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Isolation of oligomeric procyanidins from *Crataegus folium cum flore* and in vitro absorption studies in Caco-2 cell culture system.

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The oligomeric procyanidins of hawthorn leaves and flowers are considered to be in part responsible for the cardiotoxic clinical activity of the herbal material. Until now, bioavailability of these compounds is still unclear. Therefore, Procyanidins B2 and C1 as well as several procyanidin-clusters with a degree of polymerization (DP) from 3 to 13 were isolated from hawthorn leaves and flowers (*Crataegi folium cum flore*) for the first time. The bioavailability of procyanidin B2 and C1, extracts and procyanidin rich fractions was tested with a Caco-2 cell model.

Combinations of different column chromatographic and liquid chromatographic methods resulted in the effective isolation of procyanidins and procyanidin-clusters. Structure elucidation of isolated compounds was performed by ESI-MS, NMR and CD.

The Caco-2 cell model was validated with respect to different parameters (integrity, morphology, cell toxicity, permeability of control compounds) prior to the transport studies.

Cell viability assays indicated that Procyanidin B2 and C1 did not influence cell viability of Caco-2 cells in concentrations between 0.1 and 1 mmol/L, whereas extracts containing procyanidins showed a concentration dependent cytotoxicity.

In vitro absorption studies resulted in a passive paracellular transport for procyanidin B2 and C1. With increasing degree of polymerization of procyanidin-clusters (DP = 4 to 6) the permeability decreases which also indicates a passive paracellular transport. The passive transcellular route for procyanidin B2 and C1 was affected by the activity of p-glycoprotein.

Transport studies showed that no procyanidin was detectable on the basolateral side after incubation of Caco-2 cells with procyanidin containing extracts. However, in cell lysates of incubated cells procyanidins were detectable. This may be a hint for adhesion of procyanidins on cells or absorption in cells.

Passive paracellular transport of procyanidin B2 was reduced significantly in presence of procyanidin rich fraction MLW RP 18c. In contrast, the active transport of glucose was not influenced by a commercial available hawthorn extract and the fraction MLW RP 18c.