

(案)

添加物評価書

ソルビン酸カルシウム

2008年5月

食品安全委員会添加物専門調査会

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1 <審議の経緯>

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0319025

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6 2008 5 26 58

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9 <食品安全委員会委員名簿>

2007 3 31

2007 4 1

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11 <食品安全委員会添加物専門調査会専門委員名簿>

2007 9 30

2007 10 1

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要 約

CAS 7492-55-9

1 I. 評価対象品目の概要 4 53 76

2 1. 用途

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5 2. 化学名 (参照 4、76)

6

7 Calcium Sorbate

8 CAS 7492-55-9

9

10 3. 分子式 (参照 4、76)

11 C₁₂H₁₄CaO₄

12

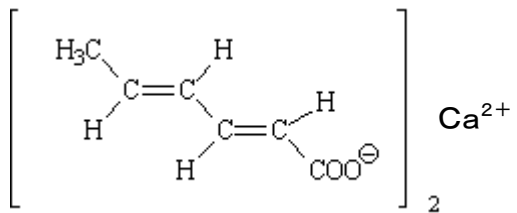
13 4. 分子量 (参照 4、76)

14 262.32

15

16 5. 構造式 (参照 4)

17



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19

20 6. 性状等 4 27 53 55 56 76

21 105 90

22 4

23 1.2 20

24 0.15% 20 28 32 20

25 58.2% 53 56 4

26

27 55 2

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29 53 76

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31 7. 評価要請の経緯

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1955

1960

80

2002 7

FAO WHO

JECFA

EU

8. 添加物指定の概要

JECFA

II. 安全性に係る知見の概要

1. 食品中での安定性

55

2

(1) 加熱処理による分解性

105

6

4,5-

4,5-oxohexenoate¹

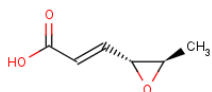
3%

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4,5-

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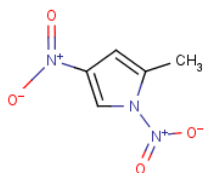
1 (2) 微生物による分解
 2 25 7 3
 3 1,3- CH₃CH=CHCH=CH₃
 4 *t,t*-2,4-
 5 (*t,t*-CH₃CH=CHCH=CHCH₂OH) *t*-4-
 6 (*t*-CH₃CH=CHCH₂CH₂CH₂OH)
 7 2- -3,5-
 8 CH₃CH(OC₂H₅)CH=CHCH=CH₂ (
 9 21)

10
 11 (3) 食品成分との反応性
 12 15 16 24 25 51
 13 52 20
 14 19
 15 ethylnitrolic acid CH₃C(=NOH)NO₂ ENA 1,4-dinitro-2-methylpyrrole
 16 DNMP ²
 17 15 16 18 24 34

18
 19 2. 体内動態 (吸収、分布、代謝、排泄)

20
 21
 22
 23
 24
 25 (1) 代謝
 26 β-
 27
 28 CH₃CH₂CH₂CH₂CH₂COOH CH₃CH₂CH₂COOH
 29 CH₃CH=CHCOOH 12
 30
 31 150 mg/
 32 5%

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3. 毒性

A. ソルビン酸類の毒性

11 18 JECFA

ADI

1 2 28

(1) 急性毒性

50%

LD₅₀

1 45

1

LD₅₀

			LD ₅₀ g/kg	
			12.50	45
			9.60	
			4.3	26
			3.6	

(2) 反復投与毒性

B6C3F1

10

20

0

1.25 2.5 5.0 10 20% 0 1,875 3,750 7,500 15,000 30,000 mg/kg

/ 4 14

20%

1

⁴ JECFA

a

	(kg)	(g/ /)	(g/kg /)
	0.02	3	150
	0.4	20	50
	10	250	25

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5.0%

59 83

(4) 生殖発生毒性

	SD		5		0	10%	0	5,000 mg/kg
/	2	120			60			
	F1		F1			70		
		F1					10	18 26
28								
			50			0	5%	0 2500 mg/kg
/	2		2		250			
2								5
						26	28	
26		28						
		2						
			50	1			0	0.1 0.5
5.0%	0	50	250	2,500 mg/kg	/	2	1,000	
			2				2	30
5.0%			252					
		0.1		0.5%				
				6		26	28	
28								
26								
	CD-1		20				0	4.6
21.4	99.1	460.0 mg/kg		6	15			17

