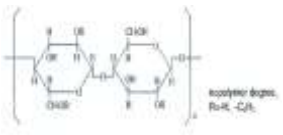
Ethyl cellulose

Ingredient synonym names

Ampacet E/C, Aquacoat, Aquacoat ECD 30, Aquacoat ECD 30FMC, Cellulose ethyl, Cellulose ethyl ether, Cellulose ethylate, Cellulose, ethyl ester, Cellulose, triethyl ether, ET 100 (cellulose derivative), ETs, ETs (Polysaccharide), Ethocel, Ethocel 150, Ethocel 890, Ethocel E50, Ethocel E7, Ethocel MED, Ethocel N10, Ethocel N200, Ethocel N7, Ethocel STD, Ethylcellulose, G 200, G 200 (polysaccharide), G 50, G 50 (Polysaccharide), 5; Nixon E/C, SPT 50CPS, T 100, T 100 (Polysaccharide), Triethyl cellulose.

IDENTIFIER DETAILS

Ingredient chemical structure



CAS Number	FEMA Number	Additive Number	Ingredient EC Number
9004-57-3	-	-	-

CAS Additional Number	FL Number	CoE Number
11097-03-3 154608-92-1 166735-68-8 51331-16-9 57307-96-7	-	-

Chemical formula: Unspecified

Ingredient CLP Classification

Ingredient REACH Registration Number

-

Acute Oral Toxicity	Eye Damage/Irritation	Carcinogenity
0	0	0
Acute Dermal Toxicity	**Respiratory Sensitisation**	**Reproductive Toxicity**
0	0	0
Acute Inhalation Toxicity	**Skin Sensitisation**	**Aspiration Toxicity**
0	0	0
Skin Corrosive/Irritant	**Mutagenicity/ Genotoxicity**	**Specific Target Organ Toxicity**
0	0	0

SPECIFICATIONS

Ethyl cellulose

Melting Point	240°C	Boiling Point	-

STATUS IN FOOD AND DRUG LAWS

Acceptable Daily Intake (ADI, mg/kg)	Not specified
Acceptable Daily Intake (ADI) comments	In 2018 The EFSA ANS Panel concluded that there was no need for a numerical ADI and that there would be no safety concern at the reported uses and use levels for the unmodified and modified celluloses. The Panel considered an indicative total exposure of around 660–900 mg/kg bw per day for microcrystalline, powdered and modified celluloses. Group ADI for modified celluloses: ethyl cellulose, ethyl hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, methyl ethyl cellulose, and sodium carboxymethyl cellulose - JEFCA (1989)
FDA Status	73.1: - Listing of colour additives exempt from certification 172.868: - Food additives permitted for direct addition to food for human consumption 182.90: - GRAS: Substances migrating to food from paper and paperboard products 573.420: - Food additives permitted in feed and drinking water of animals

CoE limits - Beverages (mg/kg)	-	CoE limits - Food (mg/kg)	-	CoE limits - Exceptions (mg/kg)	-

HUMAN EXPOSURE

Ingredient Natural Occurence (if applicable)

Not reported to occur in nature

References - Ingredient Natural Occurence

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Ingredient Reported Uses

Ethyl cellulose is used as a microcapsule material, binder and filler [FDA, 01/04/09]. This compound is also used as a food additive, rubber substitute, adhesive, lacquer and coating [FDA, 01/04/09]. It is also a key component of printing inks, and paper food packaging materials [FDA, 01/04/09].

References - Ingredient Reported Uses

FDA, CFR - Code of Federal Regulations Title 21, revised 01/04/09],

TOXICITY DATA

In Vivo Data

Acute Toxicity Data

5g/kg BW, Rat, Oral
5g/kg BW, Rabbit, Skin

In Vivo Carcinogenicity/Mutagenicity

In 2018 the EFSA ANS Panel concluded that their structural, physicochemical and biological similarities, allows for read-across between all the celluloses. Despite the limitations of some of the studies, the available data do not indicate a genotoxic concern for microcrystalline cellulose, methyl cellulose and carboxy methyl cellulose, and by read-across, of the other modified and unmodified celluloses [EFSA ANS, 2018].

References - In Vivo Carcinogenicity/Mutagenicity

EFSA ANS (2018). Re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives. EFSA Journal 2018, 16(1)5047.

