Vol. 49, No. 16
Aug. 20, 1980

ORGANOPHOSPHATE INSECTICIDE DDVP-INDUCED INCREMENT IN REGIONAL TOTAL LIPIDS AND CHOLESTEROL LEVELS: DIMINUTION OF PHOSPHOLIPID CONCENTRATION IN DIFFERENT REGIONS OF THE RAT BRAIN

K. TAYYABA AND MAHDI HASAN

Brain Research Centre, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh 202 001, India

ABSTRACT

0–0, dimethyl 2 : 2-dichlorovinyl phosphate (DDVP, 3 mg/kg body weight, i.p. injected daily for 15 days)-induced regional alterations in the brain lipid contents of male adult albino rats have been observed both 'biochemically' and 'histochemically'. Significantly increased levels of total lipids and cholesterol were found in the brain stem, cerebellum and cerebrum. But the phospholipid fraction showed diminution in all the brain regions. The biochemical findings are supported by the histochemical results.

INTRODUCTION

ORGANOPHOSPHORUS compounds are known to be cholinesterase inhibitors[1,2]. The exact mechanism of their delayed neurotoxicity is still unclear[3]. Recently, a diminution in the level of some free aminoacids[4] following 0–0, dimethyl 2 : 2-dichlorovinyl phosphate intoxication and alterations in regional monoamine concentration have been reported[5]. Mipafox-induced alterations in the brain lipids are also known[6], but comparatively little information on the regional lipid concentration of brain is available. Controversy dominates the inferences drawn by a few investigators who have ventured to obtain an insight into this problem[6,7]. The paucity of data on the effect of organophosphorus compounds on the regional brain lipid concentration prompted us to carry out the present investigation on the rat cerebrum, cerebellum and brain stem separately.

EXPERIMENTAL PROCEDURE

Sixteen male adult albino rats weighing 110 to 130 g were kept in the laboratory at room temperature and were fed a pellet diet *ad libitum* (Hindustan Lever Ltd., India) and had free access to water. Eight animals received dichlorovos (DDVP, 0–0, dimethyl 2 : 2-dichlorovinyl phosphate-Nuvan 100 EC, Ciba-Geigy India Ltd.), 3 mg/kg body weight intraperitonially (i.p.) daily for fifteen days. The control group (8 rats) was concurrently given an equal volume of physiological saline daily for the same period. On the fifteenth day all rats were decapitated to dissect out cerebrum, cerebellum and brain stem separately. Lipids were extracted according to Folch *et al.*[8] and analysed for phospholipid-phosphorus[9], total lipids[10] and cholesterol[11]. A histochemical study of the different regions of rat brain was carried out on conventional frozen sections (formol-calcium fixed, 15 μ thickness, cut on a cryotome K1310, Leitz) stained with Sudan black 'B' 1% for total lipids and by OTAN method for phospholipids as recommended by Adams[12].

* Address for correspondence: Prof. Dr. Mahdi Hasan, Brain Research Centre, Jawaharlal Nehru Medical College, Aligarh Muslim University, Aligarh 202 001 (India).

RESULTS AND DISCUSSION

Ataxia, convulsions and hyperexcitability to tactile stimuli were often detected on the fifth day of DDVP administration. These signs were intensified with the passage of time. It is evident from Table I that DDVP administration to rats significantly increases the total lipid ($P < 0{\cdot}05$) and cholesterol ($P < 0{\cdot}001$) concentrations in all the three regions of the brain while the concentration of phospholipid was significantly diminished in cerebrum ($P < 0{\cdot}05$), cerebellum ($P < 0{\cdot}05$) and brain stem ($P < 0{\cdot}001$).

As compared with the normal rats (Fig. 1), sections obtained from DDVP-treated rats (Fig. 2) show sudanophilic lipid deposits. However, at frequent sites mild deposits of phospholipid were seen in the experimental section (Fig. 4) as compared with the normal (Fig. 3).

