

BIOAVAILABILITY OF FORMULATIONS CONTAINING *CURCUMA LONGA L.* AND/OR *CENTELLA ASIATICA L.* IN RATS

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Introduction: Turmeric (*Curcuma longa* L.) is an herbaceous perennial plant containing curcumin, which is responsible for beneficial effects against neurological and cardiovascular diseases. Centella, commonly known as Gotu kola (*Centella asiatica* L.), is a perennial plant found throughout most tropical and subtropical countries. Several studies report that this plant is useful to positively affect mood disorders. The active compounds are the triterpenes asiaticoside, asiatic acid, madecassoside, and madecassic acid. Turmeric and centella are under evaluation in this research project as ingredients of nutraceuticals for brain health. However, bioavailability of these compounds seems to be poor, thus supporting the search for innovative formulations aimed to improve the bioavailability of the active components. The aims of the study were 1) to set up the analytical method able to simultaneously detect and quantify curcumin and centella triterpenes; 2) to evaluate the bioavailability of curcumin, asiatic acid, madecassic acid, asiaticoside and madecassoside in the plasma of adult male rats after repeated oral administrations of phytosomal preparations containing *Centella asiatica* L. standardized in asiaticoside 6,8% (CAP), *Curcuma longa* L. standardized in total curcuminoids 19,6% (CLP) or a mixture composed by *Curcuma longa* L. plus *Centella asiatica* L. (60:40).

Materials and methods: Curcumin, asiaticoside, asiatic acid, madecassoside, and madecassic acid were quantified in the plasma samples with SCIEX Triple Quad™ 3500 LC-MS/MS System with a method set up to simultaneously detect all the active components. Phases used were as follows: phase A: water with 0.1% formic acid; phase B: methanol and acetonitrile 1:1. Four months old male Sprague Dawley rats were treated, by oral gavage, with CAP (20-100 mg/kg), CLP (30-150 mg/kg), mixture (50-250 mg/kg) or vehicle (sterile water) for 10 days. Two hours after last administration, the plasma from each animal was collected and stored at -80°C.

Results: In the plasma of the animals treated with *Curcuma longa* L. (150 mg/kg), curcumin reached a statistically significant concentration of about 2.7ng/mL, while following treatments with 30 mg/kg of the same preparation the concentration of curcumin was 0.4ng/mL. After administration of the mixture, the bioavailability of curcumin in the plasma was reduced (0.9ng/mL) following treatment with the highest dose, and undetectable with the lowest. The plasmatic concentrations of asiatic and madecassic acids in the animals treated with *Centella asiatica* L. or the mixture showed a dose dependent fashion; the animals treated with CAP (100 mg/kg) showed significant plasmatic concentrations of asiatic and madecassic acids (around 11.5 and 4.1ng/mL, respectively) compared to the animals treated with vehicle; concentrations were similar to those obtained after administration of the mixture at the dose of 250 mg/kg (around 8.4 and 4.4ng/mL, respectively). The concentrations of asiaticoside and madecassoside appeared higher in the plasma of animals treated with the mixture at the dose of 250 mg/kg than in the plasma of animals treated with CAP.

Discussion and conclusion: A robust method to detect the active principles of turmeric and centella in one single analysis has been set up and may be used to quantify these components in nutraceutical formulations. Phytosomal formulation applied to *Curcuma longa* L. and *Centella asiatica* L. efficiently increase the plasmatic concentrations of the single active principle, in particular asiaticoside and madecassoside from CAP in rats; administration of the mixture or CAP alone resulted in similar plasmatic values of asiatic and madecassic acids. In this type of rats with this treatment period and time to plasma collection the bioavailability of curcumin is higher after administration of *Curcuma longa* L. alone than the mixture.