

o-Cymen-5-ol

PARA THYMOL

[CAS # 3228-02-2]

An Isomer of Thymol

Main Properties

- ❖ Low odor and taste.
- ❖ Highly Stable with favorable safety profile.
- ❖ Non halogen containing compound.
- ❖ Specially recommended for Skin Care products.
- ❖ For Product Protection like cosmetics.
- ❖ Wide range of Action.
- ❖ Anti Oxidant.
- ❖ Anti-microbial action better than Thymol.

Legislative details

INCI name (EC, PCPC):	o-Cymen-5-ol
EINECS no.:	221-761-7
CAS no.:	3228-02-2
Chemical name:	4-isopropyl-m-cresol
EC approval:	76/768/EEC, Annex VI/1,38, max. 0.1 % (All Cosmetic) 1223/2009, Annex V no 38, max. 0.1 % (All Cosmetic)
Japan (cosmetics):	Leave-on and rinse-off products, including the use on mucous membranes: 0.1%. For rinse-off products when not to be applied on mucous membranes: no legislative upper limit.
USA:	Cosmetic Ingredient Review: Safe at concentrations of up to 0.5%
Australia:	AICS-listed (CAS no.: 3228-02-2)
CLS 1999 listing:	Listed as 'Isopropyl Methylphenol', no. 41-103132
China listing:	IECSC listed. This ingredient is listed in the first draft of the inventory of Existing Cosmetic Ingredients in China (IECIC).

Efficacy

Several Studies have been done on the efficacy of o-Cymen-5-ol.

Phenol coefficient

The phenol coefficient refers to the bactericidal activity by a 5-10 min. contact. For Salmonella typhi and for Staphylococcus aureus, the phenol coefficient was 17, for Escherichia coli it was 19. This means the bactericidal effects of o-Cymen-5-ol appear at 1/17 - 1/19 of the concentration compared with phenol.

Bacterial effect on 60 second contact

Pathogenic Escherichia coli O157:H7 were placed at 1000 ppm, 2000 ppm, and 5000 ppm concentration of o-Cymen-5-ol for 60 seconds. At 1000 ppm number of bacteria reduced and at 2000 ppm and 5000 ppm, the bacteria were extirpated.

Efficacy against Pathogenic Organisms

o-Cymen-5-ol has been used in the treatment against Athlete's foot. It showed strong anti-bacterial activities against Parasitic micro-organisms such as Trichophyton.

Anti-viral Activities

Action on Influenza virus has been confirmed at 200 ppm

Other Uses

Industrial uses comprise disinfection of Air conditioners and Rooms and by treating Fabrics to obtain an antibacterial, deodorant and anti-fungal effect. When Fabric is treated with solution inhibition effect is observed in test using molds of S. aureus

Minimum Inhibitory Concentration

Table 2 MIC Values (%) against several species in comparison to other preservatives (literature data)

	S. aureus	B. subtilis	A. oryzae	A. niger
o-Cymen-5-OL	0.02	0.02	0.005	0.01
Benzoic Acid	0.12	0.12	0.06	0.06
Methylparaben	0.15	0.15	0.0075	0.0075
Ethylparaben	0.15	0.0075	0.038	0.038
Propylparaben	0.025	0.025	0.015	0.02
Butylparaben	0.0075	0.0075	0.015	0.015

Table 3. Minimum inhibitory concentrations.

Organism	MIC (ppm)	Organism:	MIC (ppm)
Fungi / yeast:		Gram-positive bacteria:	
Pullularia pullulans IFO 6353	75	Mycobacterium H2	50
Cladosp. Cladosporiodies IFO 6348	80	Bacillus subtilis ATCC-6633	150
Chaetomium globosum ATCC 6205	75	Bacillus fluorescens	100
Penicillium citrinum ATCC 9849	100	Bacillus cereus	150
Aspergillus niger ATCC 6275	75	Staphylococcus aureus FDA 209P	150
Aspergillus oryzae	50	Gram-negative bacteria:	
Rhizopus stolonifera S.N.32	75	Escherichia coli IFO 3301	200
Gliocladium virens IFO 6355	100	Klebsiella pneumonia IFO 13277	200
Trichophyton ferrugineum	100	Vibrio parahaemolyticus IFO 12711	250
Trichophyton rubrum	100	Salmonella typhimurium IFO 13245	200
Trichophyton interdigitale	100	Pseudomonas aeruginosa IFO 3755	500
Trichophyton mentagrophytes	100		
Zygosaccharomyces salsus	50	(data from several Sources)	
Williano anomala	50		
Candida sp.	100		
Saccharomyces sp.	100		

Safety

The safety of o-Cymen-5-ol is substantiated by a broad package of safety tests. Confirming the safety of the product. A summary is given below:

Acute toxicity

LD50 (oral) > 2.2 g/kg.

LD50 (oral): 6280 mg/kg;

LD50 (i.p.): 470 mg/kg;

LD50 (subcutaneous): 184 mg/kg.

Skin irritation

No irritation at 0.1 and 1.0 % on either intact or abraded skin (rabbit).

Primary irritation index (PII) 0.06 out of 8.0 (5% in PEG-400, rabbit).

PII 0.22 out of 4.0 (10 % in ethanol, 3 daily 24 h exposures, guinea pigs).

No reactions observed (0.5, 1.0, 2.0 and 4.0% in 50% ethanol, guinea pig).

No irritation (0.1 % and 1.0%, human, 24 h).

Eye irritation

No irritation in washed eyes (1.0%, rabbit). Some effects noted in unwashed eye after 1 and 4 h, but not observed after 24 h.

Skin sensitization

Not sensitizing, no reaction observed (2%, guinea pig, Maximization study).

Not Sensitizing in a human RIPT test (nine 24 h exposures).

Mutagenicity

Not mutagenic in a test with Salmonella typhimurium and Escherichia coli.

30-day toxicity

Animals survived doses of 0.7 and 2.0 g/kg. At 0.7 g/kg no noticeable variations were observed in body weight or food consumption.

90-day toxicity

Rats were fed 10, 100, 1000, or 2000 mg/kg for 90 days. No deaths observed. In the highest dose group, body weight gain decreased, but increased after non treatment.

Photosensitization

No evidence of photosensitization is shown (guinea pigs, up to 2 %).

Absence of estrogen-like activity

o-Cymen-5-ol did not show a significant increase in MCF-7 cell proliferation (indicative of estrogenic activity) in the range of the concentrations tested (10⁻³ to 10⁻⁷ppm). Positive control showed a clear increase in cell proliferation at (10⁻⁸ to 10⁻¹² M).

Solubility

The water solubility of o-Cymen-5-ol is rather low. As with all preservatives, it is not advised to dissolve o-Cymen-5-ol in the Fat Phase, when protecting emulsions. It is advised to make a premix of o-Cymen-5-ol in a suitable solvent (e.g. Propylene Glycol, Butylene Glycol, Phenoxyethanol or Benzyl Alcohol). The premix can be added to the final product after emulsification. It has to be made sure that o-Cymen-5-ol is well dissolved in the product, o-Cymen-5-ol has a characteristic tendency to precipitate as crystals. In mixed preparations, crystal may precipitate a long time after preparation. Particular caution is needed in emulsified or solubilized preparations.

Solvent:	Grams of o-Cymen-5-ol per 100 g solvent:
Ethanol	45
Isopropanol	40
Propylene glycol	18
Glycerine	0.1
Liquid paraffin	1.01
Water	0.015



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