

Potassium citrate

Botanical Source

Synonyms CITRIC ACID,TRIPOTASSIUM SALT;
TRIPOTASSIUM CITRATE;
C6 H5 K3 O7;
Potassium citrate monohydrate

IUPAC Name

CAS Reference 866-84-2
6100-05-6

E Number E332(ii)

Food Legislation

Council of Europe (CoE)	
Number	Comment
-	-

US Food and Drug Administration	
Number	Comment
182.1625	Approved by the US FDA. FDA 21 CFR 182.1625

Joint FAO/WHO Expert Committee on Food Additives (JECFA)		
Number	ADI	Comment
-	-	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
	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food
-

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

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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	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.

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.

Inhalation		
Published Source	Level Tested %	Comment
BAT	0.00100	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

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.
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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.

Potassium citrate

Tobacco Product Related Chemical and Biological Studies for Ingredients Tested Singly

References
Baker RR, Bishop LJ. The pyrolysis of non-volatile tobacco ingredients using a system that simulates cigarette combustion conditions. J. Anal. Appl. Pyrolysis 2005, 74, 145-170.

Potassium citrate

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	Results	Reference
Rat (numbers unspecified)	Dominant lethal assay. Citric acid doses of up to 3 g/kg bw/day administered for 5 days (route not specified). [Presumably males treated and mated with untreated females, and early foetal deaths monitored.]	Germ cell mutation	-ve	LBI, 1975a
Rat (numbers unspecified)	Chromosome aberration assay. Oral doses of up to 3 g citric acid/kg bw/day for 5 days. Bone marrow examined.	Chromosome damage	-ve	LBI, 1975a

In vitro

Test system	Test conditions	Endpoint	Activation status	Results	Reference
Human embryonic lung culture cells (WI-38)	Chromosome aberration assay. Citric acid tested up to 0.6 mg/ml.	Chromosome damage	Not known	-ve	LBI, 1975a

Chinese hamster lung fibroblast cells	Chromosome aberration/polyploidy assay. Citric acid and sodium citrate (said to be CAS 18996-35-5) tested at up to 1 mg/ml and 3 mg/ml, respectively. 48-hr incubation.	Chromosome damage and changes in chromosome number	Without	-ve (May be same study as below)	Ishidate et al. 1984
Chinese hamster lung fibroblast cells	Chromosome aberration/polyploidy assay. Citric acid and "sodium citrate" (CAS given as 68-04-2, which actually corresponds to trisodium citrate) tested up to 1 mg/ml and 3 mg/ml, respectively. 48-hr incubation.	Chromosome damage and changes in chromosome number	Without	-ve (May be same study as above)	Ishidate, 1987
<i>Drosophila melanogaster</i> [Some investigators consider this to be an <i>in vivo</i> assay.]	Citric acid [solution] tested for ability to induce sex-linked recessive lethal mutations. No further details provided.	Germ cell mutation	Not applicable	-ve (Presumably) [A mutation rate of between 0.2 and 0.5% (not further specified) was reported.]	von Brandt & Hoehne, 1951
<i>Salmonella typhimurium</i> , strains TA92, TA94, TA98, TA100, TA1535, TA1537	Ames assay. Citric acid and sodium citrate (CAS 18996-35-5) tested up to 5 mg/plate.	Mutation	With S9	-ve [Testing without S9 is also generally recommended]	Ishidate et al. 1984
<i>Salmonella</i>	Ames assay.	Mutation	With and	-ve	Fujita et

<i>typhimurium</i> , strains TA97, TA102	Potassium dihydrogen citrate, tripotassium citrate and trisodium citrate tested up to 10 mg/plate. Paper in Japanese, abstract and data tables only in English.		without S9	[Limited assay, as only two strains used. Guidelines suggest that at least four are tested.]	al. 1992
<i>Salmonella typhimurium</i> , strains TA97, TA98, TA100, TA104	Ames assay. Citric acid tested up to 2 mg/plate.	Mutation	With and without S9	-ve	Al-Ani & Al-Lami, 1988
<i>Salmonella typhimurium</i> , strains TA1535, TA1537, TA1538 and <i>Saccharomyces cerevisiae</i> , strain D4	Sodium and potassium citrates tested. No further details provided in citing source.	Mutation	With and without S9	-ve	LBI, 1975b,c
(Unspecified) laboratory species and <i>Salmonella typhimurium</i> , strains TA1530, G46 or <i>Saccharomyces cerevisiae</i> , strain D3	Host-mediated mutagenicity assay. For <i>S. cerevisiae</i> tested up to 3.5 g/kg bw (route unspecified). No further details provided in citing source.	Mutation/mitotic recombination	Host-mediated	-ve for mutation (“no clear indication of mutagenicity”) ? for mitotic recombination (+ve at low dose only) Some experts consider this to be an <i>in vitro</i> assay.	LBI, 1975a
<i>Escherichia coli</i> , strain not specified in citing sources	Citric acid [and/or possibly one or more of its simple salts] tested. No further	Mutation	With and without S9	-ve	Hayes et al. 1984

	details provided in citing sources.				
<i>Saccharomyces cerevisiae</i> , strain D3	Citric acid tested. No further details provided in citing source.	Mitotic recombination	Not known	+ve	LBI, 1975a

References

Al-Ani F.Y. & Al-Lami S.K. (1988). Absence of mutagenic activity of acidity regulators in the Ames Salmonella/microsome test. *Mutation Research* 206, 467-470 (cited in CCRIS, 1991).

BIBRA (1993). Toxicity Profile for citric acid and its common salts. P.099. BIBRA International Limited, Carshalton, Surrey.

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Fujita H. et al. (1992). Mutagenicity test of food additives with *Salmonella typhimurium* TA97 and 102 (VII). Annual Report of Tokyo Metropolitan Research Laboratory of Public Health 43, 219-227.

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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 BIBRA, 1993; FASEB, 1977).

LBI (1975c). Litton Bionetics Inc. Mutagenic evaluation of compound FDA 75-12 (006132-04-3) sodium citrate, USP, FCC hydrous, granular. Contract No. 223-74-2104 (cited in BIBRA, 1993; FASEB, 1977).

von Brandt H & Hoehne G. (1951). Mutagenic action of some chemicals. *Drosophila Information Service* 25, 132-133.