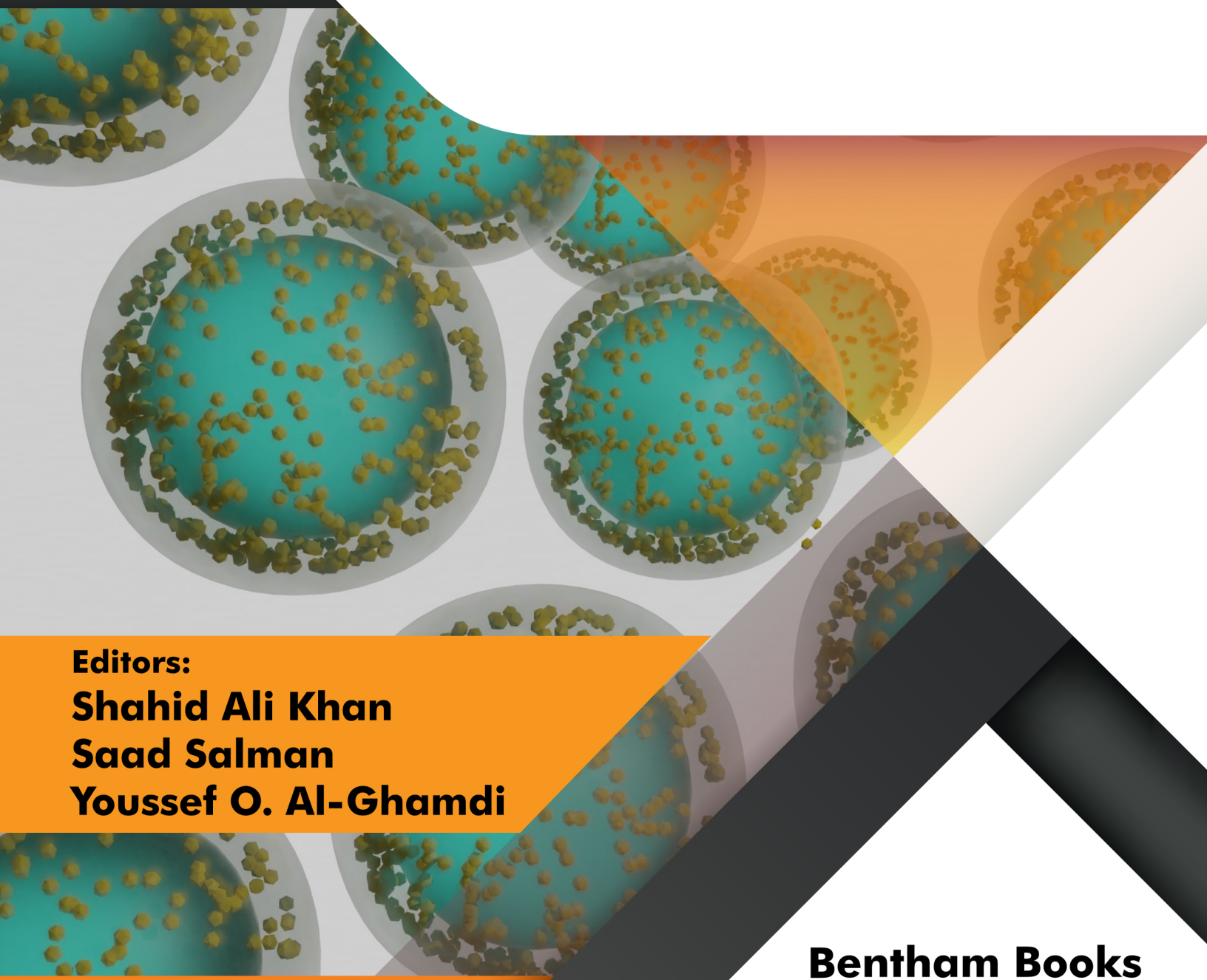
NANOTHERAPEUTIC STRATEGIES AND NEW PHARMACEUTICALS

PART I



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Nanotherapeutic Strategies and New Pharmaceuticals *(Part 1)*

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Nanotherapeutic Strategies and New Pharmaceuticals (Part I)

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ISBN (Online): 978-981-5036-69-5

ISBN (Print): 978-981-5036-70-1

ISBN (Paperback): 978-981-5036-71-8

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PREFACE

Therapeutic agents have an impressive history in drug discovery and development which led to the identification of numerous phenomenal lead drug candidates. The current therapeutic regimens are allied with several inverse biological effects. Therefore, there is an urgent need for innovative and technological strategies to help in medical diagnosis and management. With the advancement of new technologies in medicinal chemistry, several highly specific, biocompatible, and non-toxic therapeutic agents are discovered and successfully applied for diverse clinical applications. Nanotechnology has perceived historic progress in the last few decades and recently proved its efficacy in every field of science and technology. Nanotechnology-based pharmaceuticals offered multifaceted and alternative methodologies to an overwhelmed conventional limitation of clinical therapies. Expertise in designing and developing nanoformulation helped in targeted drug delivery. Recently, the use of innovative therapeutic agents, particularly in nanomedicine, has accounted for a significant portion of the global pharmaceutical market and is predicted to continue to grow rapidly in the near future.

Dr. Shahid has worked on a variety of scientific platforms over the years. He has authored multiple research publications and is well-known for his scientific knowledge. In 2019, he envisioned creating a comprehensive book on nanotherapeutics in the biological sector, which had previously been spread across the literature. Dr. Saad Salman and Dr. Youssef O. Al-Ghamdi, the co-editors, later joined hands in this scientific voyage. This book is the result of over ten years of research and the diverse contributions of more than 50 fertile brains. Many well-known scientists from various countries, including the United States, the United Kingdom, Italy, Pakistan, Malaysia, India, and Bangladesh, contributed numerous book chapters to the premises of the book titled “Nanotherapeutic strategies and new pharmaceuticals” in this book, which resulted in part I and part II. For instance, COVID-19: an outbreak, application of nanotherapeutics agents in disease control, wound healing, surgery, stem cell, central nervous, haematology, cancer therapy, Gene therapy/editing and many more. Volume-I contains 9 chapters and each chapter has a minimum of 6,000 words. This indicates that each chapter has been meticulously detailed and structured.

Furthermore, each chapter is written by specialists in respective fields, and it was made mandatory to keep it as easy as possible to make it accessible to both beginners and experts. As a result, this book is one of the best for a wide range of readers. Furthermore, this book is structured to address a wide range of topics relevant to chemists, biologists, pharmacists, and material scientists.

We are very thankful to all the authors who spare time from their busy schedules and contributed their ideas and knowledge to this book. In addition, we also pay our sincerest gratitude to the team of Bentham Science, who made great efforts to make this book series possible.

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About the Editors

Shahid Ali Khan (Editor)

Dr. Shahid Ali Khan did his master of science (MSC) in 2010 in organic chemistry from Kohat University of Science and Technology, and Master of Philosophy (MPhil) in Natural Product and Medicinal Chemistry in 2014 from ICCBS Karachi and Ph.D. in Nanocatalysis in 2017 from King Abdulaziz University, Saudi Arabia. Dr. Khan got the best Ph.D. thesis award. Dr. Khan joined the University of Swabi as Assistant Professor in Feb. 2018 and still working in the same University. During his stay at the University of Swabi, Dr. Khan has supervised 7 MSC students and Co-supervised 8 Mphil students. Currently, many students of Dr. Khan's research group are involved in the synthesis and designing of nanocatalyst and hydrogels for various technological applications. During this period, Dr. Khan have completed 2 projects as a PI and 4 projects as a Co-PI, while many projects are under progress.

