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Comparative study of binding interactions between porphyrin systems and aromatic compounds of biological importance by multiple spectroscopic techniques: A review

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ABSTRACT

The specific spectroscopic and redox properties of porphyrins predestine them to fulfill the role of sensors during interacting with different biologically active substances. Monitoring of binding interactions in the systems porphyrin-biologically active compound is a key question not only in the field of physiological functions of living organisms, but also in environmental protection, notably in the light of the rapidly growing drug consumption and concurrently the production of drug effluents. Not always beneficial action of drugs on natural porphyrin systems induces to further studies, with commercially available porphyrins as the model systems. Therefore the binding process between several water-soluble porphyrins and a series of biologically active compounds (e.g. caffeine, guanine, theophylline, theobromine, xanthine, uric acid) has been studied in different aqueous solutions analyzing their absorption and steady-state fluorescence spectra, the porphyrin fluorescence lifetimes and their quantum yields. The magnitude of the binding and fluorescence quenching constants values for particular quenchers decreases in a series: uric acid > guanine > caffeine > theophylline > theobromine > xanthine. In all the systems studied there are characters of static quenching, as a consequence of the π-π-stacked non-covalent and non-fluorescent complexes formation between porphyrins and interacting compounds, accompanied simultaneously by the additional specific binding interactions. The porphyrin fluorescence quenching can be explain by the photoinduced intermolecular electron transfer from aromatic compound to the center of the porphyrin molecule, playing the role of the binding site. Presented results can be valuable for designing of new fluorescent porphyrin chemosensors or monitoring of drug traces in aqueous solutions. The obtained outcomes have also the toxicological and medical importance, providing insight into the interactions of the water-soluble porphyrins with biologically active substances.

1. Introduction

Nowadays one of the most important ecological problems of humanity is growing pollution of the environment, which is the consequence of not only the industrial activity of humans, but is equally related to daily life of each of us. In recent times another group of pollutants has emerged, that is the different kinds of biologically active substances, which are often the components of drugs and pharmaceuticals, but also food and cosmetic products, as well as the wide spectrum of narcotics [1,2]. The gigantic intake or application of biologically active compounds, which are the ingredients of many preparations used for health and physical condition, means simultaneously the similar order of sewage production. Such products, which are currently ranked into so-called *emerging pollutants* (a new group of pollutants), are not involved in the regulations related to the examination of the quality of inland and sea waters [3]. Regretfully, the literature data indicate that the biologically active substances implicit in the pharmaceutical products are fairly resistant to the conventional methods of sewage treatment – even after the application of the standard methods of water treatment such substances can be detected at the sewage influx, in surface or ground waters, or in potable water. Although the pharmaceutical products occur in waters mentioned above at low concentrations (ng/L), their amount in surface waters is constantly growing [4]. The concentrations of these substances determined in surface waters are not regarded so far as the deadly threat for water organisms, but it is worth remembering that the long-standing exposure to such substances during the key stages of the developmental cycle of many organisms, as well as the probability of the synergistic activity of the mixture of the pharmaceutical substances and their metabolites with other pollutants, can bring about serious consequences for water and terrestrial ecosystems [5]. Therefore the subject of monitoring and purification of water from the residues of drugs and their metabolites, or other products containing the biologically active substances, is another problem needing solution.

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Based on the scientific literature there is no doubt that the ideal candidates for the role of sensors in different kinds of reactions with the participation of the aromatic biologically active substances are the water-soluble porphyrin systems. The characteristic porphyrins properties, as well as the variety of their applications, define this class of compounds as a very popular and desirable object of research. To demonstrate the validity of this thesis the mechanism of interactions proceeding between the chosen porphyrin systems and biologically active compounds was studied, using the proper spectroscopic techniques. Therefore the paramount goal of the investigations described in this review was to present the utility of the water-soluble porphyrins, and notably the cationic porphyrins, for monitoring of the chosen class of biologically active substances – the bicyclic aromatic compounds, in water environment and select the best model system for such type of investigations [6–10]. The second intention was to confirm the thesis that the determination of the mechanism of non-covalent association interactions in the systems containing the porphyrin structures is of great importance, both in the environmental protection and medical aspects.

2. Biologically Active Substances

Biologically active substances obtained usually from plants, or being the constituents of human or animal body, are very important group of ingredients of a wide choice of medicines, dietary supplements, drugs, cosmetic products or dyes. Both their structure and physicochemical properties are the popular subject of research in contemporary science [11–17]. Among the different biologically active substances, the bicyclic aromatic compounds are especially worthy of note, due to their accessibility, a wide spectrum of applications or a pivotal, often beneficial role in human organism functioning [18–24]. Since in the research discussed hereafter a series of methylxanthine compounds was used, the brief characteristics of chosen substances from this class of compounds were introduced below.

