## Automated Stopped-Flow Fluorimetric Sensor for Biologically Active Adamantane Derivatives Based on Zone Fluidics

Paraskevas D. Tzanavaras\*1, Sofia Papadimitriou1 and Constantinos K. Zacharis2

<sup>1</sup> Laboratory of Analytical Chemistry, School of Chemistry, Faculty of Sciences,
 Aristotle University of Thessaloniki, GR-54124, Greece
 <sup>2</sup> Laboratory of Pharmaceutical Analysis, Department of Pharmaceutical Technology, School of Pharmacy,
 Aristotle University of Thessaloniki, GR-54124, Greece

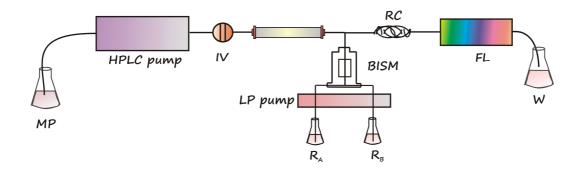
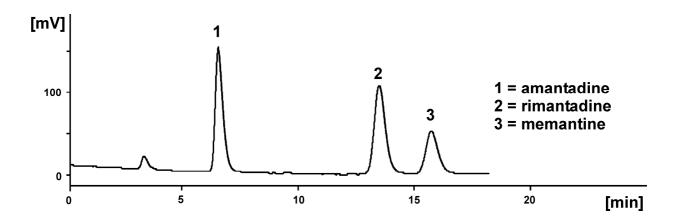


Figure S1. Schematic diagram of the HPLC-PCD setup: MP = mobile phase [50:50 v/v CH<sub>3</sub>OH:NaH<sub>2</sub>PO<sub>4</sub> (25 mmol L<sup>-1</sup>, pH = 3.0)]; IV = autosampler ( $V = 50 \mu L$ ); C = HPLC column (Prevail C18, 100 × 4.6 mm i.d.); BISM = Binary Inlet Static Mixer; LP pump = low-pressure pump; RC = knotted reaction coil (100 cm / 0.5 mm i.d.); PP = peristaltic pump; R<sub>A</sub> = OPA ( $c = 20 \text{ mmol L}^{-1}$ ,  $Q_V = 0.2 \text{ mL min}^{-1}$ ); R<sub>B</sub> = NAC (5 mmol L<sup>-1</sup>) / borate buffer (100 mmol L<sup>-1</sup>, pH = 11.0,  $Q_V = 0.2 \text{ mL min}^{-1}$ ); FL = Fluorescence detector ( $\lambda_{ex}/\lambda_{em} = 340 / 455 \text{ nm}$ ).

**Figure S2.** Reaction between OPA and the studied adamantine derivatives using N-acetylcysteine (NAC) as nucleophilic reagent; AMA = amantadine, RIM = rimantadine, MEM = memantine.



**Figure S3.** Representative chromatogram from standard mixture of the adamantane derivatives by the corroborative HPLC-PCD method; for experimental details please see sections 2.1 and 2.5.

**Table S1**. ZF sequence for the automated determination of adamantane derivatives.

| a/a | Time<br>( <i>s</i> ) | Valve position | Pump<br>action | Flow rate<br>(mL min <sup>-1</sup> ) | Volume<br>(μL) | Action description                                 |
|-----|----------------------|----------------|----------------|--------------------------------------|----------------|--|
| 1   | 1                    | 2              | Off            | _                                    | -              | Selection of NAC/Buffer port                       |
| 2   | 7.5                  | 2              | Aspirate       | 0.6                                  | 75             | Aspiration of NAC/Buffer in the HC                 |
| 3   | 1                    | 3              | Off            | _                                    | -              | Selection of OPA port                              |
| 4   | 5                    | 3              | Aspirate       | 0.6                                  | 50             | Aspiration of OPA in the HC                        |
| 5   | 1                    | 1              | Off            | _                                    | -              | Selection of sample port                           |
| 6   | 10                   | 1              | Aspirate       | 0.6                                  | 100            | Aspiration of sample in the HC                     |
| 7   | 1                    | 4              | Off            | _                                    | -              | Selection of FL detector port                      |
| 8   | 30                   | 4              | Deliver        | 0.6                                  | 300            | Deliver of the reaction mixture to the RC          |
| 9   | 60                   | 4              | Off            | _                                    | -              | Stop-flow to proceed the reaction                  |
| 10  | 120                  | 4              | Deliver        | 0.6                                  | 600            | Deliver of the reaction mixture to the FL detector |