

Anti-inflammatory Activity of Three Newly Developed *Harpagophytum procumbens* - Extracts

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Objective:

Evaluation of the anti-inflammatory activity of different extracts of *Harpagophytum procumbens* DC on interleukin-1beta stimulated rat kidney mesangium cell cultures, a model for inducible inflammatory mediators.

Material & Methods:

Tested were three newly developed ethanolic extracts (60% V/V) of *Harpagophytum procumbens*:

Extract 1: Dry plant extract, produced with maceration and percolation under elevated temperature

Extract 2: Dry plant extract, produced with high-speed extraction

Extract 3: Fresh plant extract, produced with long extraction-time

Test system:

Mesangial cell cultures of rat-kidney origin (culture passages 16,18 and 21) were pretreated with 0.5 nM interleukin-1 β (IL-1 β) for 24 h in order to stimulate cyclooxygenase-2 (COX-2) and inducible nitroxide synthase (iNOS). Cells were treated in parallel with the three Harpagophytum extracts of concentrations between 0.01-1 mg/ml in general and up to 3 mg/ml with Extract 2 and 3.

Measured were contents of nitrite, Prostaglandine PGE₂ and 6-keto-PGF_{1a}.

Results:

Extract 1: This extract was cytotoxic in concentration over 0.5 mg / ml. NO as well as PGE synthesis are stimulated. There is no inhibitory effect on IL-1beta stimulated prostaglandine synthesis, a reduction of PGE levels may be explained by the cytotoxic properties of this extract.

Extract 2: This extract is not cytotoxic. No or only little stimulation of PGE synthesis is observed without stimulation with IL-1beta. After stimulation a biphasic behaviour could be observed where in low doses a stimulation of PGE synthesis occurred and an inhibitory action in higher doses (0.5 – 1 mg/ml) was shown. This pharmacologically interesting behaviour is well known in this model from tests with synthetic COX-2 inhibitors.

Extract 3: This extract is not cytotoxic as well. It has no effect on PGE synthesis without IL-1beta stimulation. Again, a biphasic behaviour could be observed, however the inhibitory action was at a concentration higher than 1-3mg extract/ml.

Conclusion:

In this model we could show that extracts from Harpagophytum tubers were effective in reducing NO and PGE₂ synthesis. This is of particular relevance as NO is an important mediator of COX-2 induction. Thus, reduced NO may also show a reduced synthesis of prostaglandines, which was confirmed in our study.

This effect could not be shown by a dry plant extract with a different extraction method. It is well known that the extraction method may have a crucial influence on effectiveness of Harpagophytum extracts.

The partial inhibition of COX-2 may have beneficial effects on normal function of kidney cells. To date it is discussed that complete blocking of the COX-2 may have a negative impact on patient with kidney insufficiency. The above results are the base for future clinical and pharmacological research with Harpagophytum.