

Neurotoxicity of Nanomaterials and Nanomedicine

Edited by

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Academic Press is an imprint of Elsevier



Academic Press is an imprint of Elsevier
125 London Wall, London EC2Y 5AS, United Kingdom
525 B Street, Suite 1800, San Diego, CA 92101-4495, United States
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom

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Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

ISBN: 978-0-12-804598-5

For information on all Academic Press publications
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Publisher: Mica Haley

Acquisition Editor: Erin Hill-Parks

Editorial Project Manager: Tracy Tufaga

Production Project Manager: Chris Wortley

Designer: Matthew Limbert

Typeset by TNQ Books and Journals

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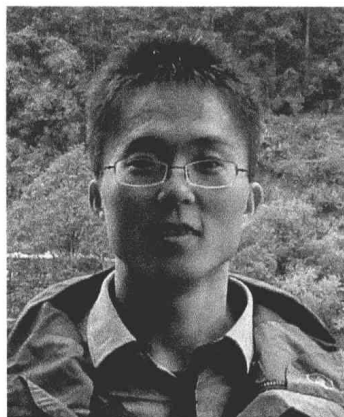
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Preface

Development of nanomaterials and nanomedicines is an impressive endeavor by researchers from chemistry, physics, engineering, biology, and medicine to improve the quality of our life. Many kinds of nanomaterials and nanomedicines are approved for human use or are under evaluation. The extensive application considerably elevates the exposure of nanomaterials and toxicity potential to human beings. Even as we enjoy the benefit from nanomaterials and nanomedicines, the toxicity potential should not be ignored.

The central nervous system (CNS) is the most important part of the human body, and should be paid serious attention when we talk about toxicity. The blood–brain barrier (BBB) has contributed to the protection of the CNS from harm by toxicants. Knowledge about BBB and the interaction between BBB and compounds has greatly expanded in the past several decades especially the past few years. The depth of knowledge about BBB enables researchers to develop nanomaterials and nanomedicines for delivering drugs or imaging probes to brain that display engaging potential for CNS disorders. However, neurotoxicity is emerging as a critical concern. The knowledge about neurotoxicity urgently needs to expand.

The chapters in this book were written by active researchers who dedicate their effort to enlarge the brain application of nanomaterials, develop brain nanomedicines, and improve the understanding of interaction of nanomaterials and the CNS. We appreciate these authors for sharing their knowledge and insights about this topic, which provide all of us, especially who work toward nanomaterials and nanomedicines, with an overview of the field and spark to think more about our research.

The early chapters provide an overview of the application of nanomaterials and nanomedicines in brain. The main routes by which nanomaterials enter brain are described. Then the excretion routes are discussed, although there are few studies related to this important topic.

A general review about neurotoxicity is provided in Chapter 4, with emphasis on the neurotoxicity mechanism. Then contributors describe in detail the application and neurotoxicity of many kinds of nanomaterials (Chapters 5–12) that are widely used, including titanium dioxide nanoparticles, iron oxide nanoparticles, silver nanoparticles, gold nanoparticles, manganese-containing nanoparticles, silica nanoparticles, carbon nanotubes, and cationic polymers. These kinds of nanoparticles represent the most commonly used nanomaterials in this field. Finally, an overview about neurotoxicity is provided with discussion of

potential strategies to reduce the neurotoxicity of nanomaterials and nanomedicines. Researchers will benefit from this knowledge to design novel nanomaterials and nanomedicines with minimum neurotoxicity.

The editors greatly thank the individual chapter contributors for kindly sharing their knowledge and ideas. It is a great pleasure to collaborate with them to develop this book. We admire the outstanding work they contributed so that researchers from nanomaterials and nanomedicines can benefit from this book and make greater success in their own work.

Xinguo Jiang

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April 2016

Introduction and Overview

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Nanoparticles (NPs) are generally described as particles of size about 0.1–100 nm, but particles that are several hundred nanometers in size are also called NPs. Thus in this book, we expand the definition of NPs to all particles around 0.1–1000 nm. The materials of NPs are called nanomaterials. One of the most important applications of NPs is delivering drugs and imaging probes to human body for disease diagnosis and treatment. These NPs are called nanomedicines.

