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Solid support counts: towards development of all-solid state sensor for ketoprofen

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Summary:
The properties of all-solid-state optical sensors based on the polyamine receptors PP-1 and PP-2 bearing pyrene fluorogenic groups able to signal selective ketoprofen, KP, binding through the enhancement of the fluorescence emission have been investigated. The series of PVC polymeric membranes, plasticized with different plasticizers and doped with fully protonated PP-2 ligand, together with TDACl or TDMACl anion exchanger in 1:1, 1:2 and 1:3eq. ratio was studied in order to tune the highest selectivity toward KP. The appropriate choice of a solid support, selecting from cellulose-based or glass materials, influences significantly the performance of sensor. The fluorescent intensity of developed optical sensors increased with KP concentration growth. The images of sensors were acquired with smartphone and digitalized with a free on-line software of image processing in order to construct calibration model. Developed chemical sensors have shown the possibility to detect KP in the concentration range 2 μM – 0.1mM, with low influence of several interfering ions of the similar structure, such as naproxen, ibuprofen and benzoate. All-solid state sensor on paper support was successfully applied for KP assessment in pharmaceutical composition OkiTask with RSD of 2.1% and recoveries in range 98-102%.

Keywords: all-solid-state fluorimetric sensors, ketoprofen, polyamine bis-pyrene receptors, pharmaceutical analysis.

Background, Motivation and Objective

The ketoprofen (KF) main action is an inhibition of prostaglandin synthesis with cyclooxygenase enzyme, that make it an effective against acute and chronic pain courses [1]. KF has been recently recognized as an emerging contaminant with high environmental impact due to its chemical stability, lack of efficient methodologies for removal from waste, and widespread consumption [2]. Hence, rapid and effective detection of KF is an actual analytical task. The chemical sensors are an effective alternative to the tedious and time-consuming standard instrumental analysis, like HPLC-MS, recommended for KF detection. Previously several types of chemical sensors and multisensor systems for KF were reported [3-7]; among them optical sensors are the most attractive since they do not require sophisticated hardware, can be wireless and their output may be estimated with common optoelectronic devices or simply through 'naked-eye' observation. Also, a fast response time, acceptable sensitivity, and selectivity, together with low cost and easiness in handling make optical sensors very requested.

In this work, 6 sensing materials were prepared by incorporating 1 wt% of PP-1 ligand and 1- 5 wt% of TDACl or TDMACl anion-exchangers inside plasticized PVC membranes, Table 1. The membrane cocktails in THF were then treated with TFA in order fully protonate fluorophore in membrane phase and to tune optical response towards KP. The 2 μl of each sensing membrane were deposited on different solid supports (glass, filter paper or cellulose fiber used as color catcher material in laundry). The performance of the obtained sensing platform in recognizing KP and interfering anions as NS^-, IB^-, $Benz^-$, ClO_4^-, SCN^-, as well as Cu^{2+} and Zn^{2+} cations was examined. For this, 5 μl of tested solution were dropped over the prepared sensing sports, the image of overall sensing platform, containing from 6 to 11 sensing spots with deposited on them solutions of KP in concentration range 2 μM – 0.1mM, and/or interfering ions was registered with a smartphone and digitalized with a free on-line software ImageJ [8] in order to construct calibration curve in co-ordinates luminescence intensity vs log[KP].

Results

The chemical structures of novel polyamine receptors PP-1 and PP-2 bearing pyrene fluorogenic groups are shown in Figure 1A. As it was previously reported, the protonated PP-1 receptor in 0.005 M TRIS-HCl/EtOH solutions (1:1 vol/vol, pH = 7), shows a significant increase of fluorescence intensity at λ_{ex} =360nm and upon titration with KP^- ions due to the inhibition of the photoinduced electron transfer (PET) process between the non protonated amines and the pyrene units in receptor structure [9].

Table 1. Composition of tested polymeric membranes, doped with 1 wt% of PP-2.

N	Plasticizer	PP-1:TDACl, mol : mol	TFA, eq.
Mb1*	TOP	1 : 0.7	-
Mb1	TOP	1 : 0.7	3 eq
Mb2	DOS	1 : 0.7	3 eq
Mb3	DOS	1 : 0.7	-
Mb4	DOS	1 : 1.5	3 eq
Mb5	DOS	1 : 2.8	3 eq

Fig. 1. (a) Chemical structures of KP-H, PP-1 and PP-2; (b) the photogram of PP-2-based all-solid-state optodes deposited on glass support; (c) the photogram and (d) relative luminescence intensity of membrane Mb5 deposited on filter paper support for 40 μM KP and different interfering ions the extracted from (c). λ_{ex} =360nm

Through addition of trifluoroacetic acid, TFA, in polymeric membranes Mb1, Mb2, Mb4 and Mb5, in 1:1 ratio in respect to PP-1 amount, the protonated (on -NH groups) form of fluorophore was obtained. These membranes were deposited on solid support (glass or paper) and their response towards KP and selectivity properties were studied, Figure 1c,d. The optimized all-solid-state optodes have shown the linear increase of fluorescence intensity upon illumination at 365 nm in presence of KP in the concentration range 2 μM – 0.1mM, and few influence of all tested interfering ions, Figure 1d. The membrane Mb5 based on fully protonated PP-2 ligand, with TDMACl anion exchanger in ratio 1:3 eq. in respect to fluorophore, and plasticized with DOS plasticizer, had the best optical response, and was applied for KP assessment in pharmaceutical composition OkiTask with RSD of 2.1% and recoveries in range 98-102%.

The detailed discussion on all-solid-state optodes selectivity evaluations, influence of solid support material and the applications for ketoprofen assessment in real samples as waste waters and biological samples (urine of patients in treatment several hours after KP assuming) will be illustrated in our presentation.

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