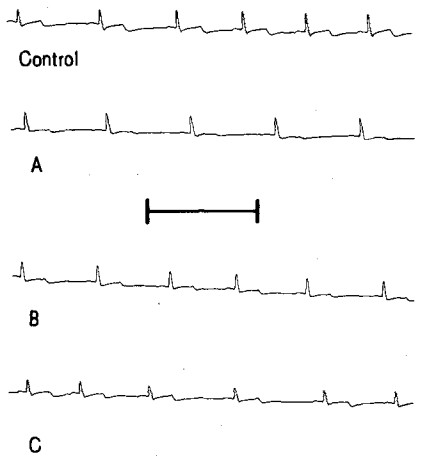
Plasma levels (ng/ml) of TZ and metabolites after oral TZ*

Time after administration	(TZ) Thioridazine	Thioridazine-2-sulfoxide (Mesoridazine)	Thioridazine 5-sulfoxide	Thioridazine 2-sulfone
0.5 h	75±23	135±44	52±16	23±18
1.5 h	50± 6	123±28	105±39	30±10
3.0 h	93±24	128±43	130±35	73±53
8.0 h	85±36	108±20	132±22	100±35
20.0 h	90±37	78±29	103±66	67±33

* TLC-fluorescence assay[7] values are mean ± SEM for 3 dogs after 6 mg/kg TZ.



Effects of infusion of thioridazine HCl on the T-wave of dog electrocardiogram. After infusion of 67 mg (A), marked flattening occurs. Recovery is observed during continued infusion (B). Notching is evident and persists after infusion of a total of 84 mg, despite near-normal T-wave amplitude (C). Calibration mark denotes 1 sec.

wave anomalies in humans, the use of i.v. infusion may be potentially useful for studying such effects. Although the present data are only suggestive, the lack of EKG effects of direct administration of TZSO at a dose equivalent to that of TZ which did produce T-wave effects, supports the view that additional research is needed to clarify the relationship between EKG effects of TZ and metabolite profiles.

1 This study was supported, in part, by a Grant-in-Aid from Boehringer-Ingelheim, Ltd. Sandoz, Inc. kindly provided thioridazine HCl (Mellaril®) and thioridazine-5-sulfoxide.
2 H.G. Kelly, J.E. Fay and S.G. Laverty, Can. med. Ass. J. *89*, 546 (1963).
3 T.A. Ban and A.St. Jean, Can. med. Ass. J. *91*, 537 (1964).
4 R.L. Dillenkoffer, R.B. George, M.P. Bishop and D.M. Gallant, in: Advances in Biochemical Psychopharmacology, vol. 9, p. 487. Ed. I.S. Forrest, C.J. Carr and E. Usdin. Raven Press, New York 1974.
5 R. Axelsson, Curr. ther. Res. *21*, 587 (1977).
6 E.C. Dinovo, L.A. Gottschalk, R. Biener and B.R. Nandi, Proc. west. Pharmac. Soc. *21*, 311 (1978).
7 L.J. Traficante, B. Hine, S. Gershon and G. Sakalis, Commun. Psychopharmac. *1*, 407 (1977).

Effect of organophosphate pesticide Sumithion (Fenitrothion) on some aspects of carbohydrate metabolism in a freshwater fish, *Sarotherodon* (Tilapia) *mossambicus* (Peters)[1]

P.R. Koundinya and R. Ramamurthi

Department of Zoology, Sri Venkateswara University College, Tirupati (India), 5 March 1979

Summary. A lethal (Lc_{50}/48 h - 6 mg/l) concentration of the organophosphate (OP) pesticide Sumithion increased blood glucose levels and phosphorylase activity, but hepatic glycogen registered a fall which indicated that the observed hyperglycemia was due to breakdown of hepatic glycogen.

It was found that the organophosphate (OP) pesticide Sumithion suppressed tissue respiration[2], inhibited aerobic enzyme systems and enhanced lactic dehydrogenase activity[3] in the fish *T. mossambica.* Exposure of the fish *Cyprinus carpio* to OP compounds like malathion, dipterex, and ddvp increased blood glucose levels and decreased liver glycogen content[4]. The present communication describes the effect of a lethal (Lc_{50}/48 h) concentration of Sumithion on some aspects of carbohydrate metabolism in *Sarotherodon mossambicus.*

Material and methods. Maintenance, size and weight range of fish used have been described earlier[3]. The concentration which is sufficient to kill 50% of test population (Lc_{50}) after 48 h of exposure computed by the probit method[5] was 6 mg/l[3]. Prior to the estimations, fish were killed by stunning. Glucose content was estimated by the method of Mendel et al.[6] and glycogen concentration by the method of Carrol et al.[7]. Phosphorylase ('a' and 'ab') was assayed in the direction of glycogen synthesis[8]. Protein content of the tissues was estimated by the method of Lowry et al.[9]. Sumithion (dimethyl-3-methyl 4-nitrophenyl phosphorothionate) which is extensively sprayed in rice fields locally, was obtained from Tata Fison Co.

