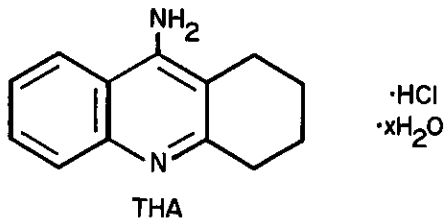
CAPSULES
preliminary notes and applications from Bioanalytical Systems, Inc.

Determination of THA



THA

Figure 1. Structure of THA

Purpose

THA (F1, 9-amino-1,2,3,4-tetrahydroacridine) is an experimental drug that has shown some promise for the treatment of Alzheimer's disease. Alzheimer's is a progressive disease of the brain characterized by the formation of neurofibrillary tangles (clumping of fibers within nerve cells) and amyloid plaques (bundles of abnormal nerve axons and protein). Disease symptoms progress from memory loss, disorientation and depression to halucinations, severe dementia and death. THA has shown remarkable ability to improve some of these symptoms in preliminary studies; it appears to work by inhibiting acetylcholinesterase and thus raising acetylcholine levels in the brain. At the time of this writing, however, the FDA had halted clinical studies of the drug because about 20% of test subjects had experienced changes in liver chemistry.

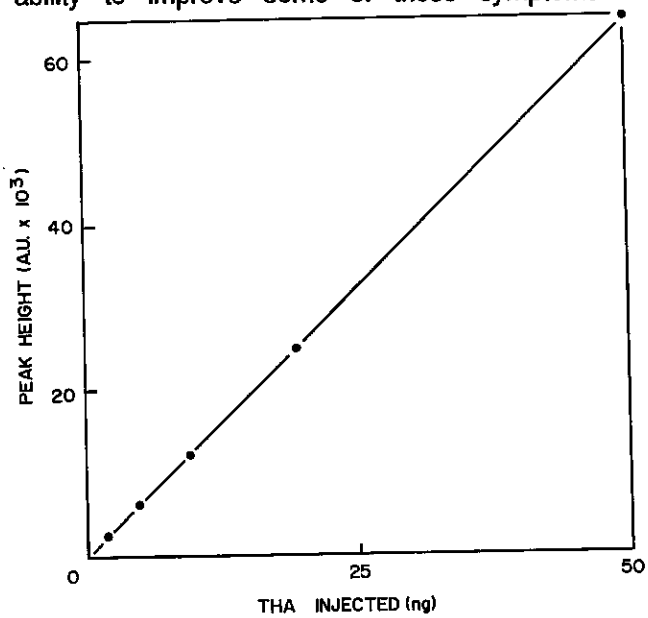


Figure 2. Calibration curve for injected standards. Each point represents the mean of two determinations.

Figure 3. Sample chromatogram of 200 pg injected standard.

Existing Methods

We are aware of no published LC methods for the determination of THA.

Conditions

System: BAS 400 Liquid Chromatograph
Detector: UV-108 variable wavelength (240 nm)
Column: BAS 3 µm Phase II Octyl reverse-phase (100 x 3.2 mm) (PN MF-6214)
Mobile Phase: 82.5% (v:v) 0.05 M KH_2PO_4 adjusted to pH 2.3 with phosphoric acid), 17.5% acetonitrile. One gram (0.1%) dimethylamine was added to this solution. Flow rate was 0.9 mL/min.

Detection Limit: 25 pg injected standard (S/N = 3)
Linear Range: 100 pg - 50 ng injected standards

Sample Preparation

Appropriate amounts of THA-hydrochloride (adjusted for the amount of free base) were dissolved in mobile phase and injected in 20 µL aliquots.

Notes

A calibration curve for injected standards is presented in F2, and a sample chromatogram is presented in F3.

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