

## GREEN SYNTHESIS IN NANOMEDICINE AND HUMAN HEALTH

EDITED BY Richard L. K. Glover Daniel Nyanganyura Maluta Steven Mufamadi Rofhiwa Bridget Mulaudzi





CRC Press Taylor & Francis Group

Regional Office for Africa

International

Science Council

## Green Synthesis in Nanomedicine and Human Health



## Green Synthesis in Nanomedicine and Human Health

Edited by Richard L. K. Glover Daniel Nyanganyura Maluta Steven Mufamadi Rofhiwa Bridget Mulaudzi



CRC Press is an imprint of the Taylor & Francis Group, an **informa** business First edition published 2021 by CRC Press 6000 Broken Sound Parkway NW, Suite 300, Boca Raton, FL 33487-2742

and by CRC Press 2 Park Square, Milton Park, Abingdon, Oxon, OX14 4RN

© 2021 Taylor & Francis Group, LLC CRC Press is an imprint of Taylor & Francis Group, LLC

Reasonable efforts have been made to publish reliable data and information, but the author and publisher cannot assume responsibility for the validity of all materials or the consequences of their use. The authors and publishers have attempted to trace the copyright holders of all material reproduced in this publication and apologize to copyright holders if permission to publish in this form has not been obtained. If any copyright material has not been acknowledged please write and let us know so we may rectify in any future reprint.

Except as permitted under U.S. Copyright Law, no part of this book may be reprinted, reproduced, transmitted, or utilized in any form by any electronic, mechanical, or other means, now known or hereafter invented, including photocopying, microfilming, and recording, or in any information storage or retrieval system, without written permission from the publishers.

For permission to photocopy or use material electronically from this work, access www.copyright.com or contact the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923, 978-750-8400. For works that are not available on CCC please contact mpkbookspermissions@tandf.co.uk

Trademark notice: Product or corporate names may be trademarks or registered trademarks and are used only for identification and explanation without intent to infringe.

Library of Congress Cataloging-in-Publication Data

Names: Glover, Richard L. K., editor. | Nyanganyura, Daniel, editor. | Mulaudzi, Rofhiwa Bridget, editor. | Mufamadi, Maluta Steven, editor. Title: Green synthesis in nanomedicine and human health / Richard L. K. Glover, Daniel Nyanganyura, Rofhiwa Bridget Mulaudzi, Maluta Steven Mufamadi Description: First edition. | Boca Raton, FL : CRC Press, [2021] | Includes bibliographical references and index. | Summary: "Green synthesis is an emerging method for deriving nanoparticles present in natural plants for use in nanomedicine. Written by experts in the field, Green Synthesis in Nanomedicine and Human Health showcases the exciting developments of this specialty and its potential for promoting human health and wellbeing. This book gives practical information on novel preparation methods for identifying nanoparticles present in natural plants. It discusses applications of nanoparticles in combating communicable, non-communicable and vector-borne diseases. It also explores the potential for nanoparticles to combat antimicrobial resistance through improvements in treatment methods, diagnostics, and drug delivery systems. Features scientific evidence of opportunities for integrating indigenous flora into nanomedicine to develop cost-effective therapeutic and diagnostic solutions for diseases including cancer, tuberculosis, malaria and diabetes. Places green synthesis and nanomedicine in the African orthodox and traditional healthcare context. Provides policy makers with scientific evidence to inform policies for controlling or mitigating dangerous diseases. This book is essential reading for students, scientists, policymakers and practitioners of nanotechnology, and will appeal to anyone with an interest in integrating traditional African healthcare and Western medicine" -- Provided by publisher. Identifiers: LCCN 2020042728 | ISBN 9780367710811 (paperback) | ISBN 9780367902162 (hardback) | ISBN 9781003023197 (ebook) Subjects: LCSH: Nanomedicine. | Nanotechnology. | Biosynthesis. Classification: LCC R857.N34 G74 2021 | DDC 610.28--dc23 LC record available at https://lccn.loc.gov/2020042728

ISBN: 9780367902162 (hbk) ISBN: 9780367710811 (pbk) ISBN: 9781003023197 (ebk)

Typeset in Times by Deanta Global Publishing Services, Chennai, India

## Contents

List of Figures	ix
List of Tables	xi
Foreword	xiii
Acknowledgements	XV
Editors	xvii
Contributors	xix

#### SECTION I Green Synthesis of Nanoparticles from Natural Plant Parts

Maluta Steven Mufamadi, Rofhiwa Mulaudzi, Richard L.K. Glover and Daniel Nyanganyura

#### SECTION II Nanotechnology for Treatment of Non-Communicable Diseases

Chapter 1	Cancer Nanotheranostics: Next-Generation Early Detection and Treatment Prioritization for Cancers Using Phytonanotechnology17
	Maluta Steven Mufamadi, Marian Jiya John, Mpho Phehello Ngoepe and Palesa Rose Sekhejane
Chapter 2	Green Synthesis of Nanoparticles Using Plant Extracts: A Promising Antidiabetic Agent
	Rofhiwa Bridget Mulaudzi, Mahwahwatse Johanna Bapela and Thilivhali Emmanuel Tshikalange
Chapter 3	Green Nanoparticles: An Alternative Therapy for Oral Candidiasis
	Razia Z. Adam, Enas Ismail, Fanelwa Ajayi, Widadh Klein, Germana Lyimo and Ahmed A. Hussein

#### SECTION III Nanotechnology for Treatment of Communicable Diseases

Chapter 4	Nanotechnology and Nanomedicine to Combat Ebola Virus Disease
	Maluta Steven Mufamadi
Chapter 5	Application of Next-Generation Plant-Derived Nanobiofabricated Drugs for the Management of Tuberculosis81
	Charles Oluwaseun Adetunji, Olugbenga Samuel Michael, Muhammad Akram, Kadiri Oseni, Ajayi Kolawole Temidayo, Osikemekha Anthony Anani, Akinola Samson Olayinka, Olerimi Samson E, Wilson Nwankwo, Iram Ghaffar and Juliana Bunmi Adetunji

#### SECTION IV Nanotechnology for Treatment of Vector-Borne Diseases

Chapter 6	Biogenic Nanoparticles Based Drugs Derived from Medicinal	
	Plants: A Sustainable Panacea for the Treatment of Malaria 10	3

Charles Oluwaseun Adetunji, Olugbenga Samuel Michael, Wilson Nwankwo, Osikemekha Anthony Anani, Juliana Bunmi Adetunji, Akinola Samson Olayinka and Muhammad Akram

#### SECTION V Nanotechnology in Combating Antimicrobial Resistance

Chapter 7	Bioengineering of Inorganic Nanoparticle Using Plant Materials to Fight Extensively Drug-Resistant Tuberculosis
	Mpho Phehello Ngoepe and Maluta Steven Mufamadi
Chapter 8	Recent Advances in the Utilization of Bioengineered Plant- Based Nanoparticles: A Sustainable Nanobiotechnology for the Management of Extensively Drug-Resistant Tuberculosis
	Charles Oluwaseun Adetunji, Olugbenga Samuel Michael, Muhammad Akram, Kadiri Oseni, Olerimi Samson E, Osikemekha Anthony Anani, Wilson Nwankwo, Hina Anwar, Juliana Bunmi Adetunji, and Akinola Samson Olayinka

#### Contents

Chapter 9	Green Synthesis of Nanoparticles and Their Antimicrobial Efficacy against Drug-Resistant <i>Staphylococcus aureus</i>
	Nonhlanhla Tlotleng, Jiya M. John, Dumisile W. Nyembe and Wells Utembe
Chapter 10	Green Metal-Based Nanoparticles Synthesized Using Medicinal Plants and Plant Phytochemicals against Multidrug-Resistant <i>Staphylococcus aureus</i>
	Abeer Ahmed Qaed Ahmed, Lin Xiao, Tracey Jill Morton McKay and Guang Yang
SECTIO	N VI Cross-Cutting Issues
Chapter 11	Polymer-Based Protein Delivery Systems for Loco-Regional Administration

Muhammad Haji Mansor, Emmanuel Garcion, Bathabile Ramalapa, Nela Buchtova, Clement Toullec, Marique Aucamp, Jean Le Bideau, François Hindré, Admire Dube, Carmen Alvarez-Lorenzo, Moreno Galleni, Christine Jérôme, and Frank Boury

