Commission of the European Communities

food - science and techniques

Reports of the Scientific Committee for Food

(Thirteenth series)

Report

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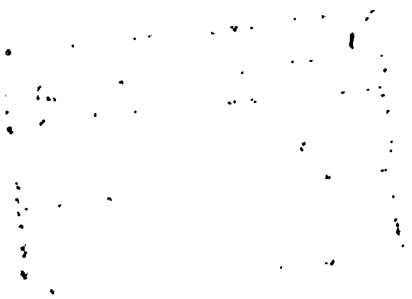

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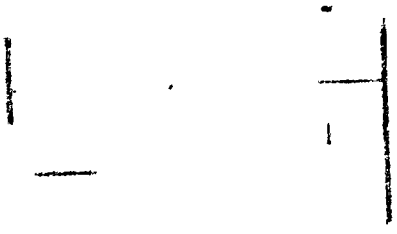

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S U M M A R Y

REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON ACRYLONITRILE MONOMER

(Opinion expressed 15 January 1981)

TERMS OF REFERENCE

To evaluate the hazards to human health arising from the migration into food of acrylonitrile monomer present in certain plastic materials and articles intended to come into contact with foodstuffs.

DISCUSSION

The Committee considered the available technological and toxicological information as well as the epidemiological data on acrylonitrile monomer (AN) presented to it during 1978 and 1979 and suggested at that time that before making a final decision it should see the results of ongoing studies. In the intervening period the Committee recommended that on the basis of the then available evidence AN should not be detectable in food or beverages by an agreed method. The Committee's views were made known to the responsible authorities. Since that time other information has become available and the Committee has now reviewed all the data.

The toxicological data show that AN administered to rats orally or by inhalation induces tumours in various specific organs in a dose-related manner primarily in the central nervous system, Zymbal gland, tongue and forestomach. This increase is induced by concentrations in the diet above 1 mg/kg. AN also induces foetal malformations and early resorptions in rats. AN is mutagenic when tested in some bacterial systems but not in others. The mutagenicity tests in eukaryotic systems with and without metabolic activation yield no conclusive results.

The epidemiological studies indicate an increase in total tumour frequency, but there is so far no clear evidence for an increased occurrence of specific tumours among exposed workers. An increased incidence of symptoms relating to the central nervous system, cardiovascular system and haematopoetic system has been reported in exposed workers.

CONCLUSIONS AND RECOMMENDATIONS

The Committee considers AN to be carcinogen for animals and possibly for man. The aim should therefore be to take all possible steps to reduce all forms of exposure to AN. The Committee recommends that the levels of AN monomer residue in materials and articles, intended to come into contact with foodstuffs, should be reduced as much as possible. In every instance AN should not be detectable in food by a method of analysis which would be applicable generally to most foods by most control laboratories.

The analytical methods available today have a limit of detection of 0.005-0.01 mg/kg. Attempts should be made to develop a method with greater sensitivity.

The Committee also recommends that the situation be reviewed at intervals in the light of further data collected in member countries and as progress is made in manufacturing technology.

REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON VINYLIDENE CHLORIDE MONOMER

(Opinion expressed 15 January 1981)

TERMS OF REFERENCE

To evaluate the hazards to human health arising from the migration into food of vinylidene chloride monomer (VDC) present in certain plastics materials and articles intended to come into contact with foodstuffs.

DISCUSSION

The Committee first considered the technological and toxicological information on vinylidene chloride monomer (VDC) available to it in 1978/79. The Committee was informed at that time of the progress of ongoing investigations in a number of countries. The data examined showed that VDC was carcinogenic when tested in mice. There was no evidence of carcinogenicity when tested in rats and hamsters and such human epidemiological evidence as was available from occupational exposure provided no evidence of a carcinogenic risk for man. The Committee also received evidence that significant migration of VDC from packaging materials and articles into food did not occur. On this basis the Committee was prepared to accept provisionally the continued use of packaging material made from VDC on condition that more information was supplied on exposure to VDC via food which is in contact with packaging material and articles containing VDC. In addition, the results of ongoing studies on the toxicology and epidemiology of VDC were requested to be made available to the Committee. The Committee recommended that in the meantime every effort should be made to reduce the levels of VDC in packaging materials and articles to the minimum . These views were made known to the responsible authorities.

The Committee has now considered the additional technological and toxicological information on VDC which has become available since its earlier review. This additional evidence includes information on the bio-chemistry, metabolism, pharmacokinetics, reproduction and teratology, carcinogenicity and mutagenicity of VDC following both oral administration and exposure by inhalation.