Moreover, Dr. Khan is working on multi-dimensional projects including Natural product chemistry, medicinal chemistry, Nanocatalysis and self-assembled hydrogels for diverse applications. Dr. Khan is also involved in the designing and synthesis of thin films as solid support for the stabilization of zero-valent metal nanoparticles for functional group transformation. Dr. Khan teaches various courses in Organic Chemistry, Physical chemistry, and spectroscopy to BS, MS, and Ph.D. students.

In brief, Dr. Khan has published 62 publications with a cumulative impact factor of 255 and has published 8 book chapters in various international journals of high repute.

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Dr. Saad Salman is a Lecturer at the Department of Pharmacy, The University of Lahore (Islamabad Campus), teaching Undergraduate and Postgraduate students. He is a Certified Health Researcher from NIH, USA. He has over twenty-one International publications, two International books, two book chapters, and thirty abstracts published. He is the founder and CEO of Research and Publication Inc.,which provides solutions to research students. He had received numerous awards at various conferences. He is an active member of the American Society of Pharmacology and Experimental Therapeutics (ASPET), the American Pharmacist Association, and the American Society of Consultant Pharmacists.

Youssef O. Al-Ghamdi (Co-Editor)

Youssef O. Al-Ghamdi received a bachelor's degree in Chemistry from Umm AL-Qura University, Makkah, Saudi Arabia, in 2008. Dr. Alghamdi received his master's degree in Organic Chemistry from King Khalid University, Abha, Saudi Arabia, in 2012, and the Ph.D. degree in Organic Chemistry, Polymers King Abdulaziz University, Jeddah, Saudi Arabia in 2018. He joined the College of Science at Al-Zulfi branch, Majmaah University, and currently chair the department of chemistry. Dr. Alghamdi is heading several units such as Planning and Development and Unit of Scientific Affairs. He is a member of the College Council, College of Science, Al-Zulfi, Majmaah University and a member of Labs and Facilities. **Dr. Youssef O. Al-Ghamdi** is involved in teaching various courses in Organic Chemistry, to BS and he has published 20 publications.

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CHAPTER 1

Advances in Nanotherapeutic Agents

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Abstract: Nanotechnology is an emerging field of science covering all the technological fields. Likewise all other fields, the medical field is also encountered by nanotechnology. In this regard, nanopharmaceuticals has gained the attention of researchers, leading to the development of nanomedicines. Nanopharmaceuticals are biologicals active molecules used for the effectiveness of drug therapies on the nanoscale. Nanomedicines in the fast-developing area have shown very fruitful results. Nanomedicines offer varieties of properties, for example, it has the capability to cross the cell barriers in order to reach the targeted organelles. It also overcomes the multidrug-resistant and prevents the effect on healthy cells. Drug delivery based on nanoparticles has many applications. Nanoparticles-based drug delivery system delivers the specified drug to the cells of the targeted tissue by controlled release. Thus, it has overcome the limitations of conventional therapies. The anti-cancer drug delivery to the cancerous cells is one of the examples of nanocarriers-based therapy. Nanoshells are used in this regard. Nanoshells load the specified anticancer pharmaceuticals, penetrate the cells and attack the targeted organelles within cells. The main and important properties of this therapy are the prevention of healthy cells from the drug effect. Nanotechnology is also used in diagnosis. It is used in the diagnosis of bone fractures, cardiovascular diseases, cancerous cells identification, and the detection of tumors in the brain. Nanolaser-based surgery is also the emerging field of nanotechnology. For this purpose, nano microscopy was used. In nano microscopy, surgery nano-based tools are used in which have the ability to penetrate the cells and remove/ kill the infected organelles. In this chapter, almost all the aspects of nanotechnology have been discussed, with a special focus on nanocarriers.

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Keywords: Nanoscience, Nanomedicines, Nanobots, Nanoendoscopes, Nanolasers, Nanotechnology in Radiology.

1. OVERVIEW OF NANOSCIENCE

The study of natural, synthetic, or semisynthetic substances at the submicroscopic level is called nanoscience. At the nano level, the features of various elements vary significantly as compared with the outdated microscale [1]. Nanostructured substances exhibit extraordinary features due to their high surface capacity and hence, are used in every field of science and medicine. Even in daily life, they are most liked by the public due to two distinctive features, *i.e* small size, and big function. This science is so broad that a particular worldwide accepted description, but generally, they are defined from the size of the particles they possess. According to IUPAC and EU, the nanoparticles have a size that ranges from one nanometer to 100 nanometers [2]. On the other hand, the size of medical nanomaterials is about 20-200 nm or maybe more than that [3]. Pokropivny, V. *et al*., taxonomized nanostructured materials as zero-dimensional things (nanospheres), one-dimensional (nanotubes), two dimensional (nanosheets), and three-dimensional (structures made out of individual squares in the nanometer scale, or mass materials) [4]. Early Egyptian peoples of 9th century BC made use of artificial stain to decorate utensils, and the stain was formulated from nanosized gold or silver. Another example is "Egyptian blue" which was used in the 3rd century BC [5].

In the modern age, the field of nanoparticles was developed by Michael Faraday (1875). He made gold at the nanoscale from aurum chloride through electrolysis [6]. In 1959 Richard Feynman established the foundation of current nanotechnology through his well-known speech, "There is plenty of room at the bottom [7]. In the 1980s, Buckminster fullerenes (by Buckminster) were introduced that further strengthen the field of nanotechnology. Carbon nanotubes were also developed in this period [8]. For the observation of nanoparticles, various techniques were developed at the beginning of the 20th century. These techniques include TEM, SEM, scanning tunneling microscope, and atomic force microscopy [9 - 11].

1.1. Nanomedicine–A Chronological Perception and Functions

Now a day's nanotechnology is applied in medical fields where nanomedicine exhibit higher therapeutic value than ordinary medicine. Due to the improved therapeutic value, nano-sized medicine has very high efficacy as compared to traditional medicine. Furthermore, nanosized drug delivery systems, nanosized

imaging, and diagnostic systems are also introduced with the same properties i-e small size and high efficacy. In 1909, Paul Ehrlich introduced the concept of "magic bullet", for drugs, launched the current therapeutic investigation [12]. Variation of the pharmacokinetics of a drug (which is necessary for its biological action) *via* its structural reformation is constrained by the structural requirement. Nanotechnology offers the likelihood to bypass this restriction by controlling the pharmacokinetics (increased absorption rate of the drugs). In 1960 Horne and Bangham reported the self-assembling properties of phospholipids. They self-assemble their structure like a plasma membrane. They can form vesicular masses of nano-size and the nanovesicles were called "liposomes" [13]. In the 1970s that drug designers employed nanocarriers for drug delivery.

In 1976 a nano-pharmaceutical scientist, Peter Speiser, studied the polyacrylamide (PAAM) based nanoparticles for vaccination and were adjuvants in nature [14]. These NP's were spherical with a size of fewer than 80 nanometers which form real colloidal aqueous solutions. The NP's were compatible to deliver antigenic material (tetanus vaccine and human intravenous immunoglobulin G) and administered parenterally. These preparations show intact biological activity and high antibody production in animals.

In 1979, Couvreur *et al*., shown the highly lipophilic characteristics of nanosized polyalkylcyanoacrylate and built up the first decomposable nanocapsules for anticancer drug delivery, and displayed successful endocytic application in calf serum [15].

Papahadjopoulos, along with Bangham, independently in 1967, studied the characterization of smectic mesophases, worked on the methods of water-soluble materials into phospholipidic vesicles, and Gregory Gregoriadis in 1971 showed that liposomes could deliver enzymes for therapeutic purposes [16].