Dermal Toxicity

No data identified

References - Dermal Toxicity

No data identified

Reproductive/ Developmental Toxicity

The development toxicity of Aquacoat ECD ethylcellulose aqueous dispersion was assessed by Freeman et al. (2000) in sets of 25 Charles River Sprague-Dawley CD rats. These rats were presumed to be pregnant and were exposed by oral gavage to doses of 0, 903, 2709 and 4515 mg/kg/day of Aquacoat ECD once a day on days 6-15 of gestation. On day 20 of gestation the surviving foetuses were removed by caesarean section, weighed, and killed. Gross and microscopic examination of the dams revealed no toxic effects, with foetal sex ratios and body weights being similar to controls. Skeletal examination of the foetuses revealed ossified or waxy ribs in foetuses receiving 4514 mg/kg/day; also an increase in incidence of thickened ribs was observed at doses of 2709 mg/kg/day and higher. These findings were deemed statistically significant. No statistically significant changes were observed in any of the mothers [Freeman et al., 2000].

Concerning reproductive and developmental toxicity, data are available for microcrystalline cellulose, methyl cellulose, hydroxypropyl cellulose and sodium carboxy methyl, cellulose. The substances were tested in mice, rats, hamsters and/or rabbits with oral dosing via gavage. Adverse effects on reproductive performance or developmental effects were not observed with modified and unmodified celluloses at doses greater than 1000 mg/kg bw by gavage (often the highest dose tested). Specific toxicity data were not always available for all the celluloses for all endpoints. In general, the most complete data sets were available for microcrystalline cellulose and sodium carboxy methyl cellulose. Given the similarities in their structure, relevant physicochemical, metabolic and toxicological properties, the EFSA ANS Panel considered it possible to read-across between all the celluloses [EFSA ANS, 2018].

References - Reproductive/ Developmental Toxicity

Freeman C, Palmieri MA, Kotkoskie LA. (2000) Developmental toxicity study of Aquacoat ECD ethylcellulose aqueous dispersion administered orally to rats. Food Chem Toxicol. 38 (1):71-4.

EFSA ANS (2018). Re-evaluation of celluloses E 460(i), E 460(ii), E 461, E 462, E 463, E 464, E 465, E 466, E 468 and E 469 as food additives. EFSA Journal 2018, 16(1)5047.

Inhalation Toxicity

No data identified

References - Inhalation Toxicity

No data identified

Cardiac Toxicity

No data identified

References - Cardiac Toxicity

No data identified

Addictive Data

No data identified

References - Addictive Data

No data identified

Behavioral data

DeMerlis et al. (2005) performed neurobehavioural tests on equal numbers of rats from each dose group that had been exposed to an aqueous Ethyl Cellulose dispersion in the subchronic test. Over four different staggered sessions the following evaluations were implemented: home cage evaluations, handling evaluations, open field evaluations, reflex assessments, grip strength, landing foot splay, proprioception, air righting ability and body weight. None of these evaluations revealed any adverse effects.

References - Behavioral data

DeMerlis CC, Schoneker DR, Borzelleca JF. (2005) A subchronic toxicity study in rats and genotoxicity tests with an aqueous ethylcellulose dispersion. Food Chem Toxicol.; 43 (9):1355-64.

In Vivo - Other Relevant Studies

Kotkoskie and Freeman (1998) studied the effects of dosing Sprague-Dawley rats with Aquacoat ECD ethyl cellulose aqueous dispersion via oral gavage at doses of 903, 2709 or 4515 mg/kg BW for 90 days. When compared with control rats no statistically significant changes in body weight, food consumption, organ weight or haematology were observed. However, in male rats receiving more than 2709 mg/kg; there was an elevation of ALT and AST levels and a reduction in total protein and globulin levels. Histopathology revealed no adverse effects. The NOAEL was deemed to be greater than 4.5 g/kg BW in female rats and 903 mg/kg BW in male rats [Kotkoskie and Freeman, 1998].

Another study exposed groups of 80 rats orally to 1.2% Ethyl cellulose for 8 months; this is equivalent to 182 mg/rat/day. No changes in appearance, behaviour or growth occurred in any of the animals. Gross pathology and histology revealed no adverse effects [Patty’s Industrial Hygiene and Toxicology 3rd Ed].