The previously observed carcinogenic effect in mice is now considered to be specific for this species and related to the cytotoxic action on the mouse kidney as the primary target organ rather than to any direct interaction with cellular DNA. This view is based on the observation that VDC and its metabolites with an epoxide structure are eliminated essentially by reaction with glutathione or bind covalently with cellular macromolecules, though only a minimal extent with DNA.

The toxicological data now available from other species have shown the absence of any significant toxic potential of VDC for the rat, the Chinese hamster and the rabbit with regard to reproduction and teratology as well as carcinogenicity and include one long-term study. Thesr studies are, however, insufficient to establish a TDI*.

The technological data have revealed that with the exception of a few oily food wrapped in films coated with VDC/VC copolymer, the levels of VDC in food generally are very low and of the order of 0.001 mg/kg food. In the few oily foods wrapped in films coated with VDC/VC polymer which have been examined, the levels of VDC ranges from 0.02-0.31 mg/kg food.

CONCLUSIONS AND RECOMMENDATIONS

The Committee has no objection on toxicological grounds to accepting the continued use of plast materials and articles made with VDC and intended to come into contact with foodstuffs. Nevertheless because the Committee was unable to establish a TDI for this monomer, it recommend that the levels of VDC monomer residues in materials and articles intended to come into contact with foodstuffs should be reduced as much as possible.

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*Tolerable Daily Intake : See Reports of the Scientific Committee for Food, 6th Series (1978)

REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON HYDROLYSED LECITHIN

(Opinion expressed 12 June 1981)

TERMS OF REFERENCE

To give an opinion on the acceptability from the point of view of public health of the use in food of hydrolysed lecithin as an alternative to non-hydrolysed lecithins.

BACKGROUND

When purity criteria for lecithins (E 322) were being drawn up, a number of questions were raised on whether it was possible to include "hydrolysed lecithins" within the term "lecithins". The Council decided that the Commission should make further enquiries before these materials could be approved for use at Community level.

As part of its investigation, the Commission has asked the Committee to advise on the safety aspects.

CURRENT REVIEW

The Committee was informed that food grade lecithin, obtained from soya beans or other sources, is a mixture containing about 60% phospholipids and 40% of triglycerides, sterols and carbohydrates in various proportions. Hydrolysed lecithin has been proposed as a replacement of lecithin and is the product of partial hydrolysis of food grade lecithin following digestion with pancreatin.

The available specification shows that hydrolysed lecithin contains about 51% phosphatides, 18% total free fatty acids, 1% moisture and 24% of triglycerides, sterols, commercial pancreation and carbohydrates in variable proportions.

Hydrolysed lecithin is biochemically closely related to lecithin from which it is derived by enzymatic hydrolysis. It therefore contains additional free acids and glycerophosphate fragments. The pathways of phosphatide synthesis and catabolism are well known. The average diet provides a daily intake of several grams (1-5 grams of lecithin).

A three week feeding study in rats comparing lecithin, hydrolysed lecithin and a control purified diet containing 10% ground nut oil showed no essential difference between lecithin and hydrolysed lecithin with respect to effects on body weight, food intake and growth. Levels of 20% or more in the diet produced adverse effects on haematopoiesis and enlargement of the kidneys[1].

Another rat study extending over 90 days with a similar design showed that the feeding of lecithin or hydrolysed lecithin at levels of 5% or less in the diet induced no adverse effects and no clear dose-related effect was seen at dietary levels up to 20%. The renal lesions observed were considered to be specific to the Colworth rat and are therefore not significant for human health[1, 2].

CONCLUSIONS

Hydrolysed lecithin is produced in the gut as a result of normal digestion. There appears to be no specific toxicological effect in rats due to feeding of hydrolysed lecithin. This substance can therefore be regarded metabolically and toxicologically as an alternative to lecithin.

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SECOND REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON MODIFIED STARCHES

(Opinion expressed 12 June 1981)

TERMS OF REFERENCE

The Committee was asked to give an opinion on the safety of the chemically modified starches, permitted on a temporary basis until 31 December 1980 and listed in groups B and C of the Appendix to its report.

BACKGROUND

In its first report on modified starches of 1976* the Scientific Committee for Food requested further studies on the appearance and mechanism underlying the observed pelvic nephrocalcinosis as well as certain studies on individual modified starches. The results of these studies were to be reviewed before the 31 December 1980.

On the other hand the Committee noted that among starches, previously classified in its earlier report in group C, those modified by epichlorhydrin were no longer used by industry, although the results of toxicological studies have become available for some of these modified starches. The Committee noted that the specifications in the Annex to its Report of 1976 had been reexamined by the Commission and that a number of modifications had been made that were not essential to the toxicological evaluation.

