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SCIENTIFIC OPINION

Scientific Opinion on the use of Gum Acacia modified with Octenyl Succinic Anhydride (OSA) as a food additive[1]

EFSA Panel on Food Additives and Nutrient Sources added to Food[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

The Panel on Food Additives and Nutrient Sources added to Food provides a scientific opinion on the use of OSA modified gum acacia as an emulsifier for flavourings, and other uses. The SCF in 1990 and 1999 considered that the existing data on gum acacia (E 414) did not point to any toxicological concern. In 2009, JECFA allocated a temporary ADI "not specified" to OSA modified gum arabic. The Panel notes that OSA modified gum acacia is not of concern with respect to mutagenicity. From a 90-day study in the rat, NOAELS of 3411 and 4052 mg/kg bw/day (the highest dose tested), for male and female rats, respectively, were derived. The Panel considers that reading across from data on gum acacia (E 414) and food starch sodium octenyl succinate (E1450) there would be no requirements for additional toxicity data on OSA modified gum acacia. The Panel considers the available toxicological dataset to be insufficient to derive an ADI. The mean dietary exposure to OSA modified gum acacia from its combined uses as an emulsifier in flavour-oil emulsions and other emulsifier uses ranges from 4.1 mg/kg bw/day in female adults, to 12 mg/kg bw/day in children (age 1.5-4.5 years). The highest potential exposure (97.5th percentile) ranges from 12 mg/kg bw/day in male adults to 33 mg/kg bw/day in children. Given these intake estimates and taking the lowest derived NOAEL (3411 mg/kg bw/day), a margin of safety of about 280 for male adults and of about 100 for children can be calculated. The Panel considers in this case these margins adequate. Based on the results of the available studies, the information on gum acacia itself and on other OSA modified starches, the Panel concludes that the use of OSA modified gum acacia as an emulsifier in foods at the proposed uses and use levels is of no safety concern.

KEY WORDS

Gum acacia modified; Octenyl succinate modified gum acacia; gum arabic; hydrogen octenylbutanedioate; CAS 455885-22-0; acacia gum (E 414; CAS 9000-01-5), starch sodium octenyl succinate (E 1450).

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SUMMARY

Following a request from the European Commission, the Panel on Food Additives and Nutrient Sources added to Food (ANS) was asked to provide a scientific opinion on the use of gum acacia modified with n-octenyl succinic anhydride as an emulsifier for flavourings and other uses.

The present opinion deals with the safety of gum acacia modified with n-octenyl succinic anhydride (OSA) for use as an emulsifier in various in foods.

The Panel notes that no ADME studies on OSA modified gum acacia are available.

Studies in animals show that gum acacia itself is almost completely digested and degraded in the caecum. A study in humans shows that gum acacia is metabolised in the colon.

The Panel, however, notes that chemical modification reduces the extent of enzyme-catalyzed hydrolysis in starch and gives rise to a modified food starch with increased levels of slowly digestible starch and resistant starch. Therefore, the Panel considers that the OSA-modification of gum acacia could also result in a reduction in digestion/fermentation by colonic microflora of the large intestine as compared to gum acacia itself.

The acute oral LD50 in rats for OSA modified gum acacia has been demonstrated to be greater than 2000 mg/kg bw.

In a 90-day subchronic dietary study in the rat, administration of OSA modified gum acacia in the diet for 13 weeks did not produce any adverse effects. Microscopic evaluation of selected organs and tissues revealed no unusual lesions or patterns of distribution that would suggest an adverse effect of exposure to OSA modified gum acacia in the diet. From this study, the No-Observed-Adverse-Effect Levels (NOAELs) were determined to be 3411 and 4052 mg/kg bw/day, the highest dose tested, for male and female rats, respectively.

The Panel considers that reading-across from available data on gum acacia (E 414) and food starch sodium octenyl succinate there would be no requirements for additional toxicity data on OSA modified gum acacia.

The Panel notes that the allergenicity of OSA modified gum acacia might be similar to that of other gums.

The Panel considers that the available toxicological dataset is insufficient to derive an ADI.

The potential dietary exposure to OSA modified gum acacia from its combined uses as emulsifier in flavour-oil emulsions and other emulsifier uses was calculated.

The mean potential exposure to OSA modified gum acacia from its combined uses as emulsifier in flavour-oil emulsions and as emulsifier for other specified uses, ranged from 4.1 mg/kg bw/day in female adults, to 12 mg/kg bw/day in children (aged 1.5-4.5 years).