Chapter 12	Nanomedicines for the Treatment of Infectious Diseases: Formulation, Delivery and Commercialization Aspects	271
	Admire Dube, Boitumelo Semete-Makokotlela, Bathabile Ramalapa, Jessica Reynolds and Frank Boury	
Chapter 13	Green-Synthesized Nanoparticles as Potential Sensors for Health Hazardous Compounds	291
	Rachel Fanelwa Ajayi, Sphamandla Nqunqa, Yonela Mgwili, Siphokazi Tshoko, Nokwanda Ngema, Germana Lyimo, Tessia Rakgotho, Ndzumbululo Ndou,and Razia Adam	



## List of Figures

Figure 1.1 AuNPs to ind	Schematic diagram illustrating the mechanisms of AgNPs and duce cytotoxicity in a cancerous human cell	22
Figure 2.1	General methods of nanoparticle synthesis	36
Figure 3.1	HRTEM image of ZnO nanoparticles	54
<b>Figure 3.2</b> µml ZnO-NI	Standard well diffusion test on <i>Candida albicans</i> biofilm; 100 Ps (inhibition zones = 24–26 mm)	55
Figure 6.1	Management of malaria	105
Figure 6.2 production a	Informatics and applications in drug discovery, formulation, nd treatment of malaria	111
Figure 7.1	Antimicrobial mechanism of NPs and their ions	127
Figure 7.2	Mechanism of drug resistance in <i>M. tuberculosis</i>	128
Figure 7.3 mediated syr	Diagram summarizing the possible mechanism of biologically thesis of nanoparticles	131
Figure 7.4 TB-infected	Inorganic nanoparticles ligand attachment for targeting macrophages	137
Figure 7.5	Labelling of inorganic nanoparticles for biomedical applications	139
Figure 10.1 green metal-	Typical various approaches for the synthesis and evaluation of based NPs	183
Figure 10.2 nanoparticles permission f	Biological (green) synthesis and the applications of metal s in biomedical and environmental fields. (Reproduced with rom Singh et al., 2016)	183
Figure 10.3 multiple resis	Historical review of MDR S. aureus strains and their emerging stance to drugs	187
Figure 10.4 cells. (c and c illustrating si with permiss facile green si dactylifera a Complement .1155/2018/18	SEM micrograph of MRSA. (a and b) Untreated control d) Cells treated with 25 and 50 $\mu$ g/ml of AgNPs; red arrows tructural deformities and irregular cell surface. (Reproduced ion from Ansari, M.A., and Alzohairy, M.A. 2018. "One-pot synthesis of silver nanoparticles using seed extract of <i>Phoenix</i> nd their bactericidal potential against MRSA". <i>Evidence-Based</i> <i>ary and Alternative Medicine</i> 2018:1–9. doi: https://doi.org/10 860280)	202

Figure 10.5 (b and c) Trea attachment ar outermost lay with permissi facile green s <i>dactylifera</i> ar <i>Complementa</i> 1155/2018/18	HR-TEM micrograph of MRSA. (a) Untreated control cell. ated with 25 and 50 µg/ml AgNPs. Red arrows indicate the ad penetration of NPs and degradation and destruction of the ters of cell wall and cytoplasmic membrane. (Reproduced ion from Ansari, M.A., and Alzohairy, M.A. 2018. "One-pot ynthesis of silver nanoparticles using seed extract of <i>Phoenix</i> and their bactericidal potential against MRSA". <i>Evidence-Based</i> <i>ary and Alternative Medicine</i> 2018:1–9. doi: https://doi.org/10 160280)	203
Figure 10.6	Possible mechanism of actions for green metal-based NPs	205
Figure 11.1	Advantages of protein therapeutics for clinical applications	252
Figure 11.2	Common polymer-based systems for drug delivery applications	256
Figure 11.3	Examples of micro/nanoparticle preparation process	257
Figure 11.4 internal struc	A simplified representation of a fibrous scaffold and its ture	261
Figure 11.5 (Adapted from of diabetic uld epidermal gro T.G. Kim, T.C nanofibers for (2006) 1108–	Different modes of protein loading into a fibrous scaffold. n J.S. Choi, K.W. Leong, H.S. Yoo, <i>In vivo</i> wound healing cers using electrospun nanofibers immobilized with human owth factor (EGF), Biomaterials. 29 (2008) 587–596 and G. Park, Surface functionalized electrospun biodegradable. r immobilization of bioactive molecules, Biotechnol. Prog. 22 1113)	262
<b>Figure 12.1</b> <i>M. tb</i> and HIV typically cont nucleus. In m intracellular s	Schematic diagram illustrating the intracellular locality of V pathogens, and the various types of nanoparticles. <i>M. tb</i> is tained within phagosomes, while HIV is located within the ost cases, nanoparticles will need to penetrate the cellular host/space and/or nucleus to deliver therapeutic payload	275
Figure 13.1	Structure of hydrazine	293
Figure 13.2	Structure of nitrobenzene	293
Figure 13.3	Basic structure of an electrochemical sensor	295
Figure 13.4 the synthesis	An illustration of the top-down and bottom-up approaches for of nanoparticles	296

## List of Tables

Table 2.1	Brief Descriptions of the Types of Diabetes	. 33
Table 2.2 with Antidi	Metal Nanoparticles Synthesis Using Different Plant Extracts abetic Activity	. 38
Table 3.1	Common Risk Factors for Oral Candidiasis (Patil et al., 2015)	.46
Table 3.2 Strains	Green-Mediated Au Nanoparticles against Different Candida	. 51
<b>Table 3.3</b> <i>Candida</i> St	Recent Plant-Mediated Ag Nanoparticles against Different rains	. 52
<b>Table 3.4</b> Nanoparticl	Recent Studies Using Plant-Mediated Synthesis of Zinc Oxide	. 53
Table 3.5	Plant-Mediated Zinc Oxide Nanoparticles and Candida Species	. 53
Table 6.1	Pharmacotherapeutic Agents for Malaria Treatment	106
Table 6.2	Nanomaterial Employed for the Treatment of Malaria	109
Table 7.1 Synthesized	Various Inorganic Nanoparticles with Antimicrobial Activity I Using Green Chemistry	133
<b>Table 10.1</b> Extracts aga	Green Synthesis of GAgNPs from Different Medicinal Plants ainst S. aureus Strains	194
<b>Table 10.2</b> Extracts aga	Green Synthesis of GAuNPs from Different Medicinal Plants ainst <i>S. aureus</i> Strains	197
<b>Table 10.3</b> Plants Extra	Synthesis of Different Green NPs from Variety of Medicinal acts against <i>S. aureus</i> Strains	199
<b>Table 10.4</b> Stabilization	Plant Phytochemicals Involved in the Formation and n of G-NPs	225
<b>Table 12.1</b> Main Trans	List of Common Infectious Diseases, Pathogen Involved and mitting Agent	272
Table 13.1	A List of Green-Synthesized Gold Nanoparticles	302
Table 13.2Application	A List of Green-Synthesized Silver Nanoparticles with Potential in Electrochemical Sensors	303
Table 13.3 Nanoparticl	Examples of Green Method Synthesized Platinum les with Potential Application in Electrochemical Sensors	304



### Foreword

Nanotechnology is considered one of the most promising, cutting-edge and disruptive technological advancements. This technology can be applied in numerous industrial and biomedical sectors. Several factors, which include the versatility of nanomaterials and the relatively low production cost of nano-enabled products, make this technology particularly suitable in low-resource settings. The application of nanotechnology in water treatment, energy, agriculture and medicine is particularly relevant in countries with struggling economies. However, several factors, which include barriers to the commercialization of nanotechnology and the unknown impact of nanomaterials on the environment and humans, can impede the development of nanotechnology.

Nanomaterials can be synthesized using a top-down or bottom-up approach. The top-down approach aims to fabricate nanoscale materials by mechanical processes such as ball milling, lithography, laser and ablation. These methods of nanomaterial synthesis can be expensive and energy-intensive, and it can negatively impact the environment. The bottom-up approach, on the other hand, is based on the self-assembly of atoms into nanoscale structures and mostly involves chemical processes. These chemical approaches are not particularly eco-friendly, and there is a growing need to develop environmentally and economically friendly processes. The most common bottom-up approach for the synthesis of metallic nanomaterials is chemical reduction of the metallic cations by inorganic reducing agents to produce colloidal nanoparticles.

