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Givaudan Roure
Flavors

March 9, 1999

Office of Premarket Approval (HF2-200)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
200 C Street, SW
Washington, DC 20204

RE: Mesquite Wood Extract

Dear Reviewer:

In accordance with the Food and Drug Administration's proposed regulation 21 CFR 170.36 (62 FR 18938; April 17, 1997), the below signed is notifying the agency of the determination that mesquite wood alcoholic extract is generally recognized as safe (GRAS) for use as a flavoring ingredient in alcoholic beverages.

This GRAS exemption claim is primarily based on scientific procedure and pertinent information in support of this claim has been gathered in accordance with the proposed rulemaking guidelines. The detailed information supporting the GRAS notification is available for the FDA review and copying, or could be sent to the FDA upon request.

Based on the information supplied, we request that the agency affirm the GRAS status for the use of mesquite wood extract.

If further information is required and for further correspondence, please do not hesitate to contact me at (513) 948-3549.

Respectfully submitted,

Nancy A. Higley, Ph.D.
Vice President, Product Safety & Regulatory Assurance

NAH/djc

Attachments

Mesquite

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Givaudan Roure Flavors Corporation
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Cincinnati, Ohio 45216

Telephone 513 948 8000
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Voluntary GRAS Notification

Of

Mesquite Wood Extract

March 1999

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General Requirements

Notifier:

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Cincinnati, Ohio 45216

Phone: (513) 948-3549
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Notified Substance:

Mesquite Wood Extract

Conditions of use:

Purpose: Flavoring substance
Use Category: Distilled spirits
Use Level: 1 lb./400 wine gallons
Consuming Public: Adults

Basis of GRAS Determination:

This GRAS exemption claim is based on scientific procedure.

Availability of Information:

The detailed information and data supporting the GRAS notification are available for the FDA review and copying at reasonable times at the specific address set out in the notice or will be sent to the FDA upon request.

Specific Requirements

A. Identity and Specifications

Preferred Name: Mesquite Wood Extract
Botanical Source: Prosopis spp.
CAS Number: 93165-66-3
EINECS Number: 296-953-7
Method of Synthesis: 1 lb. Mesquite chips/400 gallons 80 proof alcohol
Stir 2 hours with ~~X~~ no heat
Filter out chips

Typical Analysis:

Physical State: Liquid
Color: Tan to brown
Flashpoint: >50°F
Refractive Index: 1.395 – 1.392 @ 20°C
Specific Gravity: 0.84 – 0.86 @ 25/25°C
% Solids: 0.009%

Volatile Constituents:

Constituent	PPM
acetaldehyde diethyl acetal	0 026
benzaldehyde	0.004
borneol	0.001
2-butenal	0.011
1-docosene	0.082
1-eicosene	0 149
ethyl caprylate	0.001
1-hexadecene	0.059
limonene	0.010
para-mentha-1(7),2-dien-8-ol	0.005
1-octadecene	0.159
pinol	0.003

B. History of Use

Native tribes who used mesquite for culinary purposes were, among others, the Hopi, Pima, Papago, Yuma, and Seri. References indicate that whole pods contain a pulpy sweet nutritional material that is ground and made into bread, cakes, mush, and porridge. Pods are also used for making a sweet drink (atole) or fermented beer (Reference: Ethnobotany Mesquite Database).

Further information indicates that native tribes utilized mesquite extracts as poltices, infusions, and decoctions for the oral and dermal treatment of numerous ailments (References: E.F. Castetter and R.M. Underhill. 1935. The Ethnobiology of the Papago Indians; L.S.M. Curtin. 1949. By the Prophet of the Earth; F. Russel. 1908. The Pima Indians).

A review of culinary sources indicates the use of mesquite in traditional southwest food preparations and seasoning mixes. More recent food products suggest the popularity of mesquite flavored barbecue sauce.

C. Substantial Equivalence

The proposed use of mesquite extract is primarily as an alternative to oak chip extract (21 CFR 172.510 and FEMA 2794).

