Attachment 3

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LIFE SCIENCES
RESEARCH OFFICE

EVALUATION OF THE HEALTH ASPECTS OF CERTAIN COMPOUNDS FOUND IN IRRADIATED BEEF

SUPPLEMENT II
POSSIBLE RADIOLYTIC COMPOUNDS

March 1979

Prepared for

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
DEPARTMENT OF THE ARMY
FORT DETRICK, FREDERICK, MD 21701

under

Contract Number DAMD-17-76-C-6055

LIFE SCIENCES RESEARCH OFFICE
FEDERATION OF AMERICAN SOCIETIES
FOR EXPERIMENTAL BIOLOGY
9650 Rockville Pike
Bethesda, Maryland 20014

these, as well as other values obtained by extrapolation from triglyceride models may seriously overestimate the amount actually produced when beef is irradiated in a frozen state. Free fatty acids and diglycerides occur naturally in many foodstuffs, are normal digestive and metabolic products, and are authorized additions to food for desirable technical effects. The amounts produced by irradiation would be small compared with their intakes from other sources and would not be expected to have adverse health effects.

Less is known of the diol diesters, the other major product of fat irradiation. There is evidence that they are natural constituents of mammalian tissues and that they are produced in significant quantities during normal heating processes of fatty foods. Thus, tricaproin heated at 270°C for 15 hours produced ten times as much ethane dioldiester as did 60 kGy (6.0 Mrad) irradiation at 25°C. However, metabolic and toxicity data are not available on the individual members of this family, precluding any firm judgment of their possible health effects.

Based on studies with tricaproin, the only other radiolytic products present in detectable amounts were esters of fatty acids and diglycerides, aldehydes corresponding to the fatty acid components of the fat, and alkylcyclobutanones. Various aldehydes have been detected in irradiated beef in concentrations less than one part per million and were considered in the previous report to pose no hazard in these amounts to the consumer. It is believed that the esters would be hydrolyzed by gastrointestinal and tissue esterases to yield harmless levels of fatty acids and diglycerides. Nothing is known of the fate and toxicity of the alkylcyclobutanones, so no judgment can be rendered on their possible health effects.

Although relatively few radiolytic products have been detected in irradiated beef or model systems, and even fewer have been determined quantitatively, many more are possible theoretically. Many of such putative products are found in natural foods, added during food processing, produced during cooking, or present in the body as normal metabolites. As Nawar (1977) has pointed out, the nature of decomposition products formed by irradiation and heat treatment are quite similar, with many more of such compounds identified in heated or thermally oxidized, than in irradiated samples.

It is not possible to compile a complete inventory of all the components of natural foodstuffs nor of all conceivable irradiation products. The possible presence of undetected substances can never be excluded. For this reason, it is desirable to complement such chemical studies with animal feeding experiments in which the effects of irradiated and of nonirradiated beef are compared. Such experiments provide an added approach to determine wholesomeness and safety of irradiated foods.

VI. CONCLUSIONS

In the light of the foregoing considerations, the Committee concludes that:

1. Many of the radiolytic products in the concentrations estimated to be present appear to pose no hazards to consumers of beef irradiated in the described manner. Such products include the individual fatty acids and their simple esters, glycerol, mono- and diglycerides, diglyceride esters, aldehydes, and aliphatic hydrocarbons.

2. Insufficient data are available to allow judgment of the effects on health of the individual diol diesters and alkylcyclobutanones presumably present. Metabolic and toxicological studies of these compounds are desirable.

3. No evaluation can be made of other compounds theoretically possible in small amounts, but which have not been demonstrated in irradiated beef or model systems. Because no analysis, however exhaustive, can exclude the possibility of the presence of such theoretical but undetected constituents, no unequivocal demonstration of safety seems possible from consideration of individual radiolytic products alone.

4. It is desirable to couple chemical studies as described in this report with suitable animal feeding studies to provide complementary approaches to ensure the wholesomeness and safety of irradiated foods.

RECOMMENDATIONS FOR EVALUATING THE SAFETY OF IRRADIATED FOODS

FINAL REPORT

JULY 1980

Prepared for the Director, Bureau of Foods, FDA

MEMBERSHIP OF THE IRRADIATED FOOD COMMITTEE

Chairman

Dr. Lawrence R. Valcovic
Division of Toxicology

Executive Secretary

Dr. Clyde A. Takeguchi
Division of Food and Color Additives

Members

Dr. Anthony P. Brunetti
Division of Chemistry and Physics

Dr. Victor Frattali
Division of Nutrition

Mr. William B. Greear
Division of Toxicology

Dr. David G. Hattan
Division of Toxicology

INTRODUCTION AND BACKGROUND

The Irradiated Foods Committee was authorized on September 10, 1979 and established on October 23, 1979 to provide a total reassessment of all relevant issues applicable to irradiated foods. Since that time the Committee has become acquainted with the subject and accompanying problems by reviewing the relevant literature, interviewing appropriate FDA personnel and international experts knowledgeable in the area of radiation chemistry and toxicological evaluation (see Appendix I).

