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Do Irradiated Foods Cause or Promote Colon Cancer?

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Food Irradiation and Safety

Food irradiation is defined as the treatment of foods with ionizing radiation, also called ionizing energy¹. Irradiation of foods is intended to improve the quality, variety and safety of foods. For example, food products are irradiated to sterilize or disinfect them, to improve their sprouting, delay ripening, eliminate food-borne parasites, or simply enhance their appearance². The Joint Expert Committee on the Wholesomeness of Irradiated Food (JECFI) of the Food and Agriculture Organization (FAO), the International Atomic Energy Agency (IAEA), and the World Health Organization (WHO) concluded that irradiation of food up to an overall average dose of 10 kGy introduces no toxicology hazard. These organizations stated that irradiated foods are safe and nutritious³. In 1986, the United States Food and Drug Administration (FDA) approved low-dose irradiation of many foods up to 1 kGy for human consumption and the FDA approved even higher dose irradiation for several specific food classes since then⁴.

While irradiated foods have many known beneficial properties, the effect of long-term consumption of irradiated foods remains unknown. Lack of critical studies addressing the impact of long-term exposure to irradiated foods on human chronic diseases, such as cardiovascular disease, arthritis or various cancers, is considered to be a problem. Since consumption of irradiated foods is becoming more widespread, it is very important to resolve the question of an impact on the chronic diseases, particularly on cancer, with appropriate scientific methodologies. All of the studies conducted to date have been of too short a duration to verify the carcinogenic potential of irradiated foods; due to the nature of chronic disease development several decades of observation will be required.



Recent studies indicate that radiolytic compounds such as 2-alkylcyclobutanones are exclusively generated in irradiated foods⁵⁻⁷. 2-Alkylcyclobutanones formed from the chain fatty acid moiety of triglycerides present in foods might promote undesired health effects, including cancer. These four-membered ring compounds contain the same number (n) of carbon atoms as their fatty acid precursors and $n-4$ carbon atom alkyl side chains in position 2. Two recent research articles reporting on toxic and colon tumor-promoting effects of 2-alkylcyclobutanones stimulate our review on the potential health risks of the consumption of irradiated foods^{8,9}.

Dietary Fat and Colorectal Cancer

Several dietary factors including dietary lipids that vary in type and quantitatively in fatty acid composition influence the pathogenesis of several chronic diseases¹⁰. Colon cancer, multifactorial and multistep in nature, is one of the cancer types, that is largely influenced by dietary lipids. It is the second most prevalent cancer in the USA, in terms of contributing to deaths among men and women¹¹. A number of epidemiological and experimental studies support the hypothesis that consumption of animal fat and particularly saturated fat places people at high risk for colon cancer. To our knowledge there is currently no prospective epidemiological study that addresses potential colorectal cancer risk levels of humans exposed to irradiated meat vs non-irradiated meat.

Radiolytic Agents: Potential Colon Tumor Promoters?

Horvatovich *et al.* (2002)⁸ reported that administration of a 0.005% solution of 2-alkylcyclobutanone, a compound present in irradiated food, to rats resulted in the appearance of a minute fraction of agent in the adipose tissues. However, it is to be noted that prolonged exposure and thus, the presence of trace amounts of alkylcyclobutanones in the adipose tissue over long periods of time can have deleterious effects, and this requires further investigation. Ingestion of 2-alkylcyclobutanones present in irradiated



foods (specifically from the fatty acid chains) may thus contribute to the risk for the neoplastic growth in colonic (including normal, preneoplastic and neoplastic) epithelia.

Raul *et al.* (2003)⁹ published that 2-alkylcyclobutanone (0.005% w/v) promoted azoxymethane (AOM)-induced colon carcinogenesis in Wistar rats. The increase in colon tumors in animals administered radiolytic compounds is highly significant compared to control rats; however, use of only 6 rats/group and lack of vehicle controls in the experimental design raise concerns about assessing tumor outcome as the end-point. To our knowledge and in our experience with animal models of colon cancer, Wistar rats are generally more sensitive to AOM-injection than F344 or Sprague-Dawley rats. By contrast, the AOM-induced F344 rat model (two-injections protocol) is widely accepted as an ideal model to mimic human colon cancer.

Interestingly, in this above study there were no differences in total number of colonic aberrant crypt foci (ACF) in the groups treated with 2-alkylcyclobutanone-treated and untreated rats three months after the AOM-injections, but a significant difference between the groups is reported six months after AOM-injections. The data on ACF with crypt multiplicity greater than four did not support the tumor outcome in the 2-alkylcyclobutanone-treated groups in totality and no justification is given regarding the differences observed between the two results. Since the alkylcyclobutanone compounds were administered just after AOM-injections, it is possible that these compounds act differently in the initiation phase than during the post-initiation/promotion stage. This needs to be examined. It is important to understand whether these compounds are co-carcinogenic and whether they might affect people not at risk from colon cancer differently from those predisposed to it. Irrespective of the pitfalls of the study, it is indeed alarming that 0.005% w/v of solution 2-alkylcyclobutanone given in drinking water to AOM-injected Wistar rats significantly promotes colonic tumors, and total number ACF when compared to rats treated with vehicle alone. Hence, the results reported in the study by Raul *et al.* (2003)⁹ are very important and the possible public health impacts of their observation needs further investigations with established experimental designs for colon cancer.



While comparing the results of the two studies, Horvatovich *et al.* and Raul *et al.*,^{8,9} it is evident that there is a clear difference in the toxic and tumor promoting potentials between the two main forms of 2-alkylcyclobutanones, 2-(tetradeca-5'-enyl)-cyclobutanone (2-tDeCB) and 2-tetradecyl-cyclobutanone (2-tDCB). While in the first study the retention of 2-tDCB in adipose tissue is more than that of 2-tDeCB in rats fed these compounds, in the colon cancer study 2-tDeCB promoted both the appearance of colonic ACF and tumors, an effect not seen in the rats treated with 2-tDCB. An explanation for this could have been that 2-tDeCB is more potent in the colonic epithelium. The exact mechanism(s) by which 2-tDeCB specifically promotes colon cancer warrants further research. Moreover, the prolonged accumulation of these compounds in various tissues (not investigated so far) may lead to genotoxic levels and may possibly promote late but chronic effects.

Conclusion

Currently, most meat and poultry products in the United States are legally permitted to be irradiated before they reach the market place. Public consumption of irradiated foods is increasing worldwide. The levels of 2-alkylcyclobutanones in several irradiated foods of both plant and animal origins have been quantified¹². For example, the concentration of 2-alkylcyclobutanone produced by 5 kGy irradiation of minced chicken was found to be 0.2 µg/g⁶. Our main concern with regards to consumption of irradiated foods is whether 2-alkylcyclobutanones promote cancers? There are several recent reports about the toxicity of 2-alkylcyclobutanones^{9,13}. Ample preliminary evidence exists supporting the possible genotoxic effect of 2-alkylcyclobutanones¹⁴. However, further investigations are warranted to identify and assess the exact levels at which radiolytic agents may exert tumor promoting effects. Also, a full-length study investigating the cancer promoting effects of 2-alkylcyclobutanones in irradiated foods (*per se*) and their mechanism(s) of action, is urgently needed to address public health concerns. A thorough investigation of the effect of 2-alkylcyclobutanones at levels consumed by the human population and in



models (*in vitro* and *in vivo*) of various types of cancers is warranted before proposing that irradiated foods do or do not promote colon cancer.

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