The estimated worst case exposure (97.5th percentile) to OSA modified gum acacia from the proposed combined uses is equal to 12 mg/ kg bw/day in male adults, and to 33 mg /kg bw/day for children (age 1.5-4.5 years). Given these estimates and taking the lowest NOAEL derived from the 90-day study (3411 mg/kg bw/day), the Panel calculated a margin of safety of about 280

for male adults, and of about 100 for children. The Panel considers that in this case, these margins of safety are adequate.

Based on the results of the available studies, the information on gum acacia itself and on other OSA modified starches, the Panel considers the use of OSA modified gum acacia as an emulsifier in foods at the proposed uses and use levels of no safety concern.

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

Emulsifiers are regulated under Directive 95/2/EC4 of the European Parliament and the Council on food additives other than colours and sweeteners.

A manufacturer has requested the authorisation of gum acacia modified with n-octenyl succinic anhydride as an emulsifier for flavourings and other uses under Directive 95/2/EC. According to the applicant the additive is produced by the introduction of lipophilic groups to gum acacia by a controlled esterification process analogous to the production of starch sodium octenyl succinate (E 1450). The starting material acacia gum (E 414) is an authorised food additive under Directive 95/2/EC.

Gum acacia modified with n-octenyl succinic anhydride is proposed for use as an emulsifier for flavourings in a variety of applications and also for a number of other emulsifier uses including in fruit flavoured beverages, salad dressings, sauces and icing.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29 (1) (a) of Regulation (EC) No 178/20025, the European Commission asks the European Food Safety Authority to provide a scientific opinion on the safety of gum acacia modified with octenyl succinic acid anhydride as a food additive for the uses, as an emulsifier, proposed in the dossier submitted by the applicant.

[4] European Parliament and Council Directive 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners, OJ L 61, 18.3.1995, p.1.

[5] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety, OJ L 31, 1.2.2002, p.1.

ASSESSMENT

1. Introduction

The present opinion deals with the safety of gum acacia (gum arabic) modified with n-octenyl succinic anhydride (OSA) for use as an emulsifier in flavourings and in foods. In what follows the substance will be called: OSA modified gum acacia.

2. Technical data

2.1. Identity of substance

OSA modified gum acacia. CAS Registry Number 455885-22-0.

Chemical Description

The petitioner indicates that OSA modified gum acacia is produced from acacia gum (CAS No. 9000-01-5; synonyms: Gum acacia; Gum arabic; acacia gum; Indian gum); the gum is derived from the exudates of the tree species Acacia seyal or Acacia senegal. The modification involves the introduction of lipophilic groups to the polysaccharide in gum acacia by a controlled esterification processes.

The gum acacia polysaccharide chain itself consists of mainly three fractions: (i) The main fraction is a highly branched polysaccharide (MW: 3.105 g/mol) consisting of a backbone of β-(1,3) linked galactose units with linked branches of arabinose and rhamnose units and terminating in a glucuronic acid unit in the form of a magnesium, potassium or and calcium salt; (ii) A smaller fraction (~10 wt % of the total) consists of a higher molecular weight (~1.106 g/mol) arabinogalactan–protein complex (GAGP-GA glycoprotein) in which arabinogalactan chains are covalently linked to a protein chain through serine and hydroxyproline groups. The attached arabinogalactan in the complex contains ~13% (by mole) glucuronic acid; (iii) The smallest fraction (~1% of the total) has the highest protein content (~50 wt %) and consists of a glycoprotein which differs in its amino acids composition from that of the GAGP complex (Randall et al., 1988; Fenyo and Vandervelde, 1990; Islam et al., 1997; Idris et al., 1998; Goodrum et al., 2000).

2.2. Specifications

The petitioner describes OSA modified gum acacia as a hydrocolloid, soluble in cold water. The specifications as provided by the petitioner are given in Table 1. The Panel notes that these specifications are identical to those established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at its 71st meeting (JECFA, 2009).

Table 1: Chemical Specifications for OSA modified gum acacia as proposed by the petitioner and as established by JECFA.

	Specifications as proposed by the petitioner
DESCRIPTION	Off -white to light tan, free flowing powder
FUNCTIONAL USES	Emulsifier
CHARACTERISTICS	
IDENTIFICATION	Forms flocculent precipitate in lead sub-acetate solution (TS)
Solubility	1 g in 2 mL water, forms a free flowing solution, acid to litmus; insoluble in ethanol
pH of 5% solution	3.5 to 6.5
Viscosity of 5% solution	30 cps maximum (0.03 Pa.s), (5%, 25ºC)
PURITY	
Degree of esterification	Not more than 0.6%
Loss on drying	15.0% (5 hours at 105ºC)
Total ash	10% (530ºC)
Acid insoluble ash	Not more than 0.5% maximum
Insoluble matter	Not more than 1%
Starch or dextrin	(See tests) No bluish or reddish colour produced
Tannin-bearing gums	(See tests) No blackish colouration or precipitate formed
Residual OSA	(See tests) Not more than 0.3%
Microbiological criteria	*Salmonella:* Absent in 25 g; *E.coli:* Absent in 1 g
Lead	Not more than 2 mg/kg
TESTS	
Starch or dextrin	Boil a 1 in 50 aqueous solution of the sample; add about 0.1 mL iodine TS.
Tannin bearing gums	To 10 mL of a 1 in 50 aqueous solution of the sample; add about 0.1 mL ferric chloride TS
Residual OSA	Principle: HPLC method on 2-bromacetophenone-derivatised methanolic extract of a sample.

