

**A003 Antiinflammatory activity of paepalantine in rat colitis induced by TNBS**

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Paepalantine, (9,10-dihidroxy-5,7-dimethoxy-1H-naphthol(2,3c)pyran-1-one), an isocoumarin isolated from *Paepalanthus bromelioides* Silv., Eriocaulaceae (a Brazilian endemic shrub of the Serra do Cipó, MG, Brazil) shows chemical features related to several compounds with antioxidant, antiulcerogenic and anti-inflammatory activities as coumarins, flavonoids and other phenolics. For this reason, paepalantine was assayed in an experimental model of rat colitis. Paepalantine was isolated from capitula by Silica-gel column chromatography (yield 0,35%) and chemically defined by <sup>1</sup>H-NMR, <sup>13</sup>C-NMR and Infrared. Colitis was induced by administration of the 10 mg of trinitrobenzenesulfonic acid (TNBS) dissolved in 0.25 ml of 50% ethanol (v/v) by means of a Teflon cannula inserted 8 cm through the anus of animal. Rats were given 5, 10, 25, 50 and 100 mg/Kg body weight of the paepalantine orally for 3 days before colitis induction and 24 h thereafter. A TNBS control group and a normal (noncolitic) group were included for reference. Animals were killed 48 h after colitis induction and colonic segments were scored for macroscopically visible damage and assayed for biochemical determinations: colonic myeloperoxidase activity and total glutathione content. In addition, antioxidant activity of paepalantine (1-100 µM) was evaluated by inhibition of lipoperoxidation induced by ferrous sulphate plus ascorbic acid in liver membranes. All results were tested for statistical significance using one-way ANOVA. The results obtained showed that oral pre-treatment with 50, 25, 10 and 5 mg/Kg of paepalantine attenuated macroscopic colonic damage. The beneficial effect produced by administration of 5 and 10 mg/Kg was accompanied by an improvement in the oxidative status due to prevention of glutathione depletion that characterizes this model of intestinal inflammation. However, paepalantine had no effect on myeloperoxidase levels. The IC<sub>50</sub> of paepalantine on the inhibition of lipid peroxidation in rat liver membranes induced by Fe/ascorbic was 38,5 µM. All these results suggest that the antioxidant properties of paepalantine can participate in its intestinal anti-inflammatory activity.

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**A004 A glucosamino-oligosaccharide promotes early differentiation of normal human keratinocytes (NHK)**

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Carbohydrates, in particular glucosamines, are important signal transduction components of skin cells. Especially keratinocyte metabolism, growth and differentiation are influenced by carbohydrate epitopes of glycoproteins.

A dynamic cell culture system with normal human keratinocytes (NHK) and HaCaT cells was established to enable detailed investigations of effects of exogenous plant-derived poly- and oligosaccharides on cell physiology: differentiation behaviour, proliferation rate, energy metabolism and cytotoxicity can be simultaneously determined by this screening system. *In vitro* study parameters therefore are the levels of involucrin and of keratins K1 and K10 as differentiation marker, BrdU incorporation for quantification of cell proliferation, mitochondrial dehydrogenase activity and lactatedehydrogenase (LDH) as cytotoxicity marker.

Investigating the differentiation behaviour of normal human keratinocytes after incubation with different poly- and oligosaccharides a glucosamino-oligosaccharid was shown to exhibit promoting effects on cell differentiation, determined by the early protein marker involucrin and the late differentiation products keratin K1 and K10. In the same way mitochondrial dehydrogenase activity of HaCaT cells could be increased by incubation with this glucosamino-oligosaccharide while the proliferation rate was only weakly stimulated. Direct cytotoxic effects were not observed. Structure-activity relation showed that the degree of polymerisation had a significant influence on these physiological effects.

Because of its ability to promote differentiation with low stimulating effects on proliferation, short-chain glucosamino-oligosaccharides could be an promising approach in medical treatment of skin diseases and cosmetic applications.