With the expanded exploration in clinical, intra-and intercellular cycles, and huge developments in fundamental natural sciences and nanotechnology, it became clear that control of articles at the nanoscale level could take into consideration huge in the clinical field. Various materials and bodies may act as nanocarriers. Medications or proteinous drugs (*e.g*., Denileukin diftitox or hormones or enzymes) can be securely conveyed with the assistance of nanocarriers. Besides, the nanocarriers ars more efficient for drug delivery. As a result of these extensive researches, different nano antibiotics were introduced in the market, for instance, (i) AmBisome® (combination of liposomes encapsulating amphotericin B) for fungal diseases, (ii) Liposomal doxorubicin (combination of liposomes encapsulating doxorubicin) for treatment of mammary gland cancer [17], (iii) DOX/ICG Coencapsulated Liposome-Coated Thermosensitive Nanogels for

CHAPTER 2

Nanotechnology in Stem Cell Research

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Abstract: Nanotechnology encompasses the production of materials at the nanoscale level and has been applied to many fields, including medicine. Within nanoscale ranges, the physical properties of particles are dominated by quantum mechanics, thus resulting in chemical behaviours that are distinct from that of bulk substances. Nano-based therapeutics and medical devices take advantage of these specific properties in order to better image and model the underlying biochemical and biophysical changes in a system, especially in diseases that progress over time. More specifically, advances in stem cell research have been aided by the use of nanoscale materials, enabling scientists to enhance stem cell behaviours for precise gene editing, regenerative medicine, and drug delivery. The interdisciplinary application of nanotechnology has great potential in clarifying the fundamentals of stem cell biochemistry, thus accelerating the development of future regenerative therapies.

Keywords: Chemical Behaviour, Nanomaterials, Nanotechnology, Physical Properties, Regenerative Medicine, Stem Cells.

1. INTRODUCTION

Nanotechnology is an emerging field focused on the production of materials at the nanoscale level. The underlying principles of its use in various fields include the observed phenomenon that size directly affects the physiochemical properties of the substance, generating different behaviours to that of bulk structures. In recent years, the application of nanotechnology to the medical field (thus term nanomedicine has garnered substantial interest due to their flexible engineering towards therapeutics, imaging, and diagnostics. In this chapter, the prevalence of nanotechnology in stem cell research will be explored by analyzing the ways in which the physicochemical properties of specifically-engineered nanoparticles can

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supplement stem cell function in therapeutics. The advantages and disadvantages of these various technologies will also be discussed. Although much of the biochemistry behind stem cells has yet to be fully understood, they provide a promising outlook for many fields, including organ transplantation and the treatment of congenital disorders. However, limitations towards its clinical use remain, which could potentially be overcome by the incorporation of biomimetic nanoparticles.

1.1. What are Stem Cells?

Stem cells are unspecialized, with the ability to differentiate into a number of different cell types, and are present in both adult and embryonic tissues [1]. They are part of the repair system, providing a supply of correctly-differentiated cells in situations where these cells need to be continually replaced. Stem cells are characterised by their ability for self-renewal, enabling them to divide indefinitely under specific conditions [2]. This is in part due to the higher level of telomerase within stem cells as compared to other somatic cells, which allows them to replenish chromosomal cappings. However, attrition of these regions over time may lead to aberrations in replication; some stem cell types are susceptible to the formation of teratomas, which are non-cancerous tumours that contain diverse mixtures of semi-developed tissues such as teeth, hair and cartilage [3]. Stem cells are also potent, with the ability to specialise into various cell types, the diversity of which is limited by the stage of development from which the stem cell is obtained. The specialisation process is influenced by many different signals, both external and internal, including physical cell-cell contact and fluctuations in gene expression.

1.2. Types and Biogenesis of Stem Cells

The ability for stem cells to differentiate into various cell lineages is determined by the stage at which it is extracted; embryonic or adult. These cells, therefore, display different behaviours and are generated through distinct lineages. The therapeutic potential of both will be evaluated and compared.

1.2.1. Embryonic Stem Cells

Embryonic stem cells (ESCs) are derived from the inner cell mass of a human blastocyst, a structure that forms approximately five days after fertilization [4]. The zygote, the cell immediately resulting from fertilisation is totipotent. Totipotency is characterised by the ability to differentiate into any other cell line;

the developmental potency of a cell becomes more restricted as it progresses further down distinct pathways of specialisation [5]. A series of mitotic cell divisions results in a structure known as the morula, a sphere of 32-64 totipotent cells. This then develops into the blastocyst, the cell types of which are separated into the peripheral cells and the inner cell mass; peripheral cells later form extraembryonic membranes and the placenta, whereas the inner cell mass forms the foetus (Fig. **1**). Thus, the inner cell mass is not totipotent but instead pluripotent, with the ability to differentiate into any cell type excepting those derived from the peripheral blastocyst cells [6]. Cultured ESCs are pluripotent and can be engineered to differentiate into the three germ layers: ectoderm, mesoderm, and endoderm, from which all mature cell types found in the adult organism develop [7]. This presents a number of innovative applications into further understanding of the development and disease progression, as well as therapeutic tools for the treatment of currently incurable disorders such as neurological injury, type I diabetes, and cardiovascular conditions.

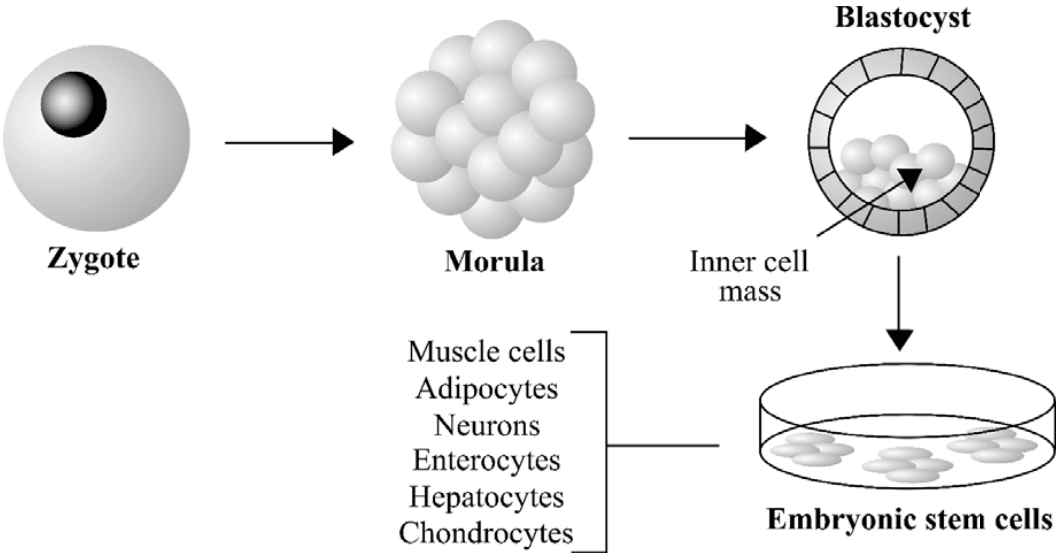

Fig. (1). Embryonic stem cell development and culture for *in vitro* differentiation into various tissues [8].

