

Toxicologie / Toxicology

# Toxicité de l'hexachlorobenzène chez *Meriones unguiculatus* : effets sur la thyroïde et le foie

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## Résumé

L'effet de l'hexachlorobenzène (HCB) sur la fonction hépatique et thyroïdienne a été recherché chez *Meriones unguiculatus*. Quatre lots d'animaux ont été gavés avec 0, 1,6, 4 et 16 mg/kg/j de HCB pendant 30 j. Le HCB n'a pas d'effet sur le poids corporel. Cependant, il entraîne chez les animaux des deux sexes une hypertrophie hépatique très accentuée, particulièrement chez les animaux traités par la plus forte dose. Des modifications de l'architecture hépatique sont également observées. Une nécrose cellulaire apparaît déjà chez les animaux recevant 1,6 mg/kg/j, accompagnée de congestions centrolobulaires et périportales et de vacuolisations cytoplasmiques chez les animaux traités avec 4 mg/kg/j. Ces mêmes lésions sont accentuées avec la dose la plus forte. L'intoxication au HCB perturbe certaines activités enzymatiques hépatiques. À forte dose, ce pesticide entraîne une augmentation de l'activité ALAT, dont le taux plasmatique est triplé chez les mâles par rapport aux témoins ( $170 \pm 24,7$  U/l vs.  $52,66 \pm 8,29$  U/l) et doublé chez les femelles ( $120 \pm 12,47$  U/l vs.  $56 \pm 5$  U/l). Ce même traitement augmente l'activité ASAT uniquement chez les femelles ( $259 \pm 29$  U/l vs.  $244,66 \pm 18$  U/l). L'impact de cette même dose de HCB sur les hormones thyroïdiennes s'est manifesté par une baisse très significative de la TT4 ( $21,95 \pm 7,46$  nmol/l vs.  $40,59 \pm 1,08$  nmol/l) chez les mâles et de la TT3 ( $1,42 \pm 0,11$  nmol/l vs.  $3,96 \pm 0,48$  nmol/l) chez les femelles comparativement aux témoins. **Pour citer cet article : L. Bitri et al., C. R. Biologies 330 (2007).**

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## Abstract

**Toxicity of hexachlorobenzene in *Meriones unguiculatus*: effects on thyroid and liver.** The effect of in vivo administered hexachlorobenzene (HCB) on liver and thyroid was studied on *Meriones unguiculatus*. HCB (1.6, 4, and 16 mg/kg of body weight) has been administered orally to meriones for 30 days. At the end of the experiment, the body weight of the animals did not show significant change. However, the higher dose of HCB treatment led to a pronounced hepatic hypertrophy comparatively to controls. Histological observations revealed many cytomorphological alterations. Cellular necrosis, periportal, and centrolobular vein congestion and cytoplasmic vacuolisation were noted and correlated with the administered doses of HCB. The higher dose of HCB induced modifications in the activities of hepatic transaminases and on thyroid hormones levels: ALAT activity level was

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more pronounced in males ( $170 \pm 24.7$  U/l vs.  $52.66 \pm 8.29$  U/l in controls) than in females ( $120 \pm 12.47$  U/l vs.  $56 \pm 5$  U/l in controls). However, ASAT activity increased significantly only in females ( $259 \pm 29$  U/l vs.  $244.66 \pm 18$  U/l in controls). Plasma total triiodothyronine (TT3) and total thyroxine (TT4) levels seemed to be sex-dependent in intoxicated animals, since TT4 decreased significantly in males ( $21.95 \pm 7.46$  nmol/l vs.  $40.59 \pm 1.08$  nmol/l in controls) and TT3 in females ( $1.42 \pm 0.11$  nmol/l vs.  $3.96 \pm 0.48$  nmol/l in controls). **To cite this article: L. Bitri et al., C. R. Biologies 330 (2007).**

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**Mots-clés :** Meriones ; Toxicité ; Hexachlorobenzène (HCB) ; Transaminases (ASAT, ALAT) ; Foie ; Hormones thyroïdiennes

**Keywords :** Meriones; Toxicity; Hexachlorobenzene (HCB); Transaminases (ASAT, ALAT); Liver; Thyroid hormones

## Abridged English version

Hexachlorobenzene (HCB) is a chlorinated aromatic hydrocarbon extensively used in the past as antifungal for the storage of crops.