Green nanotechnology is a fairly new branch of nanotechnology, which aims to produce and utilize nanomaterials in a way that is safe for living organisms and their environment. It can also involve the production of nanomaterials that can solve environmental problems. It uses the principles of green chemistry, which aims to reduce or eliminate the use or generation of hazardous substances during the synthesis of chemical products. These processes also aim to develop synthetic methods, which are more energy-efficient. Aside from the fact that green nanotechnology can be beneficial to the environment, green nanomaterials produced in this fashion can also be more biocompatible and therefore more suitable for applications in nanomedicine. The impact of nanomaterials on the environment and human health is relatively unknown. The immense diversity of nanomaterials and contradictory reports on the safety of nanomaterials further exacerbate this problem. Moreover, the absence of standardized methods makes it difficult to study the impact of nanomaterials on ecosystems.

Bioinspired synthesis methods that use biological or organic reducers of metal cations have been developed to produce green nanoparticles. A number of living organisms, which include bacteria, algae, fungi and plants, have been used as sources of these biological or organic reducers to produce colloidal metal nanoparticles. The molecular interactions between microorganisms and metals, as well as between plants and metals have been well documented. Several bacterial strains are known to produce inorganic materials, including metals. The use of microorganisms and plants to develop safer nanoparticle production methods are thus not so far-fetched. Green nanotechnology aims to reduce the production of hazardous waste during the synthesis process and to develop more energy-effective methods. Bioinspired nanoparticles are considered more biocompatible than nanomaterials produced using traditional chemical synthesis methods and are therefore more suitable for biomedical applications. Bioinspired green nanoparticle synthesis using plants involves bio-reduction reactions that are catalysed by phytochemicals such as terpenoids, flavones, ketones, aldehydes, amides and carboxylic acids. These bio-reduction reactions can occur at low temperatures, which means that these reactions are more energy-efficient than traditional chemical synthesis methods. The use of plants to synthesize green nanomaterials has given rise to phytonanotechnology, which aims to synthesize nanoparticles using eco-friendly, simple, rapid and cost-effective methods.

Some of the unique physical, chemical and optical properties of nanoparticles make these materials useful for biomedical applications. Due to their small size and high surface area to volume ratio, nanoparticles are well suited as vectors to carry molecular mediators of disease therapeutics and diagnosis. Biomolecules, which include DNA, RNA and protein as well as small-molecule drugs, can be conjugated to nanoparticles for applications in therapeutics and diagnosis. The light scattering and absorption properties of plasmonic nanoparticles make these materials useful for application in the imaging and sensing.

The use of plants in African traditional healing is deeply interwoven with cultural practices and religious beliefs. Africa thus has a rich indigenous knowledge of plants which can be explored with phytonanotechnology to develop novel solutions for the treatment and diagnosis of diseases. Green nanoparticles synthesized from plants used for medicinal purposes can potentially incorporate the medicinal properties of the plant, since the same phytochemicals that are responsible for the medicinal properties of the plant can be involved in the synthesis of nanoparticles. There is thus a unique opportunity to integrate indigenous African flora into nanomedicine to develop cost-effective therapeutic and diagnostic solutions for the devastating deadly diseases such as HIV/AIDS, TB, malaria, Ebola, hypertension, heart disease and diabetes that plague Africa.

This book showcases bioinspired green synthesis of nanoparticles from plants as an emerging method for the development of nanomedicine to promote human health and well-being. The book describes the concepts of green synthesis and reviews the application of green nanoparticles for the treatment of non-communicable and communicable diseases such as cancer, TB and Ebola. Moreover, it highlights how green nanoparticles can be used to fight multidrug antimicrobial resistance. The book also focuses on the application of this technology to develop cost-effective diagnostic systems for early disease detection. A major stumbling block in science in general is the translation of research into commercial products, and the authors therefore also present considerations for commercialization of nanomedicines.

> Prof. Mervin Meyer Professor of Biotechnology Director: DSI/Mintek Nanotechnology Innovation Centre – Biolabels Node South Africa

### Acknowledgements

The idea of publishing a book on nanotechnology had been on the cards since 2012 as part of the International Science Council Regional Office for Africa (ISC ROA) book project under the then directorship of Dr Edith Madela-Mntla and spearheaded by Prof Malik Maaza of IThemba LABS to both of whom we owe much gratitude. Owing to several factors, however, it was put on ice.

Our sincere appreciation goes to Dr Rofhiwa Bridget Mulaudzi (Romukhu (Pty) Ltd, South Africa) and Dr Maluta Steven Mufamadi (Nabio Consulting (Pty) Ltd, South Africa) through whose initiative and tacit support, the idea was revived in 2018, albeit with a shift in thematic focus. We are equally indebted to them for acting as external editors and enthusiastically putting together a Concept Paper and draft chapter outline for consideration and endorsement by ISC ROA, assisting in developing a publishing proposal to the CRC Press and recommending potential reviewers, which enabled its acceptance as well as identifying potential contributors to each chapter.

We are grateful to Dr Hazel Mufhandu (North West University, South Africa), Dr Bhekumthetho Ncube (University of KwaZulu-Natal, South Africa), Prof Ram Prasad (Sun Yat-Sen University, China) and Prof Lebogang Katata-Seru (North West University, South Africa) for reviewing the book publishing proposal.

Dr Hazel Mufhandu (North West University, South Africa), Prof Lebogang Katata-Seru (North West University, South Africa), Dr Haly Holmes (University of the Western Cape, South Africa), Dr Dennis Arokoyo (Bowen University, Nigeria), Dr Saher Islam (University of Veterinary and Animal Sciences, Pakistan), Dr Lindiwe Thete (CSIR, South Africa), Prof T.I. Nkambule (University of South Africa, South Africa), Prof Chao Zhang (Sun Yat-Sen University, China), Dr Abdelhamid Elaissari (University of Lyon, France), Dr Clinton Rambanapasi (PharmaConnect-A, South Africa) and Dr Tatenda Dalu (University of Venda, South Africa) all come up for special mention for peer-reviewing the draft chapters of this book.

Last but not least, our heartfelt thanks and appreciation go to the contributors to the various sections and chapters of this book through whose knowledge production and generous transfer, green synthesis has been vividly showcased here as an emerging method for deriving nanoparticles from natural plant parts to be used in nanomedicine for promoting human health and well-being.

> Dr Richard L. K. Glover and Dr Daniel Nyanganyura Internal Editors, ISC ROA, South Africa



### Editors



**Dr Richard L. K. Glover (Pr. Nat. Sci.)** is a biological scientist with a bias in food microbiology. Dr Glover worked as a Research Officer at the Centre for Scientific Research into Plant Medicine at Mampong-Akwapim in Ghana from 1991 to 1996 where he set up its Microbiological Screening Laboratory for validation of herbal and traditional medicinal products. He joined the Department of Applied Biology, Faculty of Applied Sciences of the University for Development Studies (UDS), Navrongo Campus, as a lecturer/researcher in microbiology in 1996. He served as Head

of Department and was Senior Lecturer when he left UDS in 2012. Dr Glover also led DANIDA-sponsored projects on Capability Building for Research in Traditional Fermented Food Processing in West Africa.

Dr Glover currently works as Programme Specialist (Biological Sciences) with the International Science Council [ISC] Regional Office for Africa (formerly International Council for Science [ICSU] Regional Office for Africa), Pretoria, South Africa. Dr Glover has participated in several international training programmes and conferences. He has over 20 peer-reviewed journal publications as well as several conference proceedings to his credit. He is the Regional Programme Officer (RPO) and member of the Steering Committee of the International Network for Government Science Advice (INGSA) Africa Chapter. He is a member of the South African Council for Natural Scientific Professions (SACNASP) with Registration Number 115865.



