EFFECTS OF THE CAULIFLOWER EXTRACT OD74 ON XENOBIOTIC METABOLIZING ENZYMES IN THE RAT

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Epidemiological and animal studies linking high and varied fruit and vegetable intake to lower cancer risk, suggested the theoretical possibility that regular, long-term mass administration of either isolated naturally occurring dietary constituent or plant extracts can provide a means of controlling cancer incidence. Although no exact mechanism of molecular chemoprotection is known, it is believed that the inhibition of phase-I (or an up-regulation of phase-II) drug metabolizing enzymes by phytoalexins or extracts from cauliflower, broccoli, Brussels sprouts or other members of cruciferous vegetables, could provide a strong defence against environmental mutagens and carcinogens.
With the aim to verify this hypothesis, in the present study the role of the *palmizio* cauliflower extract OD74 on P450 superfamily of isoenzymes in the animal model was investigated. Male and female Sprague-Dawley rats (aged 6-7 weeks, 150 ± 10 g) maintained on a standard laboratory diet received by mouth daily 120 or 240 mg per kg body weight of the *palmizio* cauliflower extract (PEC-OD74) for four consecutive days; controls received saline only. Rats were fasted 16 before being killed humanely in accordance with approved Home Office procedures appropriated for the species. Ten rats were used in each group; liver and lung microsomes were prepared and immediately tested for CYP content and various mononooxygenases such as ethoxyresorufin O-deethylase (CYP1A1-linked), methoxyresorufin O-demethylase (CYP1A2), pentoxyresorufin O-depenthylase (CYP2B1/2) and testosterone hydroxylase as multibiomarker (CYP2B1, CYP3A1/2, CYP2C11).
In PCE-OD74 supplemented male animals a modest induction of hepatic phase-I bioactiving enzymes such as CYP2E1, CYP1A1 and CYP3A1/2 (up to ~ 1.5 fold) was found. By contrast, in females, while this extract significantly ($P<0.01$) increased the O-depenthylation of penthoxyresorufin (up to ~ 1.5 fold, lower dose), it was also able to strongly decrease CYP2C11, CYP2A1 and CYP1A1-linked monooxygenases (up to ~ 89% loss). In the lung, PCE-OD74 markedly induced some CYP-dependent mixed-function oxidases such as CYP2B1/2, CYP2C11-linked activities (up to ~ 26.8 fold, males). In female rats, a notable decrease of CYP1A1/2 and CYP3A1-supported oxidases (up to ~ 86% loss) was recorded. All differences were statistically highly significant as compared to controls ($P<0.01$, Wilcoxon). Due to the recognized role of oxygen free radicals as a factor that advances the incidence of human cancer, the electron paramagnetic resonance (EPR) spectroscopy coupled to a spin-trapping technique was used to evaluate the contribution of CYPs induced by PCE-OD74 on reactive oxygen species (ROS) production. An association between CYP induction and ROS over-generation in both liver and lung was observed.
Without here discuss the validity of the hypothesized protective (anticancer) role of mass administration of natural constituents (either as single molecule or extracts) as regular dietary supplements be able to down-regulate phase-I enzymes, in the present investigation it was found that PCE-OD74 simultaneously produces a powerfully induction or a strong inactivation of metabolising enzymes. In addition to an alteration of endogenous metabolism and cellular functions linked to these catalysts, the observed CYP-changes, far for behaving as chemopreventive, can actually be associated to non-genotoxic carcinogenesis (e.g. co-carcinogenicity and promotion).