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41 49

Wistar 19 22 0
3.4 15.8 73.3 340.0 mg/kg 6 15
20

41 49

(5) 遺伝毒性

IARC

EPA

a. DNA 損傷試験

Bacillus subtilis H17 M45 DNA Rec-assay
5.0 mg/disk S9mix 68

b. 復帰突然変異試験

Salmonella typhimurium TA98 TA100 TA1535
5,000 mg/plate S9mix
17 68

S. typhimurium TA98 TA100
2.0 mg/plate S9mix

70

S. typhimurium TA1535 TA1537 TA1538 TA98 TA100
2.0 mg/plate S9 mix

1			67	70	
2		<i>Saccharomyces cerevisiae</i> D4			
3	2.5%	S9 mix			67
4					
5	c. 遺伝子突然変異試験				
6					
7			V79		
8		1,050 µg/mL			
9	65				
10					
11					
12			V79		
13	800 µg/mL	200 µg/mL	1.5 mM		
14	65				
15			CHO		
16	1,000 µg/mL				70
17					
18					
19			V79		
20	20,000 µg/mL				65
21			CHO		
22	20,000 µg/mL				70
23					
24	d. 不定期 DNA 合成 (UDS) 試験				
25					
26		A549	DNA	UDS	
27	2,000 µg/mL	S9 mix			17
28					
29	e. DNA 切断試験				
30					
31		A 549	2,000 µg/mL		DNA
32		S9 mix			17
33					
34					
35		0 400 800 1,200 mg/kg			2
36	DNA			17	
37					
38	f. 染色体異常及び姉妹染色分体交換 (SCE) 試験				

1
 2 V79
 3 SCE 1,050 µg/mL
 4 SCE 1,050 µg/mL 65
 5 5,000 mg/kg SCE
 6 17
 7
 8
 9 CHO SCE
 10 1,000 µg/mL 70
 11 V79 SCE
 12 800 µg/mL 400 µg/mL 3.0
 13 mM SCE 200 µg/mL 65
 14 200 mg/kg
 15 200 mg/kg
 16 70
 17
 18
 19 Don
 20 SCE 40 mM 20 mM
 21 SCE 10 mM
 22 63
 23 V79
 24 SCE 20,000 µg/mL 20,000 µg/mL
 25 SCE 10,000 µg/mL
 26 65
 27 CHO
 28 SCE 20,000 µg/mL 70
 29
 30 g. 小核試験
 31
 32 5,000 mg/kg
 33 17
 34
 35
 36 200
 37 mg/kg
 38 200 mg/kg 24

B. ソルビン酸類に由来する副生成物

18

(1) 発がん性

Wistar SPF 48 1,000 ppm
 5-hydroxy-2-hexanoic-acid -lactone⁷
 1.2% 600 mg/kg / 2

47 JECFA

28

(2) 遺伝毒性

4,5-

105 6 4,5-
S. typhimurium TA100 TA1535
 5,000 µg/plate S9 mix
 S9mix 10%
 S9mix 30%