In the present report, the increase in total lipid concentrations in cerebrum, cerebellum and brain stem, irrespective of their regional variations, can be explained on the basis of the observation of Caley and Jenson[7] who detected inhibition of lipase activity following organophosphate administration. Since the enzymes are very specific regarding interaction with substrates, it appears that phospholipase remained uneffected by the organophosphate intoxication and hence phospholipid concentration was not increased. On the other hand Nelson and Barnum[13] observed the inhibition of phospholipid biosynthesis by organophosphate. It appears more likely that the decrement in the phospholipid content in the present study may

TABLE I

DDVP-induced alterations in the total lipid, cholesterol and phospholipid contents of cerebrum, cerebellum and brain stem

	mg/g fresh tissue					
	Cerebrum		Cerebellum		Brain stem	
	Control	Experimental	Control	Experimental	Control	Experimental
Total lipid	106·2 (9·2)	129·4* (6·3)	127·8 (7·0)	149·3* (9·7)	128·5 (10·7)	159·6* (6·1)
Cholesterol	31·4 (6·1)	64·0*** (8·1)	25·7 (4·7)	47·6* (6·6)	44·0 (0·8)	66·5*** (3·4)
Phospholipid	56·9 (6·1)	41·9* (4·0)	55·9 (3·0)	40·5* (3·5)	59·0 (4·7)	44·0*** (4·2)

* Indicates $P < 0·05$; ** $P < 0·02$; *** $P < 0·001$.

Values in brackets indicate ± Standard error.

