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FILE: ▪Echinacea (*Echinacea angustifolia*)
▪Pharmacokinetics
▪Alkamides

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RE: Evaluation of the Pharmacokinetics of Alkamides of Echinacea Root

Woelkart K, Koidl C, Grisold A, et al. Bioavailability and pharmacokinetics of alkamides from the roots of *Echinacea angustifolia* in humans. *J Clin Pharmacol.* 2005;45:683–689.

Alkamides are lipophilic, nitrogen-containing organic compounds with long fatty-acid chains found in the roots of *Echinacea angustifolia* and *E. purpurea*, and in the aerial parts of all of the three main medicinal species, including *E. pallida*, whose roots do not contain alkamides. They have demonstrated in vitro anti-inflammatory and macrophage-stimulating properties in previous studies, but the absorption of specific compounds and its presence in the blood after ingestion had not been documented. The authors first characterized the compounds in *E. angustifolia* root, then conducted a randomized, open, single-dose crossover study to evaluate the pharmacokinetics of alkamides from *E. angustifolia* root.

Fresh roots from 2-year-old *E. angustifolia* plants (Heilpflanzen Sandfort GmbH & Co Kg [Olfen, Germany]) were processed using supercritical CO_2 by Finzelberg (Andernach, Germany), yielding 1.30% of a 77:1 extract. CO_2 extraction entails forcing pressurized carbon dioxide into a chamber filled with plant material. The CO_2 heats to approximately 95–100^o F and functions as a solvent, extracting oils, pigments, resins, and other substances from the plant matter. Because the temperatures are much lower in the supercritical CO_2 extraction process compared to steam distillation, which reaches temperatures of 140–212^o F, supercritical CO_2 extraction preserves the less stable compounds that are destroyed at higher temperatures.

After extraction the material was subjected to semipreparative high-performance liquid chromatography (HPLC) and 6 alkamides were isolated. They were undeca-2*E*/*Z*-ene-8,10-diynoic acid isobutylamide (8.44 ng/ml; designated #1), dodeca-2*E*,4*Z*-diene-8,10-diynoic acid isobutylamide (11.78 ng/ml; designated #2), dodeca-2*E*-en-8,10-diyonic acid isobutylamide (5.60 ng/ml; designated #3), dodeca-2*E*,4*E*,8*Z*,10*E/Z*-tetraenoic acid isobutylamide (31.62 ng/ml; designated #4), dodeca-2*E*,4*E*,8*Z*-trienoic acid isobutylamide

(4.45 ng/ml; designated #5), and dodeca-2*E*,4*E*-dienoic acid isobutylamide (5.71 ng/ml; designated #6).

In the second part of the study, eleven volunteers (5 men, 6 women) aged 25–36 years (mean 30.1 ± 4.7 years) were given a single dose of 2.5 ml of a 60% ethanol *E. angustifolia* extract or placebo at 8:30 AM following an overnight fast. All subjects were healthy at the time of the study. Excluded from the trial were people with any progressive systemic illness (e.g., tuberculosis, leukemia, connective tissue diseases, multiple sclerosis or other autoimmune diseases) and anyone with a history of allergy to plants in the Asteracea/ Compositae family, since *E. angustifolia* is in this plant family and cross-reactivity could result. A baseline blood sample was drawn at 8:00 AM, and additional samples were taken 10, 15, 20, 25, 30, 35, 50, 65, and 180 minutes after dosing.

The presence of alkamides in plasma samples was determined by liquid chromatography electrospray ionization ion-trap mass spectrometry (LC-ESI-IT-MS/MS). The mean maximum plasma concentration of alkamides (ng • min /ml) occurred within 30 minutes after ingestion. The fastest absorbed molecule was compound 1, which attained a mean maximum concentration (115.25 ± 86.87) after 20 minutes. The mean maximum concentration of all other alkamides was detected 30 minutes after dosing, except for compound 6, which remained below the detectable limit in all samples. The mean maximum concentration was 128, 75 ± 82.79 for compound 2, 101.36 ± 45.68 for compound 3, 1029.14 ± 500.72 for compound 4 and 195.48 ± 119.55 for compound 5. Due to the overall rapid absorption of the alkamides the authors speculated that a significant amount of absorption must have taken place in the mucous membranes of the mouth and esophagus.

Not all volunteers absorbed the compounds at the same rate. The authors detected two different absorption kinetics in the volunteers whom they labeled as "fast" and "slow" absorbers. The maximum concentration of compound 1 was detected after 10 minutes in 4 volunteers, but not until 30 minutes in 7 of the volunteers.

This study demonstrated for the first time the absorption kinetics in humans of lipophilic alkamides from *E. angustifolia* root. All compounds absorbed and detected contained double bonds in their fatty acid chain. Additional research may add to this data by evaluating the in vivo immunological effects of these alkamides.

—John Neustadt, ND

The American Botanical Council has chosen not to reprint the original article.