Biochemical and Biophysical Research Communications 503 (2018) 3167–3173

Contents lists available at ScienceDirect

Biochemical and Biophysical Research Communications

journal homepage: www.elsevier.com/locate/ybbrc

Low doses of multi-walled carbon nanotubes elicit hepatotoxicity in rats with markers of oxidative stress and induction of pro-inflammatory cytokines

Isaac A. Adedara [a], Osemudiamen O. Anao [a], Gilead E. Forcados [a], Ifeoluwa O. Awogbindin [a], Agatha Agbowo [a], Olufunke E. Ola-Davies [b], Anita K. Patlolla [c], Paul B. Tchounwou [c], Ebenezer O. Farombi [a, *]

[a] Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, Ibadan, Nigeria
[b] Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[c] College of Science Engineering and Technology, NIH-RCMI Center for Environmental Health, Jackson State University, Jackson, MS, USA

ARTICLE INFO

Article history:
Received 13 August 2018
Accepted 17 August 2018
Available online 24 August 2018

Keywords:
Multiwalled carbon nanotubes
Liver damage
Cytokines
COX-2
i-NOS

ABSTRACT

The investigation into the potential health risks associated with the use of engineered nanoparticles is a major scientific interest in recent years. The present study elucidated the involvement of pro-inflammatory cytokines, cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) in carboxylated multi-walled carbon nanotubes (MWCNTs)-induced hepatotoxicity. Pubertal rats were exposed to purified MWCNTs at 0, 0.25, 0.50, 0.75 and 1.0 mg/kg for 5 consecutive days. Results indicated that exposure to MWCNTs caused liver damage evidenced by significant elevation in serum activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) when compared with control. Moreover, MWCNTs significantly decreased superoxide dismutase (SOD) and glutathione S-transferase (GST) activities as well as glutathione level whereas it significantly increased catalase (CAT) and glutathione peroxidase (GPx) activities in liver of the treated rats. Moreover, the dose-dependent increase in hepatic hydrogen peroxide (H_2O_2) and lipid peroxidation levels were accompanied by marked increase in micronucleated polychromatic erythrocytes (MNPCE) in the MWCNTs-treated rats. Administration of MWCNTs significantly increased serum concentrations of pro-inflammatory cytokines namely interleukin-1β (IL-1β), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α) in the treated rats. Immunohistochemical analysis showed significantly increased COX-2 and iNOS protein expressions in the liver of MWCNTs-treated rats. In conclusion, carboxylated MWCNTs induces hepatic damage *via* disruption of antioxidant defense systems, promotion of pro-inflammatory cytokines generation and expression of COX-2 and i-NOS in rats.

1. Introduction

The exceptional properties of carbon nanotubes have motivated their incorporation into innovative products globally. Carbon nanotubes can exist as single-walled (SWCNTs) which consists of a single sheet of graphene rolled to form a cylinder or multi-walled (MWCNTs) which consist of several concentric graphene tubes with diameters of up to 100 nm [1]. Both forms of carbon nanotubes are widely used in medicine, nanoelectronics, engineering, agriculture and daily consumable products [2,3]. There is an increasing research attention on these nanoparticles in recent years because excessive exposure to them has been demonstrated to pose great health risks to both animals and humans [4,5]. Indeed, exposure to MWCNTs is a global concern due to their potential similarities to hazardous asbestos fibers [6,7].

Previous studies have independently demonstrated several toxicological effects of MWCNTs in different experimental models. Moreover, research into the hepatotoxicity induced by MWCNTs is important because the liver is the major site of xenobiotic metabolism. Earlier studies on MWCNTs-induced hepatotoxicity indicated that oral administration of single dose of MWCNTs at 60 and

* Corresponding author. Drug Metabolism and Toxicology Research Laboratories, Department of Biochemistry, College of Medicine, University of Ibadan, Nigeria.
E-mail address: olatunde_farombi@yahoo.com (E.O. Farombi).

https://doi.org/10.1016/j.bbrc.2018.08.112
0006-291X/