity of the cigarette smoke condensate was not increased by the addition of the ingredient.

Neutral red

Published Source	Level Tested %	Comment
BAT	0.00100	Within the sensitivity of the test system the in vitro cytotoxicity of the cigarette smoke condensate was not increased by the addition of the ingredient.
Philip Morris	0.00010	Within the sensitivity of the test system the in vitro cytotoxicity of the cigarette smoke was not increased by the addition of the ingredient.

Inhalation

Published Source	Level Tested %	Comment
Philip Morris	0.00010	The data indicate that the addition of the ingredient, when added with one of three groups, did not increase the inhalation toxicity of the smoke.

Mouse Skin Painting

Published Source	Level Tested %	Comment
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Cinnamic acid

Toxicological Data on the Unburnt Ingredient

In vivo Studies

Species	Test Conditions	End Point	Results	Reference
Human	A 48-hour occluded patch test with cinnamic acid in petrolatum on the backs of 25 healthy, male volunteers. Dose = 4%	Skin Irritation	No Irritation	Letizia et al, 2005
Rabbit	Irritation evaluated in a dermal LD ₅₀ study. Dose = 100%	Skin Irritation	Slight erythema	Bickers et al, 2005
Rabbit	Cinnamic acid applied to intact or abraded skin for 24 hours, under occlusion. Dose = 100%	Skin Irritation	Slightly Irritating	Opdyke, 1978
Guinea Pig, albino Crl:IAF (HA)-hrBR.	As part of the primary irritancy phase of a phototoxicity/photoallergy study, groups of five animals received a 2-hour covered application of 0.3 ml cinnamic acid in 3:1 diethyl phthalate:ethanol and were observed for three days. Dose = 0.1, 1, 10 or 20%	Skin Irritation	No Irritation	Letizia et al, 2005
Guinea pig, albino Ssc:AL.	As part of a sensitization study, one week following the application of Freund's Complete Adjuvant, cinnamic acid (in 96% ethanol) was applied to the skin of groups of 3 animals for 24 hours, under occlusion. Reactions were read 72 hours after application. Dose = 2-200 mg/ml [approximately 0.2-20%].	Skin Irritation	No Irritation	Letizia et al, 2005
Guinea pig, albino Ssc:AL.	One week following the application of Freund's Complete Adjuvant, 48-hour occluded patch tests with cinnamic acid in propylene glycol were carried out in 5 animals. Reactions were read 48 and 72 hours after application. Dose = 1-10%	Skin Irritation	Slight Irritation with 0% Cinnamic Acid	Letizia et al, 2005

Cinnamic acid

Species	Test Conditions	End Point	Results	Reference
Guinea pig, Hartley.	Cinnamic acid in absolute ethanol (0.02 ml) was applied to 5 areas of skin in 5 animals. Reactions were read every 10 minutes after application in the first hour, every 15 minutes in the second hour and every 30 minutes in the third hour. Dose = 15%	Skin Irritation	No irritation	Letizia et al, 2005
Mouse, Balb/c	As part of a sensitization study, cinnamic acid in 4:3:1 acetone:water:Tween 80 (0.1 ml) was applied to the skin of the abdomen and thorax of 10 females on days 0, 2, 4, 7, 9 and 11. Dose = 15%.	Skin Irritation	No irritation	Letizia et al, 2005
Rabbit and Guinea Pug	Cinnamic acid in distilled water was instilled into one eye. The untreated eye served as a control. Observations were made at 15 minutes, and at 1, 2 and 24 hours . Dose = 1 to 10 mg/ml [0.1-1%].	Eye Irritation	No irritation	Letizia et al, 2005

Sensitisation and Tolerance

Species	Test Conditions	End Point	Results	Reference
Human	A maximization test with cinnamic acid (in petrolatum) on 25 volunteers. [The test procedure typically involves an initial induction phase of five 48-hour covered patch tests, followed 10-14 days later by a 48-hour covered challenge patch.] Dose = 4%.	Skin Sensitisation	No Sensitisation	Bickers et al, 2005
Human	142 patients previously sensitized to balsam of Peru were tested with cinnamic acid. Dose = Not specified	Skin Sensitisation	Sensitization in 26 [18%] patients.	Opdyke, 1978
Human	43 female and 63 male atopic and non-atopic dermatitis patients were subjected to an occluded 20-minute patch test (reaction read 10 minutes after patch removal) and an open test in which cinnamic acid in petrolatum (0.1 ml) was applied to the upper back (reactions read 30 minutes after application). Dose = 5%.	Skin Sensitisation	Sensitization in 71 [67%] patients (closed test) and 85 [80%] patients (open test).	Letizia et al, 2005

