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Study on detection methods for 3, 4-dihydroxyphenylacetic acid in biological samples

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Abstract

3,4-Dihydroxyphenylacetic acid (DOPAC) is an important neurotransmitter molecule of catecholamine which is a major metabolite of dopamine that are widely distributed in the mammalian central nervous system. The neurotransmitter metabolites released into the cerebrospinal fluid can be a sensitive indicator of neuronal functioning in nearby diencephalon structures. Therefore, it is important to measure the metabolites level in the extracellular fluid in order to monitor neurotransmission process. A number of analytical methods have been developed to provide fast, sensitive, selective and reliable quantification for DOPAC in complex samples. In this article the studies of detection methods for DOPAC in recent years are reviewed.

Keywords: 3,4-Dihydroxyphenylacetic acid; DOPAC; neurotransmitter; determination; detection.

1. Introduction

3,4-dihydroxyphenylacetic acid (DOPAC), a water- and fat-soluble compound, is a major metabolite of dopamine (DA) which is an important neurotransmitter molecule of catecholamines which originate from a wide range of neural pathways by employing biogenic amines as neurotransmitters [1-3]. The dysfunction of the dopaminergic system is related to neurological disorders such as schizophrenia, epilepsy, Parkinson's, Alzheimer's diseases, HIV infection and retinal disease. Therefore, it is of great clinical importance to measure neurotransmitters and their metabolites level in the extracellular fluid in order to monitor neurotransmission process [4-6]. Up-to-now, different analytical methods with a high sensitivity and good selectivity have been developed for the detection of DOPAC in animal feeds, animal tissues and body liquids. In this paper, the attributes of different analytical technique for the determination of DOPAC in recent years are reviewed.

2. Analytical Methods

2.1. HPLC method. High-performance liquid chromatography (HPLC) is a powerful tool that enables the separation of complex mixtures into individual components, and is a highly sensitive and reproducible analytical technique. In recent years, HPLC has been combined with many sensitive detection techniques and has experienced continuous improvement of stationary phases, which have improved its sensitivity and specificity. HPLC is currently widely used for the analysis of drugs and dosage forms with respect to quality control, quantitative determination of active ingredients and impurities, monitoring drug blood concentration in patients, and bioequivalence assessment [7-9].

De Benedetto et al. [10] described a fast and simple isocratic HPLC method for the determination of DOPAC, norepinephrine, DA, and serotonin in homogenate samples of mouse striatum employing the direct fluorescence of the neurotransmitters. The analytes were separated on a reversed-phase column (C18) with acetate buffer–methanol as mobile phase in 15 min. The fluorescence measurements were carried out at 320 nm with excitation at 279 nm. The calibration curve for DA was linear up to about 2.5µg/ml, with a coefficient of determination of 0.9995 with a lower limit of

quantification of 0.031µg/ml. As a result, due to its simplicity, rapidity and adequate working range, the method could be used for the determination of DOPAC, DA, norepinephrine and serotonin in animal tissues.

Tsunoda et al. [11] established a sensitive and simultaneous determination method of DOPAC and homovanillic acid (HVA) using HPLC–fluorescence detection. This method adopted the column-switching system, which included an online extraction of carboxylic acids by a strong anion-exchange column followed by separation on an ODS column, coulometric oxidation, fluorogenic reaction with ethylenediamine, and fluorescence detection. The method was applicable to 50µl of rat kidney microdialysate with a sufficient accuracy and precision. The concentrations of DOPAC and HVA in rat kidney microdialysate were 131 ± 29 and 404 ± 44 nM, respectively.

Cummings et al. [12] described a HPLC method for the analysis of y-L-glutamyl-L-dihydroxyphenylalanine (gludopa) and its major metabolites L-dihydroxyphenylalanine (L-DOPA), DA and DOPAC. High sensitivity was achieved with a multi-cell coulometric detector utilizing the specific electrochemical properties of gludopa. The retention time of gludopa was both pH-dependent and sensitive to negatively charged ion-pairing agents. An alumina-based solid-phase sample preparation technique with dihydroxybenzylamine as internal standard was described for plasma and urine and an ultrafiltration technique was described for tissues. After treatment with 50 mg/kg gludopa, in excess of twenty separate catecholic metabolic peaks could be detected in rat urine, whereas in humans after 9 mg/kg the only catechols detected were L-DOPA, dopamine and DOPAC.

