Comment on a statement of the SCF on a report on 2-alkylcyclobutanones.

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We have been informed through the internet of an official statement[1] issued on July 3rd, 2002, by the Scientific Committee on Food (SCF) of the European Commission, on the report[2] we prepared concerning our study aimed at evaluating the toxicological properties of 2-alkylcyclobutanones. The results of this work were presented to the Joint Working Group on Genetically Modified/Novel Foods of the SCF in Brussels on February 1st, 2002. The European Commission was also informed by communication of the full final report, forwarded in November, 2001. This note is a comment to the SCF statement as we feel that some points need to be clarified.

In this report, we have described new reaction pathways for the chemical synthesis of saturated and mono-unsaturated 2-alkylcyclobutanones (2-ACB). This new synthesis enabled us to produce sufficient amounts of various highly pure 2-ACBs to initiate studies on the toxicological properties of these compounds. These studies included the assessment of the mutagenic properties of 2-ACBs, using the classical *Salmonella typhimurium* mutagenic reversion test, the evaluation of possible genotoxic effects of the 2-ACBs, assessed both by the Comet Assay and alkaline unwinding, the latter in the presence of DNA repair enzymes. With the aid of these techniques the induction of DNA strand breaks and oxidative damage in cultured human cells have been estimated. Finally, a promotor effect of the 2-ACBs was observed in rats enrolled in a well established chemically induced colon carcinogenesis assay.

Our conclusions indicate that 2-ACB, as pure compounds, present cytotoxic and genotoxic effects in cultured human cells, promote colon carcinogenesis in rats and accumulate in adipose tissue of rats fed with these compounds.

[1] http://europa.eu.int/comm/food/fs/sc/scf/index_en.html

[2] Burnouf D, Delincée H, Hartwig A, Marchioni E, Miesch M, Raul F, Werner D (2001). "Etude toxicologique transfrontalière destinée à évaluer le risque encouru lors de la consommation d'aliments gras ionisés / Toxikologische Untersuchung zur Risikoberwertung beim Verzehr von bestrahlten fetthaltigen Lebensmitteln – Eine französisch-deutsche Studie im Grenzraum Oberrhein". Rapport final / Schlussbericht Interreg II. Projet / Projekt No 3.171. A summary of the report is available on internet at: http://www.iaea.org/programmes/rifa/icgfi/documents/summary-press.pdf

The SCF statement appears a little bit confusing when it indicates that « it is not appropriate (...) to make a risk assessment for human health associated with the consumption of 2-ACBs present in irradiated fat-containing foods » because « the adverse effects noted refer almost entirely to *in vitro* studies... », although it acknowledges in the same statement that « promoter activity (of 2-ACBs) was seen after 23 weeks following administration of a colonic carcinogen to rats in relation to colonic tumour incidence ».

The major caveat of our study, according to the SCF statement, is that the experiments have not been done using standard procedures. We certainly agree with this point, but we would like to stress that this study was managed as a research program to identify possible toxic effects of the 2-ACBs and to elucidate the mechanisms. It was not intended just to run standard genotoxicity assays or feeding studies for regulatory purposes. Such complementary studies should be done by specialized and ISO 9002 accredited laboratories. We feel that despite the absence of standard procedures, our results nevertheless provide important information as regards the intrinsic toxicity of pure 2-ACBs.

Moreover, as it was clearly concluded in our final report, we agree that on the basis of our results, no final conclusion can be made about the impact on human health of the toxicity related to 2-ACBs present in irradiated food. However, we feel that our new data which will be published in peer-reviewed journals, raise some doubts or at least suggest that caution should be excercised before any risk to consumers by exposure to these compounds is denied. At present, knowledge about the potential toxicity of the 2-ACBs (including possible metabolites) and their toxic potency is very limited. Since these compounds are uniquely formed by irradiation and are not inherent in food, in our opinion, complementary studies are needed to make a qualified risk assessment. It needs to be shown that despite the presence of potentially cyto- and genotoxic radiation-induced agents, the consumption of irradiated fat-containing food is safe for consumers. Food safety continuously needs to be re-assessed according to the latest state of scientific knowledge. This is valid for both unprocessed food in which natural compounds exhibit toxicity (e.g. estragole) and for processed food by any processing (e.g. the recent controversy of acrylamide in heated foods). This re-assessment should also be valid for irradiated foods.

International publications

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Horvatovich, P. (2001), Formation des 2-alkylcyclobutanones à partir des triglycérides dans les aliments traités par ionisation. Doctorat de l'Université Louis Pasteur de Strasbourg.

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H. Delincée, C. Soika, P. Horvatovich, G. Rechkemmer, E. Marchioni, (2002), Genotoxicity of 2-alkylcyclobutanones, markers for an irradiation treatment in fat-containing food – Part I: cyto- and genotoxic potential of 2-tetradecylcyclobutanone, Radiat. Phys. Chem., 63, 431-435.

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Poster presentation

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H. Delincée, B.-L. Pool-Zobel (1997), Genotoxic properties of 2-dodecylcyclobutanone, a compound formed on irradiation of food containing fat. Poster presented during the 10. International Meeting on Radiation Processing, Anaheim, CA, (USA) 11-16 May 1997. (Abstract published in Conference Program and Abstracts, p. 68)

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