Analysis of oak chip extract indicates 20 volatile constituents (refer to Table 2 in Section 2). All 12 of the mesquite chip extract volatile constituents are found in the GRAS flavoring substance oak chip extract. The concentrations of the similar constituents are nearly the same. General experience concludes that the overall exposure to mesquite wood extract will be less than the oak chip extract use in distilled spirits in which the spirits often age 3 years or more in oak ressels.

similar, not the same

D. Exposure

Mesquite chip extract is used as a flavoring substance for a targeted adult population with taste preferences tending towards southwestern cuisine.

As with oak chip extract, the use of mesquite extract will be self-limiting. General experience with wood extracts provides evidence that high concentrations in finished flavor and food result in an undesirable astringent taste.

Mesquite wood extract as used at 1 lb./400 wine gallons.

Based on 1995 USDA Economic Research Survey, 1.8 gallons spirits are consumed per adult (>21 years) per year.

The per capita x 10 calculation provides a generously conservative estimate of what a "high eater" would consume. This calculation was used to calculate the constituent exposure from mesquite extract in distilled spirits. (refer to Section 4).

E. Biological and Chemical Data

A literature review of CAS 93165-66-3 as well as "mesquite extract" provide no evidence of relevant toxicity, metabolism, or pharmacological studies.

A literature search of the identified volatile constituents provided no evidence of adverse toxicity, metabolism, or pharmacological studies that would negate the support of GRAS under the conditions of use. A tabular summary of the literature search results is found in Section 3. Summary sheets for each constituent is found in Section 5. Detailed literature search results are maintained by the applicant.

All but 1-eicosene has reported qualitative or quantitative occurrence in foods. This suggests that there is currently consumption of the constituents in mesquite extract through existing dietary food sources. The use of natural occurrence (consumption ratio) is an established priority setting approach.

One safety evaluation approach, as distinguished from a toxicological evaluation, involves an evaluation of the constituents using exposure weighted safety evaluation. This review uses data on exposure to mesquite extract constituents as well as the chemical structure of individual constituents to prioritize constituents for consideration. As presented in Table 5 of Section 3, the constituents of mesquite extract are either currently GRAS or structurally related to GRAS substances. Using the well-established thresholds of concern based on structural class, the consumption of none of the constituents from mesquite extract pose a toxicological concern. Further details of the basis of the review are found in Section 3.

Based on the cumulative scientific evidence using established safety evaluation procedures for the review of flavoring substances, especially the procedures established by FEMA and JECFA, mesquite chip extract is considered GRAS for use in alcoholic beverages.

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Identity and Composition

A. Mesquite Wood

The mesquite tree can be found in warm places, e.g., the desert. The mesquite tree, Prosopsis spp., is of the family fabacea. The mesquite pods of seeds can be made into flour and the bark is used for firewood and to flavor meat. Analytical data of mesquite plant parts can be found in Section 5.

The mesquite chips used to produce the extract must not contain detectable levels of pesticides.

B. Alcohol

Alcohol used to produce the extract is food grade and undenatured. Alcohol sources include, but is not limited to, whiskey.

Ethyl alcohol meets the specifications of Food Chemical Codex, Fourth Edition.

C. Mesquite Extract

Mesquite extract is prepared by stirring 1 lb. mesquite chips in 400 gallons 80 proof alcohol for 2 hours with no heat. The finished extract is obtained by removing the chips by filtration.

The CAS Registry Number 93165-66-3 and EINES Number 296-953-7 is defined as "extractives and their physically modified derivatives such as tinctures, concretes, absolutes, essential oils, oleoresins, terpenes, terpene-free fractions, distillates, residues, etc., obtained from Prosopsis spicigera, leguminosae."