Cinnamic acid

Species	Test Conditions	End Point	Results	Reference
Human	43 female and 63 male atopic and non-atopic dermatitis patients received cinnamic acid capsules once daily on 4 days following cinnamic acid patch tests (as part of a separate study). All symptoms "were recorded over a 12-hour period". 200 mg/dose [3.3 mg/kg bw/day for a 60-kg individual].	Oral (systemic) sensitization, including subjective signs.	Erythema in 2 patients and oedema in 1 patient. Subjective symptoms such as tingling, itching, headache, nausea, diarrhoea and sweating were observed in 19 patients.	Letizia et al, 2005
Human	Cinnamic acid in petroleum (0.1 ml) was applied to the forearm of 39 male and 64 female atopic and non-atopic dermatitis patients, and reactions were read every 15 minutes for 6 hours. 5%.	Skin Sensitisation	Sensitization in 87 [84%] patients.	Letizia et al, 2005
Human	Patches containing cinnamic acid in petroleum were applied to the upper back of 105 male and female atopic and non-atopic dermatitis patients for 20 minutes. Reactions were read on patch removal. 5%.	Skin Sensitisation	Sensitization in 29 [28%] patients.	Letizia et al, 2005
Human	Patch tests carried out on 184 dermatitis patients Dose 2 or 5%	Skin Sensitisation	One sensitization reaction [0.5%] with 5% cinnamic acid.	Letizia et al, 2005
Human	Human patch test data (1978-1980) from 19 patients with cosmetic dermatitis and 23 patients with non-cosmetic eczema and dermatitis. 5%.	Skin sensitization	1 sensitization reaction (non-cosmetic eczema and dermatitis patient) [4.3%].	Letizia et al, 2005
Human	Cinnamic acid in 2-propanol:water (1:1) - 0.01 ml - was applied to the cheek of 12 male and female volunteers, covered for 10 minutes and then removed. Reactions were scored 5 and 10 minutes later. 0.5%.	Skin Sensitization	Strong "urticariogenic" effect.	Letizia et al, 2005
Human	Cinnamic acid in ethanol (0.01 ml) was applied to the upper back of 20 male and female volunteers to investigate non-immunologic contact urticaria. Observations were every 10-15 minutes for a 2-hour period. 50, 100, 250 and 500 mM [0.94, 1.88, 4.69 and 9.38%].	Skin Sensitization	50 mM: no reactions observed. 100 mM: erythema observed in 3 and oedema in 1 individual. 250 mM: erythema observed in 9 and oedema in 5 individuals. 500 mM: erythema observed in 18 and oedema in 9 individuals.	Letizia et al, 2005

Cinnamic acid

Species	Test Conditions	End Point	Results	Reference
Human	9 patients sensitized to propolis and to "other related allergens" were patch tested with cinnamic acid. 5%.	Skin Sensitization	2 patients [22%] displayed sensitization (denoted "+").	Ginanneschi et al, 1989
Guinea pig.	Buehler test. The induction phase involved three 6-hour closed patch tests with cinnamic acid, once/week for 3 weeks. 10-14 days later, the animals were challenged with a 6-hour occluded patch test. 10% (induction and challenge).	Skin sensitization.	No sensitization	Letizia et al, 2005
Guinea pig.	Ten animals were tested in a Buehler test. Induction involved a 6 hour occluded patch application with cinnamic acid in ethanol/water on days 1, 7 and 14. 10-14 days later, the animals were challenged with a 6-hour occluded patch with cinnamic acid in acetone. 10% (induction and challenge).	Skin sensitization.	No sensitization	Letizia et al, 2005
Guinea pig, albino Ssc:AL.	Magnusson-Kligman maximization test in groups of 20 animals. Intradermal injection of cinnamic acid in propylene glycol, with or without Freund's Complete Adjuvant, followed one week later with an occluded 48-hour patch application. On day 21, animals were challenged with an occluded 24-hour patch test with cinnamic acid in ethanol or dimethylisosorbide. Reactions were read 72 hours after application. Induction (intradermal): 2% Induction (dermal): 10% Challenge: 9 or 120 mg/ml [0.9% or 12%] (ethanol); 200 mg/ml [20%] (dimethylisosorbide).	Skin sensitization	One reaction at 120 mg/ml [12%] in ethanol	Letizia et al, 2005
Guinea Pig	Closed epicutaneous test (CUT) in groups of 5 animals. The induction phase consisted of six 48-hour occluded patch applications, 3 times/week for 2 weeks. On day 28, the animals were challenged with a 48-hour occluded patch. Reactions were read at patch removal, and at 24 and 48hours after patch removal. 10% (induction) 1% (challenge).	Skin sensitization	No sensitization.	Letizia et al, 2005