2.3. Manufacturing process

The petitioner indicates that OSA modified gum acacia is derived from the exudates of the tree species Acacia seyal or Acacia senegal by esterification in aqueous solution with not more than 3% n-octenyl succinic anhydride (CAS No 26680-54-6) in a process analogous with the production of starch sodium octenyl succinate (E 1450).

In the process the acacia gum is mixed with water (pH 7-8) at 80°C, filtered and transferred into a reaction vessel together with n-octenyl succinic anhydride. The pH is adjusted to 4-6. The

reaction temperature is between 38 - 63°C and the reaction time is 1-1.5 hours. After a holding period (holding time not given) the reaction mixture is heated for maximum 15 seconds at a temperature not higher than 69°C ± 0.5 and subsequently spray dried to a powder.

2.4. Methods of analysis in food

Acacia gum and other hydrocolloids are analysed according to the methods described in the United States Pharmacopeia (USP) and the National Formulary (NF). In addition, the petitioner states that special High-performance liquid chromatography (HPLC) techniques have been developed to separate the monosaccharide products of hydrolysis from gum acacia.

Gum acacia contains proteins and soluble dietary fibre and consists of arabinogalactans and other carbohydrate moieties. The petitioner indicates that it is virtually impossible to quantify the exact concentration of the gum acacia after it has been added to food, since similar compounds are almost invariably present in foods and will interfere with the analysis. Even after treatment with protease, glucosidase, amylase, etc. (AOAC method for soluble dietary fibre; AOAC, 1998) there is no existing, validated method to separate fibre mixtures into their individual fibre components.

Monosaccharides may be analyzed by specific tests with lectins and HPLC analyses (O'Donnell and Baird, 1993). HPLC analyses after hydrolysis of the OSA modified gum acacia can be performed. Various Acacia species can be identified based on galactose/rhamnose and arabinose ratios (Ward, 2005).

The European Pharmacopoeia and the British Pharmacopoeia (2000, 3rd Edition) include in their monograph for gum acacia, a method using TLC (thin layer chromatography) for separation of monosaccharides from the polymer.

The petitioner further specifies that after isolation from a food system which does not contain interfering gum components, the presence of gum acacia may be qualitatively determined by using the USP identification test and AOAC 1998 Official Methods of Analyses for soluble dietary fibre. Since the OSA modified gum acacia is typically used at low levels, the concentration of OSA in the finished food product is likely to be significantly below the detection levels for free residual OSA and bound OSA. Hence analyses should be conducted on the modified gum acacia before incorporation in food, as a quality assurance step.

The petitioner indicates that the OSA treated starches (not the finished food containing the starch) are analyzed for free OSA, based on JECFA recommendations (JECFA, 2006).

Specific tests for free or residual OSA in octenyl succinylated starch and OSA modified gum acacia have been developed as indices of stability. A methodology for analysing free and bound OSA for octenyl succinylated starches was reported (Park and Goins, 1995). The bound OSA may be used as a more specific index of the esterified moieties in the gum substrate, using gas chromatographic and mass spectrometric methods. The bound OSA in the form of an ester can be released from the starch after alkali treatment. Routine analyses for free OSA from the modified gum acacia and modified starches can be conducted based on the method in the JECFA

specifications for octenyl succinylated starches (JECFA, 2006). A limit of not more than 0.3% free OSA in octenyl succinylated starches has also been adopted for OSA modified gum acacia.

2.5. Stability, reaction and fate in food

According to the petitioner, the OSA ester linkage is stable in an aqueous solution at the pH range of foods and beverages and under usual food and processing conditions. The other components in the food serve to protect the OSA-gum ester linkage from direct degradation.

To break the ester linkage in modified gum acacia or starches, extreme alkaline or acidic conditions are required that are not typical of food processing operations. In general, the processing conditions of foods and beverage containing OSA modified gum acacia are not performed at extreme pH levels.

