Supporting Information for "Just-dip-it (Potentiometric ion-selective electrode); an innovative way of greening analytical chemistry"

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Introduction:

Ipratropium bromide (IP), 8-azoniabicyclo [3,2,1]-octane-3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl) bromide monohydrate, is a synthetic quaternary ammonium anti-cholinergic drug[1-2]. It is administered by inhalation as a bronchodilator in the treatment of chronic reversible airways obstruction, particularly in asthma and chronic bronchitis[3]. It was developed to reduce the occurrence of side effects associated with systemic absorption from such compounds as atropine. As a result of its polar nature, ipratropium bromide is poorly absorbed across lipid membranes. Therefore, it does not easily enter the systemic circulation or the central nervous system[3].

A literature review revealed that IP was determined in dosage form using HPLC with UV detection[4-5], HPLC/MS[6], CE/MS[7], radio-receptor assay [8-9], non-aqueous titration[10], kinetic and first derivative spectrophotometry[11].

One ion-selective electrode has been reported for the determination of IP using a precipitation-based technique with Na tetraphenylborate as a cationic exchanger without the incorporation of ionophores[12]. However, these electrodes were plagued by limited selectivity and did not examine the major degradation product of IP, tropic acid. Their selectivity coefficients were only tested for a few organic and inorganic cations.

Chemicals and reagents

Polyvinyl chloride (PVC) and 2-nitrophenyl octyl ether (NPOE) were obtained from Fluka Chemie GmbH (St. Louis, MO, USA), and tetrahydrofuran (THF) was obtained from BDH (Poole, England). Britton–Robinson buffer (BRB) (pH 2.0–12.0) was prepared by mixing

pre-calculated volumes of 0.04 mol L^{-1} acetic acid, 0.04 mol L^{-1} phosphoric acid, 0.04 mol L^{-1} boric acid and 0.2 mol L^{-1} sodium hydroxide.

Preparation of degradation product

A degraded sample of IP was prepared by adding 10 mL of NaOH (0.1 mol L^{-1}) to 10.0 mL of drug solution (10 mmol L^{-1}) and refluxing for 10 min. The resulting solution was tested for complete degradation by HPLC using a mobile phase of 20:80 acetonitrile : potassium phosphate buffer (100.0 mM, pH 4.0) as reported previously[5]. The degraded solution was neutralized, transferred quantitatively into a 100-mL volumetric flask and brought to volume with deionised water.

ISE characteristics using *CX6* as a sensing ionophore

The most important property of calixarenes (nano-baskets) is their ability to form supramolecular (inclusion) complexes with many appropriately sized organic ions and molecules, where the driving forces for this complexation are directed hydrogen bonding and cation–π-interactions (electrostatic attraction between the positive charge of the guest and the electron rich faces of the aromatic rings of the phenol units)[13-14].