DeMerlis et al. (2005) administered an aqueous Ethyl Cellulose dispersion orally to Sprague-Dawley CD rats (20/sex/group) at doses of 0, 2000, 3500, and 5000 mg/kg/day for a minimum of 3 months. None of the exposed animals died during the dosing stage. At 3 months the rats were euthanized; had specific organs weighed and complete macroscopic and histopathological examinations. No statistically significant adverse changes were observed in either the organ weights, macroscopic or histopathological analyses. The highest dose tested was therefore deemed to be the NOAEL (5000 mg/kg/day) [DeMerlis et al., 2005].

References - In Vivo - Other Relevant Studies

Patty's Industrial Hygiene and Toxicology, (1981) 3rd Ed, Vol 2, Part A, G.D. Clayton and F.E. Clayton, John Wiley and Sons Inc, New York, pg 2556.

Kotkoskie LA and Freeman C. (1998) Subchronic oral toxicity study of Aquacoat ECD aqueous dispersion in the rat, Food Chem Tox, 36, 705-709

DeMerlis CC, Schoneker DR, Borzelleca JF. (2005) A subchronic toxicity study in rats and genotoxicity tests with an aqueous ethylcellulose dispersion. Food Chem Toxicol.; 43 (9):1355-64.

In Vitro Data

In Vitro Carcinogenicity/Mutagenicity

DeMerlis et al. (2005) assessed the genotoxicity of an aqueous Ethyl Cellulose dispersion using the Ames and Mouse Lymphoma tests. Salmonella Typhimurium stains TA1535, TA1537, TA98 and TA100 and an Escherichia Coli strain WP2uvrA/Pkm101 were exposed to 5000 µg/plate of the dispersion, in the presence or absence of S9. No mutagenic activity was observed at the concentration tested. For the mouse lymphoma assay a subline of 3.7.2.c of mouse lymphoma L5178Y cells was exposed to 250 µg/ml for 3 (plus or minus S9) or 24 hours (minus S9). From the results it was concluded that the ethyl cellulose dispersion did not display mutagenicity.

References - In Vitro Carcinogenicity/Mutagenicity

DeMerlis CC, Schoneker DR, Borzelleca JF. (2005) A subchronic toxicity study in rats and genotoxicity tests with an aqueous ethylcellulose dispersion. Food Chem Toxicol.; 43 (9):1355-64.

In Vitro - Other Relevant Studies

No data identified

References - In Vitro - Other Relevant Studies

No data identified

Emissions and Associated Toxicity Data

The pyrolysis products of ethyl cellulose and of cigarette paper treated with ethyl cellulose was examined by Forehand et al. (1995) using two different pyrolysis methods. The first technique involved pyrolysing the sample at 600oC then analysing the products given off using GC/MS with a polar chromatographic column. The other technique also involved pyrolysing the sample at 600oC but this time used off line derivatization with BSTFA followed by GC/MS. Pyrolysis of ethyl cellulose on it's own yielded the following products: Acetaldehyde, 1,3-Cyclopentadiene, Propanal, Ethoxyethene, Ethanol, Propenal, Furan, Ethoxypropene, Ethanol and Ethoxypropanal. Some of the products generated from pyrolysis of an ethyl cellulose treated paper include: Acetaldehyde, 1,3-Cyclopentadiene, Propanal, Furan, 2-Propanone, 5-methyl-1,3-Cycloptentadiene, 2,3-

Dihydrofuran, 2-Propenal, 2-methyl-Furan and Butanal.

Trace metal analysis of ethyl cellulose ash revealed the following heavy metal concentrations: nickel 31ppm, iron 16ppm and copper 5ppm [Communication from General Cigar and Tobacco Co. 1977]. Traces of lead, cadmium and zinc were also detected at concentrations less than 3ppm.

References - Emissions and Associated Toxicity Data

Forehand J. B., Dong J. Z., Moldoveanu S. C., (1995) Pyrolysis products of ethyl cellulose and of cigarette paper treated with ethyl cellulose. Legacy:

General Cigar and Tobacco Co. (1977), Letter detailing a verbal report from Hercules Chemical Co. on ethyl cellulose ash analysis, obtained off Filenet, Item ID 003776561