2.6. Case of need and proposed uses

OSA modified gum acacia is proposed as an emulsifier in flavour-oil preparations for use in baked goods, beverages (non-alcoholic and alcoholic), breakfast cereals, processed cheese, chewing gum, flour confectionary and icings, egg products, fish products, frozen dairy, fruit ices, gelatines and puddings, gravies, imitation dairy products, instant coffee and tea, jams and jellies, meat products, milk products, other grains, processed poultry, processed fruit juices, processed vegetable juices, snack foods, soft candy, soups, and sweet sauces.

OSA modified gum acacia will also be used as an emulsifier at a level of 600 mg/kg and 1000 mg/kg in select fruit flavour drinks, 780 mg/kg in selected beverages (carbonated juice and energy drinks), and 10000 mg/kg in salad dressing, sauces and icing.

See "other emulsifier" use levels in Table 2.

Table 2: Use levels (mg/kg food) of OSA modified gum acacia as emulsifier in flavour-oil emulsions and as emulsifier for other uses as proposed by the petitioner.

Food Category	Use levels as emulsifier in flavour-oil emulsions	Use levels for other uses as emulsifier	Cumulative use levels
Baked Goods	500		
Beverages Type I, Non-alcoholic	220	780[1]	220 or 1000
Beverages Type II, Alcoholic	220		
Breakfast Cereals	300		
Cheese (processed)	120		
Chewing Gum	60		
Confectionery and Icings[2]	240, 300	10 000	10 300
Egg Products	140		
Fish Products	500		
Frozen Dairy	500		
Fruit Ices	500		

Gelatins and Puddings	500		
Gravies	400		
Imitation Dairy Products	240		
Instant Coffee and Tea	240		
Jams and Jellies	240		
Meat Products	240		
Milk products	220		
Other Grains	240		
Processed Poultry	500		
Processed Fruits (juices)	400	600[4]	400 or 1000
Beverages Containing Fruit Juice[3]	0	1000	1000
Processed Vegetable Juice	400		
Salad Dressing	0	10 000	10 000
Snack Foods	440		
Soft Candy	300		
Soups	240		
Sauces	0	10 000	10 000
Sweet Sauce	400		

[1] Other emulsifier" uses in (carbonated juice and energy drinks); [2] Includes icings only. Includes the icing portion of iced baked goods (e.g., carrot cake with icing). Assumed that all iced cakes contain 10% icing and cookie/biscuit items contain 20% icing. Peanut butter included at 240 mg/kg for flavouring use only; [3] Flavoring uses not included for beverages containing fruit juice, only "other emulsifier" uses proposed for this category; [4] Other emulsifier" uses in vitamin- or mineral-fortified juice-containing drinks only.

The petitioner states that OSA modified gum from acacia has enhanced emulsifying properties. This results in lower usage levels. The improvement of the emulsifying properties is achieved by the introduction of lipophilic groups into the polysaccharide by controlled esterification procedures (Ward, 2004).

2.7 Information on existing authorisations and evaluations

2.7.1. Gum acacia

Based on the lack of adverse effects in the available toxicity studies, JECFA in 1982 and in 1990 allocated an ADI 'not specified' to gum acacia. The Committee stressed that the evaluation covered only gum acacia from Acacia senegal and closely related species. In 1998 (51st session), the specification was changed to cover also gum acacia from Acacia seyal (JECFA, 1982a; 1990; 1998).

In the EU, Gum acacia (gum Arabic) (E 414) has not been formally evaluated in full by the SCF, but the Committee stated that the existing data do not point to any toxicological concern (SCF, 1990; SCF, 1999).

Gum acacia has been evaluated in the US as a direct food additive. In the US the approval is listed in 21 CFR 184.1330 (FDA US, 2006) and is established as GRAS for use as an emulsifier, stabilizer, thickener and formulation aid. Approved food uses include beverages and beverage bases, chewing gum, flour confectionary and icings, dairy product analogs, fats/oils, gelatines, puddings and fillings, hard candy and cough drops, nuts and nut products, frozen confection products, snack foods, soft candy, and all other food categories.

2.7.2. OSA Modified Gum Acacia

In the US, OSA modified gum acacia was granted FEMA GRAS status for use in flavourings in a variety of food categories, including baked goods, beverages (non-alcoholic and alcoholic), breakfast cereal, processed cheese, chewing gum, condiments/relishes, flour confectionery and icings, egg products, fats/oils, fish products, frozen dairy, fruit ices, gelatines/puddings, granulated sugar, gravies, hard candy, imitation dairy, instant coffee/tea, jams/jellies, meat products, milk products, other grains, processed poultry, processed fruits, processed vegetables, reconstituted vegetables, seasonings/flavours, snack foods, soft candy, soups, sugar substitutes, and sweet sauces (Smith *et al*., 2005).