2.1. Caffeine

Caffeine (1,3,7-trimethylxanthine) is one of the most popular stimulants worldwide, consumed by humans not only as drugs or dopes, but primarily as the ingredient of common drinks, including coffee, tea, cocoa and coke. This compound is as well a component of many anesthetic, anti-fever or dietary medicines. In all products containing caffeine this compound occurs in the form of solution or water mixture [6,9]. Caffeine consumed in reasonable amounts is beneficial for human organisms – except for the stimulating effects, it presents as well an anticancer activity [25]. However, the caffeine overuse is not only the reason of the disturbances in blood circulation or nervous systems, leading to *caffeinism* [26,27], but excreted with urine from human body, caffeine is the next source of pollutants, because it is not easy to eliminate this substance from sewage [1]. Although caffeine is usually well-metabolized by human organism, its presence in inland and sea waters is constantly growing, particularly in the vicinity of inhabited areas. It was found that the caffeine content in waters is relatively well correlated to *fecal coliform bacteria* and could be potentially used as a chemical indicator of the level of contamination by sanitary sources and thereby could play a role of *an anthropogenic marker* [28]. Growing amounts of caffeine and its metabolites in waters can have an adverse influence on the environment, leading to the earlier senescence of plants [29], or disturbances in photosynthesis process by decreasing of the chlorophyll *a*ctivity [30]. Therefore such situation creates the need for continued monitoring of caffeine level in water reservoirs.

2.2. Theophylline, theobromine and xanthine

Theophylline (1,3-dimethylxanthine), *theobromine* (3,7-dimethylxanthine) and *xanthine* (2,6-dihydroxypurine), coming primarily from the natural sources, including tea leaves, or coffee and cocoa beans, are the ingredients of many diuretic preparations, as well as drugs contributing to the relaxation of smooth muscles and expansion of coronary artery, what is particularly useful for the treatment of i.a. bronchial asthma or hypertension [9,31,32]. As it was found before, the methylxanthine compounds are able to interact with many organic substances playing the key functions in human organism, such as proteins or DNA, presenting concurrently the protective activity [33–43]. The interaction of methylxanthines with the systems mentioned above can hinder to a certain degree the accessibility of other intrusive compounds including polycyclic aromatic hydrocarbons (PAH) [44–46]. Long-lasting ingestion of the products with methylxanthine compounds can result as well in retardation of the gout development, the disease related to the elevated level of uric acid in blood [47].

2.3. Guanine

Guanine (2-amino-6-hydroxypurine) is one of the nucleic bases participating in the metabolism of nucleic acids, which is also associated with overproduction of uric acid, causing among other things arthritis, gout or lithiasis. Guanine is as well the exclusive additive to different cosmetic products (Uguisu mask [48]), as natural iridescent pearl essence, extracted from scales of some fishes [8,49].

2.4. Uric acid

Uric acid (2,6,8-trihydroxypurine), the final product of catabolism of the purine nucleosides in human system, plays the role of marker molecule for diseases related to alterations of the normal urate level in plasma and urine, such as lithiasis, gout, leukemia, renal impairment or cardiovascular diseases. Since the physiological level of uric acid of healthy humans is determined in the micromolar range in blood serum (between 120 and 450 mM), whereas in the pathological cases it can increase even up to 500 mM [50,51], the fast and precise determination of uric acid concentration is an urgent requirement for the correct diagnosis of many diseases [10,52].

It is well-known that the beneficial activity of biologically active compounds on humans is in certain situations disputable. The reasonable amounts of the drugs or dietary supplements, as well as the properly prescribed medicines have the pro-health activity. However, the overdosed drugs (or substances overproduced in human organism) excreted with urine are not only the further source of pollutants, but primarily they can result in different disorders in functioning of human organism. As the main route of transport of such substances in human organism is blood circulation system, there are its constituents responsible for this transport (such as blood proteins), which are directly subject to the conformational changes disturbing their physiological functions [53–57].

3. Porphyrin Compounds

Porphyrins belong to the group of naturally occurring macrocyclic compounds presenting the unique structure and physicochemical properties. The molecule of porphyrin is consisted of four pyrrole rings joined by methine bridges and forms the coupled system of double bonds, including 18 delocalized π electrons obeying the Hückel's rule ($4n + 2$, where $n = 4$). The pyrrole rings build up closed aromatic plane, playing the role of a nucleus of the compound. The flat porphyrin ring can be deformed in the process of metalation, protonation or dimerization, typical of this class of compounds. Due to the unique spectroscopic, magnetic, luminescence properties, and what is the most important, the ability of porphyrins to photoconduction and photoemission, the porphyrin compounds play a fundamental role in many processes occurring in nature. Natural porphyrins and their metal complexes, such as chlorophyll *a*nd hemoglobin, often called *the colors of life*, as well as myoglobin, cytochromes, peroxidases, bilirubin and cobalamin (vitamin B12) perform the pivotal biological functions in fauna