ESC lines are kept in the undifferentiated state *via* strictly controlled conditions in permanent culture containing bovine serum and feeder cells, which are inactivated to supply growth factors for the stem cells [9, 10]. However, the establishment of these stem cells has been ethically controversial as the extraction of the inner cell mass results in the destruction of the blastocyst in most cases. Whether blastocysts can be considered human lives has not yet been scientifically determined; thus, alternative methods of obtaining pluripotent cells have been developed in order to avoid the use of human embryos. One such method is the engineering of induced

CHAPTER 3

The Role of Nanotherapeutic Agents in Hematology and Related Diseases

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Abstract: Hematological anomalies are becoming more prevalent in the world and are comprised of blood-related diseases. They either disrupt normal blood circulation or reduce the blood volume and, consequently, death. Therapies are available to treat and alleviate these diseases, but they adversely interact with other organs/tissues to provoke them. To avoid such adverse scenarios, NT graced medicine to deliver therapeutic agents in nanocarriers that are engineered to transport them to their target site, averting untoward effects and functioning for a long time. In this chapter, we will be highlighting the role of NT in the treatment of hematological and other related diseases.

Keywords: Blood Related disease, Hematology, Nanotechnology, Targeted delivery, Treatment.

1. INTRODUCTION

Biomedical applications and pharmacology rely on nanotherapeutic agents. These applications rely on nanotherapeutic agents (NT) which is an example of a microscale form of disease treatment. A growing number of people are embracing NT in today's world, due to the transition to focused treatment [1], where medication retention capacities can be improved. As part of the treatment, healthy cells are often destroyed. However, targeted treatment only addresses the aberrant cells, which prevents any injury to the surrounding healthy cells [2]. While previous medical discoveries have made use of similar technologies, it is possible that in the future, as nanomedicine (NM) and technology come together, more solutions will be found. Due to these considerations, NM has been (and continues to be) exposed to new domains in medicine [3]. Particularly, NM has impacted the field of Hematology. In its essence, Hematology is the branch of medicine that focuses on blood, its formation, and blood-related diseases. Hematologists are physicians who look for patterns in the behavior of blood cells and interpret those

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patterns to find correlations in the Cardiovascular and Lymphatic systems [4]. Hematologists can diagnose diseases from Anemia all the way to leukemia (LA) and lymphoma. Within this chapter, you will find common diseases that hematologists diagnose and how NT has impacted treatment methods and overall results for these diseases.

2. TYPES OF BLOOD DISORDERS AND ROLE OF NANOPARTICLES

In addition, you will find a correlation between lipid-based nanoparticles and these diseases. The diseases that we will explore are Sickle Cell Anemia, High Cholesterol, Hemophilia, and LA.

2.1. Sickle Cell Anemia

Sickle cell anemia occurs when there is a deformation of the red blood cell. A mutation in the HBB gene is what causes this deformation. The HBB gene regulates the production of Hemoglobin, which binds to the oxygen molecule. Hemoglobin has four subunits: two alpha-globin subunits and two Beta-globin subunits [5]. An individual will develop Sickle cell Anemia when there is a mutation in at least one of the beta-globin subunits. The beta-globin subunit switches with hemoglobin S. This disease is an alteration in the hemoglobin, which is slightly different from B. Thalassemia. As a result, RBC will take the shape of a crescent instead of a circle, as shown in Fig. (**1**).

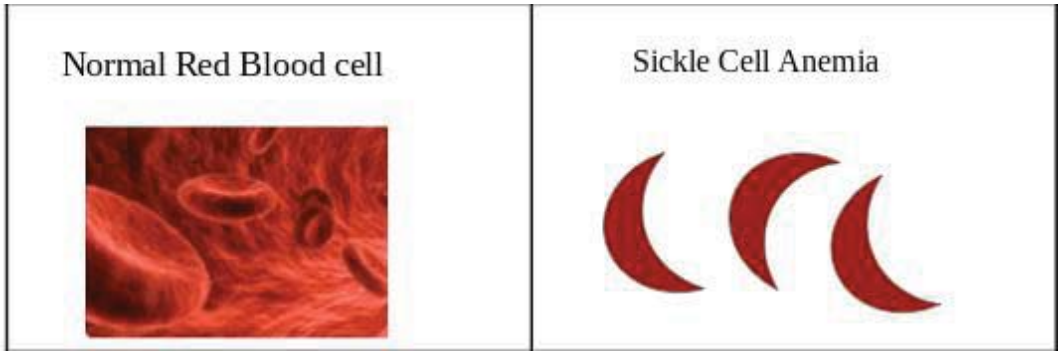

Fig. (1). Structural comparison of Normal Blood and Sickle Cell.

For individuals with sickle cell anemia, their cells cannot take adequate amounts of oxygen and transport it to the rest of the body [6]. This is why one of the most common symptoms is shortness of breath. In addition, sickle cells can also block the flow of other RBC in the blood vessels [7]. If enough sickle cells build up to

block blood flow in the blood vessels, individuals can be at risk for a stroke due to oxygen deprivation in the brain 6. Circular RBCs are shaped in such a way that they can fold and move easily throughout the cardiovascular system, unlike sickle cells. Unfortunately, there is no cure for Sickle Cell Anemia. Treatment is used to alleviate symptoms and pain and prevent further complications for patients. Some treatment methods include blood transfusions [8], stem cell transplants [9], increased vitamin intake [10], and Hydroxyurea (a chemotherapy drug) [11].

Hydroxyurea is effective in Sickle-cell Anemia because it introduces fetal hemoglobin to RBC. Due to the increase in fetal hemoglobin, the risk of organ damage is reduced [12]. However, the side effects of Hydroxyurea make this option less appealing. Common side effects include nausea, loss of appetite, diarrhea, reduction of hemolysis, and mouth sores [13, 14]. In addition, this drug can elevate hepatic enzymes, which can cause inflammation in the liver. Hemolysis is the destruction of RBC. Essentially this is the apoptosis process for RBC.

If Hydroxyurea has been shown to decrease sickle cells in the blood, then why are other treatment possibilities considered? Just because Hydroxyurea eliminates sickle cells in the blood, it does not mean that it's the most effective way without placing a toll on the body. What specifically does Hydroxyurea do to the bloodstream? Hydroxyurea can reduce the number of platelets (Thrombocytes), RBC (Erythrocytes), and white blood cells (Leukocytes) produced from the bone marrow. As a result, patients can be susceptible to infection as there are fewer white blood cells to fight bacteria. Bruising and bleeding are also common due to fewer platelets to clot the blood. Hydroxyurea can also cause Anemia - a condition where there is less healthy (RBC) in the blood. This is dangerous because individuals with Sickle Cell disease develop an Anemia, but with even lower healthy RBC, patients can be at risk for various other conditions. This is why Sickle cell patients will take Vitamin C, Iron, and even Zinc supplements to combat red blood cell loss.

With new advancements in technology, NM continues to prove promising results. NM treatment continues to be researched because it can provide patients a happier and healthier outcome with minimal side effects [15]. There are other drugs like Hydroxyurea that are similar. For the purpose of this section, we studied Hydroxyurea because it was one of the most common drugs for treatments. Other drugs used for Sickle cell Anemia include Endari, Oxybryta, and Adaveko. Endari increases the amount of glutamine (amino acid) in the blood [16]. Oxybryta strengthens the binding of hemoglobin to oxygen molecules. Adaveko, which contains an antibody, is used to mitigate pain for Sickle cell Anemia patients. For these drugs, there are unintended side effects as well. Endari can enlarge the

CHAPTER 4

Properties and Biomedical Applications of Graphene-based Nanotechnologies

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Abstract: Graphene is a 2-dimensional allotropic structure and crystalline form of carbon in which atoms of carbons are supported by sigma bonds and arranged in a hexagonal-shaped lattice. These carbon allotropes contain unpaired electrons providing them with unique physiochemical properties and are further exploited in the formation of graphene derivatives. *i.e.*, Graphene oxide and reduced graphene oxide. These graphene derivatives caused a huge revolution in nanotechnological research. The nanocomposites of graphene derivatives are employed in drug delivery, nucleic acid delivery, tissue engineering, imaging, and biosensing. This chapter is focused on discussing the physiochemical properties of graphene nanoparticles and their biomedical applications.