In 2009, JECFA allocated a temporary ADI "not specified" for OSA modified gum arabic. The ADI is temporary, pending submission of data by the end of 2011, showing hydrolysis of OSA modified gum arabic, to confirm the validity of using gum arabic data in the evaluation of OSA modified gum arabic (JECFA, 2009).

2.7.3. Other substances

Food grade starch modified with n-octenyl succinic anhydride [i.e. food starch sodium octenyl succinate (E 1450)] is approved in the EU, and is listed in the US in 21 CFR 172.892(d) as a multipurpose additive for direct addition to human food for consumption (EC, 1995; FDA, 2001).

Modified starches, including starch sodium octenyl succinate, have been reviewed by the JECFA and an ADI "not specified" was established (JECFA, 1982b).

2.8. Exposure

The petitioner provided daily exposure estimates to OSA modified gum acacia based on the proposed use-levels (Table 2) and on individual data from food consumption surveys, collected as part of the UK Dietary Survey (NDNS), of pre-school children (4-day dietary record) (Gregory et al., 1995), young people (7-day dietary record) (Gregory et al., 2000) and adults (7-day dietary record) (Henderson et al., 2002). The exposure estimates were performed for children aged 1.5 to 4.5 years, young people aged 4 to 10 years, female and male teenagers aged 11 to 18 years, and adults (male, female and adults together) aged 19 to 64 years (Technical dossier submitted by the

petitioner). NDNS food codes were matched to the food categories reported in Table 2 and then each individual potential exposure was calculated based on the assumption that OSA modified gum acacia as emulsifier in flavour-oil emulsions was present at the proposed use levels in listed categories. In addition, calculations were performed for the exposure to OSA modified gum acacia as other emulsifier for other uses, and as cumulative uses. Individual body weights were available for all population groups to calculate individual's exposure per kg bw/day. Exposure calculations for the mean and the 90th, 95th and 97.5th percentile for all persons (including non-users) and for consumers-only were provided.

The potential dietary exposure to OSA modified gum acacia from combined uses as emulsifier in flavour-oil emulsions and as emulsifier for other uses is presented in Table 3. The potential estimated mean exposure to the combined emulsifiers ranged from 171 mg/day (children aged 1.5-4.5), to 376 mg/day (adult males). Highest exposure levels (97.5th percentile) ranged from 488 mg/day (children 1.5-4.5), to 948 mg/day (adult males). Children generally have higher food intake than adults, when expressed on a body weight basis, and therefore represent the group with the highest potential exposure per kg body weight. As shown in Table 3, mean potential exposure to OSA modified gum acacia from combined uses as emulsifier in flavour-oil emulsions and as emulsifier for other uses ranged from 4.1 mg/kg bw/day in female adults to 12 mg/kg bw/day in children aged 1.5-4.5, whereas highest potential exposure (97.5th percentile) ranged from 12 mg/kg bw/day in male adults to 33 mg/kg bw/day in children aged 1.5-4.5.

Table 3: Potential dietary exposure (mg/day) to OSA modified gum acacia from combined uses as emulsifier in flavour-oil emulsions and as emulsifier for other uses[1] from all proposed food categories in the UK by population group (NDNS Data)

Population Group	Age group (years)	Exposure to OSA modified gum acacia (mg/day)		Exposure to OSA modified gum acacia (mg/kg bw/day)	
		Mean	97.5th Percentile	Mean	97.5th Percentile
Children	1.5-4.5	171	488	12	33
Young people	4-10	266	595	11	26
Female teenagers	11-18	305	749	5.8	15
Male teenagers	11-18	358	887	6.6	16
Female adults	19-64	278	792	4.1	13
Male adults	19-64	376	948	4.6	12
All adults	19-64	326	859	4.3	12

[1] see Table 2

The Panel noted that these data represent conservative estimates of potential exposure because it was assumed that OSA Modified Gum Acacia would be present in all foods for which it is proposed for use. For individual food categories this might be realistic since consumer loyalty and individual preferences might cause a person to always choose particular brands containing the additive. However, when potential exposures from all foods are combined the scenario becomes less likely.

3. Biological and toxicological data

3.1. Absorption, distribution, metabolism and excretion

According to the petitioner, there are currently no absorption, distribution, metabolism and excretion (ADME) data available for OSA modified gum acacia.