TOXICOLOGICAL EVALUATION

a) Studies of nephrocalcinosis (PN)

The Committee has now been supplied with a number of documents (1, 2, 3, 4, 5, 6, 7, 8) relating to this problem. The review by Dr. F.J.C. Roe appraised the relevant literature on mineral deposition in the renal pelvis of rats. Probably the most important factors contributing to renal manifestations of dietary mineral and vitamin imbalance in rats were the dietary levels of Ca, Mg, P and vitamin B_6. Three kinds of nephrocalcinosis can be distinguished: 1) pelvic nephrocalcinosis; 2) corticomedullary nephrocalcinosis; and 3) calculus formation. Acute Tubular nephropathy is also frequently observed. All four conditions are relatively common in untreated laboratory rats, particularly in older animals, and strain and sex difference have also been observed.

Many sugars, sugar alcohols and more complex carbohydrates, including dextrins and modified starches, enhance the absorption of calcium from the gut. It seems that low digestibility and delayed absorption of cabohydrate in the jejunum is associated with caecal enlargement and degradation of the carbohydrate in the ileum and caecum by bacterial enzymes. The absorption of degraded carbohydrate, particularly the monosaccharides, at those sites is associated with increased calcium absorption, and in turn leads to increased excretion of calcium in the urine.

High dietary concentrations of slowly digestible carbohydrates such as lactose, the occurrence of excess dietary Ca and P, an incorrect Ca/P,ratio, too little Mg or too little vitamin B_6 all contribute to the induction of renal changes, particularly in rats and mice. In turn his leads to PN in long-term feeding studies, particularly in rats.

A long-term feeding study in mice of modified starches and other substances revealed only slight evidence of PN and none of carcinogenic activity. A two-year chronic toxicity and multigeneration study in rats and two chemically modified maize starches showed a similar incidence of PN in controls as in test animals. The 30-60 days studies in hamsters fed modified starches in an incidentally Mg-deficient diet showed acute

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*Reports of the Scientific Committee for Food, Second Series (1976)

tubular necrosis of variable degree of severity especially when propylene oxide-modified starches were fed. No renal lesions were seen, if the Mg level was about 2-3.5 times the officially recommended level in the diet.

Metabolism studies on weanling rats fed modified starches at high dietary levels for 1 year showed little evidence of PN despite higher total Ca and P outputs. Similar studies on rats aged 9 months to 18 months produced clear evidence of PN especially if the basic diet contained excessive Ca and P levels. A further elaborate study on rats fed modified starch at a high dietary level failed to induce PN but there was evidence of corticomedullary calcification. The incidence and severity of the lesions was reduced by lowering the P content, increasing the Ca/P ration or increasing the Mg level tenfold. Propylene oxyde modification led to increased urinary Mg, Ca and P cpncentrations.

b) Additional studies on modified starches in group B and C

The Committee also reviewed additional short-term, long-term and reproduction studies on starches previously classified into group B or C (9, 10). They noted that none of these studies determined any dose-response relationships. Information was also received about the results of two lifespan studies in rats on epichlorhydrin, a modifying agent for starch, which showed this substance to have carcinogenic activity. The substance is als strongly mutagenic. No lifespan studies are available on propylene chlorohydrin, that will arise from modifying starch with propylene oxide, except for positive mutagenicity tests.

CONCLUSIONS

1. The Committee considered the evidence on the appearance and mechanism of formation of pelvic nephrocalcinosis (PN). This incidence of this lesion increased apparently with the degree of substitution of the starch, and with the age of animals when first exposed. The rat appeared to be a particularly sensitive species for developing PN, the finding being much rarer in mice and not present in the hamster. Slow degradation of carbohydrates in the upper intestine led to the formation of absorbable breakdown products in the lower intestine. This was associated with enhanced Ca absorption. The Committee considered this finding to be peculiar for the rat as the most sensitive species and to have little relevance for the safety assessment of modified starches for man.

2. For these reasons the Committee was of the opinion that modified starches in group B can now be regarded as acceptable. Because these modified starches also contribute to the energy balance of the diet, the Committee considered it unnecessary to establish individual ADIs provided technological usage remained at present-day levels. The Committee requested that this aspect should be kept under review by the Commission.

3. Starches modified with epichlorhydrin should not be used in food because of the carcinogenicity of epichlorhydrin.

4. As regards baby foods the Committee accepted that starches in group B could be used in infant foods and foods for young children provided the maximum limits of 5% was not exceeded. The Committee however reaffirmed its previous advice that propylene oxide-modified starches should not be used in foods for infants and young children.

5. The Committee considers that modified starches in group C, modified with propylene oxide (E 1440 and E 1442), could be transferred to group B provided residues of chlorohydri do not exceed 0.1 mg/kg as determined by an agreed method.