Typical analysis of mesquite extract is:

Physical state:	Liquid
Color:	Tan to brown
Flashpoint:	>50°F
Refractive Index:	1.395 – 1.392 @ 20°C
Specific Gravity:	0.84 – 0.86 @ 25/25°C

D. Constituent Analysis of Mesquite Chip Extract

GC Column: RTX-5 0.32mm x 60m x 1.0um film thickness

GC Temperature Program: 60°C for 5 min, increased at 3°C/min to 240°C and held for 20 min.

Internal Standard: Chlorocyclohexane at 10 ppm.

Volatile Constituents: See Table 1
Dissolved non-volatiles: 0.009%
Balance: 80 proof alcohol (ethanol: water, 60:40)

E. Substantial Equivalence with Oak Chip Extract

GC Column: RTX-5 0.32mm x 60m x 1.0um film thickness
GC Temperature Range: 60°C for 5 min, increased at 3°C/ min to 240°C and held for 20 min.
Internal Standard: Chlorocyclohexane at 10 ppm

Volatile Constituents: See Table 2
Dissolved non-volatiles: 0.007%
Balance: 80 proof alcohol (ethanol:water, 60:40)

Table 1: Volatile Constituents of Mesquite Chip Extract

	Constituent	CAS	PPM
p32	Acetaldehyde diethylacetal	105-57-7	0.026
34	Benzaldehyde	100-52-7	0.004
36	Borneol	507-70-0	0.001
38	2-butenal	123-73-9	0.011
40	1-docosene	1599-67-3	0.082
44	1-eicosene	3452-07-1	0.149
42	Ethyl caprylate	106-32-1	0.001
46	1-hexadecene	629-73-2	0.059
48	Limonene	5989-27-5 and 138-86-3	0.010
53	para-mentha-1(7),2-dien-8-ol	(none)	0.005
54	1-octadecene	112-88-9	0.159
56	Pinol	2437-97-0	0.003

Table 2: Volatile Constituent of Oak Chips Extract

Constituent	CAS	PPM
Acetaldehyde diethyl acetal	105-57-7	0.027
Benzaldehyde	100-52-7	0.001
Borned	507-70-0	0.001
2-butenal	123-73-9	0.010
1-docosene	1599-67-3	0.107
1-eicosene	3452-07-1	0.186
Ethyl caprylate	106-32-1	0.001
2-furfural	98-01-1	0.005
1-hexadecene	629-73-2	0.080
Limonene	138-86-3	0.002
Para-mentha-1(7),2-dien-8-ol	(none)	0.006
Para-mentha-1(7),2-dien-8-0l acetate	(none)	0.002
5-methoxyvanillin	134-96-3	0.03
5-methyl furfural	620-02-0	0.001
1-octadecene	112-88-9	0.159
2-phenoxyethanol	122-99-6	0.009
Pinol	2437-97-0	0.002
Pinol hydrate	42370-41-2	0.003
Vanillin	121-33-5	0.001
Cis-whiskey lactone	55013-32-6	0.001

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Biological and Chemical Data

A. Literature Search

Literature search criteria include CAS search of the following databases: RTECS, MEDLINE, TOXLINE, AGRICOLA, LIFESCI, BIOSIS, CANCERLIT, EMBASE, TOXLIT.

Table 3 provides the hit frequency – Pertinent data is presented in Section 5. There is no evidence of adverse toxicity, metabolism, or pharmacological studies that would negate the GRAS use of mesquite extract under the conditions of use.

Table 4 provides the frequency of the natural occurrence of the constituent in food. The occurrence in food suggests that there is consumption of the constituents of mesquite extract in the current diet.

B. Safety Evaluation

In the practical sense, safety assessment of natural complexes such as mesquite chips extract must employ an exposure weighted safety evaluation that takes into account the relevant toxicity data for the individual constituents. Such a review provides a data-based practical certainty that the extract is safe under the conditions of use.

