OraChrom, Inc.
The Vanguard of Liquid Chromatography.

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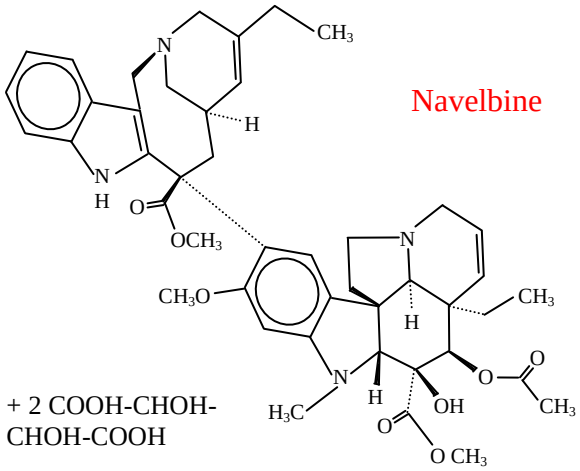
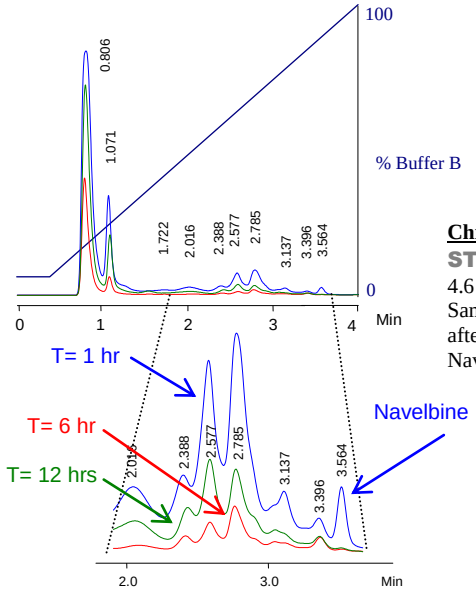
APPLICATION NOTE

Navelbine: Fast Detection in Urine Sample with STYROS™ 2R/XH.

Navelbine is a semi-synthetic vinca alkaloid with antitumor activity. It is the ditartrate salt of Vinorelbine.



The clinical pharmacology suggests that the drug's action results in its interference with microtubule assembly.
Navelbine concentration in plasma rapidly decreases after intravenous injection. This represents the peripheral distribution to the point of saturation. The excess drug is flushed out in urine within an hour.
Using urine samples from the patient one can monitor excess drug and therefore adjust the injected amount to prevent any unnecessary and rather harmful overdose.



Chromatogram 1
STYROS™ 2R/XH 4.6 X 50 mm
Samples of urine taken after injection of Navelbine.

The chromatograms show the speed and accuracy with which the treating physician can access this crucial information to make an informed judgment during treatment.
At present, the only short term guide is the patient's symptoms during the following days. The long term side effects as well as the cumulative ones are less clear. Often times the symptoms are irreversible and the treatment needs to be discontinued.

Table 1. Operating parameters for the chromatograms.

HPLC System.	Agilent 1100
Column	STYROS™ 2R/XH 4.6 X 50 mm
Mobile Phase	A: 0.075% TFA in H2O B: 0.075% TFA in ACN:H2O (95:5)
Flow rate	1 ml/min (360 cm/hr)
Gradient	5% B for 0.3 min., to 100% B in 4 min.
Temperature	37°C
Detection	252 nm
Injection volume	25 µl
Sample:	As indicated.

The metabolisms of vinca alkaloids are known to be mediated by hepatic cytochrome P450 isoenzymes in the CYP3A subfamily. It is therefore important to consider any hepatic dysfunction as well as any potent metabolic inhibitor when administering the drug to these patients.
The metabolites of Vinorelbine in excess doses have been detected in the blood, plasma and urine. However, in therapeutic doses of up to 30 mg/m2, hardly any metabolite can be detected either in the blood or in the urine.
The present application shows how one can effectively gauge the excess drug after its intravenous administration during a short chromatographic run.
Judging by the patient's blood count, Vinorelbine's effect can be seen for up to 14 days. However, no detectable peek can be recorded after 12 hrs during chromatographic run using urine samples.