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Review

Analytical techniques for the determination of biologically active quinones in biological and environmental samples

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ABSTRACT

Quinones are compounds that have various characteristics such as biological electron transporter, therapeutic agent and harmful environmental pollutant. Therefore, an effective analytical method for quinones is useful in many fields including biomedical, clinical and toxicological studies. This review describes the principle and feature of analytical techniques for quinones including high-performance liquid chromatography with ultraviolet, fluorescence, chemiluminescence, electrochemical detection and mass spectrometry, gas chromatography with mass spectrometry and capillary electrophoresis. Furthermore, the sensitivity and the sample preparation method for the determination of several quinones such as vitamin K, ubiquinone, doxorubicin and polycyclic aromatic hydrocarbon quinone in biological and environmental samples are summarized.

Contents

1. Introduction

Quinones are interesting compounds which have unique characteristics and several important roles. Quinones are widely distributed in the nature including plant and animal tissues.

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Quinones have an important role in the electron transport chain to maintain biological functions of plants and animals. It is well known that plastoquinone is involved in the light-dependent photosynthetic reactions in plants. In the animal system, ubiquinone (UQ, other name for coenzyme Q_{10}(CoQ_{10})) acts as an electron carrier in the mitochondrial electron transport chain and participates in aerobic cellular respiration and energy production [1,2]. Also, quinone structures are related to some vitamins. Vitamin K is a structurally related group of 2-methyl-1,4-naphthoquinone derivatives having either a phytyl side chain (phylloquinone (PK), vitamin K_1), or a side chain with repeated isoprenoid units (menaquinones (MKs), vitamin K_2). It was known that vitamin K has a beneficial role in blood coagulation, bone metabolism and growth [3–5]. α-Tocopherol, known as vitamin E, is oxidized to tocopherylquinone during the process of antioxidation [6]. It is conceivable that tocopherylquinone concentrations may be increased under pathological conditions. Recently, it has been reported that pyrroloquinoline quinone is nutritionally important as a vitamin in mammals [7].

In addition to these biological roles, quinones have been used in a wide variety of clinical practice and industrial application. For example, doxorubicin (DXR) is an anthraquinone (AQ) antibiotic that has been used clinically in the treatment of malignant tumors [8]. AQ derivatives such as rhein, the principle active constituents of traditional Chinese herb rhubarb, have immunosuppressive and anti-inflammatory effects [9]. The structures of these AQ drug are shown in Fig. 1. Vitamin K is clinically applied for the treatment of several diseases including osteoporosis and vitamin K deficiency symptoms [5]. In addition, AQ derivatives are used as a large class of dyes and pigments [10].

While quinones have several beneficial effects mentioned above, they are regarded as a class of toxins which can cause a variety of hazardous effects on living cells. For example, quinones act as a generator of reactive oxygen species (ROS) through the redox cycle in biological system and ROS can induce several types of oxidative damage such as lipid peroxidation [11,12]. Additionally, some quinones such as 9,10-phenanthrenequinone (PQ) serve as an inhibitor of certain enzymes, for example, nitric oxide synthase or glyceraldehyde-3-phosphate dehydrogenase, by the covalent binding to the active site of enzymes [13,14]. In the atmospheric environment, the presence of polycyclic aromatic hydrocarbon quinone (PAHQ) including PQ was confirmed [15]. It was thought that PAHQs are formed by photo-oxidation of polycyclic aromatic hydrocarbons (PAHs) that are mainly released from motor vehicle engines in atmosphere (Fig. 2). PAHQ in atmospheric environment is considered to be involved in the pathogenesis of respiratory diseases [16].

From these aspects, the determination method of quinones in biological and environmental samples should be important in various fields including the investigation of physiological properties of quinone, therapeutic monitoring of quinone drugs and the estimation of risk of toxic quinones on human health. In this review, the principle and the feature of analytical techniques for biologically active quinones especially vitamin K, UQ, DXR and PAHQ are described according mainly to the recent reports. Furthermore, the sensitivity and the sample preparation procedure for the determination of these quinones in biological and environmental samples are summarized in tables.

2. Analytical techniques for quinones

Until now, various analytical methodologies have been developed for the determination of quinones. In the following section, the principle and the feature of analytical techniques for quinones are described.

2.1. High-performance liquid chromatography (HPLC)

Chromatographic separation is one of the techniques of choice for the analysis of various compounds in complicated matrices. Thus, HPLC is one of the most frequently used tools for the analysis of quinones in biological and environmental samples. Several detection techniques including ultraviolet (UV), fluorescence (FL), chemiluminescence (CL), electrochemical detection (ECD) and mass spectrometry (MS) have been coupled with HPLC analysis.

2.1.1. HPLC-UV

HPLC with UV detection method is most common and widespread due to its easy handling nature. Various HPLC-UV methods for quinones have been developed because most of quinones have absorbance at UV region [17–20]. However, the sensitivity of UV detection is insufficient to determine trace amount of quinones. Also, the selectivity of UV detection is generally low because co-existing UV-absorbing compounds can interfere with the detection of quinones. Even though the low sensitivity and selectivity, HPLC-UV has been frequently utilized for the simultaneous determination of quinones and other types of compounds owing to its universality. For example, vitamin K and UQ were determined with other fat soluble vitamins such as retinol (vitamin A) and α-tocopherol in biological fluids [17,18]. Also, simultaneous determination method for co-administered anticancer drugs including DXR and 5-fluorouracil was developed by HPLC-UV in order to explore the synergistic effects between these drugs [19].

2.1.2. HPLC-FL

Since FL detection is usually sensitive and selective than UV detection, a large number of chemicals were measured by HPLC with FL detection technique. Among quinones, AQ derivatives such as DXR and rhein have strong FL itself, thus these compounds were determined directly by HPLC-FL [21,22]. However, most of quinones do not have intrinsic FL. Therefore, several FL derivatization reactions were developed for the conversion of non- or weakly fluorescent quinone to strongly fluorescent derivative.

The most simple derivatization reaction is the reduction of quinone to fluorescent hydroquinone and this reaction has frequently been applied to determine vitamin K in biological samples by HPLC-FL. Vitamin K (NQ derivative) was reduced to corresponding hydronaphthoquinone and it was detected at excitation and emission wavelengths of 240 or 320 and 430 nm, respectively. Several chemical reductants such as sodium borohydride, zinc and platinum were used for the FL derivatization of vitamin K. Sodium borohydride solution was used as a post column derivatization reagent [23]. Zinc was usually packed in a stainless steal column and it was incorporated as an on-line reactor between an analytical column and a fluorescence detector [24]. A platinum catalyst reduction column was also used as an on-line reactor for the reduction of vitamin K [25] and it was known that the durability of platinum was higher than that of zinc. In addition to chemical reduction, electrochemical or photochemical reduction was also employed for the FL derivatization of vitamin K. In an HPLC system coupled with an on-line electrochemical reactor, vitamin K was reduced prior to fluorescence measurements by applying a negative voltage [26,27]. A photochemical reactor constructed of PTFE tubing coiled around a low-pressure mercury lamp could reduce vitamin K to hydronaphthoquinone in the presence of sodium dodecyl sulfate (SDS) and methanol [28]. The direct reductive derivatization reaction was also applied for quinones other than vitamin K. Pollok and Melchert developed an HPLC-FL system with on-line photoreactor for the determination of tocopherylquinones in human serum [29]. In this HPLC system, tocopherylquinones were reduced to corresponding tocopherylhydroquinone under UV irradiation and they were detected at 331 nm with an excitation at 294 nm. Also,