Keywords: Diagnostics, Drug Delivery, Graphene, Nanoparticles, Nucleic Acid Delivery, Physiochemical Properties, Tissue Engineering.

1. INTRODUCTION

Modern branches of science, like solid-state physics, organic chemistry and molecular biology, are ultimately based on the principles of quantum mechanics. While some people have pondered on the limits of the universe, others have strived to answer the fundamental question: What is everything made of? What is the smallest possible unit? All these led to the discovery of the atom and paved the way for a new science called quantum mechanics, the science of the subatomic

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world. Humans discovered the strange behavior of subatomic particles. Nothing acts like a point particle at such scales – but exhibit a wave-like behavior as well, with an intrinsic uncertainty that never allows us to simultaneously know, with certainty, its momentum and position. All these have given rise to philosophical debates and the theory of the parallel universe. But on the other hand, it has also given rise to more practical technologies as well. A question that inevitably arises at this point is whether we could manipulate the particles at that scale to create drastic results in the output. The answer is yes. This is where nanotechnology comes into play.

Nanotechnology refers to the technology dealing with the manipulation of atoms at the atomic, molecular, or supramolecular scale [1, 2]. According to the National Nanotechnology Initiative, nanotechnology is the manipulation of matter with at least one dimension sized from 1 to 100 nanometres [3, 4]. Quantum-mechanical effect becomes significant at such scales, and thus, this science is very different from the macroscopic sciences. It is one of the most promising sciences that have sprung up from researches in the physical sciences. Nanotechnology holds the promise of developing new materials, which may have an unimaginable significance in the fields of engineering, medicine, and more [5, 6].

As we move from larger to smaller scales, things become more and more complex. Modern synthetic chemistry is capable of preparing small molecules for any structure. A wide variety of useful substances, like Graphene, can be prepared this way, thus making this technology a highly important one in pharmaceuticals.

Nanomedicine refers to the field which deals with the medical applications of nanotechnology. Nanotechnology makes it possible to transport drugs to specific target cells in the body, a process known as drug delivery. This way, it can be ensured that the drug is consumed, in the right amounts, only by the target cells. This helps to minimize side effects and has great potential in medicine. Currently, complex drug delivery systems are under development.

Tissue engineering is another field where nanotechnology is applied. Tissue engineering refers to the replacement or modification of existing tissue using a combination of cells, nanoparticles, and other methods. Further research is going on to develop nanoparticles for a wide range of applications.

2. APPROACHES IN NANOTECHNOLOGY RESEARCH

There are many approaches that are used in nanotechnology research. Two major approaches are the top-down approach and the bottom-up approach [7, 8].

Simply put, top-down refers to the approach of synthesizing smaller nanoparticles/devices while using larger particles to do so. This approach seeks to miniaturize current technologies and is an easy and convenient method since the parts are patterned and built-in place. On the other hand, the bottom-up approach does the opposite. The bottom-up method seeks to arrange smaller units in more complex patterns. It is, thus, basically a self-assembly process. The ultimate achievement of the bottom-up way would be to recreate life itself; since the Urey-Miller experiment justifies, life on earth was formed due to simple units clustering together to form complex molecules [9, 10].

Both the above approaches are important and successful enough in their respective applications. Top-down approaches are good for producing structures with long-range order and for making macroscopic connections, while bottom-up approaches are suitable for assembly and establishing short-range order at nanoscale dimensions. The integration of top-down and bottom-up techniques is expected to provide the best combination of tools for nanofabrication eventually.

Researchers are optimistic enough to believe that, one day, autonomous nanobots could be inserted into the body for sensitive medical operations without having to develop any cut in the body. It is beyond doubt that nanotechnology holds the key to a better understanding of the complex biochemical processes that give rise to life. At the same time, nanoparticles may have certain unintended effects. As research in nanotoxicology suggests, the manufacture and use of nanoparticles on an industrial scale can ultimately be harmful to the environment. Thus, like all new technology, the debate whether the use of nanotechnology should be regulated or not goes on.

2.1. Graphene

Graphene is a single layer of graphite, as it is the first material that is 2D, which means that it is one layer of atoms thick. This material is an allotrope (2 or more different physical forms in which an element can exist) of carbon, and these carbon atoms are bonded in a very special way. Graphene is a layer of interlocking hexagonal rings of carbon atoms. Each carbon atom is covalently bonded to 3 others in its giant 2D structure. In 2004 at Manchester University, the scientists Andre Geim and Konstantin Novoselov obtained the crystals of Graphene by sticking sticky tape onto a graphite rock and pulled it off [11]. They viewed the piece of sticky tape under a powerful electron microscope. They were awarded the Nobel Prize in Physics 2010 “for groundbreaking experiments regarding the two-dimensional material Graphene.”

CHAPTER 5

Nanotherapeutics in Cancer Treatment

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Abstract: Nanotherapeutics is an advancing technology and promising industry of the 21st century; with further development, it may hold secrets for the medical community and society as a whole. The development of nanotherapeutics into medicine is one of the newest developments in medical science that the scientific community has taken. The conventional approach of delivering anticancer drugs towards the targeted site is remained controversial and has numerous problems such as non-specific effects to the surrounding organs other than cancer affected, anticancer drug resistance, and chronic adverse effects. Recently, biomedical scientists have turned their attention towards nanocarriers possessing incredible activity to deliver anticancer drugs towards cancer-affected areas without being disrupted by endogenous barriers, rendering lesser toxicity and promoting anticancer response. In this chapter, the overview of nanotherapeutic agents is thoroughly assessed in the treatment of cancers.

Keywords: Anticancer Drugs, Cancer, Nanotherapeutics, Resistance, Toxicity, Targeted Delivery.

1. INTRODUCTION

Nanotherapeutic agents are emerging technologies that consist of various types of nanomaterials that have a vital role in the health care sector. These agents are atomically restructured materials used to deliver medications or other substances to ameliorate the therapeutic effect or diagnose any anomaly in the body. This can remain in the form of targeted drug therapy or even the early detection of some diseases in the human body. The body lies in a state of equilibrium, and within this state, all chemical processes can be carried out. A common example, the bicarbonate buffer system, is pivotal in the regulation of blood pH levels in humans. The bicarbonate buffer system will either donate or reserve H^+ ions depending on the pH: this being too acidic or basic for the body.

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Nanotherapeutics is encompassed under a term called nanomedicine, which specifically uses nanoparticles for medical applications [1]. The alteration of said matter under the microscopic level can help form unnatural recurring properties that can benefit the use of the particles. Nanotherapeutics development requires nanoscale materials often found in the environment of the laboratory settings. This may include the biocompatible nanoparticles and nanorobots used for diagnoses, delivery of materials, sensing, and actuated purposes in a living organism [2, 3].

The most important trait of these particles is biocompatibility; they must be able to survive in the human body without the worry of the attack from the immune system as detected by a foreign agent. Rejection from the body can cause issues that can span from disease to even death for the organism. The nanorobots help with the advancement of the particles and the training into completing the multitude of tasks synchronously.

Nanomedicine has its drawbacks, comparable to any therapy that is in the modern market; these risks with nanodrugs can be unpredictable due to the variance of effects in clientele population. Repeatedly in the medical community, we have seen that the rejection of agents in the body will cause surrounding tissues within the whole system. The body functions like a factory chain. When one screw is taken out, the entire system suffers. That is mirrored in the effect of the nanoparticle rejection due to lack of biocompatibility.

