Screening and comparison of toxic activities of remedies and food derived from *Euphorbiaceæ* and *Thymelæaceæ* plants

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Traditional medicinal practices of many cultures (incl. western world) utilize parts of certain species of the botanical families of *Euphorbiaceæ* and *Thymelæaceæ* for the treatment of a wide range of disorders. Utilization as abortifacients, purgatives, vesicants, aphrodisiacs and for treatments of skin diseases, warts and cancers are examples of these traditional remedies by employing mostly small doses.

On the other hand, plant parts of the *Euphorbiaceæ* and *Thymelæaceæ* are known to exhibit severe acute and chronic toxicity in man after external or internal exposure. Most of them also exhibit conditional cancerogenic (tumorpromoting) activity in the skin of mice. The active principles responsible for these bioactivities are skin irritant esters of the structurally related polyfunctional diterpene parent alcohols phorbol, ingenol and resiniferonol, respectively. For human beings conditional cancerogenic (tumorpromoting) diterpene esters (DTE) may be considered a new non-classical category of cancerogenic risk factors.

For the assessment of acute and chronic toxicity of remedies from phytomedicinal, homeopathic and ethnomedicinal drugs, a general strategy was developed using a combination of biological testing and chemical analytics in a certain hierarchical order. For testing *in vitro* and *in vivo,* short term assays are used, *i.e.* luminol dependend chemoluminescence in human polymorphonuclear leucocytes **(LDCL-assay)**, activation of chloramphenicol-acetyltransferase in DR-CAT-Raji cells **(CAT-assay)** and irritancy on mouse ear **(mouse ear assay)**, followed up by chemical analysis of the DTE content, *e.g.* by HPLC. Due to the multiplicity of the DTE content of individual drugs the latter often requires a special strategy. As a final and crucial check, the general strategy provides testing in a highly standardized initiation/promotion protocol on the back skin of mice of the drugs as utilized to establish the presence of non-classical conditional cancerogens of the tumor promoter type, qualitatively and quantitatively. From the short term tests the general strategy is provided with rel. luminol dependend chemoluminescence concentration 50 ($RLDCL_{50}$), CAT induction concentration 50 (CAT_{50}), irritant dose 50 (ID_{50}^{24}) and from the long term test with statistically validated median latency times (t_{50}) and TPA equipotent dose ($d_{e,\,TPA}$) for tumorigenicity. The newly introduced calculated measures "irritancy factor" (IF) and "detection limit" (d_1) allow for comparison of risk materials with recognised standards of environmental prototype risk factors. Some results of testing the general strategy using as putative risk materials remedies and food from several plants *(Croton flavens, Daphne mezereum, Euphorbia cyparissias, Euphorbias ingens, Euphorbias lathyris, Euphorbia resinifera)* will be reported. It is aimed at a rational estimation in the animal experiment of the cancer risk by daily doses of risk materials and an estimation of the relation of risk/benefit for the materials investigated.

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