The Committee was charged with the following tasks:

1. To review current policy.
2. To examine the foundation and soundness of that policy and its past implementation, and
3. To establish those toxicologic requirements appropriate for assessing the safety of irradiated food consistent with the level of human exposure, where the degree of testing is consistent with the potential risk as predicated on the level of human exposure. These requirements would be analogous to, and consistent with, the philosophy supporting the Cyclic Review of direct additives.

The Committee emphasizes that this report is a policy recommendation and not a petition, petition guideline, FEDERAL REGISTER (FR) document, or a comprehensive review of all data submitted to FDA and all available scientific literature. We forsee the development of guidelines for petitioners and a FR document as tasks of future committees.

1980 POLICY RECOMMENDATIONS

The Committee's main task was: to establish those toxicologic testing requirements appropriate for assessing the safety of irradiated food, where the degree of testing is compatible with the potential risk as indicated by the level of human exposure. Based on what we have learned from our review of all aspects of food irradiation, it is apparent that any toxicological testing requirements must also be predicated on the amounts of new chemical constituents generated by the irradiation process (URPs). Hence, the components of any new policy for assessing the safety of irradiated food are: 1) projected levels of human exposure; 2) qualitative and quantitative estimates of URPs; and 3) state-of-the-art sensitive toxicological tests.

While numerous efforts to estimate food consumption have been made, it is generally recognized that no single approach provides sufficiently accurate data. Hence, our projection of human exposure to irradiated foods will necessarily suffer the same limitations. The committee utilized estimates of a) total food consumption, b) dietary items proposed for irradiation and, c) the percent of each dietary item which may be irradiated. (See Human Exposure, Appendix III). These factors will vary with the specific food under consideration; however, a rough estimate based on these factors suggests that 10% of the total diet may consist of irradiated food in the near future.

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UNITED STATES ATOMIC ENERGY COMMISSION

NYO-3320

TERMINATION REPORT—PART I

Food Irradiation and Associated Studies

September 15, 1954

Columbia University
New York, New York

Technical Information Service, Oak Ridge, Tennessee

NYO - 3320

Termination Report - Part I

Food Irradiation and Associated Studies

September 15, 1954

Contractor: Columbia University
New York 27, N. Y.

Contract No.: AT(30-1)-1186

Contractors Report No.: CU-3-54-AEC-1186-Chem.

INTRODUCTION

As originally set up and subsequently modified, Contract AT(30-1)-1186 was to cover investigations in three more or less distinct, though interrelated, areas. First, under the overall supervision of Professor C. G. King, with Drs. R. R. Becker and H. C. Kung, the effects of radiation on biochemical and nutritional qualities of whole foods and portions of them was to be studied. Next, microbiological effects of radiation and their effects on radiation sterilization process design were to be studied by Professors E. L. Gaden, Jr., and E. J. Henley. Last, the possible application of radiation to certain chemical problems were to be undertaken, also by Gaden and Henley.

With reorganization of the radiation sterilization program in 1954, the biochemical and nutritional work under AEC sponsorship was terminated and transferred to the Office of the Surgeon General and Quartermaster Corps Research and Development Command, U.S. Army. A great deal of work on (a) the nutritive value of irradiated foods, (b) effects of radiation on specific food components, and (c) the mechanism of radiation-induced destruction of certain key nutrients (ascorbic acid) had been completed and these form the subject matter of this report.

Some problems have been undertaken by the nutrition and biochemistry group which have not proceeded far enough to warrant a report here. Since they are being carried further under the O.S.G. program, they will be included in progress reports under that contract.

The microbiological and chemical phases of contract AT(30-1)-1186 will be covered in part II of this report, to be issued at the close of the current contract period, September 15, 1955.

ANIMAL FEEDING EXPERIMENT

R. R. Becker, H. C. Kung and C. G. King

A two-year feeding experiment designed to test the possible unwholesomeness of partially irradiated diets is described in this section. A preliminary account of these studies has been given (1).