Cinnamic acid

General Systemic Effects – Single Exposure

Species	Test Conditions	End Point	Results	Reference
Rat	Groups of ten rats were administered cinnamic acid by oral gavage. 3250, 3750 or 5000 mg/kg bw.	Mortality	LD50 3570 mg/kg bw. 3, 6 and 9 deaths in the low-, mid- and high-dose groups, respectively.	Letizia et al, 2005
Rat	Not Specified	Mortality	LD50 2500 mg/kg bw.	Zaitsev and Maganova, 1975
Rat	Single oral dose . 50 mg/kg bw.	Mortality and clinical signs of toxicity	Gastrointestinal changes.	RTECS, 2012
Rat	Single intraduodenal dose . 50 mg/kg bw.	Mortality and clinical signs of toxicity	Alterations to gastric secretion.	RTECS, 2012
Rat; mouse; guinea pig.	Animals were given cinnamic acid in sunflower oil by oral gavage and observed for 15 days. Unspecified Dose	Mortality.	LD50 3400 mg/kg bw.	Zaitsev and Rakhmanina, 1974
Rat; mouse; guinea pig.	Animals were given cinnamic acid in sunflower oil by oral gavage and observed for 15 days.	Mortality	LD50 >5000 mg/kg bw.	Letizia et al, 2005
Mouse	Single oral Dose Dose not specified	Mortality	LD50 5000 mg/kg bw.	RTECS, 2012
Guinea Pig	Single oral Dose Dose not specified	Mortality	LD50 5000 mg/kg bw.	RTECS, 2012
Rabbit	Four animals received a single application . 5000 mg/kg bw.	Mortality	LD50 5000 mg/kg bw.	Letizia et al, 2005

Cinnamic acid

Species	Test Conditions	End Point	Results	Reference
Mouse	Single intraperitoneal injection. Not specified	Mortality	LD50 160-220 mg/kg bw.	Opdyke, 1978
Rat	Single intraperitoneal injection. Not specified	Mortality	LD50 1600 mg/kg bw.	RTECS, 2012
Mouse	Single intravenous injection. Not specified	Mortality	LD50 380 mg/kg bw.	RTECS, 2012

General Systemic Effects

Species	Test Conditions	End Point	Results	Reference
Rat, Wistar	8 rats were subjected to a 15-minute forced swimming assay, immediately before oral gavage of cinnamic acid in 1% ethanol. They were re-treated with cinnamic acid 24 hours and 1 hour prior to a second forced swimming assay, at 48 hours after initial treatment. 0.12 mg/kg bw/dose.	Behavioural changes.	No effect	Panossian et al, 2008

In Vitro

Test System	Test Conditions	Endpoint	Activation Status	Results	Reference
Rat hepatoma cells.	Comet assay and micronucleus assay. 0.05, 0.5 or 1.5 mM [0.0074, 0.074, 0.22 mg/ml].	DNA damage and chromosome damage	Not Activated	-ve (DNA damage). +ve (chromosome damage).	Maistro et al, 2011
Salmonella typhimurium, strains TA98, TA100, TA1535, TA1537 and TA1538.	Bacterial reverse mutation (Ames) assay. Pre-incubation method used, with and without S9. Up to 1 mg/plate.	Mutation	With and Without	-ve	Letizia et al, 2005

Cinnamic acid

Test System	Test Conditions	Endpoint	Activation Status	Results	Reference
Salmonella typhimurium, strains TA98, TA100.	Bacterial reverse mutation (Ames) assay and a "micro-suspension mutagenicity assay", with activation. Up to 0.1 mg/plate.	Mutation	with	-ve	Mohtashamipur and Norpoth, 1984
Salmonella typhimurium, strains TA98, TA100.	Bacterial reverse mutation (Ames) assay, with and without S9 . Not specified	Mutation	With and without	-ve	Min et al, 1987
Salmonella typhimurium, strain TA100.	Pre-incubation assay, with and without S9. Tested at concentrations up to an unspecified cytotoxic dose level. Not specified	Mutation	With and without	-ve	Eder et al, 1991
Escherichia coli, strain B/r WP2s	Mutagenicity assay without S9. Not specified	Mutation	Without	-ve	Letizia et al, 2005
Escherichia coli, strain PQ37	SOS chromotest, with and without S9. [Test methods not described in full.] Not specified	DNA Damage	With and without	-ve	Eder et al, 1991

