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Spectroscopic evidence of xanthine compounds fluorescence quenching effect on water-soluble porphyrins

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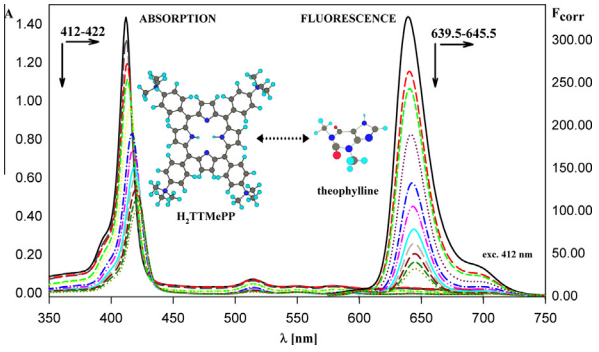
HIGHLIGHTS

- Association of water soluble porphyrins and chlorophyll with xanthine compounds have been studied.
- Xanthine compounds interact with porphyrins, quenching their emission.
- Fluorescence quenching effect is of static nature, accompanied by the additional specific binding interactions.
- The association and fluorescence quenching constants were calculated.

GRAPHICAL ABSTRACT



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ABSTRACT

The formation of π-stacked complexes between water-soluble porphyrins: 4,4′,4″,4‴-(21*H*,23*H*-porphine-5,10,15,20-tetrayl)tetrakis-(benzoic acid) (H_2TCPP), 5,10,15,20-tetrakis(4-sulfonatophenyl)-21*H*,23*H*-porphine (H_2TPPS_4), 5,10,15,20-tetrakis[4-(trimethylammonio)phenyl]-21*H*,23*H*-porphine tetra-*p*-tosylate (H_2TTMePP), 5,10,15,20-tetrakis(1-methyl-4-pyridyl)-21*H*,23*H*-porphine tetra-*p*-tosylate (H_2TMePyP), the Cu(II) complexes of H_2TTMePP and H_2TMePyP, as well as chlorophyll a with xanthine, theophylline (1,3-dimethylxanthine) and theobromine (3,7-dimethylxanthine) has been studied analysing their absorption and steady-state fluorescence spectra in aqueous (or acetone in case of chlorophyll a) solution. During titration by the compounds from xanthine group the bathochromic effect in the porphyrin absorption spectra as well as the hypochromicity of the porphyrin Soret maximum can be noticed. The fluorescence quenching effect observed during interactions in the systems examined suggests the process of static quenching. The association and fluorescence quenching constants are of the order of magnitude of $10^3 - 10^2$ mol^{-1}. The results obtained show that xanthine and its derivatives can quench the fluorescence of the porphyrins according to the number of methyl groups in the molecule of quencher.

Introduction

One of the increasingly popular objects of study in contemporary chemistry is the physicochemical behaviour of biologically active substances with curative properties. The example of such compounds are xanthine (XT) and its methyl derivatives: caffeine (1,3,7-trimethylxanthine, CF), theophylline (1,3-dimethylxanthine, TP) and theobromine (3,7-dimethylxanthine, TB), which are generally used as the components of many anaesthetic, anti-fever or dietary, as well as diuretic and vasodilatory drugs (Fig. 1a). Although it is just the caffeine which is the most popular drug and simultaneously the subject of study, the other xanthines equally deserve consideration. Both theophylline and theobromine, like caffeine, come from the natural sources – TP can be found primarily in tea

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leaves, whereas TB is present in cocoa beans, cola nuts, coffee beans and tea leaves [1]. Much foods and beverages, such as tea, coffee, Yerba mate and chocolate products, contain them as well [2]. TP and TB play an important role in improvement of blood circulation, contributing to the relaxation of smooth muscles and expansion of coronary artery [1,3], what is particularly useful for the treatment of bronchial asthma, chronic obstructive pulmonary disease and neonatal apnoea [4–6]. Both substances take part in the regulation of lipid metabolism and in the process of diuresis [7]. Medicinal significance of TP and TB is comparable with the importance of caffeine-containing drugs, but their usefulness is often limited by their poor solubility in water [5].

Methylxanthines (MXT) (especially caffeine) are presumably the most frequently consumed biologically active substances worldwide and the gigantic consumption of these compounds means simultaneously the similar order of sewage production. Caffeine is usually well-metabolized by human organism, initially just into TB, TP and paraxanthine (1,7-dimethylxanthine), which in turn are metabolized by xanthine oxidase to 1-methylxanthine and 1-methyluric acid [8]. Whereas XT is oxidised by xanthine oxidase to uric acid. After consumption by people the products containing both CF as well as TP and TB, these substances are excreted in different degree of metabolizing to domestic sewages and both inland and sea waters, where they can influence the conditions of environment [9].