Results and discussion. Blood glucose level rose after exposure to Sumithion. The fall in hepatic glycogen level was significant, whereas the decrease in muscle glycogen was not significant. Significant augmentation of glycogen phosphorylase was observed in both the tissues (table). The results clearly show that hepatic glycogen is the major source of hyperglycemia in *S. mossambicus.* Increased phosphorylase activity of the storage organ and the ultimate hyperglycemia due to mobilization of glucose molecules from liver to blood observed in *S. mossambicus* on exposure to Sumithion also support the earlier findings of elevated blood glucose and decreased liver glycogen in *Cyprinus carpio* exposed to other organophosphate com-

Effect of Sumithion on carbohydrate levels and phosphorylase activity in *Sarotherodon mossambicus*

Glucose concentration (mg/100 ml of blood)				Glycogen content (mg of glucose/g wt of tissue)				Phosphorylase activity (μmoles of inorganic phosphate/mg protein/h)			
Tissue	Control	Experimental	Change (%)	Tissue	Control	Experimental	Change (%)	Tissue	Control	Experimental	Change (%)
Blood	71.83±2.45	91.50±2.88	+27.38	Muscle	1.12±0.285	0.95±0.167[b]	−15.17	Muscle phosphorylase 'a'	0.342±0.031	0.421±0.026	+23.09
								'ab'	0.849±0.045	0.910±0.066[b]	+7.18
				Liver	15.91±2.67	11.43±2.70[a]	−28.15	Liver phosphorylase 'a'	0.424±0.042	0.538±0.035	+27
								'ab'	0.912±0.056	0.972±0.048[b]	+ 6.57

Changes after pesticide treatment are statistically significant. $p<0.001$; [a] $p<0.01$; [b] Not significant. Values are expressed as mean±SD of 6 animals.

pounds[4]. The fall in muscle glycogen being insignificant, despite the fact that muscle phosphorylase is stimulated, suggests increased turnover of glycogen, and that the muscle glycogen does not contribute towards hyperglycemia in Sumithion-treated *S. mossambicus*. It is likely that the observed hyperglycemia is mediated by glucagon which acts mainly only on hepatic tissue. Increased production of glucagon and depressed insulin activity were reported earlier in chick embryos treated with malathion[10].

1 This work was supported by UGC grant to R.R.

2 P. Ranganatha Koundinya and R. Ramamurthi, Ind. J. Envir. Health *20*, 426 (1978).
3 P. Ranganatha Koundinya and R. Ramamurthi, Ind. J. exp. Biol. *16*, 809 (1978).
4 Sakaguchi and Hiromi, Nippon Suisan Gakkaishi *6*, 38 (1972).
5 D.J. Finney, Probit analysis. Cambridge University Press, London 1964.
6 B. Mendel, A. Kemp and D.K. Myers, Biochem. J. *56*, 639 (1954).
7 N.V. Carroll, R.W. Longley and J.H. Roe, J. biol. Chem. *22*, 1583 (1956).
8 G.T. Cori, B. Illingworth and P.J. Keller, in: Methods in Enzymology, vol. 1, p. 200. Ed. S.P. Colowick and N.O. Kaplan. Academic Press, New York 1955.
9 O.H. Lowry, J.J. Rosebrough, A.L. Faar and R.J. Randall, J. biol. Chem. *193*, 264 (1951).
10 R. Kaliecharan and M.A. Gibson, Can. J. Zool. *50*, 265 (1972).

Toxic substances produced by *Fusarium*. X. Concerning the malformation disease of mango

S. Ghosal[1], D.K. Chakrabarti, K. Biswas and Y. Kumar

Department of Pharmaceutics, Banaras Hindu University, Varanasi (India), 14 March 1979

Summary. Accumulation of mangiferin and degraded carotenoids, in response to *Fusarium moniliforme* infection, has been suggested to be responsible for the malformation disease of *Mangifera indica* L. (Anacardiaceae).

The malformation disease of mango (*Mangifera indica* L.), in India, has rendered many superior quality mango orchards, in the Northern States, completely abortive. The disease has also destroyed many nursery beds of grafted seedlings. *Fusarium moniliforme* was reported[2] as a causal organism for the malformation disease. The fungus was found to secrete a large number of mycotoxins[3] on the infected plant parts. Mango is not only a staple food for many people, but its various parts are also used for therapeutic purposes in popular medicine. The presence of mycotoxins in the various parts of the afflicted mango plant is thus a cause for alarm from a public health view-point.

The purpose of this investigation was to determine the mechanism of malformation with a view eventually to controlling the disease. We recently reported[3] that in healthy mango twigs, mangiferin (1,3,6,7-tetrahydroxyxanthone-C_2-β-D-glucoside) occurred only as a minor entity, while in malformed shoots and twigs, infected with *F. moniliforme*, its concentration was increased very significantly. This observation prompted us to examine the role, if any, of mangiferin in mango malformation.

Material and mtehods. The crown of 2 1-year-old mango plants (cv. *Banarasi Langra*) and, healthy inflorescence (on intact mature plants), at an early stage of differentiation, were intentionally infected with *F. moniliforme* var. *subglutinans* (CMI-IMI 225231). The estimation of mangiferin on the infected parts was accomplished by maceration of the plant tissues with ethyl alcohol, preparative layer chromatography of the alcoholic concentrates, and by UV spectrophotometry of the eluted zones corresponding to authentic mangiferin. The presence of fusaric acid, a normal toxic metabolite of fusaria, in the diseased shoots and inflorescence of mango was tested according to a published procedure[3]. In a separate experiment, the ability of this fungus to form fusaric acid, in in vitro cultures, was tested. Richard's medium was used and the inoculum was incubated at 21 °C for 21 days. The role of mangiferin in supressing the fusaric acid production by this fungus was examined. Mangiferin (1×10^{-5} M) was added to Richard's solution prior to the 4th subculture stage.

The effect of the application of a large concentration of mangiferin to *M. indica* was determined. Aqeuous suspension of mangiferin (1×10^{-4} M) was administered for 7 days to the apical buds of 2 1-year-old mango plants by a wick arrangement. Only distilled water was applied to the control plants. The plants were kept in a green house, under aseptic condition, for a period of about 3 months.

The effect of the culture filtrates of *F. moniliforme* on the disease development was investigated. The fungus was grown in Richard's medium at 21 °C for 21 days and the