We have seen nanotherapeutics in the body in many ways through the medical changes we see in the body. The interventions that help treat so many conditions that affect us in the 21st century are due to the development of nanotherapeutic medicine in the pharmaceutical development of drugs.

2. HISTORY OF NANOTHERAPEUTICS

Nanotherapeutics, regardless of the advanced nature and the new technology of the 21st century, have been around forever. Since the emergence of humans from our ape ancestors' humans remained inquisitive species, and with that comes imagination. Imagination, a new idea in the first humans that stepped foot on the Earth, yet an important one because that very thing would cause a ripple of inventions to emerge from curiosity. Nanoparticles can be traced back to colloidal gold usage in ancient civilizations, used by the Damascans to create swords that contained far sharper edges [4]. The Romans used this colloidal gold to create the iridescent glassware. To this day, we praise the Roman Civilization [5].

The modern take in nanotherapeutics was credited to Élie Metchnikoff and Paul Ehrlich, who often take the "modern pioneers of nanomedicine" [6]. Together they were the recipients of The Nobel Prize for Medicine in 1908 and have caused a great shift in the world of medicine. Through their works of phagocytosis, commonly known as "cellular eating", they concluded that through cell-specific diagnostic and therapy, there was a higher yield in patients recovery. Fundamental deals with nanoparticles for nanomedicine were progressively evolved over the most recent 30 years of the twentieth century and included the use of liposomes. Now remains the key to the puzzling issues that arise in the 21st century. The use of nanoparticles in nanotherapeutics bloomed after the experiments of Metchnikoff and Ehrlich, and the knowledge that was acquired in the last century has changed the face of nanomedicine. Modern treatments for many debilitating diseases have now found it beneficial to use nanoparticles, and this science will be developed further in the future. The development of this science thus far has led to an improvement in the quality of life and advanced societal planted interests. Welfare concerns have been met with the interest of living longer, developed in trials of the use of this new technological science.

2.1. Economic Importance of Nanotherapeutics

The strides that nanotherapeutics left in the science field remain easily evident: increasing lifespan, decreasing pain in treatment, overall lower mortality rates in the human population. The hidden economic changes left after the health improvements tend to be the less recounted effect of introducing this new medical practice. The role that nanotherapeutics play on the world stage of economic growth is immense. Rising health costs are one of the biggest concerns facing the medical community worldwide. Patients often cannot afford healthcare with all the tests and treatments needed. When possible, they are left in debt for years, commonly the person's lifespan and through future generations. Nanomedicine, as a whole, yields a positive economic mark on the output of jobs for people. The new field has opened the gates for the development of new businesses, jobs, and trade markets. The National Nanomedicine Institute (NNI) remains the leader of this new initiative [12].

While the NNI grows deeper in magnitude and complexity, the nation has been allocating more funds to develop this technology as a step towards proactively lowering healthcare costs in the future. World leaders have seen the potential of this technology in healthcare settings and allocating money as it remains an assurance policy for the future of protecting national interests and health. It is imperative that nations keep monitoring and adapting the funding that is entered into this field; analysis of the funds includes the alignment of the goals nationally,

CHAPTER 6

Emerging Nanomaterials for Cancer Therapy

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Abstract: Nanotechnology has gained much interest over the past few years due to its ability to efficiently detect and treat different types of cancers. To overcome the limitations associated with traditional cancer treatment strategies such as lack of specificity, toxic effects, the pre-mature release of the drug, and multidrug resistance, nanomaterials have been widely utilized. Nanomaterials not only enhance the drug accumulation at a specific site but also improve the therapeutic efficacy of anti-cancer drugs. Some other advantages of nanocarriers include targeted and controlled drug delivery, less toxic effects, enhanced solubility and stability, and greater availability of chemotherapeutic agents to the cancer cells due to enhanced permeability and retention effect. The physicochemical properties of nanocarriers can be modified by varying their shapes, sizes, and surface characteristics (PEGylation, ligand, or functional group attachment). Various types of nanomaterials have been utilized for pharmaceutical and medical purposes, most importantly for cancer therapy, depending upon their nature and composition, such as lipid-based, polymeric-based, protein-based, carbon-based, and hybrid nanomaterials. Many of these nanocarrier drug delivery systems have been developed, among which only a few have been clinically approved for anti-cancer drug delivery. The rationale of using nanotechnology for anticancer drugs is to achieve targeted delivery via active or passive targeting and diminish the damages to healthy tissues. So, the ultimate objective of these nanocarriers is to effectively treat the diseases with fewer side effects.

Keywords: Active Targeting, Carbon Nanotubes, Mesoporous Silica Nanomaterials, Nanomaterials, Nanocarriers, Polymeric Nanocarriers, Passive Targeting.

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1. INTRODUCTION OF NANOMATERIALS

Cancer occurrence, prevalence, and mortality rates are increasing day by day, indicating the demand for novel technologies to combat it. According to WHO, cancer is a major health concern in developing countries and is a significant cause of death along with other heart diseases [1]. There are 100 different types of cancers that affect different body parts by uncontrollable cell growth and proliferation [2]. A major reason is its challenging diagnosis and detection. Advanced technologies can help in detecting cancer at earlier stages, thereby decreasing the mortality rate [3].

Nanotechnology is an innovative technology showing advancements in different fields of science and physics. The researchers are transforming human lives by formulating nanoscale things having the ability to work at smaller scales [4]. Remarkably small structures can be studied using nanotechnology. Nanotechnology is also defined as studying, forming, and applying particles and devices by managing their diameter within 1–100 nm size. Nanobiotechnology is the combination of nanotechnology and biotechnology through which conventional technologies can be manipulated and used at the molecular level [5]. Nanotechnology has attained so much attention over the last few years in many fields. National Institute of Health defined nanomedicine as the use of nanotechnology for detecting, diagnosing, monitoring, and regulating living systems. The term nanomedicine is referred to the materials having a size in nanometer-scale, which can easily be modified according to pharmaceutical applications [6]. Although the application of basic nanotechnology was started many years ago, the role of nanomedicine in cancer therapy has gained captivating interest over the last few years [7]. Nanomaterials have promising effects in drug delivery [8]. The very small size makes them appropriate for entering the human cells having a size less than 50 nm and circulating easily with the blood flow. Owing to high surface area to volume ratio, nanoparticles are able to modify the characteristics and activities of drugs. They are also capable of identifying minor changes related to tumor cells and transporting the drug moieties to the specific desired site without bothering nearby tissues and cells. Furthermore, the physicochemical properties of nanoparticles can be modified by varying their shapes, sizes and surface characteristics (PEGylation, attachment of ligand or functional groups).

Consequently, nanoparticles drug delivery vehicles can be lipid in nature or polymeric, along with that some are hybrid nanoparticles and some are peptide-based [9]. Some salient features of nanoparticles include targeted and controlled drug delivery, less toxic effects, enhanced solubility and stability, and greater availability of chemotherapeutic agents to the cancer cells due to enhanced

permeability and retention effect. The ultimate objective of nanoparticles utilization is to effectively treat the diseases with fewer side effects [10].