S9mix 4,5-
 50%

4,5-

4,5-

4,5-

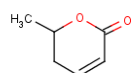
17

SCF

6

7

47



1
2 C. ソルビン酸類と他の食品添加物等の相互作用
3
4
5

6 18 SCF
7
8

9 6
10

11 (1) 発がん性
12
13

14 ① ソルビン酸と亜硝酸ナトリウム
15

16 Wistar 30
17 5% 0.1% 0.1%
18 5% 4 1
19

20 78
21

22 ② ソルビン酸とパラオキシ安息香酸エチル
23

24 SD-JCL 21
25 5.0% 5.0%
26 2.5% 2.5% 4 1
27

28 79
29

30 ③ ソルビン酸とナイシン
31

32 25 40 mg/kg /
33 2 mg/kg / 17
34 42
35

36 (2) 生殖発生毒性
37

38 25 40 mg/kg /
39 2 mg/kg / 8 F1 F4

1									
2		3.5		F1	F3				
3	F4							18	28
4	42								
5									
6	(3) 遺伝毒性								
7									
8								IARC	
9	EPA								
10									
11	ソルビン酸類と亜硝酸塩								
12	a. DNA 損傷試験								
13									
14									
15									
16	DNA							50	58
17		ethylnitrolic acid	ENA						
18			<i>in vitro</i>						
19									
20								52	
21		<i>B. subtilis</i>		Rec-assay				20	mM
22		160 mM	60	1					
23		DNA	pH				pH1.5	4.2	pH 6
24							ethylnitrolic acid	ENA	
25		1,4-dinitro-2-methylpyrrole (DNMP)					100 µg/disk	40	
26		µg/disk		71					
27									
28	b. 復帰突然変異試験								
29									
30		<i>S. typhimurium</i>	TA98	TA100					
31		200 µg/plate	ENA	150 µg/plate	DNMP		ENA	TA100	
32		DNMP	TA100	TA98			TA100		
33				71					
34			20 mM				160 mM		
35			80 mM			160 mM		pH3.5	
36	60	30		ENA	DNMP				
37						20 mM			
38				ENA	10 mM	DNMP	5 mM		

1 84)
 2 DNMP 1 mM
 3 8 mM pH6.8 37 1
 4 1-nitro-2-methyl-4-aminopyrrole NMAP *S.*
 5 *typhimurium* TA98 TA100 100
 6 µg/plate S9mix
 7 35
 8
 9 c. 遺伝子突然変異試験
 10
 11 V79
 12 pH 4.95 30 0.01
 13 0.2%
 14 0.01 1% 0.01 0.01 0.5%
 15 34
 16
 17 d. 染色体異常試験
 18
 19 15 mg/kg / 30
 20 24
 21 2 mg/kg /
 22 7.5+1 mg/kg /
 23 64
 24
 25 e. 小核試験
 26
 27 2.5 20 150 mg/kg
 28 1.25 10 75 mg/kg
 29 48
 30
 31 69
 32 200 mg/kg
 33 86
 34
 35 SCF
 36
 37 6
 38

1	② ソルビン酸と 5 種のアミン類				
2		0.33 μ M	5		
3				8	0.33 μ M
4	50	80	15		
5	5	<i>S. typhimurium</i> TA98 TA100 TA102 TA1535			
6	TA1537				5 mg/plate
7	S9 mix				<i>Escherichia coli</i>
8	PQ37	SOS spot test	DNA		S9mix
9			HeLa		DNA
10		10 mg/mL			
11					15
12					
13	③ ソルビン酸カリウムとアスコルビン酸及び 5 種の鉄塩				
14		400 μ g/disk		75 μ g/disk	5
15		Fe-EDTA			
16	9	0.5 0.9 μ g/disk	40 50	30	
17	5		<i>B. subtilis</i> H17 rec ⁺	M45 rec ⁻	
18	Rec-assay	3	Fe-EDTA		
19	DNA				
20					
21		<i>S. typhimurium</i> TA98 TA100			
22		100 μ L/plate	TA100	S9 mix	
23					
24			2.5		19
25					
26	4. ヒトにおける知見				
27					
28					
29					
30			6 18		
31				18	
32	90		4%		
33					
34		18			
35					

