EVALUATION OF THE HEALTH ASPECTS OF SODIUM OLEATE AND SODIUM PALMITATE AS SUBSTANCES MIGRATING TO FOOD FROM PAPER AND PAPERBOARD USED IN FOOD PACKAGING

1977

Prepared for

Bureau of Foods
Food and Drug Administration
Department of Health, Education, and Welfare
Washington, D.C.

Contract No. FDA 223-75-2004
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Life Sciences Research Office
Federation of American Societies for Experimental Biology
9650 Rockville Pike
Bethesda, Maryland 20014
NOTICE

This report is one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior sanctioned food substances as food ingredients, being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 223-75-2004 with the Food and Drug Administration (FDA), U.S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshalling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office (LSRO), established by FASEB in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

Qualified scientists were selected as consultants to review and evaluate the available information on each of the GRAS substances. These scientists, designated the Select Committee on GRAS Substances, were chosen for their experience and judgment with due consideration for balance and breadth in the appropriate professional disciplines. The Select Committee's evaluations are being made independently of FDA or any other group, governmental or non-governmental. The Select Committee accepts responsibility for the content of each report. Members of the Select Committee who have contributed to this report are named in Section VII.

Tentative reports are made available to the public for review in the Office of the Hearing Clerk, Food and Drug Administration, after announcement in the Federal Register, and opportunity is provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the substances covered by the report. The data, information, and views presented at the hearing are considered by the Select Committee in reaching its final conclusions. Reports are approved by the Select Committee and the Director of LSRO, and subsequently reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures the reports are approved and transmitted to FDA by the Executive Director of FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of all of the individual members of its constituent societies.

Kenneth D. Fisher, Ph. D., Director
Life Sciences Research Office
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I. INTRODUCTION

This report concerns the health aspects of using sodium oleate and sodium palmitate as they may migrate to foods from paper and paperboard used in food packaging. It has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (1) which summarizes the world's scientific literature from 1920 through 1973.* To assure completeness and currency as of the date of this report this information has been supplemented by searches of over 30 scientific and statistical reference sources and compendia that are generally available; use of new, relevant books and reviews and the literature citations contained in them; consideration of current literature citations obtained through computer retrieval systems of the National Library of Medicine; searches for relevant data in the files of FDA; and by the combined knowledge and experience of members of the Select Committee and the LSRO staff. In addition, an announcement was made in the Federal Register of September 2, 1977 (42 FR 44284-44285) that opportunity would be provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information and views on the health aspects of using sodium oleate and sodium palmitate as they may migrate to foods from paper and paperboard used in food packaging. The Select Committee received no requests for such a hearing on sodium oleate and sodium palmitate.

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the premarketing clearance that is required for food additives. It is stated in the Act and in the Code of Federal Regulations (2) [21 CFR 170.3 and 170.30] that GRAS means general recognition of safety by experts qualified by scientific training and experience to evaluate the safety of substances on the basis of scientific data derived from published literature. These sections of the Code also indicate that expert judgment is to be based on the evaluation of results of credible toxicological testing or, for those substances used in food prior to January 1, 1958, on a reasoned judgment founded in experience with common food use, and is to take into account reasonably anticipated patterns of consumption, cumulative effects in the diet, and safety factors appropriate for the utilization of animal experimentation data. FDA (2) recognizes further that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

*The document (PB-241 968/7) is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
The Select Committee on GRAS Substances of LSRO is making its evaluations of these substances in full recognition of the foregoing provisions. In reaching its conclusions on safety the Committee, in accordance with FDA's guidelines, is relying primarily on the absence of substantive evidence of, or reasonable grounds to suspect, a significant risk to the public health. While the Committee realizes that a conclusion based on such reasoned judgment is expected even in instances where the available information is qualitatively or quantitatively limited, it recognizes that there can be instances where, in the judgment of the Committee, there are insufficient data upon which to base a conclusion. The Committee is aware that its conclusions will need to be reviewed as new or better information becomes available.

In this context, the LSRO Select Committee on GRAS Substances has reviewed the available information on sodium oleate and sodium palmitate and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of these substances under the Federal Food, Drug, and Cosmetic Act.

II. BACKGROUND INFORMATION

Sodium oleate and sodium palmitate are prepared commercially by converting oleic and palmitic acids, obtained by fractionation of the hydrolyzates of animal and vegetable oils, to their sodium salts. Usual sources of the fatty acids are tall oil and inedible tallow and vegetable oils. Sodium oleate and sodium palmitate are white to yellowish powders that are soluble in water and alcohol (3, 4).

Both sodium oleate and sodium palmitate are GRAS substances listed in the Code of Federal Regulations (2) under 21 CFR 182.90 as substances migrating to foods from paper and paperboard products used in food packaging. This report concerns the evaluation of these two salts-only for this purpose.

