The organophosphate pesticide -OP- malathion inducing thyroidal disruptions and failures in the metamorphosis of the Senegalese sole, Solea senegalensis

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Abstract

Background

Organophosphate pesticides-OP-, like malathion, can alter the normal functioning of neuroendocrine systems (e.g., hypothalamus-pituitary-thyroid-HPT-axis), and to interfere on the thyroidal homeostasis. Through direct interactions with thyroid receptors, an/or indirectly via up-stream signalling pathways, from the HPT axis (i.e., negative feedback regulation), malathion possess the ability to affect integrity of thyroidal follicular tissue, and it can also block or delay its hormonal functioning. This insecticide can alter the majority of the ontogenetic processes, inducing several deformities, and also provoking decreases in the growth and survival patterns. The present study has been performed to determine the sublethal effects of malathion during the first month of life of the Senegalese sole, Solea senegalensis, and it is mainly focused on the metamorphosis phase. Different transcript expression levels (i.e. thyroid receptors, matrix and bone -Gla-proteins) and immunohistochemical patterns (i.e. thyroid hormones, osteocalcin, cell proliferation) have been analysed during the most critical phases of the flatfish metamorphosis, that is, through differentiation of thyroid system and skeletal development, migration of the eye, and further adaptation to benthic behaviours.

Results

In early life stages of the Senegalese sole, the exposure to the highest concentration of malathion (6.25 μg/L) affected to the growth patterns, showing the exposed individuals, a reduction around 60 and 92% of the total length and the dry weight, respectively. In parallel, a significant reduction of the thyroid follicles (i.e., size and number) it was also been recorded, in a dose-dependent way. Abnormal phenotypes induced in the exposed larvae, did not complete the process of metamorphosis, and displayed several morphological abnormalities and developmental disorders, which were mainly associated with the eye migration process, and with thyroidal and skeletal disorders (i.e., transcriptional and protein changes of thyroid hormones and receptors, and of matrix and bone Gla proteins distribution), that conduced to an inadequate adaptation to the benthic life.
Conclusions

In the Senegalese sole, the majority of the ontogenetic alterations induced by the exposure to malathion were mainly associated to the metamorphosis period, which is a thyroid-driven process. In fact, most crucial and transitional ontogenic events, appeared notably disturbed, for e.g., thyroid gland differentiation and functioning, migration of eye, skeletal development and benthonic behaviors.

Keywords: Eye, Malathion, Metamorphosis, Osteocalcin, Proliferation, Proteins, Skeleton, Senegalese sole, Thyroid, Transcripts
Malathion


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Organophosphate pesticides-OP-, like malathion, can alter the normal functioning of neuro-endocrine systems (e.g., hypothalamus-pituitary-thyroid-HPT- axis), and to interfere on the thyroidal homeostasis. Through direct interactions with thyroid receptors, an/or indirectly via up-stream signalling pathways, from the HPT axis (i.e., negative feedback regulation), malathion possess the ability to affect integrity of thyroidal follicular tissue, and it can also block or delay its hormonal functioning. This insecticide can alter the majority of the ontogenetic processes, inducing several deformities, and also provoking decreases in the growth and survival patterns. The present study has been performed to determine the sublethal effects of malathion during the first month of life of the Senegalese sole, *Solea senegalensis*, and it is mainly focused on the metamorphosis phase. Different transcript expression levels (i.e. thyroid receptors, matrix and bone -Gla-proteins) and immunohistochemical patterns (i.e. thyroid hormones, osteocalcin, cell proliferation) have been analysed during the most critical phases of the flatfish metamorphosis, that is, through differentiation of thyroid system and skeletal development, migration of the eye, and further adaptation to benthic behaviours.

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Malathion-Induced Oxidative Stress, Cytotoxicity and Genotoxicity in Human Liver Carcinoma (HepG₂) Cells

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Abstract

Malathion is an organophosphate pesticide that is known for its high toxicity to insects and low to moderate potency to humans and other mammals. Its toxicity has been associated with the inhibition of acetylcholinesterase activity, leading to the interference with the transmission of nerve impulse, accumulation of acetylcholine at synaptic junctions, and subsequent induction of adverse health effects including headache, dizziness, nausea, vomiting, bradycardia, and miosis. Oxidative stress (OS) has been reported as a possible mechanism of malathion toxicity in humans. Hence, the aim of the present study was to examine the role of OS in malathion-induced cytotoxicity and genotoxicity. To achieve this goal, MTT, lipid peroxidation, and single cell gel electrophoresis (Comet) assays were performed, respectively to evaluate the levels of cell viability, malondialdehyde (MDA) production, and DNA damage in human liver carcinoma (HepG₂) cells. Study results indicated that malathion is mitogenic at lower levels of exposure, and cytotoxic at higher levels of exposure. Upon 48 h of exposure, the average percentages of cell viability were 100±11%, 117±15%, 86±15%, 35±9%, and 27±7% for 0, 6, 12, 18, and 24 mM, respectively. In the lipid peroxidation assay, the concentrations of MDA produced were 12.55±0.16, 20.65±0.27, 31.1±0.40, 34.75±0.45, and 15.1±0.20 μM in 0, 6, 12, 18, and 24 mM of malathion, respectively. The Comet assay showed a significant increase in DNA damage at the 24mM malathion exposure. Taken together, our results indicate that malathion exposure at higher concentrations induces cytotoxic and genotoxic effects in HepG₂ cells, and its toxicity may be mediated through oxidative stress as evidenced by a significant production of MDA, an end product of lipid peroxidation.
Lavandulastoechas essential oils protect against Malathion-induced reproductive disruptions in male mice

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Background

The current study was conducted to evaluate the protective effect of Lavandulastoechas essential oils (LSEO) against malathion (M) exposure-caused reprotoxicity in male mice as well as the possible mechanisms implicated in such protection.

Methods

Six–eight-week-old male mice weighting 25–30 g were used and divided into four groups: normal-control, LSEO (50 mg/kg, b.w.), malathion (200 mg/kg, b.w.) and malathion + LSEO treated mice. Malathion was emulsioned in corn oil and per orally administered for 30 days. LSEO was daily administrated during the same period. LSEO chemical identification was done by Gas chromatography–mass spectrometry (GC-MS). Reproduction-damages and LSEO-benefits were assessed using histopathological, biochemical and steroidogenesis gene expression disruptions and improvements.

Results

The GC-MS analysis, allowed to the identification of 25 bioactive compounds in MCEO. In vivo, we firstly found that malathion exposure induced a clear reprotoxicity as assessed by a significant-decrease (P < 0.05) of testis/epididymis relative weights, serum testosterone level and reproductive performance. Malathion also produced lipoperoxidation, thiol (-SH) groups decrease as well as a significant-depletion (P < 0.05) of antioxidant enzyme activities such as catalase (CAT) and glutathione peroxidase (GPx), total superoxide dismutase (SOD), Cu/Zn-SOD and Mn-SOD in testis and epididymis. The histopathological examination showed marked change in both studied tissues. All these biochemical and structural changes were significantly (P < 0.05) corrected by LSEO co-administration. More importantly, malathion exposure remarkably (P < 0.05) down-regulated the
expression of StAR gene as well as, the mRNA levels of P450scc, 3ßHSD and 17ß-HSD, while LSEO-administration strangely protected against steroidogenesis disruption.

Conclusions

The potential protective effects of LSEO against malathion-induced reprotoxicity and oxidative stress might be partially to its antioxidant properties as well as its opposite effect against some gene expression involved in the steroidogenesis.

Keywords: Malathion, Mice, Steroidogenesis, LSEO, Oxidative stress, StAR gene