

CAPSULES

preliminary notes and applications from Bioanalytical Systems, Inc.

CI-958 in Plasma

Purpose

Determination of CI-958 in plasma.

IS: R₁=H

CI-958: R₁=8-OH

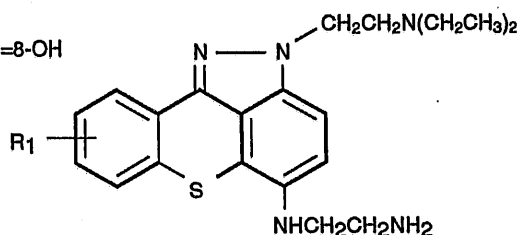


Figure 1. Structures of CI-958 and the internal standard (IS).

CI-958 [F1] is a benzthiopyranoindazole which may show anticancer activity through its action as a DNA intercalator. An LCEC method was developed to determine CI-958 in plasma, at concentrations between 1 ng/mL and 100 µg/mL [1].

Conditions

System: BAS-200 Liquid Chromatograph

Electrode: Glassy carbon

Potential: +600 mV vs. Ag/AgCl

Column: Zorbax RX[®], C₈, 250 x 4.6 mm

Temperature: 45 °C

Mobile Phase: 5%(v:v) MeOH, 2.5% *n*-propanol, 93.5% 0.05 M phosphoric acid, adjusted to pH 3.1 with NaOH, and containing 0.25 g/L Na₂EDTA and 5 g/L tetrabutylammonium bromide

Flow Rate: 1.5 mL/min

Linear Range: 1 ng/mL to 100 µg/mL

Sample Preparation

A Bond Elut[®] cyano cartridge was preconditioned by treating it sequentially with H₂O (1 mL), MeOH (1 mL), H₂O (5 mL), blank plasma (human, dog, or mouse, 0.5 mL), H₂O (2 mL), 0.1% (v:v) ethylenediamine (EDA), 0.005% (w:v) cysteine in MeOH pH 7 with HOAc, MeOH (2 mL) and H₂O (5 mL). Then 0.5 mL of sample was transferred to the cartridge and internal standard was added. The sample

was aspirated and the cartridge washed with H₂O (2 x 1 mL), then air dried for one minute. The analytes were eluted with the 0.1% EDA solution. The eluate was dried under a stream of nitrogen, then reconstituted with mobile phase containing 50 µg/mL ascorbic acid.

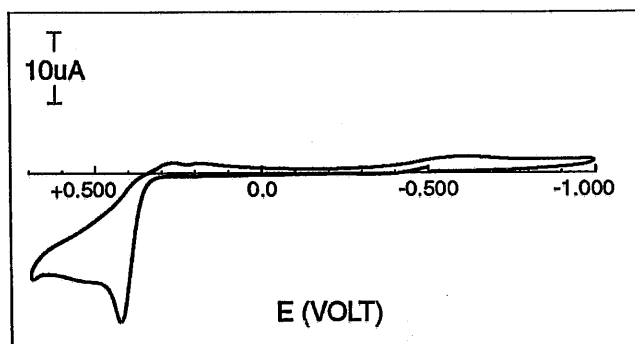


Figure 2. Cyclic voltammogram of CI-958. The working electrode was of glassy carbon, and the supporting electrolyte was phosphate buffer containing triethylamine and acetonitrile.

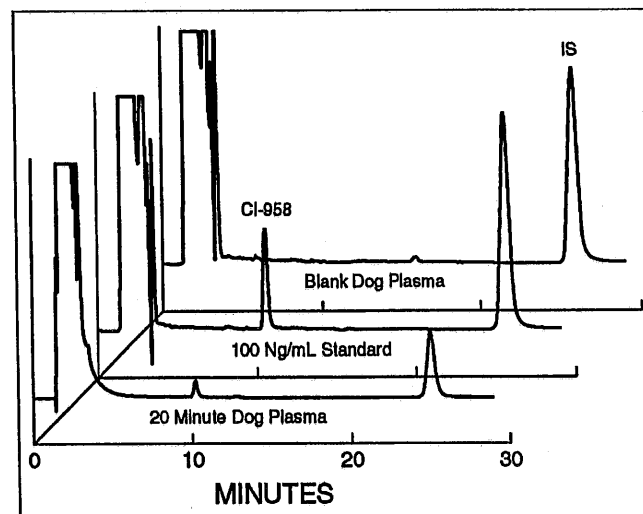


Figure 3. Chromatograms from dog plasma, compared to standards.

Notes

A cyclic voltammogram of CI-958 [F2] showed it to be easily oxidizable at potentials above +500 mV (vs. Ag/AgCl).

Chromatograms of mouse and dog plasma are presented in F3 and F4.

Pharmacokinetic profiles of CI-958 in dogs and mice are shown in F5 and F6.

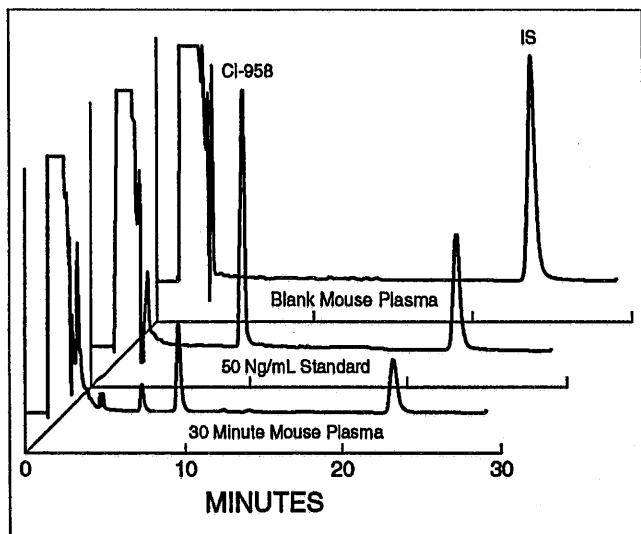


Figure 4. Chromatograms from mouse plasma, compared to standards.

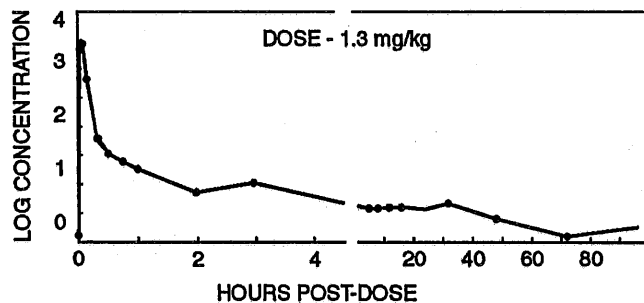


Figure 5. Pharmacokinetic profile from a dog.

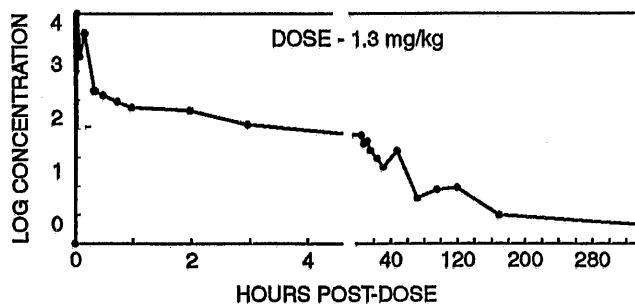


Figure 6. Pharmacokinetic profile from a mouse.

Reference

1. A. Brubaker, L. Leung, L.R. Whitfield and B. Wong, poster presented at the American Association of Pharmaceutical Scientists annual meeting (1991) Washington D.C.

