Citric acid

Botanical Source	
Synonyms	CARBOXY-3-HYDROXY-GLUTARIC ACID (3-)
IUPAC Name	
CAS Reference	77-92-9 5949-29-1
E Number	E330

Food Legislation

Council of Europe (CoE)	
Number	Comment
20	Listed by the Council of Europe as acceptable for use in food.

US Food and Drug Administration	
Number	Comment
184.1033	Approved by the US FDA. FDA 21 CFR 184.1033

Joint FAO/WHO Expert Committee on Food Additives (JECFA)		
Number	ADI	Comment
218	-	On the basis of the available data, the total daily intake arising from use levels necessary to achieve the desired effect does not represent a hazard to health

FEMA	
FEMA No.	Comment
2306	-

Natural Occurrence and Use in Food
Found in fruits and vegetables; used in fruit juices, meats,

Estimated Intake from Food and Drink	
Daily Intake mg/kg/day	FEMA Possible Average Daily Intake mg
90.54	3.13

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

Smoke Chemistry		
Published Source	Level Tested %	Comment
BAT	1.14000	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.
Philip Morris	0.01220	An overall assessment of the data suggests that this ingredient did not add to the toxicity of smoke.

Ames Activity		
Published Source	Level Tested %	Comment
BAT	1.14000	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	0.01220	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	1.14000	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	1.14000	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	0.01220	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
BAT	1.14000	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Lorillard	0.01680	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Philip Morris	0.01220	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
Lorillard	0.00001	None of the changes appeared to be substantial enough to conclude that the tumour promotion capacity of the condensate was discernibly different between condensate produced from cigarettes with the ingredient in comparison with condensate from cigarettes without the ingredient.

References

Baker RR, Pereira da Silva JR, Smith G. The effect of tobacco ingredients on smoke chemistry. Part I: Flavourings and additives. Food Chem Toxicol. 2004; 42 Suppl:S3-37.

Baker RR, Pereira da Silva JR, Smith G. The effect of tobacco ingredients on smoke chemistry. Part II: casing ingredients. Food Chem Toxicol. 2004; 42 Suppl:S39-52.

Baker RR, Massey ED, Smith G. An overview of the effects of tobacco ingredients on smoke chemistry and toxicity. Food Chem Toxicol. 2004; 42 Suppl:S53-83.

Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 1: cigarette design, testing approach, and review of results. Food Chem Toxicol. 2002; 40(1): 77-91.

Rustemeier K, Stabbert R, Haussmann HJ, Roemer E, Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 2: chemical composition of mainstream smoke. Food Chem Toxicol. 2002; 40(1): 93-104.

Roemer E, Tewes FJ, Meisgen TJ, Veltel DJ, Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 3: in vitro genotoxicity and cytotoxicity. Food Chem Toxicol. 2002; 40(1): 105-111.

Vanscheeuwijck PM, Teredesai A, Terpstra PM, Verbeeck J, Kuhl P, Gerstenberg B, Gebel S, Carmines EL. Evaluation of the potential effects of ingredients added to cigarettes. Part 4: subchronic inhalation toxicity. Food Chem Toxicol. 2002; 40(1): 113-131.

Gaworski CL, Dozier MM, Heck JD, Gerhart JM, Rajendran N, David RM. Brennecke LH, Morrissey R. Toxicologic evaluation of flavor ingredients added to cigarette tobacco: 13 week inhalation exposures in rats. Inhal. Toxicol. 1998; 10:357-381

Gaworski CL, Heck JD, Bennett MB, Wenk ML. Toxicologic evaluation of flavor ingredients added to cigarette tobacco: skin painting bioassay of cigarette smoke condensate in SENCAR mice. Toxicology. 1999; 139(1-2):1-17.

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Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly

References
Baker RR, Bishop LJ. The pyrolysis of tobacco ingredients. J. Anal. Appl. Pyrolysis 2004, 71, 223-311.

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Toxicological Data on the Unburnt Ingredient

[+ve, positive; -ve, negative; ?, equivocal; with, with metabolic activation; without, without metabolic activation]

In vivo

Species	Test conditions	Endpoint	Result	Reference
Rats	Up to 3 g citric acid/kg bw/day was administered for 5 days by an unspecified route in a dominant lethal assay.	Germ cell mutation Chromosome damage (bone marrow)	-ve -ve	LBI, 1975a

In vitro

Test system	Test conditions	Endpoint	Activation	Result	References
Cultured human cells	Treated with citric acid, concentration not specified.	Chromosome damage	not specified	-ve	LBI, 1975a
Cultured hamster cells	Citric acid and sodium citrate treatments at unspecified concentrations.	Chromosome damage	without	-ve	Ishidate *et al*. 1985
Salmonella typhimurium and *Escherichia coli*	Citric acid and its potassium and sodium salts were tested in a number of Ames tests.	Mutation	with and without S9	-ve	Al-Ani & Al-lami, 1988; Isidate *et al*. 1984; LBI, 1975a, b and c; and Hayes *et al*. 1984.
Saccharomyse cervisiae	Citric acid and its potassium and sodium salts were tested.	Mutation	with and without S9	-ve	LBI, 1975a, b and c.

References

Al-Ani F.Y. & Al-Lami (1988). Mutation Res. 206, 467.

Hayes S. *et al* (1984). Mutation Res. 130, 97.

Isidate M. Jr *et al*. (1984). Fd Chem. Toxic. 22 (8), 623.

LBI (1975a). Litton Bionetics Inc. Summary of mutagenicity screening studies: host-mediated assay, cytogenetics, dominant lethal assay, compound FDA 71-54, citric acid. Contract No. FDA 71-268 (cited in FASEB, 1977).

LBI (1975b). Litton Bionetics Inc. Mutagenic evaluation of compound FDA 75-4 (006100--05-6) potassium citrate, NF, FCC granular. Contract No. 223-74-2104 (cited in FASEB, 1977).

LBI (1975c). Litton Bionetics Inc. Mutagenic evaluation of compound FDA 75-12 (006132-0403) sodium citrate, USP, FCC hydrous, granular. Contract No. 223-74-2104 (cited in FASEB, 1977).