observed an increase in OS in elderly urban inhabitants (59 vs. 27%,p<0.001); thus, the urban elderly have a 2.86 greater risk of presenting OS than the rural elderly, and higher for male sex (OR=4.25). Adjusted for different confounders, living in Mexico City, overweight(27≥kg/m²) and sleep ≤6 h/day, represented risk factors of OS.

Conclusions: The greatest percentage and intensity of OS in urban area is not accompanied by an antioxidant compensatory mechanism.

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INHIBITION OF ETHANOL-INDUCED APOPTOSIS BY *UNCARIA TOMENTOSA* IN HEPG2 CELLS

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Excessive consumption of alcohol and increased production of TNF" cause apoptosis in liver. Uncaria tomentosa (UT) is an herbal medicine from the Peruvian Amazon that is widely used for inflammatory disorders. Previous experiments from our laboratory have demonstrated that UT inhibits free radicals and modulates the expression of genes associated with cell death. The purpose of this study was to determine whether UT protects hepatic cells (HepG2) against ethanol-induced apoptosis. UT was prepared as an aqueous extraction then concentrated by freeze-drying. Cells were exposed to -ethanol (EtOH, 100 mmol/L), TNF" (30 ng/mL), hydrogen peroxide (300μM), EtOH+TNF" -followed by incubation for 24 hours, with UT (10 μg/ml) administered as a 2 hour pretreatment. Apoptosis was quantified by cell death detection ELISA. Administration of EtOH, TNF", H_2O_2 or EtOH+TNF" induced apoptosis ($P < 0.05$) in HepG2 cells. Pretreatment of cells with UT decreased ($P < 0.05$) apoptosis in EtOH (79.3%), TNF" (48.6%), H_2O_2 (54.5%), and by EtOH+TNF" (62.1%). These results demonstrate that UT exerts protective effect agaisnt oxidative stress generated by the metabolism of alcohol. In conclusion, these findings suggest that consumption of UT may alleviate liver deterioration by decreasing the exacerbated cytotoxicity caused by ethanol and TNF", which occurs in alcoholic liver disease.

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AGE-RELATED DECLINE IN Nrf2-DEPENDENT GSH SYNTHESIS: IMPROVEMENT BY LIPOIC ACID

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One of the hallmarks of aging is a decline in steady-state antioxidant levels. Glutathione (GSH) declines in the aging rat liver by 35±5%; however, feeding R-a-lipoic acid (LA) (0.2% w/w) for 2 wks reverses this loss. The mechanism(s) of GSH decline and its restoration by LA treatment may be due to decline in levels or activity of g-glutamyl cysteine synthetase (g-GCS), the rate-controlling enzyme in GSH synthesis. To examine this hypothesis, we measured g-GCS activity and protein content in young (3 mo) & old (24 mo) F344 rats. Results showed g-GCS activity declines (p=0.03) 35% with age. To examine whether there was also a decline in protein content, levels of heavy (g-GCS_h) & light (g-GCS_l) chains were determined. g-GCS_h & g-GCS_l declined by 20 & 60%, respectively (p>0.02). Treatment with LA (40mg/kg bw) over 48 h reversed the age-related decline & g-GCS activity. In part, basal g-GCS levels are controlled by Nrf2, a transcription factor that regulates genes with the antioxidant response element. We determined whether the lower g-GCS levels were due to altered Nrf2-mediated transcription. Results showed basal nuclear Nrf2 levels declined by 70-85% with age; LA treatment reversed this decline. These results suggest that the age-related decline in GSH levels is, in part, due to Nrf2-dependent transcriptional dysregulation of g-GCS & LA may act to increase basal transcription of g-GCS.

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IN VIVO DETECTION OF VITAMIN E-DEPENDENT PROTECTION AGAINST FREE RADICAL FORMATION AND OXIDATIVE STRESS IN SKIN TREATED WITH CUMENE HYDROPEROXIDE.

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Organic peroxides, widely used in the chemical and pharmaceutical industry, are considered to be one of the key factors contributing to skin tumor promotion via free radical production. In vitro experiments have demonstrated metal-catalyzed formation of alkoxyl, alkyl, and aryl radicals in keratinocytes incubated with cumene hydroperoxide. The present study investigated in vivo free radical generation in lipid extracts of mouse skin exposed to cumene hydroperoxide. The ESR spin-trapping was used to detect the formation of alpha-phenyl-N-tert-butylnitrone (PBN) radical adducts, following intradermal injection of 180 mg/kg PBN. After topical exposure (30 min), cumene hydroperoxide (12 mmole/kg) induced free radical generation in the skin of female Balb/c mice kept for 10 weeks on vitamin E-deficient diets. In contrast, hardly discernible radical adducts were detected when cumene hydroperoxide was applied to the skin of mice fed a vitamin E-sufficient diet. Total antioxidant reserve, levels of GSH, ascorbate and vitamin E decreased 34%, 46.5%. 27% and 98%, respectively, after mice were kept for 10 weeks on vitamin E-deficient diet. PBN adducts detected by ESR in vitamin E-deficient mice provide direct evidence for in vivo free radical generation in the skin after exposure to cumene hydroperoxide.

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MECHANISTIC ASPECTS OF QUERCETIN NEUROTOXICITY

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Our studies investigate the molecular basis for the potent neurotoxic effects of quercetin on primary cortical neurons. Quercetin (0.3-30 μM) induced concentration-dependent damage to neurons as assessed by the MTT assay which correlated with a strong activation of caspase-3. Furthermore, quercetin exposure resulted in a dose- and time-dependent reduction in the basal level of Akt/PKB phosphorylation/activation, a potent cell survival enzyme in neurons. However, there was no measurable effect on the basal phosphorylation of JNK1/2. Both methylated forms of quercetin were less neurotoxic than the aglycone which was reflected in a lower activation of caspase-3. However, 3'-*O*-