Methoxy-3-methyl pyrazine (2 or 5 or 6-)

Botanical Source

Synonyms METHOXY-3-METHYL PYRAZINE (2-);
METHYL-3-METHOXY PYRAZINE (2-);
METHOXY-3 or 5-METHYL PYRAZINE (2-);
METHOXY-6-METHYL PYRAZINE (2-)

IUPAC Name

CAS Reference 68378-13-2
2847-30-5

E Number

Food Legislation

Council of Europe (CoE)	
Number	Comment
2266	Listed by the Council of Europe as acceptable for use in food at up to 5 ppm.

US Food and Drug Administration	
Number	Comment
-	-

Joint FAO/WHO Expert Committee on Food Additives (JECFA)		
Number	ADI	Comment
788	ND	No safety concern at current levels of intake when used as a flavouring agent.

FEMA	
FEMA No.	Comment
3183	Generally recognised as safe as a flavour ingredient:GRAS List Number 8

Natural Occurrence and Use in Food
Found in coffee, potatoes, sprouts; used in baked goods, candy, ice cream.

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.
Philip Morris	0.00020	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	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	0.00020	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	0.00020	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	0.00100	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Philip Morris	0.00020	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.

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.

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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

In vivo

Species	Test conditions	Endpoint	Results	References
Mouse (males and females; 4 per group)	A mixture of the 2-methoxy-, 5-methoxy- and 6-methoxy-3-methylpyrazine isomers (minimum 70% 2-methoxy isomer) was tested in a bone marrow micronucleus assay. A single intraperitoneal injection with up to 248 mg/kg bw was given and the animals were killed 30 hours later.	Chromosome damage	-ve	Wild et al. 1983
Drosophila melanogaster	A mixture of the 2-methoxy-, 5-methoxy- and 6-methoxy-3-methylpyrazine isomers (minimum 70% 2-methoxy isomer) was tested in a basc test for sex-linked recessive lethal mutations. Up to 10 mmol/l [1.24 mg/ml] was given in the diet to male flies which were then mated with untreated females.	Mutation	-ve	Wild et al. 1983

In vitro

Test system	Test conditions	Endpoint	Activation status	Results	References
Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538	A mixture of the 2-methoxy-, 5-methoxy- and 6-methoxy-3-methylpyrazine isomers (minimum 70% 2-methoxy isomer) was tested in an Ames test with up to 3.6 mg/plate.	Mutation	With and without S9	-ve (a good quality test)	Wild et al. 1983

References

Wild D et al (1983). Study of artificial flavoring substances for mutagenicity in the Salmonella/microsome, basc and micronucleus tests. Food and Chemical Toxicology 21, 707-719.