The Panel, however, notes that data in literature show that arabic gum (i.e. gum acacia) is almost completely digested by guinea-pigs (O'Dell *et al*., 1957). Studies in the rat show that gum arabic degradation occurs in the caecum and that it is associated with increased methane excretion, increased volatile fatty acids (VFA) concentration and changes in the proportions of various VFAs in the feces (Ross *et al,* 1981).

In a study in humans, gum arabic administered to men for 21 days at a dose of about 350 mg/kg bw/day, had little effect on glucose tolerance and stool weight, but decreased the serum cholesterol. There was no significant increase in fecal bile acids and neutral sterols. Gum arabic could not be recovered from the stool, which according to the authors suggests that gum arabic is metabolised in the colon (Ross *et al.*, 1983).

There are ADME data available for approved modified food starches produced by esterification in a similar way as for the production of OSA modified gum acacia. Approved modified starches include: distarch phosphate (E 1412); phosphate distarch phosphate (E 1413); acetylated distarch phosphate (E 1414); starch acetate (E 1420); starch acetate esterified with vinyl acetate (E 1421); acetylated distarch adipate (E 1422); hydroxypropyl distarch phosphate (E 1442); starch sodium octenyl succinate (E 1450); acetylated oxidized starch (E 1451).

Kelley (1991) indicates that OSA provides hydrophobic domains that enhance the emulsifying ability of starch. The digestion of both starch and modified food starch is known to occur via enzyme-catalyzed hydrolysis (Han and BeMiller, 2006). The modifications made to starch via methods such as hydroxypropylation, *n*-octenylsuccination, and combinations of crosslinking and substitution reduce the extent of enzyme-catalyzed hydrolysis and produce a modified food starch with increased levels of slowly digestible starch and resistant starch. Therefore, the Panel considers that the OSA-modification of gum acacia may be expected to also result in a reduction in digestion/fermentation by colonic microflora of the large intestine as compared to gum acacia itself.

3.2. Toxicological data

3.2.1. Acute oral toxicity

The petitioner provides data from two acute oral studies in rats (PSL, 2002; PSL, 2003a).

In a first study, OSA modified gum acacia with specifications as in section 2.2, was used in a single-dose acute oral study in male and female Sprague-Dawley albino rats. Ten animals (5 male/5 female) were administered a dose of 2000 mg/kg bw via gavage. The petitioner indicates that the study was conducted to comply with Good Laboratory Practices (GLP) (EPA/TSCA and FDA). Animals were observed for 14-days post-exposure for mortality, signs of overt toxicity, behavioural changes and body weight. No overt signs of toxicity were observed and no gross abnormalities were noted at necropsy. Therefore, the single dose acute oral LD50 value for OSA modified gum acacia is considered > 2000 mg/kg bw in male and female rats.

A second similar GLP study was conducted with OSA-10 (modified using 10% n-octenyl succinic acid anhydride) in female Sprague-Dawley albino rats only. Five female rats were administered a dose of 2000 mg/kg bw via gavage. The same observations as in the first study were carried out. All animals survived, gained weight and appeared healthy. No overt signs of toxicity were observed and no gross abnormalities were noted at necropsy. Therefore, the single-dose acute oral LD50 value for this OSA modified gum acacia is considered > 2000 mg/kg bw for female rats. The petitioner indicates that the increased degree of substitution (esterification) had no effect on the LD50 compared with the 3% level in the OSA modified gum acacia used in the first study.

3.2.2. Short-term and subchronic toxicity

A dietary palatability study was conducted to select dietary levels for a subsequent 90-day dietary study in rats (Eurofins/PSL, 2006).

In this study, OSA modified gum acacia was administered in the diet for 14 days to 40 Hsd:Sprague Dawley SD rats (5 male and 5 females/group) at dose levels of 0, 15 000, 30 000 or 50 000 mg/kg rat feed. According to the petitioner this is equivalent to mean daily intakes of OSA modified gum acacia of 0, 1237, 2534 and 4198 mg/kg bw/day in male rats and 0, 1325, 2674 and 4481 mg/kg bw/day in female rats.

Dose levels of 0, 10 000, 25 000 and 50 000 mg/kg rat feed were identified and proposed for the 90-day dietary study. The petitioner indicates that the upper dose level for the subsequent 90-day study was set based on an upper limit concentration of 5%, which typically will not result in nutritive effects/imbalance in the animals. The petitioner states that at concentrations above 5%, there are worries about adding confounders to the study because the nutritive value of the diet fed

to the animals may be adversely affected. The 14-day palatability study examined the 5% concentration level in the diet and was conducted to evaluate firstly if the animals would accept the diet, and secondly to look for any evidence of toxicity that would assist in setting dose levels in the definitive 90-day trial.

