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CLINICAL

Application Notes

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Determination of paracetamol and vitamin C in pharmaceuticals

empresa innovadora de base tecnológica reconocida por ANCES e!bt

Determination of paracetamol and vitamin C in pharmaceuticals

» INTRODUCTION

Acetaminophen or **paracetamol** (APAP) is a widely used analgesic and antipyretic drug, formulated in a variety of dosage forms. It is used for the relief of fever, headaches and other minor aches and pains. Their determination in pharmaceuticals is of paramount importance, since an overdose of APAP can cause fulminating hepatic or renal necrosis and other toxic effects. Hepatic toxicity begins with plasma levels of APAP in the 120 µg/ml range 4 h after the ingestion and an acute damage is presented with plasmatic levels up to 200 µg/ml 4 h after the ingestion.

The hydrolysis of APAP principally generates ***p*-aminophenol** (*p*AP) which could be present in pharmaceutical preparations as a degradation product of APAP or as a synthetic intermediate.

Ascorbic acid (AA) or **vitamin C** is present in some APAP formulations since it has been reported to have a protective role in vivo with respect to APAP hepatotoxicity.

Microfluidic electrophoresis systems in combination with **electrochemical detection** open the gate to new analytical methods for quality control of pharmaceutical formulations. Thus, these systems enable features such as high selectivity and sensitivity, fast analysis and low cost.

Therefore, **microfluidic systems** could improve the conventional methodologies for the **analysis of pharmaceuticals**.

» EXPERIMENTAL

Samples: Acetaminophen and related compounds standard solutions. Paracetamol tablets.

Injected sample: < 100 pL.

Instrumentation: MicruX® HVStat / iHVStat. Holder DC series.

Microfluidic device: SU8/Pyrex microchips with integrated Pt electrodes (*MCE-SU8-Pt002T*).

Conditioning: 0.1 M NaOH – 30 min.
Deionized water – 15 min.
Buffer solution – 10 min.

» RESULTS

Microfluidic electrophoresis system has been used in the separation and detection of acetaminophen (APAP), ascorbic acid (AA) and *p*-aminophenol (*p*AP).

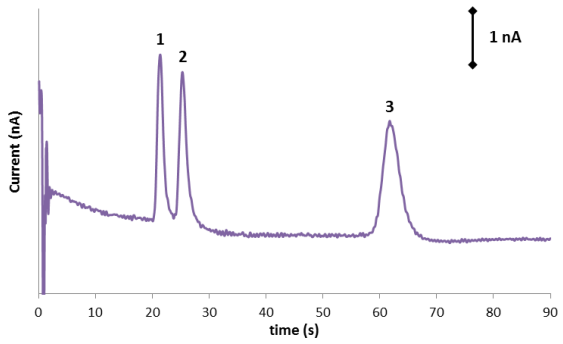

***Figure 1**. Electropherogram for a sample mixture of **(1)** pAP 100 µM, **(2)** APAP 200 µM and **(3)** AA 500 µM using a SU-8/Pyrex microchip with integrated Pt film end-channel detector. Conditions: V_{inj} = +750 V, t_{inj} = 3 s, V_{sep} = +1000 V, E_d = +0.8 V (vs. Pt) and 20 mM MES, pH = 6.0 as running buffer.*

The separation of the active ingredient, APAP and related compounds is accomplished in less than **80 s** (***Figure 1***).

Thus, the analytical methodology based on microfluidic platforms can be used in the simultaneous determination of APAP, *p*AP and AA in pharmaceuticals, paracetamol tablets.

*p*AP is limited to the low level of 50 ppm (0.005 % w/w) in the drug raw material and 0.1 % w/w in tablet formulations by the European, United States, and Chinese Pharmacopoeias. The low level ensures paracetamol drug safety, because *p*AP has significant nephrotoxicity and teratogenic effects.

Microfluidic platform enables the *direct detection* of APAP and related compounds. Paracetamol tablets are simply solved in the buffer solution and transfer to the platform.