It is to be noted that these and other salts and esters of other fatty acids are also cited elsewhere in the Code: the sodium salts of fatty acids in 21 CFR 172.863, as substances that may be safely used as binders, emulsifiers, and anticaking agents in foods and in the manufacture of food components in accordance with good manufacturing practice; aluminum oleate and aluminum palmitate in 21 CFR 182.90 as substances migrating to foods from paper and paperboard products; vitamin A palmitate in 21 CFR 182.5936 as a substance that may be safely added to foods as a nutrient and/or dietary
supplement; and the ethyl ester of oleic acid in 21 CFR 172.515 as a synthetic food flavoring substance and adjuvant. The evaluation of the aluminum salts and vitamin A-fatty acid esters as food ingredients has been or will be covered in other reports of the Select Committee (5, 6). Oleic acid and palmitic acid are esterified components of the triglycerides of coconut oil, peanut oil, soybean oil, fish oil, tall oil, and tallow, which have also been evaluated in other reports of the Select Committee (7-11).

The Food Chemicals Codex (12) provides no specifications for food grade sodium oleate or sodium palmitate. However, the Code of Federal Regulations (2) identifies those salts of fatty acids, including sodium oleate and sodium palmitate, that may be used safely as food additives [21 CFR 172.863]. Food industry specifications with respect to free fatty acid, ash, moisture, and alkalinity are available for sodium oleate and sodium palmitate added to food as thickeners and emulsifiers at 1 to 5 percent levels (13). The Joint FAO/WHO Expert Committee on Food Additives (14) has specified that food grade sodium palmitate should contain no more than 3 mg arsenic per kg nor more than 10 mg heavy metals (as Pb) per kg. The FAO/WHO Expert Committee did not consider sodium oleate.

III. CONSUMER EXPOSURE DATA

A report of a National Research Council (NRC) subcommittee (15) on the use of GRAS substances in foods contains no data on possible intakes of sodium oleate and sodium palmitate resulting from their use in paper and paperboard food packaging products since such data were not requested. No other sources of information in this regard have been found. However, the Select Committee believes that only minute amounts of sodium oleate and palmitate might enter the human food supply from paper and paperboard packaging materials containing these substances as ingredients, and that the amounts would be extremely small in comparison with the substantial amounts of oleic and palmitic acids and sodium that are ingested daily as natural components of food.

The Joint FAO/WHO Expert Committee on Food Additives (16) has set no limit on the acceptable daily intake of sodium palmitate provided the contribution of sodium ions does not significantly change the normal body load. The FAO/WHO Expert Committee did not consider sodium oleate.
IV. BIOLOGICAL STUDIES

Absorption, metabolism, excretion, and acute toxicity

No information directly concerned with the absorption, metabolism, excretion, or acute toxicity of sodium oleate and sodium palmitate as such was found by the Select Committee. However, the following three studies are relevant:

Carroll and Richards (17) fed rats for 16 days on diets containing various sources of fat and found that oleic acid was less well absorbed (73 percent) than triolein (99 percent); 40 percent of fed palmitic acid was absorbed while only 22 percent of fed tripalmitin was absorbed. These percentages were based on analyses of feces for unabsorbed lipids. Dietary doses of the fats were approximately 1.2 to 1.4 g per rat per day (about 7 to 8 g per kg per day).

Bergström et al. (18) administered by gastric intubation 0.5 ml of \(1^{-14}\text{C}\) oleic acid (about 1.8 g per kg) to 250 g male rats with cannulated thoracic ducts. After 24 hours, an average of 78 percent of the labeled oleic acid had been absorbed. Of the absorbed oleic acid recovered in lymph from the thoracic duct, about 2 percent was in the form of phospholipids. About 16 percent of the carbon-14 label was recovered as expired \(^{14}\text{CO}_2\) in 24 hours.

Similar experiments were conducted by Bloom et al. (19) who administered \(^{14}\text{C}\)-palmitic acid in corn oil enterally. Thoracic duct cannulations were performed on ten male rats, six received the free fatty acid and four received tripalmitin. In 19 to 24 hours, 81 to 95 percent of the labeled palmitic acid was recovered from the thoracic duct lymph. An additional four rats were prepared by cannulation of their larger mesenteric lymph ducts; 69 to 84 percent of the labeled palmitic acid was recovered from the fatty acid fraction of the intestinal lymph.

Oleic and palmitic acids are components of many foods and GRAS food ingredients (6-10). Their sodium salts dissociate in the gastrointestinal tract and the fatty acid moieties are transported into the mucosal cells, where they are esterified into triglycerides. A small amount of the free fatty acids is dispersed in the chylomicrons and transported into the general circulation (20).
Short-term and long-term studies

Few studies have been reported concerning the sodium salts of oleic or palmitic acids as such, and these, as well as relevant studies on the feeding of the corresponding fatty acids, have usually employed dosage levels that are orders of magnitude higher than would be expected in food due to migration of these salts from packaging materials.