8

9 Fe-EDTA

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18 38 39

5. 一日摂取量の推計等
(1) わが国における評価

13

1997

19.6 mg/ / 89
2003 13.6 mg/ / ADI 25
mg/kg / 1.08% 90%

31

16

31.1 mg/ / ADI 25 mg/kg /
2.5% 88

(2) 米国における評価

1987

NAS/NRC GRAS

1,670 758 1,660

753 10 33

1983

25 mg/ 23 26 mg/kg /6 24

22

(3) EU における評価

1984 1986

29.4 mg/ / 87

¹⁰ 241 1986 17.2 mg/ /

1 ADI

2 25 mg/kg /

3 40

4

5 Ⅲ. 国際機関等における評価

6 1. JECFA における評価

7 JECFA 1961 1965

8 1973 17

9 NOEL 2,500 mg/kg / 100 0 25 mg/kg

10 / ADI 28

11 JECFA 1985 29

12

13

14

15 ADI 91

16

17 2. FDA における評価

18 FDA

19

20 26

21 GRAS

22 GMP 7

23

24 3. EU における評価

25 SCF 1994

26 1974 JECFA National Food

27 Agency

28

29

30 1

31

32 2 10%

33

34 3 *in vivo* *in vitro*

35

36

37

38

1	4					
2	5					
3						
4						
5	6					
6						
7						
8		750	5,000 mg/kg	/		
9	NOEL	750 mg/kg	/	700	1,400 mg/kg	/
10		NOEL 1,400 mg/kg	/			
11	2,500 mg/kg	/			JECFA	1974
12	NOEL 5.0%	2,500 mg/kg	/			
13	6					
14						
15		SCF			NOEL5.0%	
16	2,500 mg/kg			100	ADI 0 25 mg/kg	/
17		6				
18						
19						
20		E203	5			
21						

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
		3		5		0 1.0 2.0 5.0 10% 0 500 1,000 2,500 5,000 mg/kg /		26 28
		3		8		0 1.0 2.0% 0 250 500 mg/kg /		26 28
発がん性		64		50		0 2.5 5.0% 0 3,750 7,500 mg/kg /	64	60 61
		17		25		40 mg/kg /		26 42
		80		48 50		0 1.0 5.0 10% 0 1,500 15,000 mg/kg /	5.0% 10% 1.0% 1,500 mg/kg / 5.0% 10% NOEL NOEL	41 48
		104		48		0 1.5% 630 mg/kg / 850mg/kg / 10% 4,330 mg/kg / 5,690 mg/kg /	10% 1.5% 10% NOEL 5%	41 43
	ラット	60		6		0.1% 50 mg/kg / 0.3% 150 mg/kg /		44

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
発がん性(つづき)	ラット	104		150		0 2.5 5.0% 0 1,250 2,500 mg/kg /	5.0%	59 83
生殖発生毒性		120		5		0 10% 0 5,000 mg/kg /	F1	10 18 26 28
		60						
		F1 70						
		250		50		0 5% 0 2,500 mg/kg /	NOEL:5% 2,500 mg/kg / JECFA	26 28
		2 252		30		0 0.1 0.5 5.0% 0 50 250 2,500 mg/kg /	0.1 NOEL:5% 2,500 mg/kg / JECFA	26 28
		6 15 (17)		20		0 4.6 21.4 99.1 460.0 mg/kg		41 49
		6 15 (20)		19 22		0 3.4 15.8 73.3 340.0 mg/kg		41 49
遺伝毒性	<i>In vitro</i>	DNA Rec-assay	<i>Bacillus subtilis</i> H17 M45			5.0 mg/disk	S9 mix	68
			<i>S. typhimurium</i> TA98 TA100 TA1535			5,000 mg/plate	S9 mix	17 68
	<i>In vitro</i>		<i>S. typhimurium</i> TA98 TA100			2.0 mg/plate	S9 mix	70