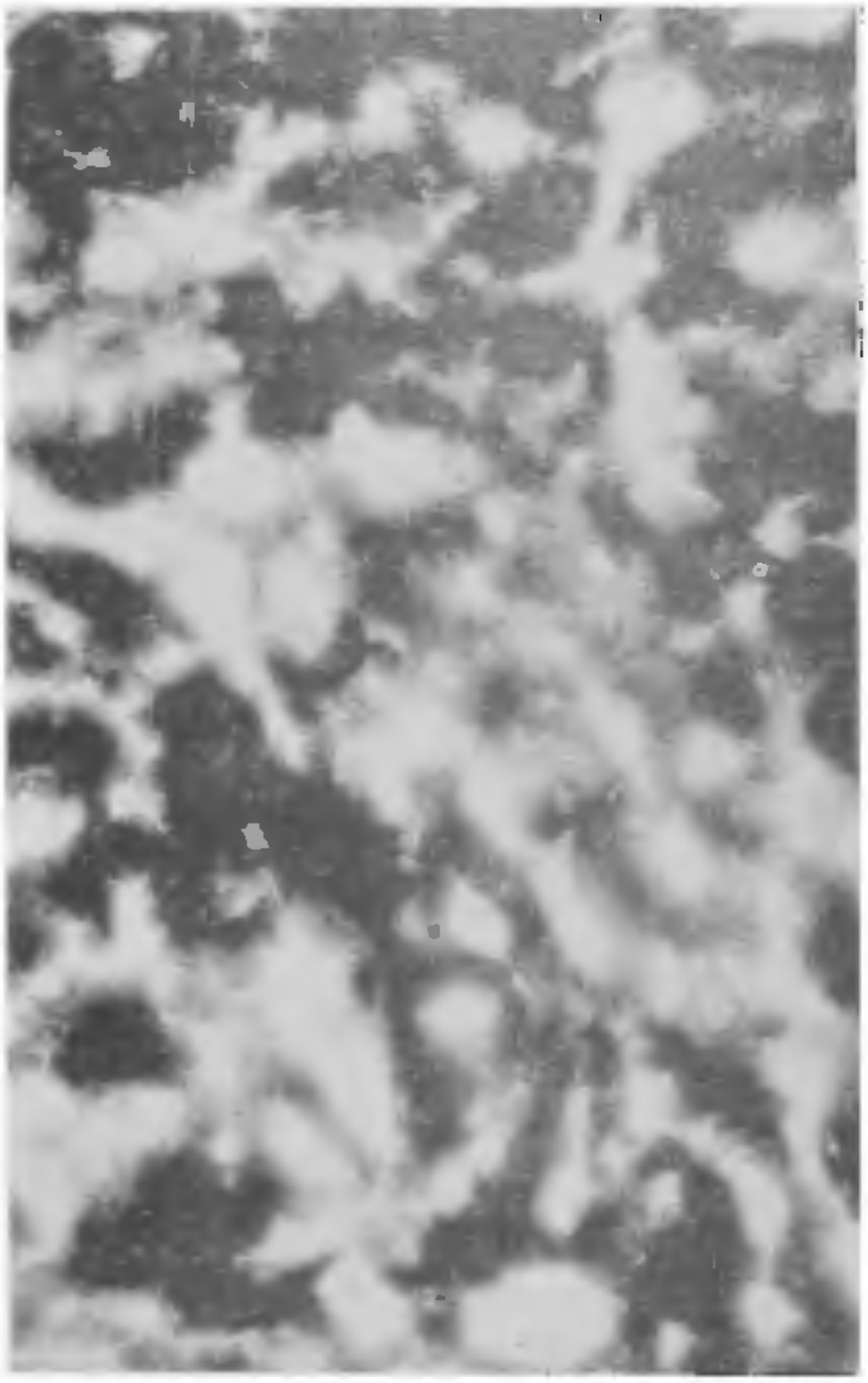

FIG. 1. Frozen section, cerebral hemisphere of untreated albino rat showing total lipid concentration (Adam's method) (× 600).

