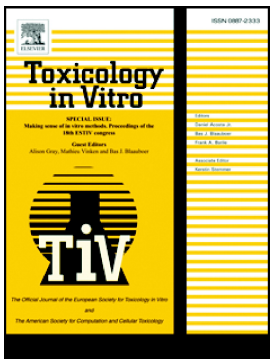

Sub-toxic exposure to lindane activates redox sensitive kinases and impairs insulin signaling in muscle cell culture: The possible mechanism of lindane-induced insulin resistance

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ABSTRACT

Lindane exposure is claimed to be involved in pathogenesis of type 2 diabetes mellitus (T2DM) and insulin resistance state by an as yet unknown mechanism. The redox sensitive kinases (RSKs) and heat shock proteins (HSPs) interfere with insulin signaling and induce insulin resistance. The present study was designed to explore the mechanism of insulin resistance induced by sub-toxic lindane exposure. In an *in vitro* study, exposure to 60mg/L and 120mg/L of lindane for 18hrs on rat L6 myoblasts derived myotubes significantly increased malondialdehyde level & superoxide dismutase activity, decreased total antioxidant level and insulin-induced glucose uptake in a dose dependent manner. The extent of activation of RSKs and HSP25 as measured by western blot from the extent of phosphorylation of IκBα, p38 MAPK, JNK & HSP25 in lindane-exposed myotubes was higher. HSP70 was induced and insulin signaling as measured from tyrosine phosphorylation of insulin receptor (IR) & insulin receptor substrate-1 (IRS-1) and serine phosphorylation of Akt was attenuated in comparison to those in untreated myotubes. We conclude that sub-toxic lindane exposure induces oxidative stress, activates RSKs & HSP25 and induces HSP25. These in turn, impair insulin signaling to impart insulin resistance in myotubes induced by sub-toxic lindane exposure.

Keywords: Lindane, redox sensitive kinases, insulin signaling, insulin resistance, type 2 diabetes mellitus.