IDENTIFICATION OF AN ACTIVE PRINCIPLE OF ANTITUMOR ANTIBIOTIC JAWAHARENE WITH A MIXTURE OF LONG CHAIN FATTY ACIDS

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(Received for publication August 25, 1981)

Jawaharene[1] an antitumor antibiotic complex was obtained from the mycelia of a strain of *Aspergillus niger*. Its antitumor[2~7], antiviral[1,8] and antimicrobial[9,10] properties were studied in detail. In the present study, jawaharene has been fractionated by silica gel column chromatography and an antitumor active fraction designated JF_1 has been obtained. This fraction shows a single spot in thin-layer chromatorgram (TLC) using different solvent systems. JF_1 has been found by others to inhibit Ehrlich ascites carcinoma (EAC) and sarcoma-180 (S-180) ascites tumor in Swiss mice. It also inhibits the oxygen uptake and glucose uptake by EAC and S-180 cells, *in vitro*. The results will be published in a separate communication.

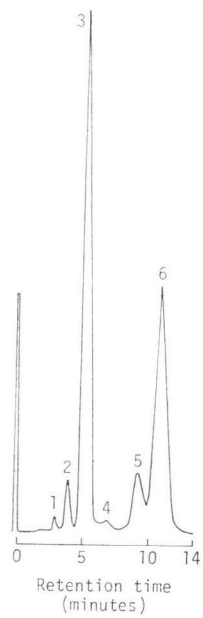
The methyl esters of JF_1 were made with diazomethane[11] and the ester-mixture was purified by silica gel column chromatography and preparative TLC. All the eluates were concentrated and dried *in vacuo*.

The indication that JF_1 is a mixture of long chain fatty acids was obtained from its various spectral data. The IR spectrum suggested the presence of carboxylic acid groups, long methylene chains and olefinic double bonds. The same conclusions could be drawn from the NMR spectrum of the methyl esters of JF_1. The mass spectrum of the methyl ester preparation indicated it to be a mixture of methyl esters of straight chain aliphatic acids. The molecular ion peaks corresponding to the constituent fatty acid methyl esters were observed at *m/z* 214, 242, 268, 270, 296 and 298. Finally the methyl esters of the fatty acids constituting JF_1 were quantitatively determined by GLC in Pye Unicam, GCD-chromatograph, using a 15% DEGS column on Gaschrom Z (80~100 mesh). Methyl esters of fatty acids were identified by comparison with authentic samples. The peaks 1, 2, 3, 4, 5 and 6 corresponding to lauric, myristic, palmitic, palmitoleic, stearic and oleic acid were observed (Fig. 1) with their relative abundance of 0.2, 0.86, 43.26, 2.0, 11.6 and 42.5%, respectively.

Thus JF_1, the antitumor active fraction of jawaharene, has been found to consist of six different long chain fatty acids of which palmitic (43.26%) and oleic (42.5%) are the major constituents. Among these six fatty acids oleic acid (commercial) has been found to be most active against EAC and S-180 cells comparable to JF_1. There are reports of antitumor active fatty acids (palmitic, stearic, octadecaenoic and octadecadienoic) isolated from the mycelia of some fungi[12,13] *viz. Penicillium crustosum, P. tardum, Cephalosporium diospyri, Sepedonium ampullosporum*.

The fatty acids constituting JF_1 occur commonly in the lipids of almost every organism. However, the antitumor properties of such fatty acids and their role as dietary constituents warrant further investigation in detail.

Fig. 1. GLC of methyl esters of JF_1.



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Acknowledgements

The authors express their sincere thanks to Prof. J. DUTTA, Bose Institute, Calcutta, and Dr. N. ROY, Indian Association for the Cultivation of Science, Calcutta for the measurement of GLC and NMR spectra respectively.

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