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483

N-Nitroso Compounds: Analysis and Formation (International Agency for Research on Cancer Publication No. 3)

P. BOGOVSKI, R. PREUSSMAN, E. A. WALKER and W. DAVIS (Editors)

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By any criterion *N*-nitrosamines are among the most potent and most important classes of chemical carcinogens. It was appropriate therefore for the International Agency for Research on Cancer to organize in October 1971 a conference concerned with the detection and estimation of *N*-nitrosamines and with the conditions under which they may be found either outside or inside the body by the interaction of nitrite with secondary or tertiary amines. The published proceedings of that conference are the subject of this review.

Nitrosodimethylamine and nitrosopyrrolidine may be formed in meat when nitrite is used to preserve it. Concentrations as low as 2.5p.p.m. of nitrosodimethylamine over a period of 30 days are fatal for mink and 0.5p.p.m. of nitrosodimethylamine is on the borderline of carcinogenicity for the rat. The food analyst has been required to develop methods capable of detecting and measuring concentrations at least 100-fold less than this (i.e. within the 1–10p.p.b. range). Most of the many nitrosamines that have been adequately tested have been found to be actively carcinogenic for laboratory animals. So also have several nitrosamides. For the purposes of safety evaluation of foods it has therefore been necessary to seek ways of measuring, not just individual nitrosamines, but nitrosamines and nitrosamides as classes of compound. It has, not unreasonably, been speculated that some human cancers might be caused by exposure to nitrosamines in food, alcoholic beverages etc. Accordingly food eaten by persons in communities where cancers, such as cancers of the liver or oesophagus, are rife has been the object of careful analysis for nitrosamines. Unfortunately, some of the earlier studies of this kind were based on the use of doubtful analytical procedures. This briefly is the background to the first section of the book, which begins with a survey (A. E. Wasseman) of the analytical procedures that have been used and a series of contributions on the detection of nitrosamines in foods and beverages, and culminates in a brief 'Report of the Sub-committee on Analytical Methods for *N*-Nitroso Compounds'.

G.l.c. and mass spectrometry after clean-up comprising steam-distillation, liquid–liquid extraction with dichloromethane, ion-exchange or silica-gel chromatography, and volume reduction by evaporation or freeze-drying provide a generally reliable and sensitive technique for the detection of volatile nitrosamines. In laboratories where mass spectrometry is not available improved sensitivity and specificity can be achieved by forming from nitrosamines derivatives with electron-capturing or strongly fluorescent properties. Acceptably reliable methods for the determination of non-volatile *N*-nitroso compounds have not yet been developed.

In the case of most toxins that may reach man via his food, protection may be effected by analysis of samples of foodstuffs for the toxin in question. The possibility of exposure to nitrosamines, however, may escape this net insofar as they may be formed by the interaction of nitrites and secondary amines during cooking or after ingestion. Some drugs (e.g. oxytetracycline, aminopyrine) are secondary amines, and it has been shown that nitrosamines can be formed by the interaction of these with nitrite under the warm and acid conditions existing in the human stomach. According to E. Boyland the rate of nitrosation in the stomach may be greatly increased by many factors, including the presence of bromide or iodide ions and the concentration of thiocyanate in saliva. P. Bogovski and his colleagues have shown, on the other hand, that tannins inhibit the formation of nitrosamines. Gut organisms and bacteria causing urinary-tract infections in man can nitrosate secondary amines in the presence of excess of nitrate, and M. J. Hill and G. Hawksworth have found nitrosamines in the urine of rats with experimental urinary infections when they were given high-nitrate drinking water.

This book conveniently assembles information previously scattered throughout the scientific literature, and usefully points to the most reliable analytical methods, drawing attention to the snags in their application. As such it will be essential reading for analysts who find themselves involved in nitrosamine determinations. But the book is also of value in that it will help the general reader to understand why cancer research scientists are currently so fascinated by the complexities of nitrosamine research.

FRANCIS J. C. ROE