**Dr Daniel Nyanganyura** is Regional Director for the International Science Council for Science (ISC) Regional Office for Africa (ROA) from February 2017 and acted in this position from June 2016 to January 2017. He holds a PhD in Atmospheric Physics (2007), an MSc in Agricultural Meteorology (1999), a BSc 4th Year Honours in Physics (1997) from the University of Zimbabwe and a Licentiate Degree in Education in the Specialty of Physics and Astronomy from Enrique José Varona Higher Pedagogical Institute, Havana, Cuba (1991). He was Programme

Specialist for Physics, Mathematics and Engineering Sciences at the International Council for Science Regional Office for Africa (2008–2016); Air Pollution Research Scientist at the Max Planck Institute for Chemistry in Mainz, Germany (August 2007–July 2008); Physics Lecturer at the University of Zimbabwe (2000–2007) and A-Level Physics and Computer Science Teacher (1991–1998). At ISC ROA, he manages and oversees ISC scientific programmes/activities in Africa. He is a member of the South African Institute of Physics; South African Society for Atmospheric Sciences; European Geophysical Union; the Air Pollution Information Network for Africa; and International Society for Agricultural Meteorology.



**Dr Maluta Steven Mufamadi** is the founder and managing director of Nabio Consulting (Pty) Ltd. He has earned his PhD in (nano)pharmaceutics from Wits University, entrepreneurship short courses from University of Pretoria and Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland. His interest is in the health applications of nanotechnology, entrepreneurship and commercialization. He has authored and co-authored three patents, one of which is an international patent, several peer-reviewed scientific publications and book chapters. He received the awards as interna-

tional inventor from the Wits Enterprise & Wits University Innovation Forum, and for the best peer-reviewed research paper of pharmaceutics (nanomedicine) from South African Academy of Pharmaceutical Sciences. In 2017, he was supported for UNESCO-Kalinga Prize for the popularization of nanotechnology in South Africa by the South African National Commission for UNESCO. From 2014, he is member of the national nanotechnologies committee (ISO TC229) at the South African Bureau of Standards (SABS).



**Dr Rofhiwa Bridget Mulaudzi** is the Founder and Managing Director of Romukhu (Pty) Ltd, She holds a PhD in Ethnobotany and MSc in Botany from the University of KwaZulu-Natal. She holds an Honours degree in Biochemistry and BSc degree in Biochemistry and Microbiology from the University of Venda and is registered with the South African Council for Natural Scientific Professions (SACNASP) as a Professional Natural Scientist. Apart from university degrees, Rofhiwa completed formal certificate courses in Basic, Intermediate and Advanced

Project Management at the University of South Africa and a Certificate in Bio-Entrepreneurship Training Programme at Coach Lab, the Innovation Hub, Pretoria, South Africa. Dr Mulaudzi was a Researcher in Medicinal Plants at the Agricultural Research Council. Her current research projects are focusing on the Research and Development (R&D) of both medicinal plants and indigenous vegetables as medicine for human health and well-being. Dr Mulaudzi has published peer-reviewed articles in international journals and contributed chapters to books. Her current research interests include development of nanomedicine drugs using African indigenous plants and using African leafy vegetables as source of medicine. She won the Best Researcher of the year award in Plant Science presented by the Rn. Abuthahir. S, President of World Research Council, RULA Awards 2020.

### Contributors

#### Razia Z Adam

Faculty of Dentistry, University of the Western Cape Cape Town, South Africa

#### Juliana Bunmi Adetunji

Nutritional and Toxicological Research Laboratory, Department of Biochemistry Sciences, Osun State University Osogbo, Nigeria

#### Charles Oluwaseun Adetunji

Microbiology, Biotechnology and Nanotechnology Laboratory, Department of Microbiology Edo University Iyamho Edo State, Nigeria

#### Abeer Ahmed Qaed Ahmed

Department of Biomedical Engineering, College of Life Science and Technology, Huazhong University of Science and Technology Wuhan, PR China

#### Fanelwa Ajayi

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### Muhammad Akram

Department of Eastern Medicine, Government College University Faisalabad Punjab, Pakistan

#### **Carmen Alvarez-Lorenzo**

Departamento de Farmacologia, Farmacia y Tecnología Farmacéutica, R & D Pharma Group, Facultad de Farmacia, Universidade de Santiago de Compostela Santiago de Compostela, Spain

#### Osikemekha Anthony Anani

Laboratory of Ecotoxicology and Forensic Biology, Department of Biological Science, Faculty of Science, Edo University Iyamho Edo State, Nigeria

#### Hina Anwar

Department of Eastern Medicine, Government College University Faisalabad Punjab, Pakistan

#### **Marique Aucamp**

School of Pharmacy, University of the Western Cape Bellville, South Africa

#### Mahwahwatse Johanna Bapela

Department of Plant and Soil Sciences, University of Pretoria Hatfield, South Africa

#### Jean Le Bideau

Université de Nantes, CNRS, Institut des Matériaux Jean Rouxel IMN, Nantes, France

#### Frank Boury CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France

#### Nela Buchtova

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France

#### **Admire Dube**

School of Pharmacy, University of the Western Cape Bellville, South Africa

#### Moreno Galleni

Laboratory for Biological Macromolecules, Center for Protein Engineering, Institut de Chimie B6, University of Liège Sart-tilman, Liège, Belgium

#### **Emmanuel Garcion**

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France

#### Iram Ghaffar

Department of Eastern Medicine, Government College University Faisalabad Punjab, Pakistan

#### **Richard Lander Kwame Glover**

International Science Council Regional Office for Africa (ISC ROA) Pretoria, South Africa

#### François Hindré

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France

#### Ahmed A. Hussein

Natural Product Chemistry Research Group, Department of Chemistry, Cape Peninsula University of Technology Cape Town, South Africa

#### **Enas Ismail**

Natural Product Chemistry Research Group, Department of Chemistry, Cape Peninsula University of Technology Cape Town, South Africa

#### **Christine Jérôme**

Center for Education and Research on Macromolecules (CERM), Université de Liège Liège, Belgium

#### Marian Jiya John

Nabio Consulting (Pty) Ltd Pretoria, South Africa

#### Widadh Klein

Faculty of Dentistry, University of the Western Cape, Cape Town, South Africa

#### Germana Lyimo

Faculty of Dentistry, University of the Western Cape Cape Town, South Africa

#### Muhammad Haji Mansor

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France and Center for Education and Research on Macromolecules (CERM), Université de Liège Liège, Belgium

#### Contributors

#### **Tracey Jill Morton McKay**

Department of Environmental Sciences, School of Agriculture and Environmental Sciences, University of South Africa Florida, Roodepoort, Johannesburg, South Africa

#### Yonela Mgwili

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### **Olugbenga Samuel Michael**

Cardiometabolic Research Unit, Department of Physiology, College of Health Sciences, Bowen University, Iwo Osun State, Nigeria

#### Maluta Steven Mufamadi

Nabio Consulting (Pty) Ltd Pretoria, South Africa

#### Rofhiwa Bridget Mulaudzi

Romukhu (Pty) Ltd Pretoria, South Africa

#### Ndzumbululo Ndou

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### Mpho Phehello Ngoepe

Department of Oral Biology, University of the Witwatersrand, Johannesburg Parktown, South Africa

#### **Daniel Nyanganyura**

International Science Council Regional Office for Africa (ISC ROA) Pretoria, South Africa

#### Nokwanda Ngema

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### Sphamandla Nqunqa

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### Wilson Nwankwo

Informatics and CyberPhysical Systems Laboratory, Department of Computer Science, Edo University Iyamho Auchi, Edo State, Nigeria

#### **Dumisile W Nyembe**

Ngwane Teachers College Eswatini

#### Akinola Samson Olayinka

Department of Physics, Faculty of Science, Edo University Iyamho Edo State, Nigeria

#### Kadiri Oseni

Department of Biochemistry, Faculty of Basic Medical Sciences, Edo University Iyamho Edo State, Nigeria

#### **Tessia Rakgotho**

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### **Bathabile Ramalapa**

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France and Laboratory for Biological Macromolecules, Center for Protein Engineering, Institut de Chimie B6, University of Liège, Sart-tilman, Liège, Belgium and Council for Scientific and Industrial Research Brummeria, Pretoria, South Africa

#### Jessica Reynolds

Department of Medicine, School of Medicine and Biomedical Sciences, University at Buffalo Buffalo, New York, USA

#### Olerimi Samson E.

Department of Biochemistry, Faculty of Basic Medical Sciences, Edo University Iyamho Edo State, Nigeria

#### Palesa Rose Sekhejane

Africa Institute of South Africa, Human Sciences Research Council Pretoria, South Africa

