Nanoscale carbon-based materials in protein isolation and preconcentration

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This review provides an overview of the current research on nanoscale carbon-based materials as new adsorption materials in the isolation and preconcentration of protein species from biological sample matrices for ensuing bioscience investigations, or achieving enrichment prior to detection. In addition, we discuss future perspectives in related research fields.

Keywords: Adsorption; Biological; Carbon nanomaterial; Detection; Enrichment; Isolation; Nanoscale; Preconcentration; Protein; Sample pretreatment

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1. Introduction

Nanoscale carbon-based materials have gained extensive attention in various fields of research because of their attractive physical and chemical properties, including low cost, diversity of morphologies (powders, fibers, sheets, tubes and composites) which facilitate processing into desired devices, and relatively inert electrochemistry. It is worth mentioning that the huge surface/volume ratio and tunable surface properties of these materials have enabled their wide applications as powerful sorbents in the sample pretreatment process, especially the isolation and preconcentration of trace level of proteins of interest.

Proteomics analysis is a very attractive area for design and optimization of bioprocesses, and the acquisition of high-purity proteins is the primary basis for successful, comprehensive understanding of protein functions and regulations. Tissue specimens, cell suspensions, blood plasma and other body fluids are the most frequently used materials in proteomics analysis. This is due to the increasing interest in exploring the functional mechanisms of diverse protein species in these matrices, and the desire to obtain special functional protein product of high quality for clinical and therapeutic applications. These biological matrices are usually very complex, and might contain thousands of protein species in a very large range of concentrations. There is a wide range of cellular protein species, which can be as great as six orders of magnitude between the most abundant and the least abundant proteins in cells or 10^{10}–10^{12}-fold for biological fluids (e.g., plasma) [1,2]. Although there have recently been great achievements in identifying abundant protein species, knowledge about low-abundance proteins is still a challenge for scientific research. For most biological systems, the absolute concentration limit of low-abundance proteins remains unknown. The ability to detect these trace proteins relies on the absolute minimum limits of detection (LODs) of current technologies. The detection of rare proteins below the detection threshold of these technologies may depend on further instrument improvements. Detection of low-abundance proteins is often masked by the presence of massive amounts of one or several proteins. Interference from other protein species needs to be eliminated prior to quantitative assay and applications where highly purified samples are needed. At this point, LOD and interference issues might be overcome by exploiting appropriate sample-pretreatment protocols, forcing samples to fall within the detection capabilities of the instruments to get a protein species with satisfactory purity.

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Solid-phase extraction (SPE) is one of the most widely-employed sample-pretreatment techniques that can be performed using off-line or on-line systems. SPE is generally simple and has the advantage of being easy to automate [3]. The retention of the analyte of interest on the appropriate solid sorbent and the ensuing elution process with suitable solvent contribute greatly to the desired results (i.e. elimination of potential interferences and contaminants, and preconcentration of analyte that improves the sensitivity of the determination method applied).

Sorbent materials used in SPE should fulfill the requirements for performance of analysis (e.g., satisfactory selectivity, appropriate affinity and sorption capacity). The discoveries of new materials and their applications have significant impact on the performance of pretreatment for sample matrices of different origins. On this point, the wide applications of carbon materials in sample processing by SPE have provided successful examples. Carbon materials comprise a wide range of allotropic forms of carbon, including diamond, fullerenes, single-walled carbon nanotubes (SWCNTs), multi-walled carbon nanotubes (MWCNTs), carbon onion and graphene/graphene oxide (G/GO), due to the mutable hybridization states, as illustrated in Fig. 1 [4]. Use of these carbon materials in SPE is among the most important applications due to their attractive physical and chemical properties (e.g., establishment of π-π interactions and Van der Waals interactions with other molecules, large surface area, favorable chemical and thermal stability, and ease of surface functionalization or modification). The applications of carbon materials in the isolation and preconcentration of organic and inorganic species have been reviewed [5–7].

The aim of this work is therefore to provide an updated critical review of the most important features and applications of nanoscale carbon materials, including carbon nanofiber, nanodiamond (ND), fullerenes, CNTs and G/GO, as powerful SPE materials in the isolation and preconcentration of protein species. We emphasize description of the different works that have provided interesting results in obtaining protein of high purity from complex biological sample matrices or achieving a certain extent of enrichment prior to MS and spectroscopic detection. We expect this review article to inspire broader interests across various disciplines and to promote further investigations in this promising field of research. In this respect, we describe future perspectives in the related research fields.

2. Carbon nanofiber

Carbon fibers are fibrous carbon materials with a micro graphite crystal structure. They are classified by the source materials (e.g., rayon, polyacrylonitrile and pitch). Carbon nanofiber (CNF), like other one-dimensional nanostructure (e.g., nanowires and nanotubes), is recognized as one of the most promising materials due to its large length-to-diameter ratio. This material is expected in various areas of applications. It can be used as catalyst or catalyst support, a selective adsorption agent for various target species and promising energy-storage device [8].

Nowadays, there is growing demand for the development of downstream purification approaches that are capable of separating large quantities of biotherapeutic proteins in a short period of time. Thus, new adsorption media with operating properties of high capacity and improved sample throughput are increasingly in great demand. Recently, CNF was demonstrated to be an excellent protein-adsorption medium with appropriate capacity [9]. After being functionalized by attaching carboxylic-acid groups, CNF becomes hydrophilic and shows an adsorption capacity of up to 200 mg/g for lysozyme, which is twice as high as that achieved by the

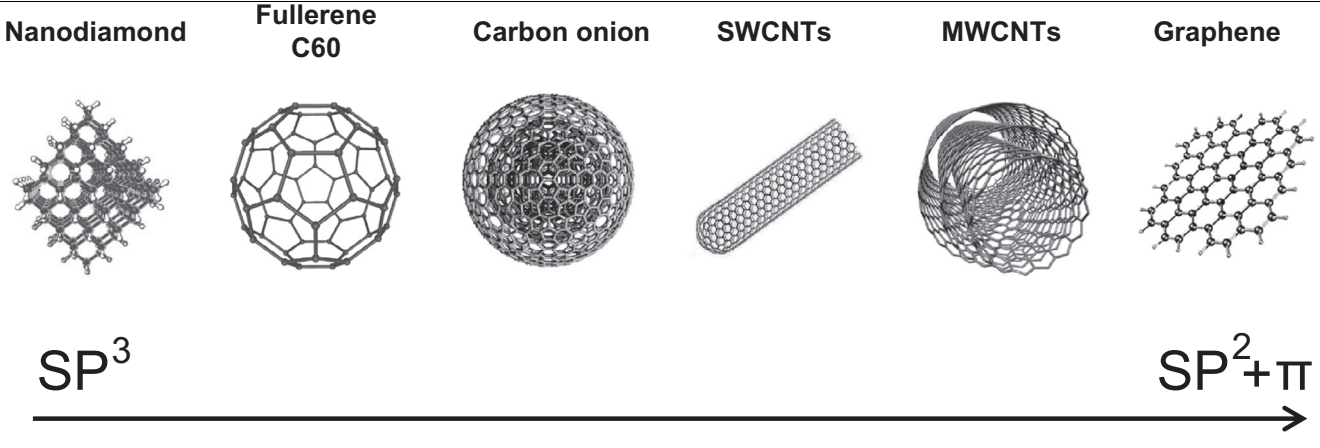

Figure 1. Hybridization states of nanoscale carbon-based materials (From [4] with permission).