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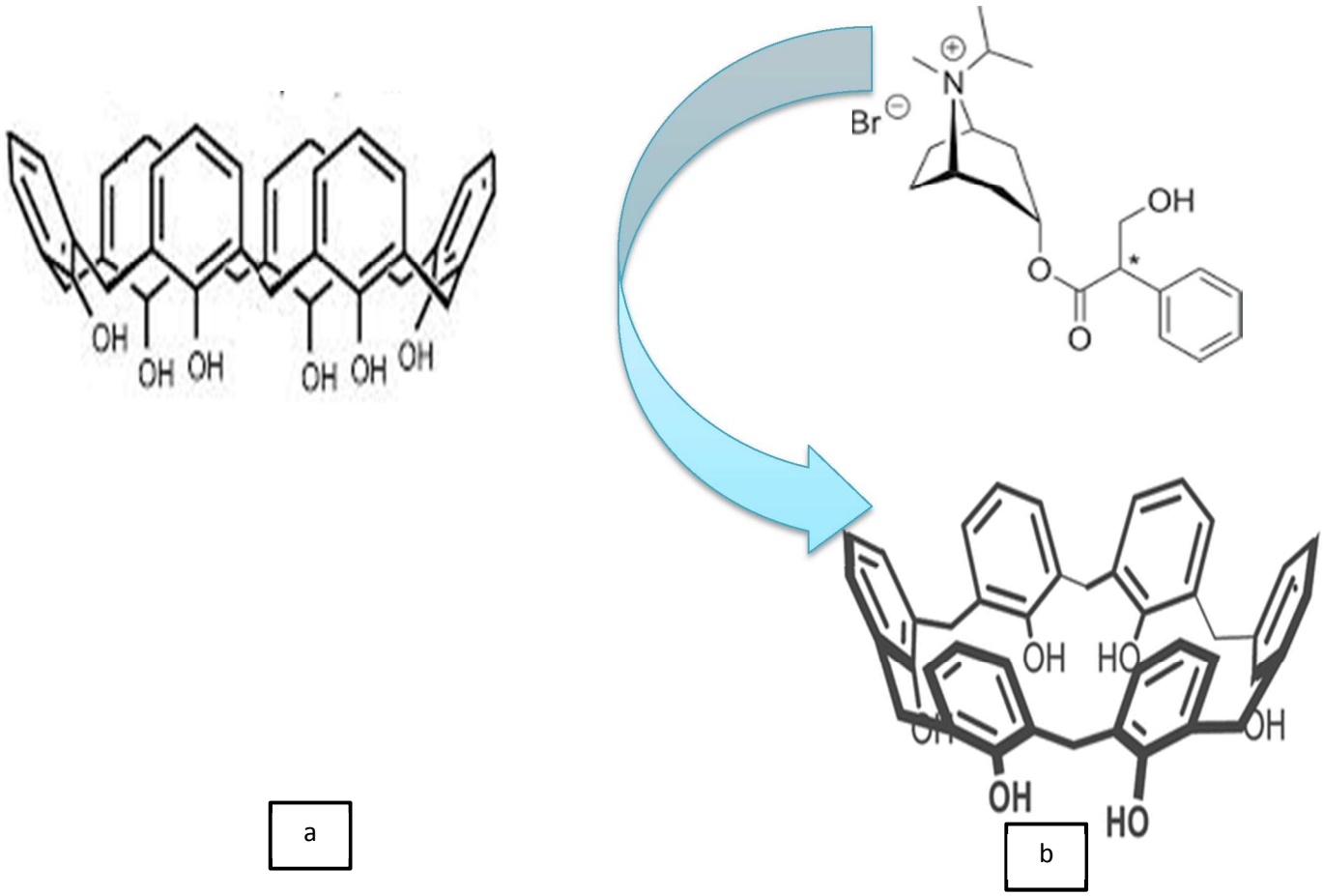

Figure S1. (a) Chemical structure of the calix[6]arene molecule. (b) Mode of attachment between IP and the ionophore (calix[6]arene)