2.2. Electrochemical method. Since the early 70s electrochemistry has been used as a powerful analytical technique for monitoring electroactive species in living organisms. The biological activity of DOPAC was believed to be related to its redox chemistry, which made its electrochemical behavior in aqueous solution become the subject of recent studies. But the measurements were complicated due to the presence of possible interferences such as ascorbic acid (AA) and uric acid (UA), which oxidized at the same potential at bare electrode, which resulted in rather poor selectivity and sensitivity. In order to avoid these problems, chemically modified electrodes have been employed for the selective and stable determination of DOPAC. Numerous materials, such as metal nanoparticles, polymers, carbon nanotubes, graphenes, and enzymes, have been used as modifiers to construct highly sensitive and selective DOPAC biosensors [13-15].

Kalimuthu et al. [16] reported the highly sensitive and selective electrochemical determination of DOPAC using an ultrathin electropolymerized film of 5 - amino -1,3,4-thiadiazole-2-thiol (p-ATT) modified glassy carbon electrode (GCE) in 0.20M phosphate buffer solution. The p-ATT modified electrode not only separated the voltammetric signals of AA, DOPAC and UA, but also enhanced their peak currents. The amperometric current response was increased linearly with increasing DOPAC concentration in the range of 4.0×10^{-8} to 1.0×10^{-5} M and the detection limit was found to be 150pM.

Liu et al. [17] proposed a strategy for the preparation of tyrosinase biosensor to determine DA metabolite of DOPAC. They successfully used an amino-polysaccharide chitosan as matrix to entrap tyrosinase on GCE surface on basis of tyrosinase conjugated with chitosan. The sensor was operated at -0.15V. The current linearly increased with the increasing concentration of DOPAC over the concentration of 6 nM to 0.2 mM. The sensor could be used to selectively determine nanomolar DOPAC in the presence of physiological level of AA, UA, acetaminophen, neurotransmitters including DA, L-dopa, adrenaline and noradrenaline.

Raj et al. [18] synthesized 4-(Dimethylamino)pyridine capped gold nanoparticles (DMAP-AuNPs) in aqueous medium and then immobilized them on 1,6-hexanedithiol modified Au electrode for the selective determination of DOPAC in the presence of AA. The current response was increased linearly with increasing AA and DOPAC in the concentration range of 4.0×10^{-9} to 1.0×10^{-5} M and a detection limit was found to be 5.6×10^{-10} M and 3.7×10^{-10} M for AA and DOPAC, respectively. The present modified electrode was also successfully used for the determination of 40 nM DOPAC in the presence of 2500-fold excess of common interferents such as Na^{+}, Mg^{2+}, Cu^{2+}, Ca^{2+}, NH^{4+} , urea and glucose.

2.3. Other methods. In addition to these main approaches mentioned above for DOPAC detection, still a few special techniques with high sensitivity have been applied. Drujan et al. [19] described a fluorometric method for the determination of urinary DOPAC and 3,4-dihydroxymandelie acid (DOMA). This method was based on ethyl acetate extraction, electrophoretic separation, and conversion of these compounds to highly fluorescent ethylenediamine condensation products and measurement of the fluorescent intensity. Duncan et al. [20] developed a gas chromatographic/mass spectrometric methodology for simultaneous assay of salsolinol, DA, Norepinephrine, DOPAC and Dihydroxyphenylethanol.

3. Conclusions

The DA metabolism can be assessed in the prefrontal cortex by measuring the extracellular levels of DOPAC. Therefore, the concentration of DOPAC is a sensitive indicator for neuronal functioning in nearby diencephalons structures. Usually, DOPAC exists as very low concentration along with AA and UA in blood

serum and urine. Thus, the selective and sensitive determination of DOPAC is very important not only in the fields of biomedical chemistry and neurochemistry but also for diagnostic and pathological research [21]. This review has highlighted the significant developments in rapid and alternative techniques for the detection of DOPAC in recent years. New developed methods with better sensitivity and specificity, along with more simplicity and lower cost is still the future direction.

Acknowledgments

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