#### Boitumelo Semete-Makokotlela

Council for Scientific and Industrial Research, Chemicals Pretoria, South Africa

#### Ajayi Kolawole Temidayo

Section of Integrative Bioenergetics Environmental and Ecotoxicological Systems, Department of Microbiology, Faculty of Life Sciences, University of Ilorin Ilorin, Nigeria

#### Nonhlanhla Tlotleng

National Institute for Occupational Health, National Health Laboratory Services Johannesburg, South Africa

#### **Clement Toullec**

CRCINA, INSERM, Université de Nantes, Université d'Angers Angers, France and Center for Education and Research on Macromolecules (CERM), Université de Liège Liège, Belgium and Université de Nantes, CNRS, Institut des Matériaux Jean Rouxel, IMN, Nantes, France

#### Siphokazi Tshoko

SensorLab, Chemistry Department, University of the Western Cape Bellville, South Africa

#### Thilivhali Emmanuel Tshikalange

Department of Plant and Soil Sciences, University of Pretoria Hatfield, South Africa

#### Wells Utembe

Nabio Consulting (Pty) Ltd Pretoria, South Africa

#### Lin Xiao

Department of Biomedical Engineering, College of Life Science and Technology, Huazhong University of Science and Technology Wuhan, PR China

#### **Guang Yang**

Department of Biomedical Engineering, College of Life Science and Technology, Huazhong University of Science and Technology Wuhan, PR China

## Section I

# Green Synthesis of Nanoparticles from Natural Plant Parts



### **General Overview**

Maluta Steven Mufamadi, Rofhiwa Mulaudzi, Richard L.K. Glover and Daniel Nyanganyura

#### CONTENTS

The History of Nanotechnology	4
Green Synthesis of Nanoparticles: Concepts and Scientific Context	5
Application of Green Synthesized Nanoparticles in Human Health	7
Antimicrobial Mechanism of Action	7
Anticancer Mechanism of Action	8
Non-Communicable Diseases	8
Communicable Diseases	9
Nanomedicine Innovations: New Trend	9
Commercialization Aspects	10
References	10

Green synthesis of nanoparticles (NPs) has gained extensive attention as a reliable, sustainable and eco-friendly protocol for synthesizing a wide range of materials/ nanomaterials, including metal/metal oxides nanomaterials, hybrid materials and bioinspired materials (Singh et al., 2018). It is regarded as an important tool to reduce the destructive effects associated with the traditional methods of synthesis for nanoparticles commonly utilized in the laboratory and industry. The green synthesis method is also known as biological synthesis or biogenic synthesis (Salem and Fouda, 2020). It is required to avoid the production of unwanted or harmful by-products through the build-up of reliable, sustainable and eco-friendly synthesis procedures.

In recent years, green synthesis of nanoparticles from natural plant parts and/or plant crude extracts has gained a lot of attention in both medical and pharmaceutical applications (Mukherjee et al., 2014; Mufamadi et al., 2019). There are different methods of nanoparticles synthesis such as chemical, physical and biological (i.e. green) synthesis methods. Traditionally, nanoparticles production is achieved by employing physical and chemical methods. However, both methods are very expensive, and chemical method and use of harsh toxic solvents limit their applications in clinical fields and are also harmful to both human health and the environment (Caroling et al., 2015). Green synthesis methods use various green sources such as bacteria, fungi, enzyme, algae and yeast as well as plant extracts for nanoparticles production (Kaviya et al., 2011; Mufamadi and Mulaudzi, 2019; Salem and Fouda, 2020). The advantages of using plant and/or plant crude extracts during green synthesis of nanoparticles are that they contain many compounds like proteins, polysaccharides, amino acids and secondary metabolites like

flavonoids, phenolic acid, alkaloids, tannins and terpenoids that are responsible for the bioreduction, capping and stabilization of metallic ions during nanoparticle formation (Aromal and Philip, 2012; Ali et al., 2020). Plant-based synthesis is an ideal approach for nanoparticles formation because it doesn't require high temperatures, energy, pressure and harmful chemical solvents. Furthermore, plant-based synthesis of nanoparticles is environment-friendly, cost-effective and easy to scale up for large-scale synthesis of nanoparticles (Benakashani et al., 2016).

The success in green synthesis of nanoparticles from natural plant parts has opened an opportunity for low- and middle-income countries such as African countries to start to elevate their research and development (R&D) in the nanomedicine area in order to address the burden of diseases that they are currently facing today. The advantages of using plant-based synthesis of nanoparticles are that it is easy to synthesize, uses single-step process, requires low or just room temperature for nanoparticles production, is easy to scale up for large-scale synthesis of nanoparticles, is easy to maintain and is inexpensive and/or economically viable. African countries, particularly those that are in sub-Sahara Africa (SSA), are facing many burdens of non-communicable diseases (NCDs), communicable diseases (CDs) and vector-borne diseases, as well as antimicrobial resistance. In order to overcome these challenges, African countries need to start to harness science-based health innovations (e.g. Green synthesis of nanoparticles from natural plant parts) as a way to achieve affordable and efficient health and medical solutions.

The main objective of this book is to showcase green synthesis as an emerging method for deriving nanoparticles from natural plant parts to be used in nanomedicine for promoting human health and well-being. It also looks at the advancement in nanoparticles production using plant parts/plant crude extracts (i.e. green synthesis) to combat non-communicable diseases (e.g. cancer, diabetes and oral candidiasis), communicable diseases (e.g. Ebola and tuberculosis) and vector-borne diseases (e.g. malaria), as well as antimicrobial resistance (extensively drug-resistant tuberculosis and antibiotic-resistant *Staphylococcus aureus*) in the African context. Furthermore, it unearths the prospects of utilizing nanoparticles to address cross-cutting disease and drug-related issues.

#### THE HISTORY OF NANOTECHNOLOGY

The idea of nanotechnology was first discussed in 1959 by American physicist Richard Feynman at an American Physical Society meeting at the California Institute of Technology (Caltech), in his talk entitled "There's Plenty of Room at the Bottom". In this speech, Feynman discussed the importance "of manipulating and controlling things on a small scale" and how they could "tell us much of great interest about the strange phenomena that occur in complex situations" (Feynman, 1960). The term "nanotechnology" was first introduced by the Japanese scientist Norio Taniguchi in a 1974 paper on production technology that creates objects and features on the order of a nanometre (Taniguchi, 1974). In 1986, Eric Drexler began to promote and popularize nanotechnology through his book *Engines of Creation: The Coming Era of Nanotechnology*. The invention of scanning tunnelling microscope in 1981 by

Gerd Binnig and Heinrich Rohrer at IBM Zurich Research Laboratory allowed scientists to see materials at an atomic or molecular level (Binning and Rohrer, 1986). The National Nanotechnology Initiative (NNI) in the US Federal Nanotechnology Research and Development Program defines nanotechnology as *the understanding and control of matter at dimensions of roughly 1–100 nm, where unique phenomena enable novel application*. The term nanotechnology encompasses nanoscale science, engineering and technology and involves imaging, measuring, modelling and manipulating matter at this length scale. A nanometre is one-billionth of a metre (NNI, 2020; Bhattacharya et al., 2009). Currently, there are two unique approaches for synthesizing nanoparticles: top-down and bottom-up. Top-down approach is when bulk material is broken down or cut down until it reaches the size of nanoparticles by applying external force, e.g. mechanical milling, drilling, grinding and laser ablation, while bottom-up approach refers to self-assembly of atoms, molecule by molecule until nanosize particles are formed, using chemical or physical forces, e.g. chemical reduction and biological (green) synthesis (Iqbal et al., 2012).