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3. A preliminary report of a thirty day study in hamsters fed modified starches : Dr. P. Newberne and M.L. Buttolph.

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5. Final Protocol for studies of modified food starch in hamsters : Dr. P. Newberne.

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10. Personal Communication from Dr. G. Van Esch.

SECOND REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON FLAVOURINGS

(Opinion expressed 11 December 1981)

The Committee was asked as a matter of urgency to give its opinion on the proposal that nature-identical flavouring substances and natural flavouring materials should be regulated by using the negative list principle (i.e. substances and materials not expressly prohibited are to be considered as acceptable).

In view of the constraints of time imposed on the Committee the present report should be considered as a summary of conclusions that can be justified with detail should the need arise.

The Committee recognises the complexities of classification, specification and toxicological evaluation of the large number of substances involved and the problems of enforcement entailed by the elaboration of a list of permitted flavourings. The Committee reiterates the statement in its 10th Report that before an additive is accepted for use in food it should have been subjected to an adequate toxicological evaluation, and sees no reason, on the information available to it about flavourings to depart from this principle.

A system which proposes that a substance or material could be used in food without evaluation until proof of danger would not be compatible with the Committee's interpretation of what was needed to protect public health.

The fact that a substance occurs in food or has been synthesised to be identical to a substance occuring naturally in food or natural source material is no proof of its inherent safety.

It is clear that nature identical substances, more than natural flavourings, are likely to be used in food in quantities exceeding the levels in which they are found in nature. The committee accepts the concept that nature identical substances do not differ fundamentally from their natural counterpart. However, toxic substances are found in nature and some occur in food and this justifies the position of the Committee that a positive list for nature identical substances and for source materials for the production of natural flavouring preparations is desirable.

In its 10th Report the Committee acknowledged that special considerations may apply when evaluating the safety-in-use of flavourings and that priorities need to be established regarding the substances to be evaluated. At the same time due consideration should be given to the extent of the minimum toxicological examination required.

Given the large number of substances involved an evaluation will take time and the Committee can understand those who state that the list of acceptable substances cannot be drawn up immediately. Indeed the Committee could accept that the list would have to be drawn up in stages according to agreed criteria for priorities. Experience and information has been accumulated by the Council of Europe, WHO, national authorities and organisations such as IOFI and the US F.E.M.A. on the usage, physico-chemical characteristics and toxicological properties of flavouring substances. Therefore it should be possible to evaluate many flavourings in use on the basis of these data and to assess their acceptability or non-acceptability. The task should be carried out in such a way as to avoid duplication of effort among the various scientific bodies concerned in advising governments and international organisations.

The Committee recognizes that there are political, legal and economic implications which have to be considered by the responsible authorities. Nevertheless it draws to their attention the conclusion of the Council of Europe's expert group that "any effective legal control must be based on positive lists". The Committee also notes that the application of the provisions of the 6th amendment to the Council Directive on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances[1], will influence the situation.

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[1] 79/831/EEC of 18.9.1979, OJ L 259 of 15.10.1979, p. 10

REPORT OF THE SCIENTIFIC COMMITTEE FOR FOOD ON STYRENE MONOMER

(Opinion expressed 5 March 1982)

TERMS OF REFERENCE

To evaluate the hazards to human health arising from the migration into food of styrene monomer present in certain plastic materials and articles intended to come into contact with foodstuffs.

DISCUSSION

The Committee considered the technological and toxicological information available to it in 1978/1979 and suggested at that time that before making a final decision it should see the results of ongoing studies. In the intervening period the Committee recommended that on the basis of the then available evidence it would be necessary to achieve the lowest level of residual styrene monomer (SM) in the materials and articles that was technologically feasible and then to reduce migration of SM into food. These views were made known to the responsible authorites.

Since that time other information has become available, including additional data on the toxicological effects of SM on man, experimental animals, and certain biological systems. Estimates have also been provided of the likely intake of SM in the human diet, which may range from 1-4 µg/day.

The Committee has reviewed again all presently available data and concluded that the new information confirms the Committee's previous opinion that the data do not lead to the conclusion that SM is carcinogenic to animal species or to man. The available toxicological data are still insufficient to establish a TDI*. However, the Committee is aware of further ongoing studies and will review the situation when these data become available to it.

CONCLUSION AND RECOMMENDATIONS

The Committee has no objection on toxicological grounds to accepting the continued use of plastic materials and articles made with SM and intended to come into contact with foodstuffs. Nevertheless because the Committee was unable to establish a TDI for this monomer it recommends that the levels of SM residues in materials and articles intended to come into contact with foodstuffs should be reduced as much as possible.

*Tolerable Daily Intake: see Reports of the Scientific Committee for Food, 6th Series (1978)

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