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Table 1. Analytical parameters for the separation of acetaminophen and related compounds using a SU8/Pyrex chip with integrated Pt electrode

	*p*AP	APAP	AA
» *Repeatability i_p (RSD %)*	2%	6%	8%
» *Repeatability t_m (RSD %)*	0.5%	0.5%	2%
» *Theoretical plate number (N|m^{-1}):*	37.000	41.000	25.000
» *Resolution (R_s):*	0.7	3.3	
» *Linear range (µM):*	10 – 300	10 – 1000	25 – 650
» *Sensitivity (pA·µM^{-1}):*	39	23	14
» *LOQ (µM):*	10	10	25
» *LOD (µM)*:*	7	9	20

**Limit of detection considers a signal-to-noise ratio, S/N = 3.*
Conditions: 20 mM MES, pH = 6.0; V_{inj} = +750 V, t_{inj} = 3 s, V_{sep} = +1000 V, E_d = +0.8 V (vs. Pt). pAP (50 µM), APAP (100 µM), AA (250 µM).

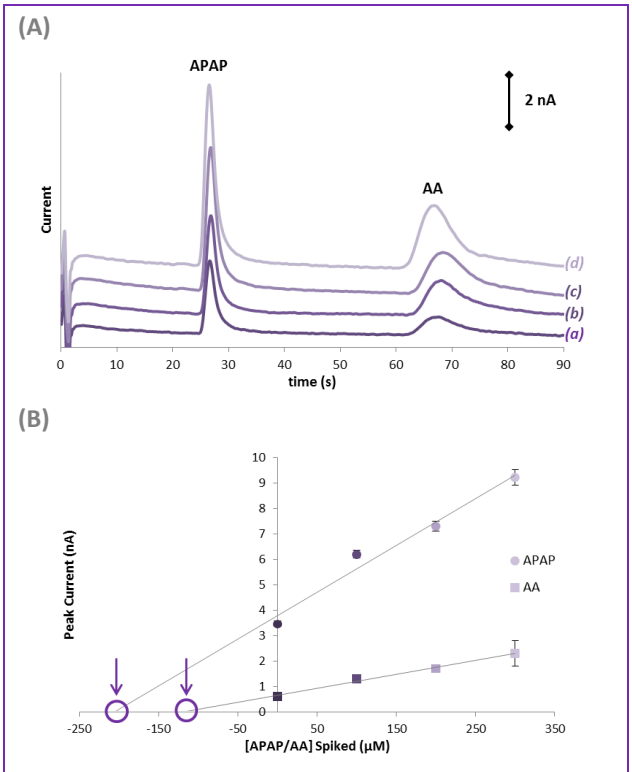

***Figure 2**. **(A)** Electropherograms for a 100-fold dilute paracetamol tablet with successive additions of APAP/AA: 0 (a); 100 (b); 200 (c) and 300 µM (d). **(B)** Standard additions calibration plot. Conditions: V_{inj} = +750 V, t_{inj} = 3 s, V_{sep} = +1000 V, E_d = +0.8 V (vs. Pt) and 20 mM MES, pH = 6.0 as running buffer.*

Paracetamol tablets are evaluated using the *standard additions method* in order to avoid any matrix effect and get a better precision (***Figure 2***).

***Table 2.** Analysis of paracetamol tablets*

Sample	Analyte	Stated value (mg)	Found (mg)	Recovery (%)
Efferalgan	APAP	1000	1020 ± 30	102
Efferalgan Vitamin C	APAP	330	332 ± 14	101
	AA	200	197 ± 15	99

Therefore, establishment of a simple, economical, and accurate analytical method for the simultaneous determination of *p*-aminophenol, paracetamol and related compounds would be useful to medical manufacturers for investigation of the stability of paracetamol, for pharmaceutical analysis, and for quality control.

The automated portable microfluidic system could be validated for pharmaceuticals quality control and currently, it is used as educational tool (*Teaching Packs*) in Universities.

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TECHNOLOGIES

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