Animals were observed daily for viability, overt signs of toxicity and behavioural changes, and weekly for a battery of clinical observations. Body weights and food consumption were recorded. Gross necropsies were performed on all animals. No mortality was observed during the course of the study. No treatment-related changes were noted in clinical observations, food consumption/efficiency, body weight/body weight gain, or at gross necropsy. A No-Observed-Adverse-Effect Level (NOAEL) of 50 000 mg/kg rat feed (equivalent to about 4200 mg/kg bw/day for male rats and to about 4500 mg/kg bw/day for in female rats) was identified.

In the 90-day study, OSA modified gum acacia was administered in the diet to 80 Hsd:Sprague Dawley SD rats (10 male and 10 females/treatment group) at levels of 0, 10 000, 25 000 or 50 000 mg/kg rat feed. According to the petitioner this is equivalent to mean daily intakes of OSA modified gum acacia of 0, 679, 1715, and 3411 mg/kg bw/day in male rats, and 0, 799, 2032 and 4052 mg/kg bw/day in female rats. The study was conducted in compliance with OECD guidelines and FDA Redbook 2000 guidance (FDA, 2003).

Signs of toxicity were examined daily, and body weights weekly. Ophthalmological examinations were conducted prior to and during treatment. A functional observational battery and motor activity evaluation were conducted prior to test termination. Food consumption was measured weekly and food efficiency calculated. Haematology, clinical chemistry and urinalysis examinations were conducted on samples collected prior to test termination. All animals were sacrificed and necropsied at the end of the study. Histological examination of tissues and organs from the control and high dose groups were conducted. No mortality or clinical signs of toxicity were observed during the course of the study.

OSA modified gum acacia consumption had no significant effect on body weight parameters or food consumption. There were no adverse changes in haematology, coagulation, urinalysis, or clinical chemistry parameters in male or female rats at any dose level. No significant macroscopic and organ weight changes were noted upon necropsy. No histopathological evidence of toxicity was produced at doses up to 50 000 mg/kg rat feed in the diet.

The NOAEL in this study is 50 000 mg/kg rat feed, the highest dose level tested, equivalent to 3411 mg/kg bw /day in male rats and 4052 mg/kg bw/day in female rats (Eurofins/PSL, 2007).

3.2.3. Genotoxicity

The petitioner provided data from a commissioned Ames assay on OSA modified gum acacia using *Salmonella* strains TA97a, TA98, TA100 and TA1535, and *E. coli* strain WP2 *uvr*A (328), both in the presence and absence of metabolic activation (Aroclor induced rat liver S9). The study was conducted in compliance with Good Laboratory Practice and the OECD test guidelines 471 and 472 (OECD, 1997).

Test article concentrations of 5, 10, 50, 100, 500, 1000, 2500 and 5000 µg per plate were tested in the plate incorporation assay and 100, 500, 1000, 2500 and 5000 µg per plate were assessed in the confirmatory pre-incubation assay. No test concentration resulted in a mean number of revertants two times greater than the mean of the concurrent controls. Therefore, under the conditions of the study, OSA modified gum acacia was negative for the induction of mutagenicity in the bacterial reverse mutation assay and was not considered genotoxic (Next Century Incorporated, 2006).

From an Ames assay with OSA modified gum acacia (CAS No 455885-22-0) carried out under the same experimental conditions and in compliance with the same guidelines as the test described above, Schmitt *et al.* (2008) also concluded that there are no indications that OSA modified gum acacia possesses mutagenic potential.

3.2.4. Chronic toxicity and carcinogenicity

No experimental data have been provided.

The Panel notes that studies on carcinogenicity of gum arabic (acacia gum) in mouse (B6C3F, both sexes) and rat (F344, both sexes) are available. As regards the mouse, in a 103-weeks feeding study with acacia gum at levels up to 5% in the diet (equivalent to about 7500 mg/kg bw/day), there was no site at which an increase in tumour incidence could be clearly associated with the administration of the chemical (NTP, 1982).

Similarly in a 103-week feeding study in the rat with acacia gum at levels up to 5% in the diet (equivalent to about 2500 mg/kg bw/day), no effects of the test compound were reported with respect to clinical signs, survival, or incidence of gross or microscopic lesions (NTP, 1982).

3.2.5. Reproductive and developmental toxicity

No experimental data have been provided.

3.2.6. Other studies

No data on oral intolerance of OSA modified acacia gum have been provided. The petitioner states that the production of OSA modified gum acacia does not alter the small fraction (~ 10 wt % of total) of high molecular weight arabinogalactan-protein complex present in the gum acacia polysaccharide chain.

