

Dimethyldihydrofuranolone (2,5-)

Botanical Source

Synonyms

HYDROXY-2,5-DIMETHYL-3(2H)-FURANONE (4-);
FURANEOL;
DIMETHYL-4-HYDROXY-2,3-DIHYDROFURAN-3-ONE(2,5-);
HYDROXY-2,5-DIMETHYL-2H-FURANONE-3 (4-);
DIMETHYL-4-HYDROXY-3-FURANONE (2,5-);
DIOXY HEXANONE;
ALLETONE;
PINEAPPLE KETONE;
PINEAPPLE FURANONE;
STRAWBERRY FURANONE;
DIMETHYL HYDROXY FURANONE (2,3,5[H]-);
FURALON;
ENHANSOL;
2,5-DIMETHYL-3-HYDROXY-4-OXO-4,5-DIHYDROFURAN;
2,5-DIMETHYL-4,5-DIHYDROFURAN-3-OL-4-ONE

IUPAC Name

2,5-DIMETHYL-4-HYDROXY-2,3-DIHYDROFURAN-3-ONE

CAS Reference

3658-77-3

E Number

Food Legislation

Council of Europe (CoE)

Number	Comment
536	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
1446	5254	No safety concern at current levels of intake when used as a flavouring agent

FEMA

FEMA No.	Comment
3174	Generally recognised as safe as a flavour ingredient:GRAS List Number 3

Natural Occurrence and Use in Food	
Found in beef, maple syrup, cassia oil; used in frozen dairy goods, baked goods, candy.	

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

Dimethyldihydrofuranolone (2,5-)

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

Smoke Chemistry		
Published Source	Level Tested %	Comment
BAT	0.00300	At maximum application level this ingredient is not associated with significant increases in levels of Hoffmann analytes in smoke.
Philip Morris	0.00010	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	0.00300	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	0.00300	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	0.00300	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 and specificity of the 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	0.00300	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
Lorillard	0.00001	The results indicate that the addition of the ingredient had no discernible effect on the inhalation toxicity of mainstream smoke.
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
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.

Dimethyldihydrofuranolone (2,5-)

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.

Dimethyldihydrofuranolone (2,5-)

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	
Mouse, 5-6 males per dose level	Single intraperitoneal administration at 0, 0.5, 1 or 1.5 g/kg bw, and peripheral lymphocytes were examined for micronuclei at 24, 48 and 72 hr.	Chromosome damage	+ve	Hiramoto <i>et al.</i> 1998	
Mouse, 10/group	Intraperitoneal administration of 0, 186, 371 or 928 mg/kg bw. Bone marrow cells examined for micronuclei. Further details of the study are difficult to deduce from this paper in Chinese.	Chromosome damage	+ve study quality cannot be determined	Xing <i>et al.</i> 1988	
Mouse	Intraperitoneal administration of 0, 186, 232 or 309 mg HDMF/kg bw. Cells [unclear which] examined for sister chromatid exchanges. Further details of the study are difficult to deduce from this paper in Chinese.	Chromosome effects	+ve study quality cannot be determined	Xing <i>et al.</i> 1988	
Mouse, males, numbers unclear	Intraperitoneal administration of 0, 232, 464 or 928 mg/kg bw, sperm examined for morphological defects. Further details of the study are difficult to deduce from this paper in Chinese	Germ cell effects	+ve study quality cannot be determined	Xing <i>et al.</i> 1988	

Mouse (males)	Germ cells of treated mice were examined for micronuclei induction. No further details were given in the citation, the original paper is in Chinese.	Chromosome damage	+ve study quality cannot be determined	Tian <i>et al.</i> 1992
---------------	---	-------------------	---	-------------------------

In vitro

Test system	Test conditions	Endpoint	Activation	Result	References
<i>Salmonella typhimurium</i> Strains TA97, TA98, TA100, TA102	Tested at four concentrations (0.5-4 mg/plate. Further details of the study are difficult to deduce from this paper in Chinese.	Mutation	With and without S9	+ve	Xing <i>et al.</i> 1988
<i>Salmonella typhimurium</i> strains TA98 and TA100	Ames test, at up to 10 mg/plate	Mutation	With and without S9	+ve	Hiramoto <i>et al.</i> 1996
<i>Bacillus subtilis</i> H17(rec+), M45(rec-)	Tested at five concentrations (20-120 µg/plate in a rec assay (measuring differential strain killing). Further details of the study are difficult to deduce from this paper in Chinese.	DNA damage (indicative test)	Without	+ve study quality cannot be determined	Xing <i>et al.</i> 1988
Supercoiled plasmid pBR 322 DNA	Incubated overnight at 2.6-780 uM, and DNA examined for strand breaks	DNA damage	Without	+ve	Hiramoto <i>et al.</i> 1996

DNA fragments from the human p53 tumour suppressor gene	DNA incubated with the test compound, either without added metal ions or co-incubated with copper II or iron III ions.	DNA damage	Without	-ve (without added metal ions) +ve (extensive with copper, weaker with ferric ions)	Yamashita <i>et al.</i> 1998
---	--	------------	---------	--	------------------------------

References

Hiramoto K *et al* (1996). DNA strand break by 2,5-dimethyl-4-hydroxy-3(2H)-furanone, a fragrant compound in various foodstuffs. *Mutation Research*, 359 (1), 17-24.

Hiramoto K *et al* (1998). Absorption and induction of micronucleated peripheral reticulocytes in mice after oral administration of fragrant hydroxyfuranones generated in the Maillard reaction. *Mutation Research*, 415 (1-2), 79-83.

Tian Q *et al* (1992). Genotoxic study of furaneol on mice germ cells. *Weishing Dulixue Zazhi*, 6, 26-28 (cited in Hiramoto *et al.* 1996).

Xing B *et al* (1988). Mutagenic studies on HDMF. *Chung-Hua Yu Fang I Hsueh Tsa Chih* (Chinese J Prevent. Med.), 22 (2), 85-87.

Yamashita N *et al* (1998). Superoxide formation and DNA damage induced by a fragrant furanone in the presence of copper(II). *Mutation Research*, 397 (2), 191-201.