Reproductive and Developmental Toxicity

Species	Test Conditions	End Point	Results	Reference
Rat, albino	Cinnamic acid given orally throughout gestation to groups of 14 or 15 animals. On day 20 of gestation, 50% of the females were killed and embryos examined (embryonic lethality, weight, anatomical changes, skeletal ossification and liver nucleic acid content). The remainder were allowed to deliver normally and the offspring (body weights, size, survival, development) assessed for 1 month. Up to 50 mg/kg bw/day.	Embryotoxic effects, developmental effects.	No statistically significant differences between treated and control groups.	Zaitsev and Maganova, 1975

Cinnamic acid

Species	Test Conditions	End Point	Results	Reference
Rat, albino	Groups of 6 rats given daily intraperitoneal injections on days 1 to 10 of gestation. Assessment for anti-fertility effects (number of implantation sites on day 10 and number of viable foetuses day 19 of gestation). For animals allowed to deliver normally, the pups were observed for at least 1 month. 0 or 40 mg/kg bw/day.	Reproductive and developmental effects.	There were decreases in the number of pregnant rats (by 50%, presumably as assessed by rats with implantation sites and/or viable foetuses) number of implantations/rat, number of viable foetuses/rat and percentage resorptions in treated rats.	Kurup and Rao, 1988

In vitro

Species	Test Conditions	End Point	Results	Reference
Rat, Sprague-Dawley	Standardized oestrogen receptor competitive binding assay. Uteri were obtained from non-pregnant rats ten days after ovariectomy . Including 1 mmol [approximately 500 mg/kg bw].	Oestrogen receptor binding.	No binding to the oestrogen receptor; considered inactive.	Letizia et al, 2005

References

- Eder, E., Deininger, C., Muth, D., 1991
Genotoxicity of *p*-nitrocinnamaldehyde and related α,β -unsaturated carbonyl compounds in two bacterial assays. *Mutagenesis*, 6, 261-269.
- Ginanneschi, M., Acciai, M.C., Sertoli, A., Bracci, S., 1989
Propolis allergy: synthesis and patch testing of γ,γ -dimethylallyl caffeic acid ester and its *o*-methyl derivatives. *Contact Dermatitis*, 21, 267.
- Kurup, A. and Rao, M.N.A., 1988
Antifertility activity of cinnamic acids. *Indian J. Pharm. Sci.*, 50, 341-342.
- Letizia, C.S., Cocchiara, J., Lapczynski, A., Lalko, J., Api, A.M., 2005
Fragrance material review on cinnamic acid. . *Fd Chem. Toxic.*, 43, 925-943.
- Maistro, E.L., Angeli, J.P., Andrade, S.F., Mantovani, M.S., 2011
In vitro genotoxicity assessment of caffeic, cinnamic and ferulic acids. *Genet. molec. Res.*, 10(2), 1130-1140.
- Min, S., Chaigneau, M., Courtois, Y.A., Festy, B., 1987
Genotoxic activity of organic esters likely to form from chloro-2 ethanol generated during sterilization by ethylene oxide. *Ann. pharm. fr.*, 45, 353-359.
- Mohtashamipur, E. and Norpoth, K., 1984
Nonmutagenicity of some wood-related compounds in the bacterial-microsome plate incorporation and microsuspension assays. *Int. Archs occup. envir. Hlth*, 54, 83-90.
- Opdyke, D.L.J., 1978
Monographs on Fragrance Raw Materials: Cinnamic acid. *Fd Cosmet. Toxicol.*, 16, 687-690.
- Pannossian, A., Nikoyan, N., Ohanyan, N., Hovhannisyan, A., Abrahamyan, H., Gabrielyan, E., Wikman, G., 2008
Comparative study of Rhodiola preparations on behavioral despair of rats. *Phytomedicine*, 15(1-2), 84-91

Cinnamic acid

RTECS, 2013

Registry of Toxic Effects of Chemical Substances. Record for cinnamic acid (621-82-9). Last updated April 2012.

Zaitsev, A.N. and Rakhmanina, N.L., 1974

Toxic properties of phenylethanol and cinnamic alcohol derivatives. *Vop. Pitan.*, (5), 48-53.