

## Documents

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**Development of volumetric absorptive microsampling for analysis phenytoin levels and its application to monitoring therapy in epilepsy patients**

(2023) *Journal of Applied Pharmaceutical Science*, 13 (11), pp. 75-81.

DOI: 10.7324/JAPS.2023.125948

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### Abstract

Phenytoin (PHT) is an anticonvulsant drug used as monotherapy or combination therapy to treat seizures. However, PHT has a narrow therapeutic index range of 10–20 µg/ml, so it is necessary to monitor drug levels. This study aims to obtain optimum sample preparation conditions and a validated analytical method for the analysis of PHT in volumetric absorptive microsampling with carbamazepine as an internal standard using high-performance liquid chromatography and apply it for monitoring blood levels of PHT in epilepsy patients who meet the inclusion and exclusion criteria required in this study. The analytical method developed was validated according to the Food and Drug Administration guidelines in 2018 with a lower limit of quantification value of 0.1 µg/ml with a calibration curve range of 0.1–30.0 µg/ml and a correlation coefficient of  $r \geq 0.9995$ . PHT levels were monitored in 30 epilepsy patients; the range of PHT levels was from 0.81 to 17.45 µg/ml. 9 out of 30 subjects were in the range of appropriate drug therapy, while the other 21 subjects had levels of PHT that were lower than the expected therapeutic range. © 2023 Rizka Mardhiani et al. This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0/>).

### Author Keywords

carbamazepine; HPLC; Phenytoin; therapeutic drug monitoring (TDM); validation; volumetric absorptive microsampling (VAMS)

### Index Keywords

anticonvulsive agent, carbamazepine, clobazam, lamotrigine, levetiracetam, phenytoin, topiramate, valproic acid; accuracy, adult, analysis, analytic method, Article, blood level, blood sampling, body weight, chromatography, chromatography by mobile phase, clinical article, drug dose increase, drug selectivity, drug stability, drug therapeutic index, epilepsy, female, Food and Drug Administration, high performance liquid chromatography, human, injection, male, monitoring, monotherapy, sampling, seizure, ultrasound, volumetric absorptive microsampling

### Chemicals/CAS

carbamazepine, 298-46-4, 8047-84-5; clobazam, 22316-47-8; lamotrigine, 84057-84-1; levetiracetam, 102767-28-2; phenytoin, 57-41-0, 630-93-3; topiramate, 97240-79-4; valproic acid, 1069-66-5, 99-66-1

### Tradenames

Zorbax Eclipse Plus, Agilent

### Manufacturers

Agilent; Branson; Shimadzu; Soccorex; Thermo; Waters

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**Publisher:** Open Science Publishers LLP Inc.

**ISSN:** 22313354

**Language of Original Document:** English

**Abbreviated Source Title:** J. Appl. Pharm. Sci.  
2-s2.0-85176374315

**Document Type:** Article

**Publication Stage:** Final

**Source:** Scopus

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