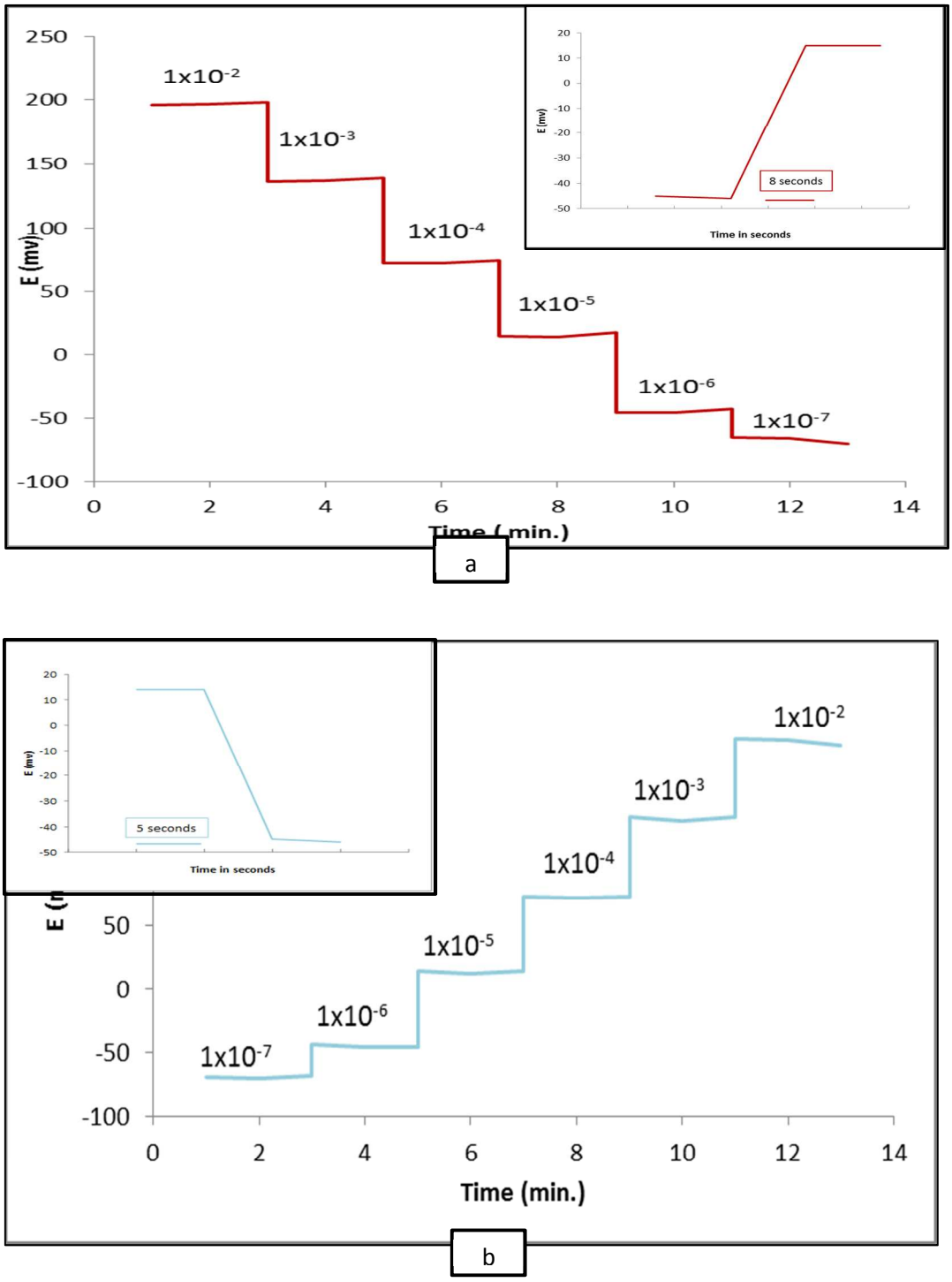

Figure S2. Dynamic response time and reversibility of sensor 2 by changing IP concentration in steps of 1 order of magnitude in the 10^{-7}–10^{-2} M range, a) from the uppermost concentration to the lowermost one, b) from the lowermost concentration to the uppermost one.