It was previously demonstrated that methylxanthines, through the process of hetero-association, can form stacking non-covalent complexes with several aromatic compounds, like anticancer drugs [10,11], fluorescence dyes [12–16], mutagens [17,18], neurotoxins [19,20] and others [21,22]. Such behaviour confirms the protective abilities of MXT against the cytostatic and cytotoxic effects of some aromatic molecules, e.g. polycyclic aromatic hydrocarbons (PAH) or acridine mutagens, by reduction of their mutagenic activity in the aftermath of their diminishing bioavailability [1,2,10]. Formation of complexes between MTX and aromatic drugs may diminish temporally the concentration of free drug molecules available for the cells [10], what may be used to reduce some side effects associated with the high local concentrations of these drugs in the initial phase of their administration. Long-term consumption of MXT might protect as well against development of gout, the disease resulting from the elevated level of uric acid in human blood [23].

Therefore xanthine and its methyl derivatives form an interesting class of compounds for examining the effect of the nature and position of the substituents on their fluorescence quenching ability towards the different aromatic biologically active agents, e.g. bovine serum albumin (BSA) [24], human serum albumin (HSA) [4,25], lysozyme [7], trypsin [26], as well as acridine orange [2]. However, their interactions with water-soluble porphyrins have not been studied as yet (except the earlier work of the author [9]).

The water-soluble porphyrins are the group of macrocyclic organic molecules with the specific spectroscopic and redox properties, as well as the ability to electron transfer, very sensitive to the subtle changes of pH, porphyrins and ligands concentration or form of complexing with metal ions proceeding in a reaction environment. The representatives of the class of water-soluble porphyrins are the cationic porphyrins, which have the great ability to interact not only with DNA chain and its particular elements [27–34], but also with different kinds of biologically active compounds, like caffeine [9] and paraoxon [35], as well as with toxic metal ions [36]. Spectral analysis of such interactions plays a pivotal role in better understanding of organisms functioning, what is particularly useful from a therapeutic point of view, in identification of ligands with potential anticancer activity [37], in studies of telomerase inhibitors [37,38] or photodynamic diagnosis and therapy of cancer (PDT) [29–31]. It has been also reported that cationic porphyrins possess anti-prion properties [39,40]. Moreover, the water-soluble cationic porphyrins can be successfully applied in biomimetic catalysis [41–43] and designing of porphyrin-based electrochemical sensors [44].

The studies described in this paper were focused on the spectroscopic analysis of binding interactions between biologically important molecules. The primary objective of presented research was to specify the mechanism of interactions of the chosen compounds from the class of water-soluble porphyrins with xanthine, theophylline and theobromine and verify as well the usefulness of the porphyrins as chemical indicators of xanthine compounds. In previous work the methods of absorption and fluorescence quenching analysis proved to be a powerful tool to describe the conformational changes of porphyrins during their stacking interactions with cyclic organic compounds, such as nucleic bases [33], caffeine [9] and guanine [34]. Therefore to determine the xanthine compounds – porphyrins relations the absorption and steady-state fluorescence

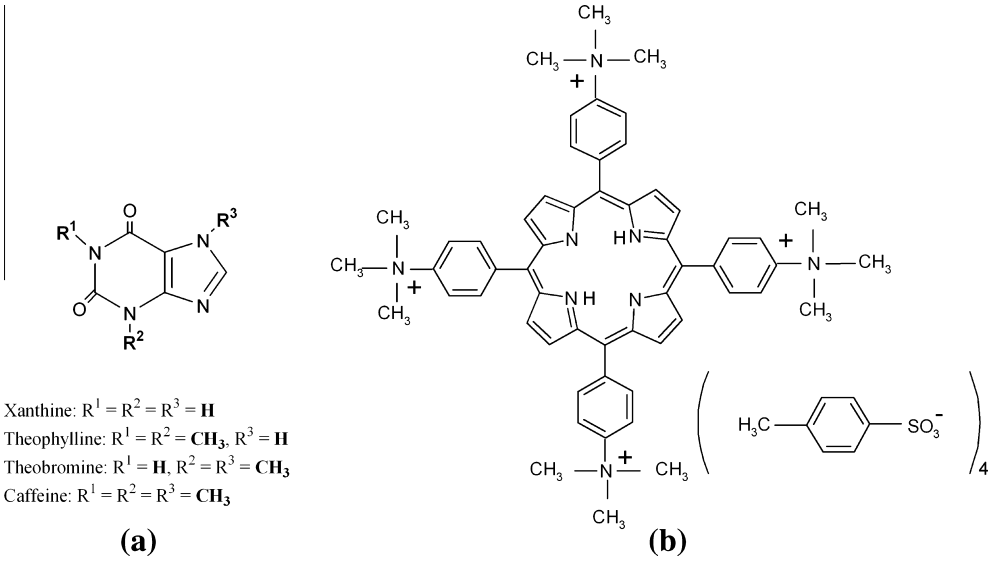

Fig. 1. The molecular structures of (a) xanthine compounds (xanthine, theophylline, theobromine, caffeine) and (b) H_2TTMePP (5,10,15,20-tetrakis[4-(trimethylammonio)phenyl]-21*H*,23*H*-porphine).