Although its production was prohibited in many countries, this dioxin-like compound is still present in the environment as a by-product of various chemical processes. The HCB is known for its high chemical stability and persistence, and global water and air pollution is still observed at faraway locations from the production or utilization sites.

Humans or animals' chronic exposure to HCB induces various adverse effects on health. HCB has been reported to be hepatotoxic, immunotoxic, and genotoxic; it is even at the origin of diseases, such as porphyria, and of endocrine disturbances in thyroid and reproductive functions.

This study was conducted to determine the effects of a subchronic exposure to various doses of HCB on liver and thyroid functions in *Meriones unguiculatus*, a rodent, which, in the wild state, lives near farms where pesticides are regularly used.

Animals maintained at 12L/12D in room with controlled temperature ( $22 \pm 1^\circ\text{C}$ ) were provided with commercial rat food and water ad libitum. Daily doses of 0, 1.6, 4 and 16 mg HCB/kg BW in olive oil were administered by force-feeding between 9 and 10 AM over a period of 30 days. At the end of the experiment, the animals were decapitated.

After having been weighed, livers were fixed for histological analysis and plasma samples were frozen at  $-30^\circ\text{C}$  before ASAT, ALAT, TT4, and TT3 determinations.

While no modification in body weight was noted in HCB-treated animals compared to controls, high doses of HCB led to a pronounced hepatic hypertrophy with a dose effect. The relative weight (liver/body%) increases with increased HCB doses. Liver histological studies revealed many cytomorphological alterations with a dose effect: centrolobular congestion and some cellu-

lar necrosis (1.6 mg HCB), centrolobular and periportal vein congestion, more cellular necrosis and cytoplasmic vacuolization (4 mg HCB), same histological modifications, but more pronounced, with important vacuolization and disappearance of cellular junction (16 mg HCB).

Concerning transaminase activities, only the highest dose of HCB induces modifications in ALAT activity with a significantly higher level in males ( $170 \pm 24.7$  U/l vs.  $52.66 \pm 8.29$  U/l in controls,  $p < 0.01$ ) compared to females ( $120 \pm 12.47$  U/l vs.  $56 \pm 5$  U/l in controls,  $p < 0.01$ ). However, for ASAT activity, no significant variation is observed.

Plasma thyroid hormones levels are only affected in the group receiving the highest dose of HCB (16 mg/kg BW). This effect seems sex-dependent: TT4 decreased significantly only in males ( $21.95 \pm 7.46$  nmol/l vs.  $40.59 \pm 1.08$  nmol/l in controls,  $p < 0.01$ ), while a strong diminution of TT3 was noted in females ( $1.42 \pm 0.11$  nmol/l vs.  $3.96 \pm 0.48$  nmol/l in controls,  $p < 0.01$ ).

It can be concluded that the best index for environmental pollution by HCB (or PCBs) is the relative weight of the liver, with a clear dose effect. Plasma thyroid hormones or transaminase activities seem to be modified only with high doses of pollutant and are not a good indicator of a slight pollution.

The existence of sex-dependent differences in the plasmatic rates of thyroid hormones seems well to emerge. A combined effect of the thyroid function with the reproductive axis should be then envisaged and would deserve to be thorough.

## 1. Introduction

Les biphényles polychlorés (BPC) constituent une classe d'hydrocarbures aromatiques chlorés dont les propriétés physicochimiques remarquables expliquent le grand intérêt qu'elles représentent pour l'industrie.

Ces produits sont réputés pour leur inertie vis-à-vis des réactifs chimiques et de la chaleur, leur ininflamma-

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