

Meeting abstract

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Bioavailability of dodeca-2E, 4E, 8E, 10E/Z-tetraenoic acid isobutylamides after oral administration in rats and distribution in various tissues

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Background

Preparations from *Echinacea* are among the best-selling phytopharmaceuticals worldwide and have been widely used for the treatment of common cold and various upper respiratory infections. The most relevant active principles of *Echinacea* extracts are alkamides, caffeic acid derivatives (CADs) and glycoproteins/polysaccharides [1]. The main alkamides in *Echinacea* preparations are the isomeric dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides ("tetraenes"). Until now, a limited number of pharmacokinetic studies with alkamides have been reported, but no data exist about their distribution in tissues and transport through the blood-brain barrier (BBB). Therefore, we evaluated the pharmacokinetics of dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides after a single oral dose administration of 2.5 mg/kg in plasma as well as in liver and four different brain regions (hippocampus, cerebral cortex, striatum and cerebellum).

Methods

Plasma and tissues were collected after 8, 15, 30 minutes and 1, 2, 3, and 6 hours after oral dosing and the concentrations were determined by a liquid chromatography tandem mass spectrometry (LC-MS/MS) method with benzanilide as internal standard using the respective [M-

H]⁺ ions, m/z 248/152 for the dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides and m/z 198/105 for the internal standard.

Results

The lipophilic constituents were rapidly absorbed and well distributed to the examined tissues. The highest concentration was found in the striatum. The total tetraene amount in plasma was calculated as AUC_{0-∞} (794 min · ng/mL), which was about 13-45% of that found in different brain parts (1764-6192 min · ng/mL), and 63% of that in liver tissues (1254 min · ng/g). The C_{max} in plasma was 26.4 ng/mL, while the C_{max} in the different brain regions varied between 33.8 ng/g and 46.0 ng/g.

Conclusion

The results demonstrate that the dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides are bioavailable in rats with a rapid passage across the blood-brain barrier.

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