Nanomedicine is the medical application of nanotechnology. It uses nanoscale materials (1-100 nm) for health innovation to improve various kinds of diseases treatment, diagnosis, prevention and monitoring (Tinkle et al., 2014). The use of nanotechnology in the development of new medicines offers an enabling tool for providing new and innovative medical solutions to address unmet medical needs (Sadikot and Rubinstein 2009; Soares et al., 2018). The advantage of using nanotechnology in medicine includes target drug delivery, i.e. the capability of delivering biological or small molecules - active pharmaceutical ingredients (APIs) -to where they will be most effective. To achieve target drug delivery, APIs encapsulated nanoparticles are surface functionalized with different receptor ligands such as protein, peptide, antibody, folic acid, receptors, polysaccharide and polynucleotide so that they can be localized at the disease-specific site, without affecting the normal cells and/or healthy tissues. Site-specific drug delivery system reduced side effects and improved therapeutic efficacy and safety of therapeutic molecules (Bazak et al., 2015). The use of nanotechnology with natural products in nanomedicine is a rapidly developing innovative field that brings multiple advantages: it improves the effectiveness of natural compounds in disease treatment and prevention and/or offers better treatment outcome (Watkins et al., 2015). Incorporation of nanoparticles increases the bioavailability, targeting and controlled-release profiles of the natural products.

#### GREEN SYNTHESIS OF NANOPARTICLES: CONCEPTS AND SCIENTIFIC CONTEXT

The goal of using green methods for the synthesis of nanoparticles – "green nanotechnology" – was to produce nanomaterials and nano-products that are safe for human health and are environment-friendly, an alternative method for chemical and physical synthesis methods. Both chemical and green synthesis methods utilize the concepts of bottom-up approach for nanomedicine manufacturing. Green synthesis strategy uses existing principles of green chemistry and green engineering for the production of green nanomaterials and/ or nanomedicine products (Anastas and Warner, 1998). In medicine, nanotechnologies are designed to focus on the human health, environmental impact and social and economic benefits. Moreover, nanomaterials and nano-products production are achieved without the use of toxic ingredients, at low temperatures and less energy. Green synthesis strategy is cost-effective and requires low maintenance with relative reproducibility (Kalaiarasi et al., 2010). Plant extracts or microorganisms become "chemical factories" for greener nanomaterials or nano-products. During nanoparticle synthesis, both plant extracts and microorganisms can act as reducing/capping and stabilizing agents. However, plantbased synthesis approaches for nanoparticles formation are more ideal than those employing microorganism-based synthesis. Plant-based synthesis is easy and faster to formulate, and it produces nanoparticles that are more stable compared to those that are fabricated employing microorganisms-based synthesis approaches (Roy and Das, 2015; Ali et al., 2020; Salem and Fouda, 2020). In addition, plants are easily available and have a broad variety of novel metabolites or "green sources" from plant crude extracts, such as protein, vitamins, antioxidants, amino acids, enzymes, polysaccharides and secondary metabolites (e.g. flavonoids, phenolic acid, alkaloids, tannins and terpenoids). Different green sources extracted from various plant parts such as stem, root, leaves, fruit, flower, seed, callus and peel have been used as green "bio" reductants and capping agents during green synthesis of nanoparticles (Awwad and Salem, 2012; Ahmed et al., 2015; Mufamadi and Mulaudzi, 2019; Alphandery, 2020). African scientists are also using different plants parts or extracts for green synthesis of metallic nanoparticles such as Moringa oleifera (Leaf). Thevetia peruviana (leaf), Aloe vera (whole plant), Agathosma betulina (leaves), Combretum molle (leaves), African Galenia africana (whole plant), Hypoxis hemerocallidea (whole plant), Microsorum punctatum (leaf), Cassia fistula (leaf), Melia azadarach (leaf) and many more (Chiguvare et al., 2016; Oluwaniyi et al., 2016; Elbagory et al., 2017; Moodlev et al., 2018; Nate et al., 2019; Kedi et al., 2020; Naseer et al., 2020). Metallic nanoparticles include silver (Ag), gold (Au), iron (Fe), copper (Cu), zinc (Zn), palladium (Pd), platinum (Pt), lead (Pb), selenium (Se), titanium dioxide (TiO<sub>2</sub>), zinc oxide (ZnO), iron oxide (FeO) and copper oxide (CuO) (Ramesh et al., 2014; Shah et al., 2015; Avoseh et al., 2017; Chung et al., 2017; Singh et al., 2018; Mufamadi and Mulaudzi, 2019; Verma et al., 2019; Naseer et al., 2020). The mechanism of metallic nanoparticle synthesis using plant extracts involves the reduction of the silver metal ion (Ag<sup>+</sup>) into metallic silver nanoparticles (Ag<sup>0</sup> or AgNPs) with a size of 1–100 nm and different shapes (e.g. spherical, hexagonal and cuboidal). The green synthesis of nanoparticles protocol is a one-step synthesis involving the assembly of zero-valent metals or metal oxides or metal salts together with plant extract broth containing metabolites (i.e. phytochemicals) as reducing, capping and stabilizing agent (Roy and Das, 2015). The formation of metallic nanoparticles is confirmed by the colour change, e.g. AgNPs from initial reagent yellow solutions to dark brown mixture solution (Moodley et al., 2018). Dynamic light scattering (DLS), scanning electron microscopy (SEM), atomic force microscopy (AFM), transmission electron microscopy (TEM), X-ray diffraction (XRD), ultraviolet and visible spectrophotometry (UV-vis), Fourier-transform infrared spectroscopy (FTIR), low-energy ion

scattering (LEIS) and energy-dispersive spectroscopy (EDS) are used for further validation and physicochemical characterization of the metallic nanoparticle (e.g. size, shape, morphology and surface properties).

#### APPLICATION OF GREEN SYNTHESIZED NANOPARTICLES IN HUMAN HEALTH

Eco-friendly and the unique properties of green synthesized nanoparticles from plant extracts (i.e. phytochemical) make them excellent candidates for medicine and pharmaceutics applications. The novel properties of the green synthesized nanoparticles of plant extracts include optical or fluorescent properties, thermal, biosensing, photocatalyst, photodynamics, immunotherapeutic, antiangiogenesis, antibacterial, antifungal, antiparasitic, antioxidant, antiviral and anticancer activities. The applications of green synthesized nanoparticles on human health include therapy, drug delivery, diagnostics, biosensing, theranostics (a combination of therapy and diagnosis) and bio-imaging. According to Mukherjee et al. (2014), metallic nanoparticles synthesized from plant parts are promising to offer a multifunctional biomedical system, a 4-in-1 system that comprises biocompatibility, bio-imaging and antimicrobial and anticancer activities. The presence of Olax scandens leaf extract acted as a bio-reducing as well as stabilizing/capping agent during the formation of green AgNPs. The red fluorescence activity of AgNPs synthesized employing methanolic extract of Olax scandens leaf extract inside cancer cell makes it a potential diagnostic tool for cancer disease in the future. The optical and fluorescence properties of the green synthesized AgNPs and AuNPs could make them suitable candidates for replacing radiolabelled isotopes for tumour detection in the future, and ultimately they will reduce the side effects associated with radiotherapy (Ovais et al., 2016). A recent study by Varghese et al. (2020) demonstrated that green synthesized AgNPs from neem leaf extracts have biosensing and photocatalytic properties, and this was evaluated using mancozeb (MCZ) agrofungicide and optimum surface plasmon resonance (SPR). Riley and Day (2017) demonstrated the photothermal therapy employing green synthesized AuNPs. The study showed the green synthesized AuNPs to be capable of absorbing incident photons and converting them to heat to destroy cancer cells and/or tumours.

Many studies reported antimicrobial and anticancer activities employing green synthesized metallic nanoparticles from plant extract or phytochemical extracted from different parts of plants, e.g. leaves, fruit, flower, stem and root (Awwad and Salem, 2012; Chiguvare et al., 2016; Oluwaniyi et al., 2016; Elbagory et al., 2017; Kedi et al., 2020; Naseer et al., 2020). However, the antimicrobial and anticancer mechanism of action of green synthesized nanoparticles is still not fully understood. Various mechanisms have been proposed to illustrate the activity of green synthesized nanoparticles as antimicrobial and anticancer agents:

#### **ANTIMICROBIAL MECHANISM OF ACTION**

- Disabling the respiratory of chains
- · Cell membrane disruption and leakage of its cellular contents

- Binding to functional group of proteins causing protein denaturation and cell death
- Blocking the DNA of replication
- Denaturation of proteins and cell death through binding to functional groups of proteins

#### ANTICANCER MECHANISM OF ACTION

- Cytotoxicity that disturbs the cell membrane permeability and cellular internalization resulting in cell death through a cascade of events
- Inducing apoptosis through caspase-dependent and mitochondrial dependent pathways
- Generation of reactive oxygen species (ROS) that leads to induction of ROS resulting in cellular damage
- Trigger upregulation of p53 protein and caspase-3 expression through apoptosis pathway activation leading to cell death
- pH-dependent release of metal ions from green synthesized nanoparticles leading to cancerous cells death
- Inhibiting the function of vascular endothelial growth factor (VEGF)induced angiogenesis

Green synthesized nanoparticles from plant extract shown to have the potential to enhance the diagnosis and treatment of non-communicable diseases (e.g. cancer, diabetes and oral candidiasis), communicable diseases (e.g. Ebola and tuberculosis) and vector-borne diseases (e.g. malaria) as well as antimicrobial resistance (extensively drug-resistant tuberculosis and antibiotic-resistant *Staphylococcus aureus*) are discussed in this book.