EXPERIMENTAL

Twenty-four rats, twelve males and twelve females, obtained from Professor Sherman's high generation rats, served as the initial group of experimental animals. They were devided into two groups of twelve each. The first group, the control, had been fed a control diet, Sherman diet 16, consisting of 1000 grams of ground whole wheat, 200 grams of whole milk powder and 20 grams of salt. The second group, the experimental, had been fed an irradiated diet which was prepared by mixing 1000 grams of ground whole wheat, 147 grams of skim milk powder, 53 grams of irradiated butterfat and 20 grams of salt. The butterfat was irradiated in Pyrex glass tube by gamma-radiation from a "kilocurie" Cobalt-60 source at an average dose of 1,680,000 roentgens. Both the control and irradiated diets were supplemented with halibut liver oil for vitamin A and D. "Haliver" oil (Parke-Davis & Co.) diluted with Wesson oil (1:2 by volume) had been adopted to feed the rats one drop at a time, twice in a week.

When the rats of the same litter reached sixty-three days of age, the males and the females were placed together and mated in eight cages. Pregnant females were isolated until their offspring reached twenty-eight days of age, then the mother was put back in the original cage. Thirty-two rats, sixteen males and sixteen females, of the second generation (the offspring of the first generation) and the same number of the third generation were tested in the same way as described above. The rats were weighed once a week, and growth and breeding data recorded.

RESULTS AND DISCUSSION

The average body weight of the first, second, and third generation male rats is given in Table I. The data show that the average body weight of the control and experimental males increased in the same pattern from twenty-eight days up to seven hundred days of age. As is shown in Figures I, II, and III, the growth data were somewhat irregular in the later stages, with the controls evidencing slightly higher and more consistent weights.

The average body weights of the three generation female rats from twenty-eight to seventy days of age are given in Table II and Figure IV. There is no significant difference between the growth of the control and the experimental animals.

All the twelve females, six controls and six experimental, of the initial group (first generation) proved to be fertile. Forty-one litters, 280 young rats, were delivered by the six control females as compared with twenty-eight litters, 193 young rats, by the six experimental females (Table III). This difference, thirteen litters or eighty-seven young rats, is significant. The difference in fertility between the control and experimental groups of the first generation can also be seen from the number of litters per female and the number of young per female as shown in Table IV and V respectively. The average body weight of their young (the second generation) at 28 days of age of the control group was 39 grams while that of the experimental group was 37 (about 5% difference).

The results obtained from the breeding record of the second and third generation rats are similar to those from the first generation, except that the differences between the control and the experimental groups are less significant than those of the first generation as is shown in Tables III, IV, and V. The breeding period of the second generation females was almost complete when the experiment was terminated. One female of this group on the experimental diet was sterile.

From the breeding record (Table III, IV, and V) especially of the first generation, it is evident that the fertility of the female rats fed the irradiated diet had been somewhat impaired. For this reason some studies on the destruction of vitamin E by gamma irradiation were carried out, with the cooperation of Dr. Stanley R. Ames of Distillation Products Industries. Samples of butterfat and wheat germ oil were irradiated (dose: 1.2×10^6 r) in our Co^{60} source, and assayed both chemically and biologically by Dr. Ames' group. The results are summarized in Table VI. By chemical assay, there was an apparent increase in the total tocopherols following irradiation. Biological tests show an 82% destruction of tocopherols in butterfat and 14% in wheat germ oil.

Table III

Generation	I		II		III	
Diet	control	irrad.	control	irrad.	control	irrad.
Number of female mated	6	6	8	8	8	8
Number of litters born	41	28	47	39	40	33
Number of young born	280	193	307	293	269	239
Number of young reared*	239	161	264	262	215	215
Number of female reared*	131	87	135	142	109	108
Number of male reared*	108	64	129	120	106	107
Average body wt. of young at 28 days	39	37	42	39	41	38

* Young rats were reared to 28 days of age, then either kept for experiment or sacrificed.

Table IV

Number of litters per Female

Generation	Control mean ± P.D.*	Experimental mean ± P.D.*
I	6.8 ± 0.5	4.7 ± 0.6
II	5.9 ± 0.7	4.9 ± 0.8
III	5.0 ± 0.5	4.1 ± 0.5

* Probable deviation of the mean.

Table V

Number of Young per Female

Generation	Control mean ± P.D.*	Experimental mean ± P.D.*
I	46.7 ± 4.2	32.2 ± 4.8
II	38.4 ± 4.6	36.5 ± 5.4
III	33.6 ± 4.5	29.9 ± 3.7

* Probable deviation of the mean.