Wood creosote, the principal active ingredient of seirogan, an herbal antidiarrheal medicine: a single-dose, dose-escalation safety and pharmacokinetic study

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＜和文タイトル＞

健常被験者に複数用量を単回投与した正露丸の主成分である木クレオソートの安全性、薬力学試験

[Abstract]

Study Objective: To assess the safety, tolerability, and pharmacokinetics of escalating single doses of wood creosote, an herbal antidiarrheal and antispasmodic agent.

Design: Randomized, double-blind, placebo-controlled study.

Setting: Clinical research center.

Subjects: Forty (32 men, 8 women) healthy volunteers aged 19-42 years.

Intervention: By random assignment, 22 men and 8 women received escalating single doses of wood creosote (45, 90, 135, 180, and 225 mg) and 10 men received placebo (for each of the five dose levels, 6 subjects received active substance and 2 subjects received placebo).

Measurements and Main Results: Vital signs, laboratory tests, and electrocardiograms were assessed; no dose-related or clinically significant changes were noted. Serial blood samples were obtained to determine the pharmacokinetics of four major active components of wood creosote: total (conjugated plus free) guaiacol, creosol, *o*-cresol, and 4-ethylguaiacol. The most common adverse events were mild headache and dizziness, with no dose-related trends being apparent. Area under the concentration-time curve from time zero to infinity increased in a dose-proportional manner for total guaiacol, creosol, and *o*-cresol and was not assessed for total 4-ethylguaiacol owing to lack of data at the low dose level. No apparent differences by sex were noted for any of the four active components. All four components were rapidly eliminated.

Conclusion:. Single oral doses of wood creosote up to 225 mg were safe and well tolerated in healthy men and women. Also, the doses of wood creosote were rapidly absorbed, conjugated, and eliminated. Such a rapid onset and short duration of action would appear desirable in the treatment of acute nonspecific diarrhea.