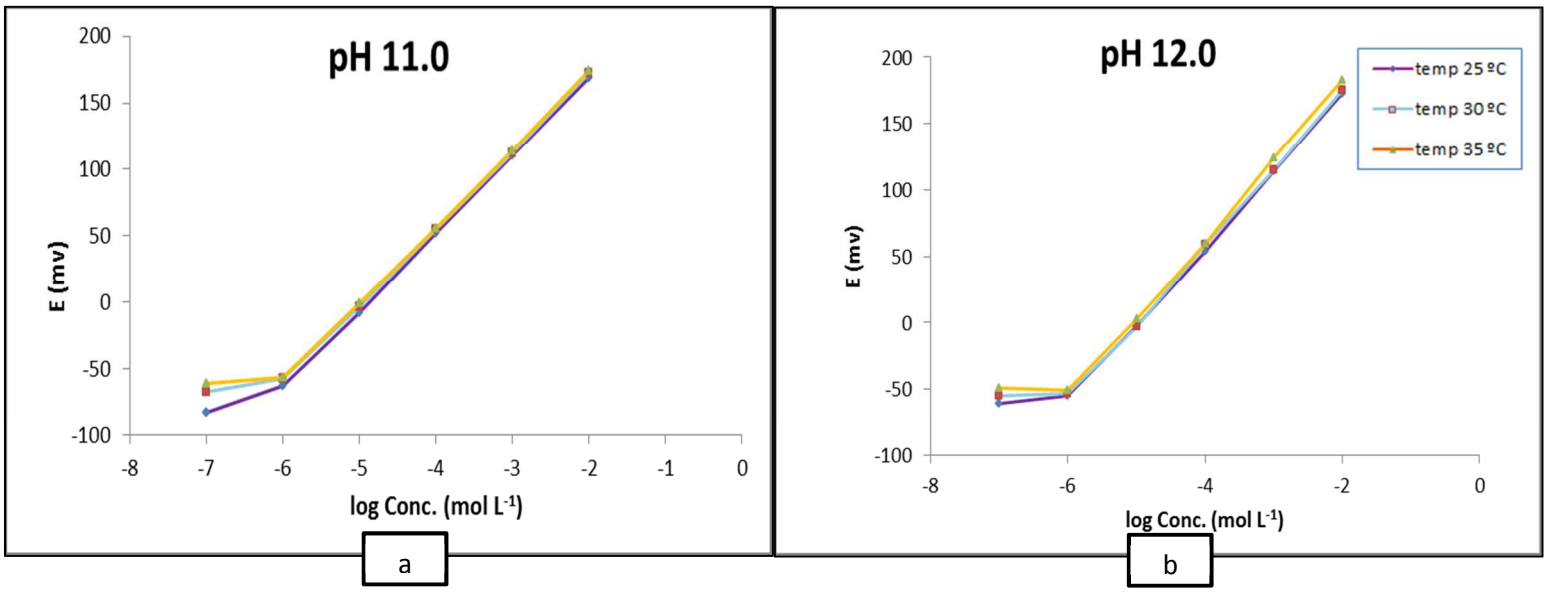

Figure S3. Profile of the potential in mV versus log concentration of IP (a) at pH 11.0 (b) at pH 12.0 at different temperatures.

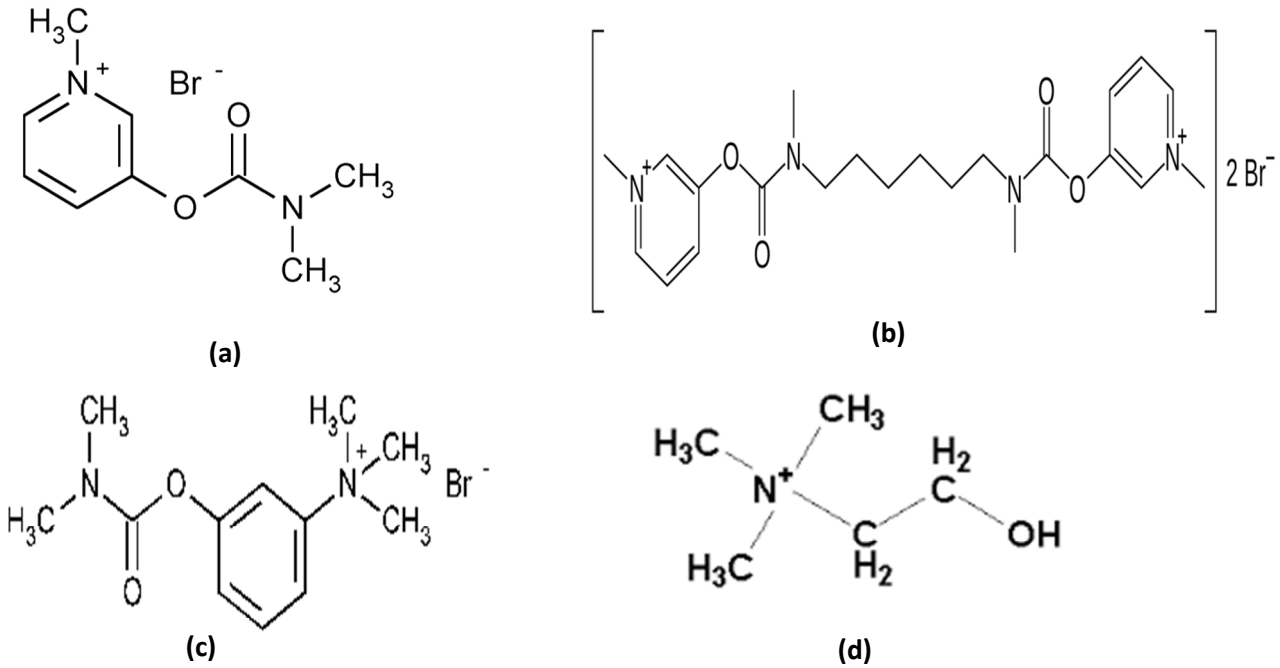

Figure S4. Chemical structure of (a) pyridostigmine bromide, (b) distigmine bromide, (c) neostigmine bromide and (d) choline.