#### NON-COMMUNICABLE DISEASES

NCDs are a diverse group of chronic diseases that are not communicable and cannot be passed from person to person. NCDs are responsible for the premature mortality around the world. According to the World Health Organization (WHO), the four main risk factors for major NCDs are high consumption of alcohol, tobacco consumption, lack of physical activity and unhealthy diet (WHO, 2015). According to Marquez and Farrington (2013), by 2030, NCDs such as cancers, diabetes, cardiovascular diseases (like heart attacks and stroke) and chronic respiratory diseases (pulmonary disease and asthma) will become the leading cause of death in sub-Saharan Africa. The challenge of treating NCDs is that most of them can only be diagnosed at a late stage of affliction, making it very difficult to treat or manage, e.g. cancer diseases present at a late stage (5-years later) and/or once the tumour has already formed (Mulisya et al., 2020). Combating these NCD burdens demands immediate measures and tools that could enable early and rapid diagnosis and treatment, such as nanomedicine (Chandarana et al., 2018). Nanomedicine promises to offer better approaches towards identifying NCDs at an early stage and to overcome treatment challenges associated with them.

Therapeutic benefits of using nanomedicine in NCDs include improved drug circulation times, target delivery that enhances treatment efficacy and the ability to act as a therapeutic (Sanna et al., 2014; DiSanto et al., 2015; El-Readi and Mohammad, 2019; Lafisco et al., 2019). Moreover, nanomedicine promises to provide better diagnostic tools, medical imaging and theranostics, by the combination of therapy and diagnosis in a single application (Mukherjee et al., 2014; Chandarana et al., 2018).

#### **COMMUNICABLE DISEASES**

CDs or infectious diseases are communicable, which means that they can be passed from person to person either directly or indirectly by disease-causing agents, humans or animals (Nash et al., 2015). The disease-causing agents include viruses, bacteria, fungi and parasites, and account for approximately 15 million deaths worldwide (Singh et al., 2017). Africa has the highest prevalence of CDs in the world. HIV/AIDS, tuberculosis, acute respiratory infections, malaria and diarrheal diseases are on top in the list of the deadliest CDs in Africa. Four of them combined are predicated to be responsible for nearly 80% of the total infectious disease burden and claiming more than 6 million people per year (Boutayeb, 2010). Since the establishment of the sustainable development goals (SDGs), Africa has set new ambitious targets which include ending the prevalence of HIV/AIDS, TB and malaria by 2030 (Narayan and Donnenfeld, 2016). However, the rising cost of the antibiotics, antimicrobial and antiparasitic resistance and also the adverse side effects due to prolonged drug use indicate that the battle against CDs is far from over (Blecher et al., 2011). Therefore, in order to envision a future without these CDs, it will require an improved antimicrobial agent or newer and more effective therapies. The unique physical and chemical properties of nanoparticles make them an ideal candidate to improve the therapeutic effects associated with current conventional therapies and/or to end the prevalence of HIV/AIDS, TB and malaria by 2030. The roles that nanomedicine is promising to play in CDs include improved therapeutic, diagnostic and prevention/vaccination approaches (Blecher et al., 2011; Dube, 2019). In the case of CD diagnostics, nanomedicine promises to offer cheap and quick diagnostic test. When it comes to CD treatments and vaccine, nanomedicine promises to offer immunotherapy that is capable of neutralizing viruses and to improve drug circulation times, target delivery, combination therapy, pharmacokinetics and pharmacodynamics.

#### NANOMEDICINE INNOVATIONS: NEW TREND

The convergence of material science, biotechnology, engineering and nanomedicine is promising to transform medical technology and the pharmaceutical industry. Moreover, the improved nanomedicine is promising to offer accurate diagnoses, targeting therapies with fewer side effects, and providing better medical imaging and personalized medicine (de Smet et al., 2011; Zhang et al., 2017). A new trend in nanomedicine technology is influenced by the advancement in nanoformulation that led to a new type of nanomedicine:

- Stimuli-responsive nanomedicines that trigger drug release in an ondemand manner or influence by stimulus, e.g. pH, light, thermal, redox and magnetic and electronic fields
- Nanotheranostics (i.e. smart pill) that combines therapeutics with imaging agents into one pill
- Polytherapy (i.e. polypill), which combines multiple active pharmaceutical ingredients into one pill
- Nanosensors that can diagnose certain diseases through analysing human exhaled breath, and thus recognizing the biomarker gases related to diseases in human exhalation
- Fully autonomous DNA nanorobot that is capable of transporting vaccines and drugs to the targeted site

The development of these new types of nanomedicines was to address the issue of multidrug resistance (MDR) in current antimicrobial and anticancer agents (Fattal and Tsapis, 2014; Tangden, 2014; Kim et al., 2017; Zhang et al., 2017; Li et al., 2018; Zhou et al., 2018). In addition, it was to overcome challenges associated with conventional nanomedicine such as poor stability, poor bioavailability, drug toxicity and hurtful side effects (Fattal and Tsapis, 2014).

#### **COMMERCIALIZATION ASPECTS**

Many different nanomedicines have been developed over the years to improve the therapeutic efficacy, target drug delivery system and safety for various types of diseases (Ventola, 2012; Curley et al., 2017). According to Metselaar and Lammers (2020), more than 50 nanomedicine formulations are currently approved for clinical use by the Food and Drug Administration (FDA) and many others are currently undergoing clinical trials. However, none of those approved nanomedicine formulations are from Africa. Although nanomedicines have the potential to provide affordable and efficient medical solutions, only few African countries are prioritizing on it: South Africa, Egypt, Morocco and Nigeria (Mufamadi, 2019). African countries need to start embracing their own health innovation, research and/or local technologies and stop depending on the international market for every technology they need (Singer et al., 2008). If African scientists need to commercialize their nanomedicines, they need to find a commercialization strategy that matches their potential and sustainability, such as licensing, equity investment, strategic alliances and private consortium or cluster alliance (Mufamadi, 2019). Moreover, they need to make a substantial investment towards the infrastructure along with the increase in human capacity building and nanomedicine-based products. Furthermore, they need to find a way of attracting investment from local or international investors and big pharmaceutical companies.

#### REFERENCES

Ahmed, S., Ahmad, M., Swami, B. L., Ikram, S. 2015. "A review on plants extracts mediated synthesis of silver nanoparticles for antimicrobial applications: A green expertise." *Journal of Advanced Research* 7: 17–28. DOI: 10.1016/j.jare.2015.02.007.