Radiotherapy and surgical therapy help in eliminating localized cancers, but advanced stages of cancers are cured using chemotherapy. However, chemotherapy is not much effective because of its limited availability to cancerous cells. Some other limitations of chemotherapy are lack of specificity, potential toxic effects, and multidrug resistance. Therefore, because of the limitation of conventional therapies and their associated challenges, they are not considered effective for treating different types of cancers, so developing novel strategies for targeting cancerous cells is the necessity of time [11]. As the cancer progression is diverse, cancer treatment is complex due to different responses of therapy among different patients [12]. Therefore, along with recent advancements in nanomedicine-based cancer therapy, the pathophysiology of tumors and their microenvironment are supreme factors that should be kept in mind to overcome the hindrances in their production and commercialization [13]. However, chemotherapeutics agents can be effectively delivered to the tumors with the help of nanoparticles-based drug delivery systems showing improved therapeutic effects [14].

Moreover, the conjugation of nanoparticles with targeting ligands helps in targeting the overexpressing factors of tumor cells. The therapeutic efficacy of nanomedicines is also affected by their circulation time in the body and interactions with different types of proteins [15]. A variety of nanoparticles-based drug delivery systems have been approved for treating different types of tumors, and numerous products are in clinical trials [10]. In this chapter, we have discussed different types of nanoparticles and their roles in cancer therapy. Then we have explained the targeting strategies and surface modification of nanoparticles for improving their targeting and circulation time. In the end, we discussed the future aspects of nanomaterials, most particularly for cancer therapy.

2. TYPES OF EMERGING NANOMATERIALS

Various types of nanomaterials are being utilized for pharmaceutical and medical purposes depending upon their nature and composition, and their roles are briefly described in this section. The graphical illustration of these emerging nanomaterials is given in (Figs. **1** and **2**) .

CHAPTER 7

Toxicity of Silver Nanoparticles

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Abstract: Silver nanoparticles (AgNPs) are metallic nanoparticles that are used for different biological purposes. Few toxic traits of Silver nanoparticles (AgNPs) producing plants are expressed; however, lesser is known about their genotoxic properties. This work discovered the cytotoxic and genotoxic risks of the entire concentrate from AgNPs of ethereal parts. Few studies had demonstrated that exaggerated reactions were not emerged by the four strains of Salmonella typhimurium, presented to fixations up to 5 mg/plate, with or without mammalian metabolic actuation (liver microsomal S9 division from Wistar rodents). In cytogenic cells and culture studies, higher doses (25–100 µg/mL) demonstrated a significant decrease in cell viability. In sister chromatids, chromosome distortions portrayed that AgNPs are genotoxic at the most noteworthy fixation utilized when clear cytotoxic impacts were also observed. Though, no expansion in micronuclei recurrence in bone marrow cells was identified when the extract was administered orally to mice (100, 500, and 2000 mg/kg dosages). The information was acquired to set up the most far-reaching extract on the genotoxic capability of AgNPs. Furthermore, it is noteworthy that the plant extracts plus AgNPs can cause *in-vitro* DNA hindrance at cytotoxic doses.

Keywords: Biological Properties, Chemical Properties, Physiochemical Properties, Plant Extract, Silver Nanoparticles.

1. INTRODUCTION

Silver nanoparticles (AgNPs) are prepared from different plants obtained from Brazil, North America, Malaysia, China, India, and Pakistan [1 - 4]. It is routinely

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utilized as a solution for some sicknesses and accounted for by the decoctions and colors acquired from the leaves and underlying foundations of the plant, for instance, antirheumatic, ant syphilitic, hors d'oeuvre, diaphoretic, diuretic, emollient, purgative, and narcotic exercises [5 - 7]. Different properties have been guaranteed by trial pharmacology: mitigating, antimalarial, pain-relieving, antifungal, antibacterial, anticancer, antimitotic, anti-trypanosomal, and diuretics [8 - 11]. The toxic analysis of the AgNPs *in-vivo* ought to be studied [12, 13]. Genetic toxicity is one of the major poisonous impacts and its centrality is plentiful as we are thinking about the sublethal dosages prompting long haul impacts, for example, malignancy and degenerative infections [14 - 18]. Different techniques used in the synthesis of AgNPs are briefly discussed in Table **1**. While, the characterization and behaviors of AgNPs in the biological and environmental samples are briefly discussed in Table **2**. This book chapter focuses on the assessment of the normal genotoxic and cytotoxic danger of AgNPs and the extract in which it was prepared. The diverse hereditary results were examined to evaluate DNA harm at various hereditary articulation degrees. We assessed the viability of cells of AgNPs on CHO cells utilizing the MTT examination. The mutagenicity of the AgNPs on different bacterial strains. The Ames test was used for quality transformation, cytogenetic measures on cytogenic cells, culture study for chromosomal harm outside the body, andclastogenic and aneugenic impacts inside the body. The micronucleus test, in the bone marrow of mouse, is performed and the comet test was used for the assessment of DNA harm.

Table 1. Techniques used in synthesis of AgNPs adapted from Pryshchepa *et al*., 2020 [19].

Modes	**Precursor**	**Synthesis Condition**	**Preservation System**	**Result**
Physico-chemical	$AgNO_3$	2 mm cathode and 99.9% titanium anode dipped into silver nitrate solution	Citrate	AgNPs ≈ 18 nm
	$Ag_2C_2O_4$	$AgNO_3$ decomposed at 125 centigrade for 100 h Anode is platinum and cathode made up of stainless steel capillary tube immersed in silver nitrate along with fructose solution	-	AgNPs 5–20 nm
	$AgNO_3$	Laser excision of 99.9% purity silicon target	Fructose	Polydisperse irregular AgNPs
	$AgNO_3$	Solution of Silver nitrate, Nd:YAG laser, having wavelength of 355 nm and pulses less than 40 ns, power density per pulse less than 40 J/cm^2 with 5 Hz frequency.	Silica	Polydisperse irregular AgNPs
Physical	AgNPs 99.9%	Electrodes of Silver (Ø 2 milimetre with length forty milimetre), disclosed in a distinct media (distilled water and glucose 10% and 25% w/w, glycerin/distilled water 10% and 25% w/w, phenol/distilled water 5% w/w, Mg(NO3)2•6H2O/distilled water 0.01% w/w and 0,05% w/w, xylene, ethylene glycol, ethyl acetate, and phenol/toluene 5% w/w) with pulses of 5–10 A/cm2, the cathode-anode gap was≈1 mm, the NPs were separated by entrifugation and dried at 70 °C for 24 h	-	Ag@SiO_2 NPs with shell of 1-2 nm and core of 11 ± 4 nm

(Table 1) contd.....

Biological	$AgNO_3$	Filtrate of cell of fungus of 1. C. indicum, 2. Alternaria species, 3. Phoma, 4. F. oxysporum, 5. Curvularia species were cultivated on broth of potato dextrosefor almost 72 hours at 28 degree Celsius and combined with the mixture ofsilver nitrate.	Fungal cell filtrate mixture	AgNPs of 1. 7–20 n, 3. 5–23 nm, 5. 7–20 nm 2. 4–13 nm, 4. 10–31nm
		Solution of AgNO3 mixed with phosphate buffer having 7 pH contained O. limnetica homogenate were placed under fluorescence for 48 hours at 35 °C.	Composite of O. limnetica Homogenate	Quasi-spherical AgNPs having size of 3–18 nm.
		Solution of Silver nitrate combined with chrysin, 3-hydroxylflavone, galangin, flavone, kaempferol, tricetin, quercetin, apigenin, myricetin, luteolin, pH ranges from 7.2 to 10.1, the reaction was carried at 40, 23 and 70 °C.	Flavonoids	Depending on flavonoid use AgNPs ranges from size 12–39 nm.
		At 37 °C the solution of Bacillus licheniformis biomass along with silver nitrate was held for 24-h on shaker 200 rpm, then sonication and centrifugation was used to remove biomass	Compounds of Bacillus licheniformis biomass	AgNPs 40 -50 nm
		AgNPs were refined along dialysis with twelve thousand Da break-off and sucrose gradient (200.000×g for nearly 16-h at 4°C via HEPES buffer by using ultracentrifugation. Silver nitrate combined with orange peel essential oil and agitated for 48 hrs at 70°C.	Compounds of essential oil	AgNPs≈ 3 nm
		ultracentrifugation	Betanin	Spherical, shortened and triangualr AgNPs, = 15 nm
		Silver nitrate combined with orange peel essential oil and agitated for 48 hrs at 70°C.	Powdered Zingiber officinale composite	Average sizes of 11, 16, 20, 24nm that depends upon amount of silver nitrate

