

**A085 Cytotoxicity of *Plantago* spp. on tumoral cell lines**

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We have assessed the n-hexane and methanol extracts from leaves of six species of *Plantago* genus: *P. afra*, *P. bellardii*, *P. coronopus*, *P. lagopus*, *P. lanceolata*, and *P. serraria*, against four human cell lines, using etoposide and vincristine as positive controls. The tumoral cellular lines were renal adenocarcinoma (TK-10), breast adenocarcinoma (MCF-7), melanoma (UACC-62) and CORL-23. We have followed the protocols established by the National Cancer Institute (NCI) National Institute of Health (USA), using the sulphorhodamine B assay (1).

The cytotoxic activity of each extract was expressed as an IC<sub>50</sub> value (concentration of the extract in µg/ml that inhibits the cellular growth by 50%), and was calculated from the correspondence log-dose curve.

The species that showed most activity were *P. bellardii*, *P. coronopus*, and *P. serraria*, showing up *P. bellardii*, only specie which showed activity on all of the lines. The most active on MCF-7 was *P. coronopus* with a IC<sub>50</sub>=32.57±11.90 and *P. serraria* on CORL-23 with a IC<sub>50</sub>=16.98±0.62.

**References:** 1. Monks, A. (1991), J. Natl. Cancer Inst., 83(11): 757-766.

**A086 The effect of sesquiterpene lactones on the release of neutrophil elastase**

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Neutrophil granulocytes are central components of the inflammatory process. They migrate to the inflammation site and release toxic products such as proteolytic enzymes or reactive oxygen species. Cell surface receptors of chemoattractants, such as the bacterial peptide N-formyl methionyl-leucyl-phenylalanine (fMLP) or platelet activating factor (PAF) are involved in the initial process resulting in exocytosis of granules with proteolytic enzymes, e.g. the human neutrophil elastase (HNE). Under normal physiological conditions, HNE is controlled by endogenous proteinase inhibitors. However, intense neutrophil infiltration results in an imbalance between the amount of HNE and endogenous inhibitors. Accumulating HNE can then cause abnormal degradation of healthy tissue resulting in the development of diseases such as pulmonary emphysema, rheumatoid arthritis or cystic fibrosis (1).

We have recently investigated whether sesquiterpene lactones (SLs), anti-inflammatory active natural compounds from a variety of medicinal plants of the Asteraceae family, directly target HNE and could show that only few SLs were able to inhibit the protein at low concentrations (2). Here we studied nine SLs of eudesmanolide, guaianolide, pseudoguaianolide, and germacranolide type for their ability to inhibit the release of HNE, detected by p-nitroanilide (pNA) formation. Neutrophils were isolated from fresh human blood. After preincubation with different concentrations of the respective SL and cytochalasin B, the exocytosis of elastase was initiated either by PAF or fMLP. The SLs exhibited an inhibitory effect on elastase released from neutrophils challenged either by PAF or fMLP. Concentration-response curves were recorded and the IC<sub>50</sub> values ranged from 2-25 µM. Studies on isolated HNE have shown that a selective inhibition directly on HNE can be excluded. Further studies are in progress whether membrane stabilizing effects of SLs or the influence on calcium homeostasis may be responsible for the observed inhibitory activity (3).

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**References:** 1. Johansson et al. (2002) J. Nat. Prod. 65: 32-41. 2. Siedle et al., Bioorg. Med. Chem. in press. 3. Hall, I.H. et al. (1980) J. Pharm. Sci. 69 (5): 537-543.