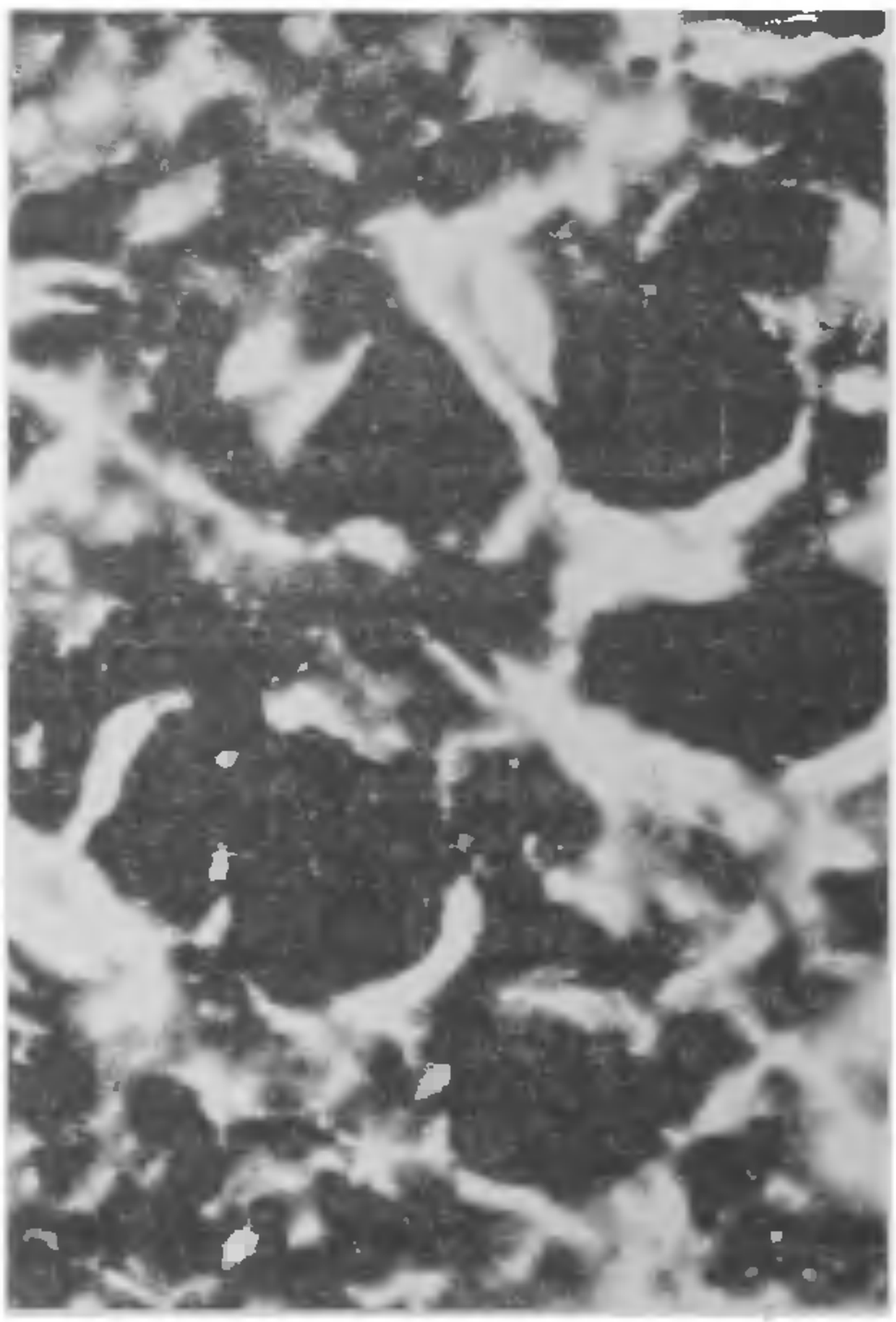

FIG. 2. Total lipid concentration after 15 days treatment by DDVP showing well-marked Sudanophillic lipid deposition (× 600).

FIG. 3. Photomicrograph showing phospholipid content of the cerebrum of the control rat (× 600).

FIG. 4. Photomicrograph showing diminution of phospholipid concentration in the cerebrum of the DDVP-intoxicated rat (× 600).

be the result of a similar mechanism. Earlier Austin[14] also favoured a similar role for diisopropyl fluorophosphonate (DEP), a potent organophosphorus compound. The increment in cholesterol level can be explained on the basis of either its increased synthesis or decreased degradation, following organophosphate intoxication. The possibility of inhibition of enzymes responsible for its degradation by DDVP appears more likely in view of the toxic manifestations of organophosphorus compounds. Another alternative explanation may be sought in the known steroid-organophosphorus antagonism[15]. Pretreatment of rats with certain steroids reduces the toxicity of organophosphates[16]. Since cholesterol is a substrate for the steroid biosynthesis it would not be unreasonable to assume that cholesterol level may rise following organophosphorus toxicosis.

The observed concordance of the biochemical results and histochemical observation of total lipid and phospholipid in different regions of brain made this facet of neurotoxicological research of great practical interest.

ACKNOWLEDGEMENTS

The authors express their gratitude to the University Grants Commission, New Delhi, for financial assistance. The senior author is a research fellow of U.G.C.

1. Durham, W. F., Gains, T. B., Mecauley, R. N. Sellae, V. A., Mattson, A. M. and Hayes, W. J., *AMA Arch. Industr. Health*, 1957, **15**, 340.
2. Coopage, D. L., Mathews, E., Cook, G. H. and Knight, T., *Pesticide Biochem. Physiol.*, 1975, **5**, 536.
3. Casida, J. E., *Science, N.Y.*, 1964, **146**, 1011.
4. Ali, S. F. and Hasan, M., *Indian J. Exp. Biol.*, 1977, **15**, 759.
5. —, — and Tariq, M., *Ibid.*, 1979, **19**, 424.
6. Majno, G. and Karnvosky, M. L., *Federation Proc.*, 1955, **14**, 250.
7. Richard, M. C. and Robert, G. J., *Lipids*, 1973, **8**, 43.
8. Folch, J., Ascoli, I., Lees, M., Meth, J. A. and LeBaron, F. N., *J. Biol. Chem.*, 1951, **191**, 833.
9. Fiske, C. H. and Subba Row, *Ibid.*, 1925, **66**, 375.
10. Woodman, D. D. and Price, C. P., *Clinica. Chim. Acta*, 1972, **38**, 39.
11. Bloor, W. R., Pekan, K. K. F. and Allen, D. M., *J. Biol. Chem.*, 1952, **52**, 191.
12. Adams, C. W. M., *J. Neurochem.*, 1958, **2**, 178.
13. Nelson, W. L. and Barnum, C. P., *Ibid.*, 1960, **6**, 43.
14. Austin, L., *Brit. J. Pharmacol.*, 1957, **12**, 356.
15. Glees, P., *German Med. Monthly*, 1961, **6**, 245.
16. Selye, H., *Arch. Environ. Hlth.*, 1970, **21**, 706.