

FLOCHROM[®] MITOTANE/DDE IN PLASMA

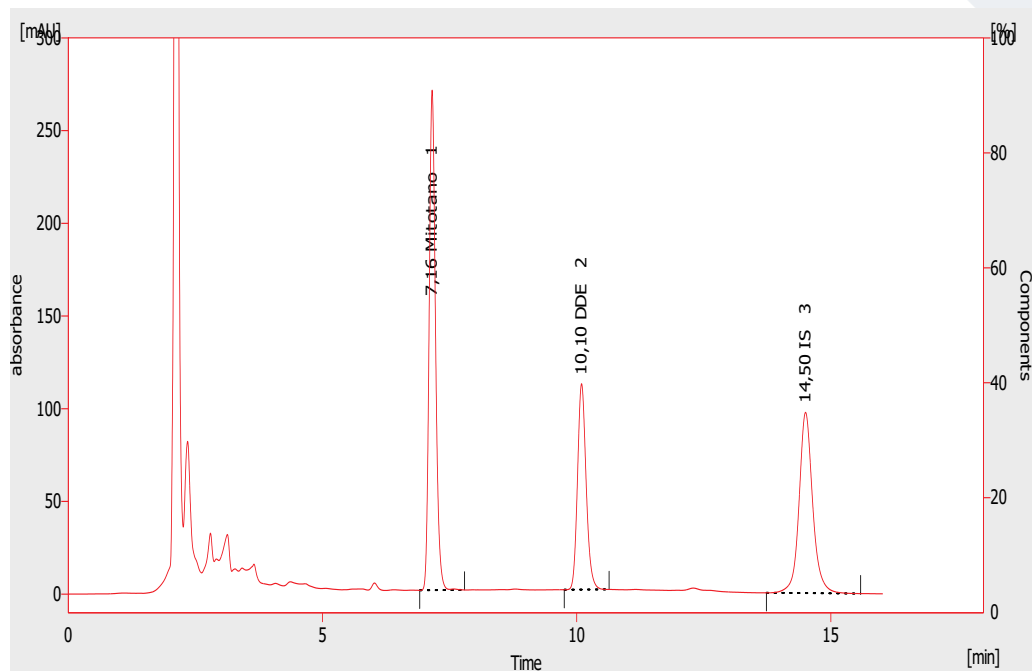
Mitotane, an analogue of DDT insecticide, is the drug of choice for unresectable, metastatic or recurrent adrenocortical carcinoma (ACC) and, due to high rates of recurrence, it is also suggested as adjuvant therapy after tumor resection.

The antitumor effect of Mitotane is related to the maintenance of adequate plasma levels of the drug.

Patients with Mitotane levels in plasma $\geq 14 \mu\text{g/mL}$ have been observed to have a response rate of 55-60%, while those with lower levels have a lower response rate. Significant side effects were generally only observed in patients with plasma levels above 20 $\mu\text{g/mL}$.

Monitoring of plasma concentration of Mitotane during treatment allows a faster achievement of the therapeutic level (14-20 $\mu\text{g/mL}$), as well as the minimization of adverse effects due to an excessively high plasma level. Intra-adrenal metabolic transformation is essential for the therapeutic effect of Mitotane, that is metabolized in DDE and DDA: DDA levels rapidly increase in response of high Mitotane levels while DDE levels increase slowly.

Long-term follow-up studies suggest that DDE plasma concentration is closely related to improvement and clinical remission.



HPLC system conditions

Injection volume: 50 µL (variable according to instrumental sensitivity)

Flow rate: 1.0 mL/min

Running time: 15 min

Column heater: 45°C

UV detector: 226 nm

Column conditioning: column should be conditioned for 10 min at flow rate of 0.8 mL/min with mobile phase

Sample preparation

- Add 100 µL of plasma
- Add 20 µL of Internal Standard and vortex
- Add 200 µL of precipitant solution and vortex
- Centrifuge for 10 min at 10000-12000 rpm
- Collect 150 µL of supernatant and transfer into an auto sampler vial
- Inject 50 µL and analyze with HPLC technique

Performance

ANALYTE	LLOD (µg/mL)	LLOQ (µg/mL)	LINEARITY (µg/mL)	CV% INTRA	CV% INTER
Mitotane	0.280	0.940	0.940 – 100	2.6% - 7.5%	5.7% - 7.1%
DDE	0.300	0.990	0.990 – 40	2.1% - 6.9%	3.9% - 6.6%

Ordering guide

EUH07050	FloChrom® Mitotane/DDE in Plasma	100 assays
EUH07051	Controls (2 Levels), lyophil.	2 x 2 x 2 mL
EUH07090	Analytical Column	1 pc

CHR-13-19-REV.3