

Meeting abstract

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Absolute and relative bioavailabilities of dodeca-2E, 4E, 8E, 10E/Z-tetraenoic acid isobutylamides after intravenous and oral single doses in rats

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Background

Dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides are the main alkamides in *Echinacea* preparations, which have been demonstrated to possess biological activities in various bio-assays, such as immune-modulating activities and effects on cannabinoid receptors [1]. Therefore, the evaluation of systemic availability of these active plant constituents is a major prerequisite for the interpretation of *in vitro* pharmacological testing. This study assessed the absolute and relative bioavailabilities of dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides (tetraenes) administered as pure compounds or as an *Echinacea purpurea* root extract preparation.

Methods

Ten rats received 0.75 mg/kg dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides orally, pure and within 158.6 mg/kg *Echinacea purpurea* extract, or intravenously to compare the absorption and pharmacokinetic properties. Pharmacokinetic parameters and bioavailability data of tetraenes were obtained by non-compartmental analysis (NCA) using WinNonlin® 5.2 software.

Results

Mean dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamide plasma area under the concentration-time curve ($AUC_{0-\infty}$ per dose) was $3.2 \pm 0.3 \text{ min} \cdot \text{ng/mL}/\mu\text{g}$ and $1.0 \pm 0.2 \text{ min} \cdot \text{ng/mL}/\mu\text{g}$ after i.v. and oral administration, respectively, and $1.5 \pm 0.2 \text{ min} \cdot \text{ng/mL}/\mu\text{g}$ after oral administration of the *Echinacea* root extract. The absolute bioavailability of dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides was 29%, which was increased to 47% (1.6 fold) by the administration of an *Echinacea* extract. The relative bioavailability was over 100%.

Conclusion

Administration of a whole *Echinacea* extract increases blood exposure with no impact on C_{max} . The high area under the curve concentration resulted in a longer elimination half-life with 123 min in comparison to 36 min after administration of the pure dodeca-2E,4E,8E,10E/Z-tetraenoic acid isobutylamides. The approximately 2-fold higher percentage of relative bioavailability achieved with the *Echinacea* root extract resulted in a 3.4 and 3.6 times higher terminal elimination half-life and mean residence time (MRT), respectively. A rapid absorption followed by a slower elimination phase was observed.

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