

**Document Type** : Thesis

**Document Title** : Toxicological studies of some lichen acids on mouse-liver mitochondria  
دراسات سمية لبعض الأحماض الأشنية علي ميتوكوندريا كبد الفأر

**Document Language** : Arabic

**Abstract** : Three lichen acids, namely (+)usnic acid (USN), vulpinic acid (VUL) and atranorin (ATR) were isolated from three lichen species: *Usnea alliculata*, *Letharia vulpina* and *Parmelia tinctorum*, respectively. - The extraction, purification and chemical identification of these three lichen acids has been worked-out and the median lethal dose (LD<sub>50</sub>) of *U. alliculata* dry chloroform extract (FCE), dry ethanol extract (DEE) and pure (+)usnic acid (USN) to mice (s.c.) was determined. According to the classification of chemicals in relation to their relative toxicities both DCE and USN are considered to be among the highly toxic compounds. However, no toxic effect was recorded for the DEE. The interesting common properties shared by the three lichen acids used in this study render them potentially active as membrane disruptors in biological systems. These lichen products exhibited characteristic uncoupling activity to mouse liver mitochondria similar to that produced by the classical uncoupler 2,4-dinitrophenol (DNP). They released respiratory control, hindered ATP synthesis, stimulated state-4 respiration (in the absence of ADP) and enhanced significantly ATPase activity. ATR was the only lichen acid with no effect on ATPase. The minimal concentrations required to cause complete uncoupling of oxidative phosphorylation were as follows: USN (1 microM), VUL (5 microM), ATR (5 microM) and DNP (50 microM). The uncoupling effect was dose-dependent in the three cases. In vivo studies using usnic acid-treated mice (injection s.c.) with a lethal dose (200 mg/kg) showed also significant uncoupling effects. It is postulated that the three lichen acids induce mitochondrial uncoupling by acting on the inner mitochondrial membrane through their lipophilic properties and protonophoric activities.

**Supervisor** : د. أحمد نبيل أبو خطوة ، د. علي أحمد الرباعي