- Ali, A., Ahmed, T., Wu, W., Hossain, A., Hafeez, R., Masum, MI., Wang, Y., An, Q., Sun, G., Li, B. 2020. "Advancements in plant and microbe-based synthesis of metallic nanoparticles and their antimicrobial activity against plant pathogens." *Nanomaterials* 10: 1146. DOI: 10.3390/nano10061146.
- Alphandery, E. 2020. "Natural metallic nanoparticles for application in nano-oncology." International Journal of Molecular Sciences 21: 4412. DOI: 10.3390/ijms21124412.
- Anastas, P.T. and Warner, J.C. 1998. *Green Chemistry: Theory and Practice*, 30. Oxford: Oxford University Press.
- Aromal, S.A. and Philip, D. 2012. "Green synthesis of gold nanoparticles using Trigonella foenum-graecum and its size dependent catalytic activity." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 97: 1–5. DOI: 10.1016/j.saa.2012.05.083.
- Avoseh, O.N., Oyedeji, O.O., Aremu, O., Nkeh-Chungag, B.N., Songca, S.P., Oyedeji, A.O., Sneha, M.S., Oluwafemi, O.S. 2017. "Biosynthesis of silver nanoparticles from Acacia mearnsii De Wild stem bark." *Green Chemistry Letters and Reviews* 10, no. 2: 59–68. DOI: 10.1080/17518253.2017.1287310.
- Awwad, A.M. and Salem, N.M. 2012. "Green synthesis of silver nanoparticles by mulberry leaves extract." *Journal of Nanoscience and Nanotechnology* 2: 125–128. DOI: 10.5923/j.nn.20120204.06.
- Bazak, R., Houri, M., El Achy, S., Kamel, S., Refaat, T. 2015. "Cancer active targeting by nanoparticles: A comprehensive review of literature." *Journal of Cancer Research and Clinical Oncology* 141, no. 5: 769–784. DOI: 10.1007/s00432-014-1767-3.
- Benakashani, F., Allafchian, A.R., Jalali, S.A.H. 2016. "Biosynthesis of silver nanoparticles using Capparis spinosa L. leaf extract and their antibacterial activity." *Karbala International Journal of Modern Science* 2, no. 4: 251–258. DOI: 10.1016/j. kijoms.2016.08.004.
- Bhattacharya, D., Singh, S., Satnalika, N. 2009. "Nanotechnology, big things from a tiny world: A review." *International Journal of Science and Technology* 2, no. 3: 29–38.
- Binnig, G. and Rohrer, H. 1986. "Scanning tunneling microscopy". IBM Journal of Research and Development. 30, no. 4: 355–369.
- Blecher, K., Nasir, A., Friedman, A. 2011. "The growing role of nanotechnology in combating infectious disease." *Virulence* 2, no. 5: 395–401. DOI: 10.4161/viru.2.5.17035.
- Boutayeb, A. 2010. "The impact of infectious diseases on the development of Africa." In *Handbook of Disease Burdens and Quality of Life Measures*, edited by Preedy V.R., Watson R.R. New York: Springer. DOI: 10.1007/978-0-387-78665-0\_66.
- Caroling, G., Vinodhini, E., Ranjitham, A.M., Shanthi, P. 2015. "Biosynthesis of copper nanoparticles using aqueous Phyllanthus embilica (Gooseberry) extract- characterisation and study of antimicrobial effects." *Journal of Nanostructure in Chemistry* 1, no. 2: 53–63.
- Chandarana, M., Curtis, A., Hoskins, C. 2018. "The use of nanotechnology in cardiovascular disease." *Applied Nanoscience* 8: 1607–1619. DOI: 10.1007/s13204-018-0856-z.
- Chiguvare, H., Oyedeji, O.O., Matewu, R., Aremu, O., Oyemitan, I.A., Oyedeji, A.O., Nkeh-Chungag, B.N., Songca, S.P, Mohan, S. and Oluwafemi, O.S. 2016. "Synthesis of silver nanoparticles using Buchu plant extracts and their analgesic properties." *Molecules* 21, no. 6: 774. DOI: 10.3390/molecules21060774.
- Chung, I.M, Rahuman A.A., Marimuthu, S., Kirthi, A.V., Anbarasan, K., Padmini, P., Rajakumar, G. 2017. "Green synthesis of copper nanoparticles using Eclipta prostrata leaves extract and their antioxidant and cytotoxic activities." *Experimental and Therapeutic Medicine* 14: 18–24. DOI: 10.3892/etm.2017.4466.
- Curley, P., Liptrott, N.J., Owen, A. 2017. "Advances in nanomedicine drug delivery applications for HIV therapy." *Future Science OA* 4, no. 1: FSO230. DOI: 10.4155/ fsoa-2017-0069.

- De Smet, M., Heijman, E., Langereis, S., Hijnen, N.M., Grüll, H. 2011. "Magnetic resonance imaging of high intensity focused ultrasound mediated drug delivery from temperature-sensitive liposomes: An in vivo proof-of-concept study." *Journal of Controlled Release* 150, no. 1: 102–110. DOI: 10.1016/j.jconrel.2010.10.036.
- DiSanto R.M., Subramanian, V., Gu, Z. 2015. "Recent advances in nanotechnology for diabetes treatment." Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology 7, no. 4: 548–564. DOI: 10.1002/wnan.1329.
- Dube, A. 2019. "Nanomedicines for infectious diseases." *Pharmaceutical Research* 36, no. 4: 63. DOI: 10.1007/s11095-019-2603-x.
- Elbagory, A.M., Meyer, M., Cupido, C.N., Hussein, A.A. 2017. "Inhibition of bacteria associated with wound infection by biocompatible green synthesized gold nanoparticles From South African plant extracts." *Nanomaterials* 7, no. 12: 417. DOI: 10.3390/nano7120417.
- El-Readi, M.Z. and Mohammad, A.A. 2019. "Cancer nanomedicine: A new era of successful targeted therapy." *Journal of Nanomaterials* 2019: 1–13. DOI: 10.1155/2019/4927312.
- Fattal, E. and Tsapis, N. 2014. "Nanomedicine technology: Current achievements and new trends." *Clinical and Translational Imaging* 2: 77–87. DOI: 10.1007/s40336-014-0053-3.
- Feynman, R.P. 1960. "There's plenty of room at the bottom." *Engineering and Science* 23: 22–36.
- Iqbal, P., Preece, J.A., Mendes, P.M. 2012. "Nanotechnology: The 'top-down' and 'bottom-up' approaches." In *Supramolecular Chemistry*. Chichester, UK: Wiley. DOI: 10.1002/9780470661345.smc195.
- Kalaiarasi, R., Jayallakshmi, N. Venkatachalam, P. 2010. "Phytosynthesis of nanoparticles and its applications." *Plant Cell Biotechnology and Molecular Biology*. 11, no. 1/4: 1–16.
- Kaviya, S., Santhanalakshmi, J., Viswanathan, B., Muthumary, J., Srinivasan, K. 2011. "Biosynthesis of silver nanoparticles using citrus sinensis peel extract and its antibacterial activity." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 79, no. 3: 594–598. DOI: 10.1016/j.saa.2011.03.040.
- Kedi, P.B.E., Nanga, C.C., Gbambie, A.P., Deli, V., Meva, F.E., Mohamed, H.E.A., Ntoumba, A.A. et al. 2020. "Biosynthesis of silver nanoparticles from Microsorum Punctatum (L.) copel fronds extract and an in-vitro anti-inflammation study." *Journal of Nanotechnology Research* 2, no. 2: 025–041 DOI: 10.26502/jnr.2688-85210014.
- Kim, S., Choi, S., Jang, J., Cho, H., Kim, I. 2017. "Innovative nanosensor for disease diagnosis." Accounts of Chemical Research 50, no. 7: 1587–1596. DOI: 10.1021/acs. accounts.7b00047.
- Lafisco, M., Alogna, A., Miragoli, M., Catalucci, D. 2019. "Cardiovascular nanomedicine: The route ahead." *Nanomedicine* 14, no. 18: 2391–2394. DOI: 10.2217/nnm-2019-0228.
- Li, S., Jiang, Q., Liu, S., Zhang, Y., Tian, Y., Song, C., Wang, J. et al. 2018. "A DNA nanorobot functions as a cancer therapeutic in response to a molecular trigger in vivo." *Nature Biotechnology* 36: 258–264. DOI: 10.1038/nbt.4071.
- Marquez, P.V. and Farrington, J.L. 2013. *The Challenge of Noncommunicable Diseases and Road Traffic Injuries in Sub-Saharan Africa: An Overview*. Washington, DC: The World Bank.
- Metselaar, J.M. and Lammers, T. 2020. "Challenges in nanomedicine clinical translation." *Drug Delivery and Translational Research* 10: 721–725. DOI: 10.1007/ s13346-020-00740-5.
- Moodley, J.S., Krishna, S.B.N., Karen Pillay, K., Govender, S., Govender, P. 2018. Green synthesis of silver nanoparticles from Moringa oleifera leaf extracts and its antimicrobial potential. Advances in Natural Sciences: Nanoscience and Nanotechnology 9: 1–9.
- Mufamadi M.S. 2019. "From lab to market: Strategies to nanotechnology commercialization in Africa." *MRS Bulletin* 44: 421–422. DOI: 10.1557/mrs.2019.134.