The evaluation of constituents by using the concept of "threshold of concern" makes use of past accumulated knowledge regarding the distribution of toxicological potency of the chemicals for which good toxicity data exists (Rulis 1986; Cramer 1978; Munro 1996). Assuming that the substance being considered is no more hazardous than the most hazardous chemical in the class of interest, a theoretical upper bound on the potency of the substance can be inferred. This upper bound on potency is used to establish a threshold below which only trivial risks can accrue and which would therefore not require further safety evaluation.

Munro et al. (1996) quantified the toxic potential of the three structural classes established using the decision tree approach (Cramer et al. 1978). The decision tree approach to flavor substance review has been extensively applied by the FEMA Expert Panel. The human exposure threshold by class is currently being used by JECFA for the review of flavoring substances.

Application of the following thresholds:

Table 1. Structural Class Definitions and their Human Intake Thresholds

Class	Description	Human Exposure Threshold[a] (mg/day)	5th Percentile NOEL (mg/kg/day)
I	Structure and related data suggest a low order of toxicity. If combined with low human exposure, these substances should enjoy an extremely low priority for investigation. The criteria for adequate evidence of safety would also be minimal. Greater exposures would require proportionately higher priority for more exhaustive study	1.8	3
II	Intermediate substances. They are less clearly innocuous than those of Class I, but do not offer the basis either of the positive indication of toxicity or of the lack of knowledge characteristic of those in Class III	0.54	0.91
III	Structural features permit no strong initial presumption of safety, or that may even suggest significant toxicity. They thus deserve the highest priority for investigation. Particularly when per capita intake of a significant subsection of the population is high, the implied hazard would then require the most extensive evidence for safety-in-use.	0.09	0.15

[a] The human exposure threshold was calculated by multiplying the fifth percentile NOEL by 60, assuming an individual weighs 60 kg and dividing by a safety factor of 100

to each of the constituents in mesquite extract is presented in Table 5. The consumption of none of the constituents from mesquite extract in alcoholic beverages exceed the threshold for its structural class.

Table 3: Constituent Literature "Hit" Frequency

Constituent	CAS#	RTECS	MEDLINE	TOXLINE	AGRICOLA	LIFESCI	BIOSIS	CANCERLIT	EMBASE	TOXLIT
1-Octadecene isomers	112-88-9	0	1	11	0	0	3	0	0	45
1-Eicosene isomers	3452-07-1	0	0	3	1	0	2	0	0	13
1-Docosene isomers	1599-67-3	0	0	0	0	0	0	0	0	10
1-Hexadecene isomers	629-73-2	1	2	29	0	0	14	0	0	56
Acetaldehyde diethy acetal	105-57-7	1	0	33	37	0	363	0	177	77
2-Butenal	123-73-9	1	0	68	0	0	0	0	0	21
Limonene	5989-27-5	1	1	246	101	0	306	0	531	719
para-Mentha-1(7),2-dien-8-01										
Benzaldehyde	100-52-7	1	116	653	187	1	660	36	342	2143
Pinol	2437-97-0	0	0	0	1	0	0	0	0	8
Borneol	507-70-0	1	0	84	64	0	186	0	84	1184
Ethyl Caprylate	106-32-1	1	0	22	15	0	10	0	2	159

Table 4: Constituent Occurrence in Food

Constituent	CAS#	Natural Occurrences
1-Octadecene isomers	112-88-9	12
1-Eicosene isomers	3452-07-1	0
1-Docosene isomers	1599-67-3	2
1-Hexadecene isomers	629-73-2	13
Acetaldehyde diethyl acetal	105-57-7	67
2-Butenal	123-73-9	16
Limonene	5989-27-5	290
para-Mentha-1(7),2-dien-8-01		
Benzaldehyde	100-52-7	280
Pinol	2437-97-0	9
Borneol	507-70-0	81
Ethyl caprylate	106-32-1	127

