TRIBUTYLTIN CHLORIDE DISRUPTS GLUCOSE AND LIPID HOMEOSTASIS ON WISTAR MALE RATS

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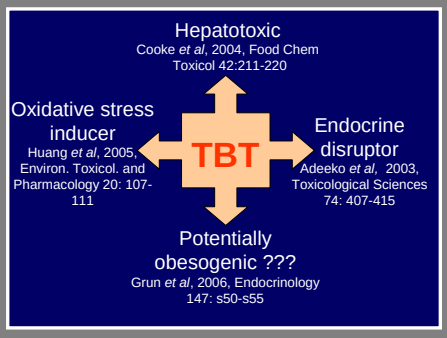
Abstract

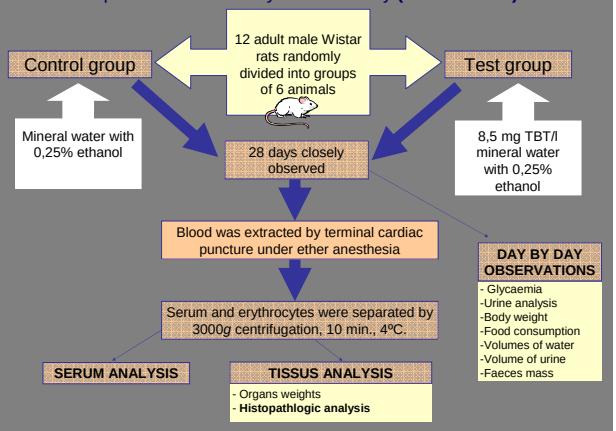
Tributyltin chloride is still a relevant water and seafood pollutant, as reported for some sites of Mediterranean and Iberian coastal waters. We evaluated TBT metabolic effect in Wistar male rats, after administration of a repeated oral dose of 8.5mg/L in ethanol 0.25%, during 28 days, according to DIR96/54/EC. Groups of six animals, individually caged, were daily observed for fast blood glycaemia and semi-quantitative urine analysis. Glycaemia levels were significantly lower on the test group along the assay, showing a tendency for fasting hypoglycaemia. Urine analysis showed the presence of ketonic bodies in test group during the treatment. At the end of test period, animals were euthanized and serum analysis was performed revealing a significant increment of cholesterol and HDL-cholesterol (9.3% and 6.7%, respectively) and a non-significant increment on triglycerides content. These results suggest that TBT disrupted glucose and lipid homeostasis. Accordingly, and considering TBT a new member of environmental obesogen family, it is most relevant to reassess the effect of chronic exposure to low doses of this pollutant.

Introduction



Materials & Methods

Repeated dose / 28 days / oral toxicity **(DIR96/54/EC)**



Results & Discussion

Daily observation

Table 1: Daily observations between animal groups

	Control group	Test group	Obs.
Body weight increase (%)	9,0 ± 0,4	8,6 ± 0,4	
Volume of water drank (cm^3)	36 ± 2,5	25,8 ± 1,0	*
Volume of urine (cm^3)	15,6 ± 1,4	8,1 ± 0,4	*
Food consumption (g)	26,2 ± 0,6	27,6 ± 0,4	
Faeces mass (g)	9,1 ± 0,4	9,4 ± 0,2	

Data are expressed as mean ± SEM for six rats.
* Significantly different in comparison to control ($p < 0,05$)

❑ At the end of the test period, a slight increase of weight was observed in both TBT treated and control groups, without significant differences between them (table 1).

❑ TBT treated animals drank always less water that the animals of the control group. In part, the explanation for that may be in the TBT flavour left on the water. Probably as a consequence, a small volume of urine was also recorded in test group. No variations were observed between the two groups in what respects to food consumption and faeces mass (table 1).