Accompanied with the development of chemistry, biology, and materials science, many kinds of nanomaterials are synthesized with impressive characteristics. Nanomedicines are also extensively designed for both peripheral diseases and central nervous system (CNS) disorders. Despite great achievements, the toxicity of nanomaterials has been emerging as an increasingly important concern. The CNS is the most important part of human being, thus the toxicity to CNS, named neurotoxicity, should be paid particular attention.

In this book, the application and neurotoxicity of nanomaterials and nanomedicines are reviewed and discussed. The book includes the following:

- The application of nanomaterials and nanomedicines in brain targeting drug delivery
- The routes by which nanomaterials and nanomedicines enter into brain
- The excretion of nanomaterials and nanomedicines from brain
- The neurotoxicity of many kinds of nanomaterials, including titanium dioxide nanoparticles, iron oxide nanoparticles, silver nanoparticles, gold nanoparticles, manganese-containing nanoparticles, silica nanoparticles, carbon nanotubes, and cationic polymers
- The general mechanism of neurotoxicity and strategies to reduce the neurotoxicity.

HOW DO NANOMATERIALS AND NANOMEDICINES ENTER INTO AND GET EXCRETED FROM BRAIN?

In the CNS, the blood–brain barrier (BBB) considerably restricts the brain distribution of nanomaterials and nanomedicines. In healthy condition, the BBB protects the CNS from harm by toxicants in blood. But in CNS disorders, the

BBB also restricts the brain access of drugs, making CNS disorders the most difficult diseases to treat. Many researchers dedicate their efforts to enhance brain drug delivery using various methods. In these methods, nanomaterials play a critical role. In Chapter 1, we discuss the general application of nanomaterials and nanomedicines in brain targeting drug delivery and then in Chapter 2, Dr. Liu and Dr. He further summarize the routes that the nanomaterials enter brain, including penetrating the BBB through receptor-mediated endocytosis, transporter-mediated endocytosis, adsorptive-mediated endocytosis, bypassing BBB through intranasal delivery, inhibiting the function of BBB by inhibition of efflux pumps, and disturbing the structure of BBB. The distribution of nanomaterials and nanomedicines in brain is influenced by many factors, such as size, shape, surface charge, and ligand modification of NPs; administration routes; chronobiology; and disease condition, which is reviewed by Dr. Gao in Chapter 3. After entering into brain, the nanomaterials could be degraded or excreted from brain, which is affected by the deformability, biodegradability, size, shape, and ligand modification of the nanomaterials and nanomedicines. The conscious state and disease condition also affect this procedure, which is discussed in Chapter 3.

WHAT IS THE NEUROTOXICITY OF NANOMATERIALS?

Because nanomaterials could enter into brain through various routes, the contact of nanomaterials and nanomedicines with CNS may cause some neurotoxicity. The common neurotoxicity includes oxidative stress, inducing cell apoptosis and autophagy, immune response and inflammation, activating specific signaling pathway, affecting BBB function, and so on, which are reviewed in Chapter 4. Many kinds of nanomaterials have been developed with potential for CNS exposure, among which the widely used nanomaterials are selected for detailed description, such as metal NPs, carbon nanotubes, and cationic polymers. The application and neurotoxicity of these nanomaterials are reviewed in Chapters 5–12. The potential mechanism and influence factors are also reviewed, such as size, shape, crystal type, charge, surface property, release of ions, and administration route. Because neurotoxicity is a critical concern in the application of nanomaterials and nanomedicines, strategies to reduce neurotoxicity are important for researchers. Based on the reasons involved in the neurotoxicity, we conclude several strategies in Chapter 13, including reducing brain exposure and decreasing inherent toxicity of nanomaterials and nanomedicines.

CONCLUSION

This book is prepared with the purpose of benefiting nanomaterial and nanomedicine researchers in the following areas:

- Fundamental knowledge about nanomaterials and nanomedicines application in CNS disorders

- Routes by which nanomaterials and nanomedicines enter into and get excreted from brain
- Common neurotoxicity of nanomaterials and the influence factors
- Mechanism of neurotoxicity and strategies to reduce neurotoxicity.

The valuable insights shared by chapter authors are intended to expand the fundamental knowledge about brain application of nanomaterials and nanomedicines and the corresponding neurotoxicity. Researchers from all related fields may further develop nanomaterials and nanomedicines with lower neurotoxicity for more satisfying application in humans.

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