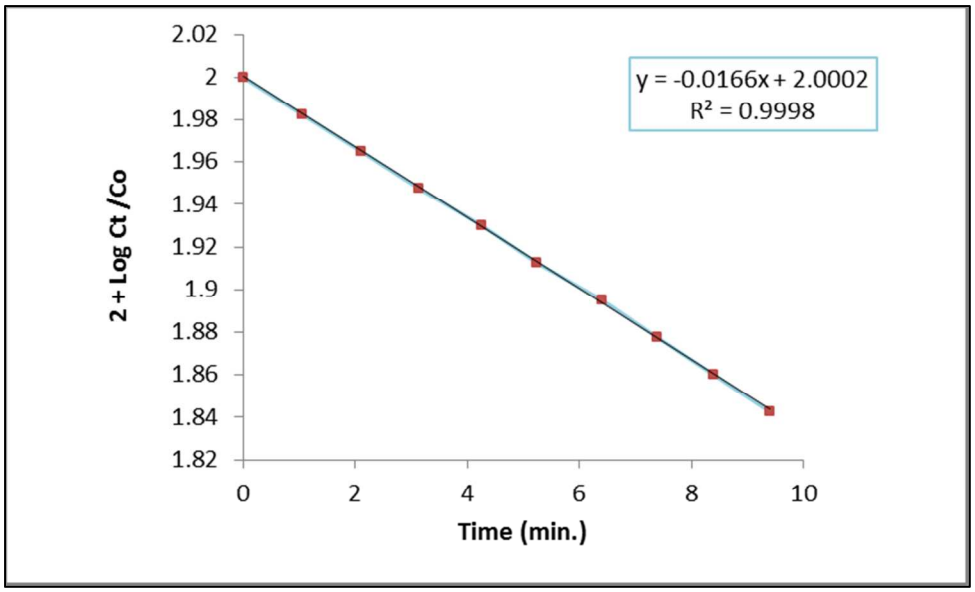

Figure S5. First order plot of the hydrolysis of IP (1 mmol L^{-1}) with a BRB of pH 12.0 at temperature 25 ºC using ISE.

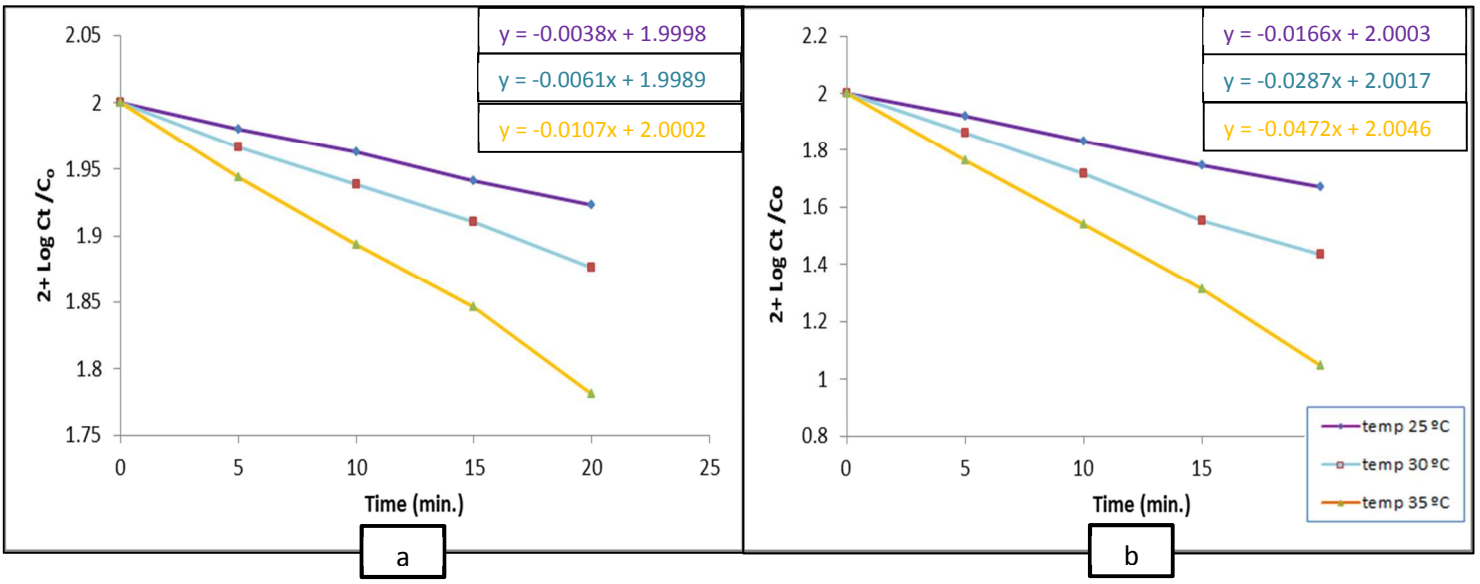

Figure S6**.** First order plots of the hydrolysis of IP with BRB of pH (a) 11.0, (b) 12.0 at different temperatures using HPLC.

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