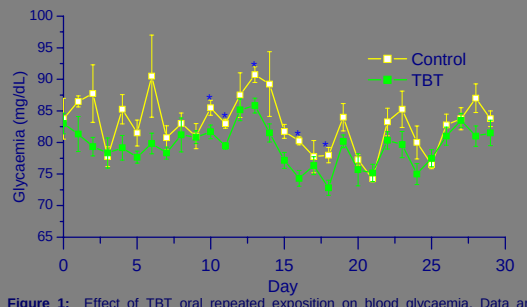


Figure 1: Effect of TBT oral repeated exposition on blood glycaemia. Data are expressed as mean±SEM of six observations. * means a significant difference is observed between groups at P<0.05

❑ The fasting glycaemia levels of the test group were, since the first day of treatment, lower than those of controls, nevertheless they can be considered normal.

The *Combur10 Test* was applied to urines collected during the night (during the feeding period). Ketonic bodies were detected, just in the test group, in the first and subsequent days of the assay. Glucose was never detected in urine.

Box 1: *Combur10 Test* urinary results

❑ The slight hypoglycaemia can not be explained by glucose urinary depletion (box 1). Furthermore, ketonic bodies observed on TBT treated rats (box 1) are consistent to a metabolic disruption on glucose homeostasis.

Post mortem observations

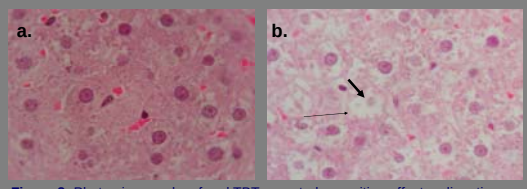


Figure 2: Photomicrographs of oral TBT repeated exposition effect on liver tissue. **a.** Control liver tissue ; **b.** TBT treated rat liver tissue: fin arrow - loss of cell membrane integrity and hydropic degenerescence ; gross arrow - nuclei necrotic changes. (Hematoxylin-eosin 400X)

❑ Histopathologic examination revealed slight liver alterations on the animal of the group expose to TBT which were: 1) cellular swelling as hydropic change and loss of cell membrane integrity; 2) degenerative and necrotic nuclei changes like nuclear membrane hyperchromatosis, pyknosis and karyolysis (figure 2).

Table 2: Serum biochemical analysis

	Control group	Test group	Obs.
Cholesterol (mg/dL)	48.5 ± 0.8	53.5 ± 1.3	*
Cholesterol-HDL (mg/dL)	33.2 ± 0.6	35.6 ± 0.8	*
Triglycerides (mg/dL)	174.7 ± 6.9	194.2 ± 16.1	
Albumin (g/L)	18.5 ± 0.3	17.6 ± 0.2	*
Total protein (g/L)	21.8 ± 0.5	21.0 ± 0.6	
ALT (U/L)	93.0 ± 3.6	114.5 ± 4.8	*
Amylase (U/L)	5003 ± 702	5138 ± 524	
Cholinesterase (U/L)	44.54 ± 2.37	46.81 ± 2.80	

Data are expressed as mean ± SEM for six rats
* Significantly different in comparison to control ($p < 0,05$)

❑Serum analysis revealed a significant increment of cholesterol and HDL-cholesterol (9.3% and 6.7%, respectively) and a non-significant increment on triglycerides content (table 2).

❑ALT activity shows an increment of 19% and albumin decreasedo of 5% in the test group (table 2).

Conclusions

Histopathologic analysis revealed liver alterations in TBT treated group, such as cellular swelling and loss of cell membrane integrity, indicating liver damage. Accordingly, serum biochemical analysis showed a significant 19% increase of ALT activity and a significant 5% decrease of albumin between TBT treated and control group. These results suggests hepatotoxicity of TBT.

Statistic analysis of data from daily blood glycaemia and urine analysis revealed that TBT treated rats presented reduced fasting glycaemic levels and ketosis. Moreover, serum analysis in the end of the test period revealed that TBT also induced a slight hypercholesterolemia. These results suggest a metabolic disruption of glucose and lipid homeostasis, probably related to the impairment of some metabolic hepatic functions. Accordingly, and considering TBT a new member of environmental obesogen family, it is most relevant to reassess the effect of chronic exposure to low doses of this pollutant.

SETAC Europe 17th Annual Meeting, *Warsaw, 25-29 May, 2008*