Chauchard et al. (21) reported that feeding sodium oleate to rats daily at 22 percent of their diet (about 22 g per kg per day) increased the excitability of the neuromuscular system, shortened nerve chronaxia, and increased muscle chronaxia. The effect was observed within 48 hours after starting the diet. The authors ascribed the effect to a dietary lipid imbalance and found it to be neutralized by addition of B vitamins. Lecoq et al. (22), in continuance of this work, observed similar effects after subcutaneous injection of sodium oleate (dose not indicated) and found that they could be reversed or prevented by daily oral administration of 100 to 200 μg doses of nicotinamide, pyridoxine or pantothenic acid. In neither study was the no-effect level of sodium oleate on neuromuscular excitability determined.

Sunde (23) reported that chicks receiving 5 percent oleic acid in their diet (about 6 g per kg per day) for four weeks showed improved feed utilization and no adverse effects.

Flesch (24) found that the administration of 10 ml of oleic acid (about 2.5 g per kg body weight) by stomach tube every other day for four days to four albino rabbits resulted in hair loss, scaling seborrheic lesions on the ears and one death. Doses of 2.5 ml of oleic acid (about 0.6 g per kg) were without adverse effects.

Herting et al. (25) fed weanling Holtzman rats a diet containing palmitic acid as 50.4 percent of the ration (about 50 g per kg body weight per day). The palmitic acid was 58 to 60 percent absorbed. Lipogranulomas were produced in adipose tissue within eight weeks. The occurrence of lipogranulomas was greater in the fat associated with the testis or ovary than in that of other tissues. Foreign body-type reactions in perigonadal fat were noted in four of five animals observed for 24 weeks. Similar results were obtained with other saturated fats (stearic acid, ethyl stearate and hydrogenated lard) when fed at about the same levels. When the saturated fat in the diet was replaced with 20 percent corn oil, prompt diminution and eventual disappearance of the lipogranulomas were observed. The investigators ascribed the effect to dietary imbalance produced by a high lipid diet of saturated fatty acids. Experiments at lower dietary levels were not conducted.
Renaud (26) gave seven rats a hyperlipemic diet (32 percent butter; 5 percent cholesterol) supplemented by 5 percent palmitic acid (about 4.6 g per kg body weight per day of palmitic acid) for a six-week period. To initiate thrombosis, a Salmonella typhosa endotoxin was injected at the end of the feeding period. Palmitic acid was the most hyperlipemic of the common fatty acids used in these experiments which also included caprylic, lauric, myristic, and stearic acids. Stearic acid was the most thrombogenic, followed by palmitic acid. Robertson et al. (27) injected five week-old male and female albino mice subcutaneously with a 5 percent emulsion of oleic acid in 0.25 and 0.5 ml volumes weekly (about 12 to 15 g per kg body weight) for 60 weeks. The growth rate of the animals was normal.

Carroll and Noble (28) fed Sprague-Dawley and Wistar rats a diet supplemented with 15 percent oleic acid (initially about 15 g per kg body weight). They appeared to develop normally and their general health appeared good after five months. Progressive reduction in spermatogenesis, and prolonged estrous cycles occurred but most females bore living young. In general, the animals resembled those subjected to diets deficient in essential fatty acids.

Special studies

No studies of the carcinogenicity, mutagenicity, or teratogenicity of sodium oleate or sodium palmitate have come to the attention of the Select Committee. It is noted, however, that Nakahara (29) found an intraperitoneal injection of 0.5 ml of a 1 percent solution of sodium oleate in mice (about 0.25 g per kg body weight) to increase their resistance to growth of subsequently transplanted Bashford adenocarcinoma 63. Sodium oleate produced no significant increase in the resistance to cancer already in situ. Sodium palmitate at about the same dosage was without effect in these experiments.

V. OPINION

Although there are no data available to the Select Committee on the amounts of sodium oleate and sodium palmitate used in fabricating food containers or the amounts that might migrate to food therefrom, it is evident that the amount of these compounds that could transfer to foodstuffs in the package would be many orders of magnitude below the quantities of the respective fatty acids normally present as triglycerides in many foods. The sodium salts of the fatty acids are toxicologically indistinguishable from the latter when consumed in small amounts. The Select Committee recognizes that large amounts of the free fatty acids can distort the physiological processes in a system that is organized to absorb and utilize the triglycerides, but such excesses would not be expected from the use of sodium oleate and sodium palmitate as food packaging material ingredients.
In light of the foregoing, the Select Committee concludes that:

There is no evidence in the available information on sodium oleate and sodium palmitate that demonstrates or suggests reasonable grounds to suspect a hazard to the public when they are used as ingredients of paper and paperboard food packaging materials in the manner now practiced or as they might be expected to be used for such purposes in the future.
VI. REFERENCES CITED


7. Select Committee on GRAS Substances. 1977. Evaluation of the health aspects of coconut oil, peanut oil, and oleic acid as they may migrate to food from packaging materials, and linoleic acid as a food ingredient (SCOGS-65). Life Sciences Research Office, Federation of American Societies for Experimental Biology, Bethesda, Md. 18 pp.


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December 22, 1977

Date

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