CHEMISTRY

Complex Formation, Isolation and Carcinogenicity of Polycyclic Aromatic Hydrocarbons

THE carcinogenic activity of some of the polycyclic aromatic hydrocarbons[1,2] present in common materials has focused considerable attention on the properties and isolation of this group of compounds. Many methods for their isolation have been reported which are based, in general, on procedures involving partition[3–6], adsorption[7–9] or complex formation[9,10], used either singly or in combination.

The present attempt to develop a more satisfactory method of isolating polycyclic aromatic hydrocarbons stems from the work of Weil-Malherbe[11] who, on the basis of an observation by Brock, Druckrey and Hamperl[12], investigated the quantitative aspects of the solubilization of a number of polycyclic aromatic hydrocarbons in many different purine solutions. 1 : 3 : 7 : 9-Tetramethyluric acid (TMU) and caffeine were shown to be the most effective purines. Although the phenomenon is not specific to polycyclic aromatic hydrocarbons[13–17], other compounds such as aromatic amines and heteropolycyclics, which form complexes and are often found in hydrocarbon mixtures, present no difficulty to an attempt to isolate polycyclic aromatic hydrocarbons.

Silica impregnated with caffeine has been used[18,19] in a thin layer chromatographic technique to separate the components of a mixture of polycyclic aromatic hydrocarbons; the preparation of a concentrate of polycyclic aromatic hydrocarbons from petroleum products with high boiling points using aqueous caffeine has been described[20] and counter current distribution with a solvent system containing TMU has been used to separate certain polycyclic aromatic hydrocarbons[17].

From a consideration of the suggestions put forward for the structure of complexes formed between polycyclic aromatic hydrocarbons and purines[11,21–24] and between polycyclic aromatic hydrocarbons and nitro aromatic compounds[25,26], it seemed likely that the complexes might migrate under the influence of an electrical potential.

Using curtain paper electrophoresis with platinum electrodes in troughs at the top and bottom of the paper, complexes of polycyclic aromatic hydrocarbons with both caffeine and TMU have been found to migrate readily. Complexes were formed before spotting on the paper; the solvent was a solution of 2 g purine in 90 ml. water–10 ml. ethanol–2 ml. ammonia and the potential and current were 30–35 V/cm and 3–4 m.amp/cm. The twenty-five complexes of polycyclic aromatic hydrocarbons examined all migrated as discrete spots which completely left the baseline. Using the same method, it was later shown that these polycyclic aromatic hydrocarbons could be separated from twelve times their own volume of 'Vaseline'.

In large scale applications of the method, as much as 1 g of hydrocarbon mixtures containing polycyclic aromatic hydrocarbons has been adsorbed on 80–100 g silica and the residue packed into a column 38 mm in diameter. By applying a potential of 1,200–1,500 V to the column and slowly eluting with the solvent already mentioned, almost all the species which could be detected by electron capture during gas-liquid chromatography have been separated from the bulk of the mixture which remained on the column. Furthermore, in experiments in which radioactively labelled polycyclic aromatic hydrocarbons were incorporated in the hydrocarbon mixture, 97–98 per cent of the labelled polycyclic aromatic hydrocarbons were isolated. The exact experimental details of the method, which is now being used with most encouraging results to examine the condensate of cigarette smoke, will be published in the near future.

The nature of the purine/hydrocarbon complexes suggested by Liquori *et al.*[22], namely a dipole – induced dipole interaction between the polar component (caffeine) and the polarizable component (polycyclic aromatic hydrocarbons), is consistent with the phenomenon which has been demonstrated and used in the present work.

Many attempts have been made to relate the complexing ability of polycyclic aromatic hydrocarbons to their carcinogenic properties, but none has so far been successful. Weil-Malherbe[11] could find no direct relationship but suggested that an affinity between hydrocarbons and the purines in nucleo-proteins might cause interference with nucleic acid metabolism. Booth and Boyland[13] also found that carcinogenic polycyclic aromatic hydrocarbons did not differ from non-carcinogenic compounds in their reaction with purines. Liquori *et al.*[22] and Van Duuren[24] have also examined the problem. The rates of electrophoretic migration of all the complexes of polycyclic aromatic hydrocarbons with caffeine and TMU examined are similar and the slight visible differences cannot be related to any carcinogenic properties of the hydrocarbons. It is nevertheless possible that the complexing property of polycyclic aromatic hydrocarbons makes an important contribution to their carcinogenicity, the differences in biological properties resulting from a combination of factors such as molecular size, geometry and general reactivity. Thus the absence of carcinogenic activity in the majority of the polycyclic aromatic hydrocarbons might arise from diffusion and transport difficulties within the cell, lack of ability to adapt to a favourable configuration at the site of action in the cell, or destruction in other biochemical reactions before reaching the site of action. As suggested by Booth and Boyland[13], the protective action of purines in carcinogenesis may result from their competition with the site of action for the polycyclic compounds.

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