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No	
遺伝毒性(つづき)	<i>In vitro</i>		<i>S. typhimurium</i> TA1535 TA1537 TA1538 TA98 TA100			2.0 mg/plate	S9 mix	67 70	
				<i>Saccharomyces cerevisiae</i> D4		2.5%		S9 mix	67
	<i>In vitro</i>			V79		1,050 µg/mL		65	
	<i>In vitro</i>			V79		800 µg/mL	200 µg/mL 1.5 mM	65	
				CHO		1,000 µg/mL		70	
	<i>In vitro</i>			V79		20,000 µg/mL		65	
				CHO		20,000 µg/mL		70	
	<i>In vitro</i>	DNA UDS		549	A		2,000 µg/mL	S9 mix	17
	<i>In vitro</i>	DNA			A 549		2,000 µg/mL	S9 mix	17
		DNA					0 400 800 1,200 mg/kg		17
	<i>In vitro</i>	SCE			V79		1,050 µg/mL	1,050 µg/mL	65

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
遺伝毒性(つづき)		SCE				5,000 mg/kg		17
	In vitro	SCE	CHO			1,000 µg/mL		70
		SCE	V79			800 µg/mL	400 µg/mL 3.0 mM 200 µg/mL SCE	65
						200 mg/kg	200 mg/kg	70
	In vitro	SCE	Don			40 mM	20 mM SCE 10 mM	63
		SCE	V79			20,000 µg/mL	20,000 µg/mL SCE 10,000 µg/mL	65
	In vitro	SCE	CHO			20,000 µg/mL		70
						5,000 mg/kg		17
						200 mg/kg	mg/kg 24	200 70
	ヒトにおける知見							
								18
				慢性蕁麻疹の90症例			4%	18

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
ヒトにおける知見(つづき)								18 38 39

B ソルビン酸類に由来する副生成物

				/				No
発がん性		2		48		1,000 ppm 1.2% 600 mg/kg /		28
遺伝毒性	In vitro		S. typhimurium TA100 TA1535	4,5-	105	5,000 6 µg/plate	S9 mix S9mix 10% S9mix 30% S9mix 4,5- 50% 4,5- 4,5-	17

C ソルビン酸類と他の食品添加物等の相互作用

				/				No
発がん性		1		30		5% 0.1% 0.1% 5% 4		78

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
発がん性(つづぎ)		1		雌雄各21		5.0% 5.0% 2.5% 2.5% 4		79
		17		25		40 mg/kg / 2 mg/kg /		42
		8 F1 F4		雌雄各25		40 mg/kg / 2 mg/kg /	F1 F3 3.5 F4	18 28 42
遺伝毒性	<i>In vitro</i>	DNA Rec-assay	<i>B. subtilis</i>	60 1		20 mM 160 mM	DNA pH pH1.5 4.2 pH 6	71
					ethylnitrolic acid ENA 1,4-dinitro-2-methyl pyrrole (DNMP)	100 µg/disk 40 µg/disk		
	<i>In vitro</i>		<i>S. typhimurium</i> TA98 TA100	ENA DNMP	200 µg/plate ENA 150 µg/plate DNMP	ENA TA100 TA98 DNMP TA100 TA100	71	

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No
遺伝毒性(つづき)	<i>In vitro</i>		<i>S. typhimurium</i> TA98 TA100		1-nitro-2-methyl-4-aminopyrrole NMAP	100 µg/plate	S9mix	35
	<i>In vitro</i>		V79			0.01 0.2% 0.01 1% 0.01 0.01 0.5%		34
		30				15 mg/kg / 2 mg/kg / 7.5 + 1 mg/kg /	24	64
	<i>In vitro</i>					2.5 20 150 mg/kg 1.25 10 75 mg/kg	48	69
						200 mg/kg		86

試験種類	動物種	試験期間	投与方法	動物数/群	被験物質	投与量	試験結果	参照No	
遺伝毒性(つづき)	<i>In vitro</i>				5	5	S9 mix	15	
						mg/plate			
		DNA				<i>Escherichia coli</i> PQ37			S9mix
		DNA				HeLa	10		
					10				
	<i>In vitro</i>	Rec-assay		<i>B. subtilis</i> H17 rec ⁺ M45 rec ⁻	5	Fe-EDTA	3	Fe-EDTA DNA	19
					400				
						75			
						5	Fe-EDTA		
						0.5 0.9			
	<i>In vitro</i>					100	TA100 S9 mix	2.5	
						μL/plate			

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