Table 5: Constituent Exposure via Mesquite Extract in Alcoholic Beverages

Constituent	CAS#	% in Extract	Constituent µg/p/d	Decision Tree Class	> Threshold?
1-Octadecene isomers	112-88-9	0.0000159	29.65	I	No
1-Eicosene isomers	3452-07-1	0.0000149	27.79	I	No
1-Docosene isomers	1599-67-3	0.0000082	15.29	I	No
1-Hexadecene isomers	629-73-2	0.0000059	11.00	I	No
Acetaldehyde diethyl acetal	105-57-7	0.0000026	4.85	I	No
2-Butenal	123-73-9	0.0000011	2.05	II	No
Limonene	5989-27-5	0.0000010	1.87	I	No
para-Mentha-1(7),2-dien-8-o1		0.0000005	0.93	I	No
Benzaldehyde	100-52-7	0.0000004	0.75	I	No
Pinol	2437-97-0	0.0000003	0.56	III	No
Borneol	507-70-0	0.0000001	0.19	I	No
Ethyl caprylate	106-32-1	0.0000001	0.19	I	No

Potential Intake

A. Conditions of Use

Flavoring substance at 1 lb./400 wine gallons.

B. Spirits Consumption

1.2 gallons/capita total population
1.8 ~~2.8~~ gallons/capita >21 years
1.7 gallons/capita >18 years

Reference: 1995 USDA Economic Research Survey

Further details are found in Section 5.

C. Mesquite Chip Extract

Extracts with large annual usage can be considered to be broadly distributed and there is virtually no difference between per capita intake and mean "eaters only" intake. As volumes become smaller, reflecting less broad use in the food supply, the probability increases that the per capita and "eaters only" intakes will diverge because of differences in the eating patterns of individuals.

The per capita x 10 calculation provides a simple, available, realistic, but generously conservative estimate of what a "high eater" would consume. This value was used to calculate constituent exposure from mesquite extract.

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Mesquite Tree

This tree can be found in warm places, like in the desert. It's a big tree with very many long narrow branches. a lot of branches. The mesquite tree can grow up to 50 feet tall. It's roots look like they are very deep and thick. The mesquite tree has greenish white little flowers and pods of seeds that can be made into flour. It has dark green leaves. It's leaves are divided into two stalks, each having many smaller leaflets. The mesquite tree is a home for birds and other animals. It serves as a nurse plant by providing shade for other plants. The mesquite tree's bark is used for firewood and to flavor meat.

PhytochemDB

Table-maker: Phytochemicals of Prosopis juliflora

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Chemical	Part	Amount (ppm)	Low (ppm)	High (ppm)
4-O-METHYL-D-GLUCURONIC-ACID	Plant			
5-HYDROXYTRYPTAMINE	Plant			
APIGENIN	Plant			
APIGENIN-6,8-DIGLUCOSIDE	Plant			
ASH	Fruit	48,000		
ASH	Leaf	85,000		
ASH	Seed		35,000	300,000
CALCIUM	Leaf	20,800		
CARBOHYDRATES	Fruit	783,000		
CARBOHYDRATES	Leaf	696,000		
CARBOHYDRATES	Seed	218,000		
CELLULOSE	Fruit	272,400		
D-GALACTOSE	Plant			
FAT	Fruit	30,000		
FAT	Leaf	29,000		
FAT	Seed		53,000	78,000
FIBER	Fruit	277,000		
FIBER	Leaf	216,000		
FIBER	Seed	28,000		
GLUCOSE	Fruit	302,500		
ISORHAMNETIN-3-GLUCOSIDE	Plant			
L-ARABINOSE	Plant			
PHOSPHORUS	Leaf	2,200		
PROTEIN	Fruit	139,000		
PROTEIN	Leaf	190,000		
PROTEIN	Seed		300,000	652,000
QUERCETIN	Plant			

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SUGAR	Fruit	330,000		
SUGAR	Seed	330,000		
TANNIN	Bark		6,000	84,000
TANNIN	Root	67,000		
TANNIN	Wood	9,000		
TANNINS	Fruit	58,100		
TRYPTAMINE	Plant			

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View Taxon model | Query by example | Query builder

ACeDB query language | Select new DB

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