Acacia gum elicited an immune response after oral dosing comparable with the specific immune response elicited by hens' egg ovalbumin, and purification of acacia gum led to a significant reduction of the immune response under in vivo test conditions (Strobel et al., 1986).

4. Discussion

The present opinion deals with the safety of gum acacia modified with n-octenyl succinic anhydride (OSA) for use as an emulsifier in flavourings and in foods.

The Panel notes that no ADME studies on OSA modified gum acacia are available.

Studies in animals show that gum acacia itself is almost completely digested and degraded in the caecum. A study in humans shows that gum acacia is metabolised in the colon.

The Panel however, notes that chemical modification reduces the extent of enzyme-catalyzed hydrolysis of starch and gives rise to a modified food starch with increased levels of slowly digestible starch and resistant starch. Therefore, the Panel considers that the OSA-modification of gum acacia could also result in a reduction in digestion/fermentation by colonic microflora of the large intestine as compared to gum acacia itself.

The acute oral LD50 in rats for OSA modified gum acacia has been demonstrated to be greater than 2000 mg/kg bw.

In a 90-day subchronic dietary study in the rat, administration of OSA modified gum acacia in the diet for 13 weeks did not produce any adverse effects. Microscopic evaluation of selected organs and tissues revealed no unusual lesions or patterns of distribution that would suggest an adverse effect of exposure to OSA modified gum acacia in the diet. From this study the NOAELs were determined to be 3411 and 4052 mg/kg bw/day, the highest dose tested, for male and female rats, respectively.

The Panel considers that reading across from available data on gum acacia (E 414) and food starch sodium octenyl succinate (E1450) there would be no requirements for additional toxicity data on OSA modified gum acacia.

The Panel notes that the allergenicity of OSA modified gum acacia might be similar to that of other gums.

The Panel considers that the available toxicological dataset is insufficient to derive an ADI.

The estimated worst case exposure (97.5th percentile) to OSA modified gum acacia from its proposed combined uses as emulsifier in flavour-oil emulsions and as emulsifier in specified food categories is equal to 12 mg/kg bw/day in male adults, and to 33 mg/kg bw/day for children (age 1.5-4.5 years). Given these estimates and taking the lowest NOAEL derived from the 90-day study (3411 mg/kg bw/day), the Panel calculated a margin of safety of about 280 for male adults and of about 100 for children. The Panel considers these margins of safety resulting from the proposed use levels of OSA modified gum acacia adequate.

CONCLUSION

Based on the results of the available studies, the information on gum acacia itself and on other OSA modified starches, the Panel considers the use of OSA modified gum acacia as an emulsifier in foods at the proposed uses and use levels of no safety concern.

DOCUMENTATION PROVIDED TO EFSA

1. Submission of OSA modified Gum Acacia for use as a food additive in the EU. Technical dossier submitted by the petitioner on 12 November, 2007.
2. Eurofins/PSL, 2006. Gum Acacia-Modified: Palatability/Toxicity Study (14-Day Dietary Study in Rats). PSL Study Number 20435, October.
3. Eurofins/PSL, 2007. Gum Acacia-Modified: Subchronic Toxicity Study (90-Day Dietary Study in Rats). PSL Study Number 20801, April.
4. PSL, 2002. Acute Oral Toxicity Study in Rats-Limit Test. PSL Study Number 11690, December 17th.
5. PSL, 2003a. Acute Oral Toxicity Up and Down Procedure in Rats. PSL Study Number 13675, August 1st.
6. PSL, 2003b. Primary Skin Irritation Study in Rabbits. PSL Study Number 13676, August 1st.

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GLOSSARY/ABBREVIATIONS

ADI	Acceptable Daily Intake
ADME	Absorption, distribution, metabolism, excretion
ANS	Panel on Food Additives and Nutrient Sources added to Foods
AOAC	Association of Analytical Communities
bw	body weight
CAS	Chemical Abstracts Service
EC	European Commission
EFSA	European Food Safety Authority
FAO/WHO	Food and Agriculture Organization/World Health Organization
FDA	Food and Drug Administration
FEMA	Flavour and Extracts Manufacturers Association
GLP	Good Laboratory Practices
GRAS	Generally Recognised As Safe
HPLC	High-performance liquid chromatography
JECFA	Joint FAO/WHO Expert Committee on Food Additives
NDNS	UK Dietary Survey
NOAEL	No-Observed-Adverse-Effect Level
NF	National Formulary
LD_{50}	Lethal Dose that kills 50% of the tested population
OECD	Organisation for Economic Co-operation and Development
OSA	Octenyl Succinic Anhydride
SCF	Scientific Committee on Food
TLC	Thin Layer Chromatography
TS	Test Solution
USP	United States Pharmacopeia