



Memorandum

Date November 9, 1988

From Div. of Toxicology, Additives Evaluation Branch (HFF-158)

Subject Gum arabic and immunogenicity; literature from Dr. D. M. W. Anderson.

To Direct Additives Branch (HFF-334)
Attn: Eric Flamm, Ph.D.

Through: G. N. Biddle, Ph.D. *Kirk Biddle, 11/9/88*
Chief, Additives Evaluation Branch (HFF-158)

GRAS REVIEW PETITION 3G0287

Beatrice Foods Co., Inc.
Chicago, Ill.

Introduction

On September 26, 1988, Dr. D.M.W. Anderson, the scientific advisor to the International Natural Gums Association for Research (INGAR), met with CFSAN representatives, primarily to discuss the wording of 21 CFR 184.1330. In response to questions from DTRE regarding the putative allergenicity/hypersensitivity of gum arabic (Acacia) in sensitive subpopulations, Dr. Anderson indicated that the body of literature he was personally acquainted with did point to a potential problem with this compound. Our previous memorandum (HFF-158 to HFF-314, March 8, 1988) reviewed the literature and concluded that "The few cases presenting minor reactions, using products containing at times substantial amounts of gum acacia, during a history of use going back more than 50 years, can be viewed as extremely weak evidence for the allergenic potential of gum arabic constituting a safety problem". Therefore, we asked Dr. Anderson to kindly provide us with references to back up his conclusion. The promised references were sent to Dr. Modderman (HFF-415) with a letter dated October 10, 1988.

Evaluation

Dr. D.M.W. Anderson submitted a list of 28 published papers, of which 13 were indexed as publications pertinent to the immunogenicity of gum arabic. Six of these papers deal specifically with the amino acid and/or protein structure of the gums and present no clinical data:

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The amino acid composition of the proteinaceous component of gum karaya (Sterculia spp.), Anderson, D.M.W., et al., Food Add. Contam. 2, 153-157 (1985).

The amino acid composition of the proteinaceous component of gum arabic (Acacia senegal(L.)Willd.), Anderson, D.M.W., et al., Food Add. Contam. 2, 159-164 (1985).

The amino acid composition of the proteinaceous component of guar gum (Cyamopsis tetragonolobus), Anderson, D.M.W., et al., Food Add. Contam. 2, 225-230 (1985).

The amino acid composition of the proteinaceous component of gum tragacanth (Asiatic Astragalus spp.), Anderson, D.M.W., et al., Food Add. Contam. 2, 231-235 (1985).

Nitrogen conversion factors for the proteinaceous content of gums permitted as food additives, D.M.W. Anderson, Food Add. Contam. 3, 231-234 (1986).

The structural significance of amino acids in some plant gums, D.M.W. Anderson, Gums and Stabilisers for the Food Industry, Vol. 4, pp. 31-37, I.R.L. Press, Oxford (1988).

Two of the publications deal with other gums, and are therefore not relevant to the discussion on gum arabic:

Evidence for the safety of gum tragacanth (Asiatic Astragalus spp.) and modern criteria for the evaluation of food additives, D.M.W. Anderson, Food Add. Contam. (in press), December 1988.

Evidence for the safety of gum karaya (Sterculia spp.) as a food additive, D.M.W. Anderson, Food Add. Contam. (in press), March 1989.

Four of the five remaining publications were reviewed in the memorandum dated March 8, 1988 (HFF-158 to HFF-314), and did not lend credence to the supposition that gum arabic is a food allergen:

Immunogenicity of foods and food additives - In vivo testing of gums arabic, karaya and tragacanth, Strobel, S., et al., Toxicol. Lett. 14, 247-252 (1982).

Immunogenicity, immunological cross reactivity and non-specific irritant properties of the exudate gums, arabic, karaya and tragacanth, Strobel, S., et al., Food Add. Contam. 3, 47-56 (1986).

Induction of oral tolerance, in mice, to gum arabic, Strobel, S. and Ferguson, A., Food Add. Contam. 3, 43-46 (1986).

Evidence for the safety of gum arabic (Acacia senegal(L.)Willd.) as a food additive - a brief review, D.M.W. Anderson, Food Add. Contam. 3, 225-230 (1986).

The only new and relevant paper supplied to the agency by Dr. D.M.W. Anderson was:

Immunological response to food, Ferguson, A., Proc. Nutrit. Soc. 44, 73-80 (1985).

Review

This paper examines the properties of the mucosal immune system, showing it to be separate and distinct from the systemic immune system. "The immune response to enteric antigens, including food, are in general under continuous suppression (oral tolerance)." An interruption of this gut property can be considered in the pathogenesis of food allergic diseases. An approach to investigating the oral tolerance in man is to define circumstances in which this property is absent, i.e., in which there is active systemic immunity to antigens which are normally only encountered in the gut. Fifty healthy blood donors were examined for antibodies to certain specific food antigens; beta-lactoglobulin (from cow's milk), ovalbumin (from chicken's egg), gliadin (from wheat) and gum arabic. These individuals were not identified as either having or not having clinically diagnosed food allergies. The following table indicates that "substantial numbers of healthy individuals have detectable antibodies to foods." The author also indicates that patients with a high antibody titre to one antigen usually had significantly high titres to several others also.

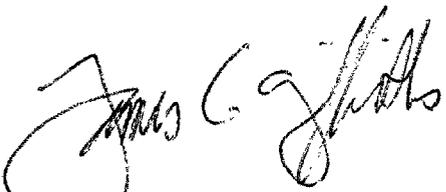
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<u>Antigen</u>	<u>negative</u>	<u>intermediate</u>	<u>high</u>
β -lactoglobulin	39	10	1
Ovalbumin	40	8	2
Gliadin	47	2	1
Gum arabic	43	5	2

The paper concedes that the usefulness of this approach is only as a screening procedure for active systemic immunity, to establish genetic predisposition to this state in healthy individuals. In conclusion, the author states that the only method for the diagnosis of a food allergy is to prove food intolerance by clinical means, with an identification of an abnormal in vitro immune response used only as a back up.

Conclusion

The literature citations from Dr. D.M.W. Anderson provided only one new reference to the previously discussed topic of "Gum arabic and immunogenicity" (memo HFF-158 to HFF-314, March 8, 1988). This single paper does not change DTRE's previous conclusion of "extremely weak evidence for the allergic potential of gum arabic". DTRE does not feel there is a significant body of data to require the labeling of gum arabic containing alcoholic creme-style liquors. However, we continue to recognize the inconsistency in having foods containing gum arabic labeled under general food labeling provisions and having gum arabic containing alcoholic beverages unlabeled.

 11/9/88
James C. Griffiths, Ph.D.
Toxicologist

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