CHAPTER 8

Boron Nanomaterials for Biomedical Applications

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Abstract: Boron belongs to the metalloid group and has an atomic number 11. Boron does have an important role in humans and animals; however, it is not well understood. According to developmental biology, boron is a necessary component of embryonic development and when it is deficient, it causes impaired embryos or necrosis. Different types of boron nanomaterials, such as nanoclusters, nanotubes, nanowires, nanoribbons, nanobelts, nanosheets, and monolayer crystalline sheets, have recently been created experimentally. Boron nanomaterials have a different bonding configuration than three-dimensional bulk boron crystals in icosahedral because of their reduced dimensionality. Furthermore, the wide range of boron nanoparticles available could serve as building blocks for mixing with other existing nanomaterials, atoms, molecules, and/or ions to create new materials with novel properties and functions. Hexagonal boron nitride (h-BN) is a new two-dimensional (2D) nanomaterial that has been employed in biomedical applications. This material exhibits semi-conductive capabilities due to its enlarged band gap, allowing it to be used as a biosensor and disparity agent. BNNs (boron nitride nanotubes) are also being investigated for use in regenerative medicine and medication delivery. Because of its bioactive properties, this particular nanomaterial (BNNs) has a lot of potential in the field of tissue engineering. The advancement of boron nanoparticles during the previous decade has been evaluated, and future directions and guidelines for biomedical applications are discussed.

Keywords: Anticancer, Antimicrobial, Boron Nanoparticles, BNCT, Nanomaterials, Nanotubes, Nanosphere.

1. INTRODUCTION

Nanomaterials are directly related to the technological interest of the peculiar physiognomies that extant in a scale of handling, *i.e.,* the sizes are in nanometers.

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Nanotechnology is a diverse field of science that is prompting the already existing technical environment like medicine. Therefore, nanomedicine appears to be a new technique that enhances the development of nanomaterial applications in the field of traditional medicine [1]. Implications of nanomedicine mean that outmoded or traditional methodologies and instrumentation of investigation are enhanced with every novel finding. Consequently, a therapeutic and diagnostic technique based on NPs offers early-stage cancer diagnosis and treatment with high sensitivity [2]. The advancement in the imaging techniques which ease cancer and other fatal diseases diagnosis is magnetic resonance imaging (MRI), positron emission tomography (PET), X-ray computed tomography (CT), and optical imaging and power tool. For therapy approaches, different techniques have been applied, such as photodynamic therapy (PDT), photothermal therapy (PTT), chemotherapeutical drug delivery. Therefore, NMs in medicine had multidirectional characteristic applications. Different NMs are investigated with numerous exceptional physiochemical possessions for the development of new nanomaterial-based tactics: pharmacokinetic analysis, fluorescent labels *via* quantum dots, approaches of separation and refinement of cells or single biomolecules, biosensing, recognition of biological samples and pathogens (*e.g*., proteins, nucleic acid), final drug or gene delivery, tissue engineering, improvement of therapeutic visualization techniques (*e.g*., magnetic resonance imaging), and cancer treatment *via* hyperthermia method. NMs have appeared as the most fertile areas for biomedical applications. NMs are measured as a therapeutic boon for the prevention, diagnosis, and treatment of cancer [3, 4]. In addition, following the advances in chemistry, nanotechnology, pharmacy, biology, imaging, and medicine in the last decade, various systems have been developed and combined; for instance, therapy and disease diagnosis as shown in (Fig. **1a**) [5, 6]. These developments stimulate the vast range of objects having nanometer-sized for their organization of cancer tissues, empowering tumors imagining, drugs delivery, and/or demolition of cancers by various healing procedures. The providence of the particles inside the body can be well projected by selecting the right shape, size, charge, and coating along with aiming moiety (Fig. **1b**) [7]. New NMs drugs express innovative possessions by virtue of their shape and size and thus gathering cumulative attention as possible multifunctional healing agents [8].

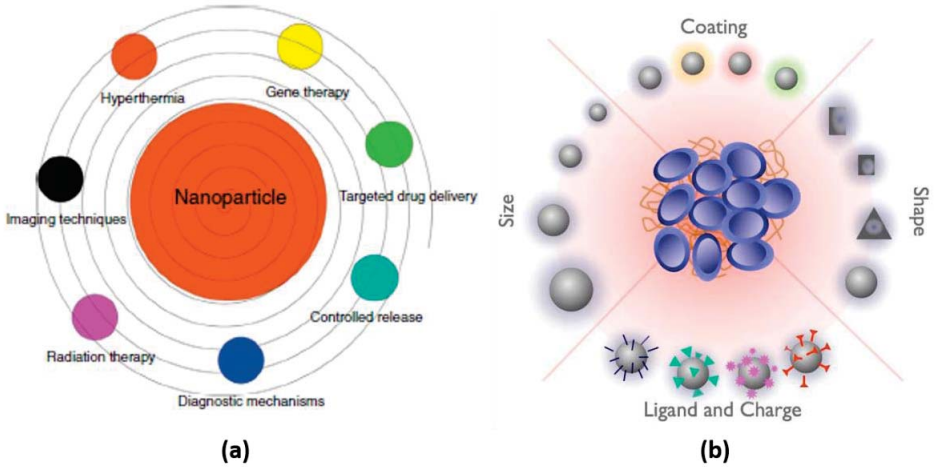

Fig. (1). (a) Theragnostic applications of NPs. Source Ref [6], **(b)** Properties of particles thatinfluence targeting, elimination, and distribution. Source: Ref [7].

Boron element is the first-row neighbor of carbon; however, the study of the boron element is far behind the carbon. For the last two centuries, carbon has been considered a leading element in chemical research. Although boron is rich in nature, it has not been utilized as a building block of its own, despite being used in dealing with carbon [9, 10]. Generally, the amount of boron element in the human body is very minute (*i.e.,* it is not more than 18 mg in an average individual [11]); however, boron compounds are considered vital micronutrients for plants and animals. Boron elements can be used in the drug design of novel pharmaceuticals because they have the potential properties to be considered as a helper in new biological accomplishments. For instance, they can help to strengthen the plant cell walls as well as support bone health in animals. It's reported that the bone lipids in femurs of male pigs were decreased resulted in a higher bending moment by taking boron deficient diet, which suggests the important role of boron in bone metabolism [12]. Therefore, stem cell differentiation could be modulated by boron because it has already been used in biomaterials for medicinal applications and has proven to be vital in bone and cell metabolism. Astonishingly, boron-containing compounds are rarely found in medicine; however, so far, there is no report showing the inherent disadvantages of boron in terms of its incorporation into medicine. Indeed, some boron-containing compounds were recently examined and utilized in clinical applications. Furthermore, more boron-based medicine is predictable due to a new emerging proton boron fusion therapy and the advancement in boron neutron capture therapy (BNCT). This chapter focuses on the biomedical applications of the recently reported novel boron NMs as shown in Fig. (**2**).

CHAPTER 9

Metal Nanoparticle Synthesis Through Biological Entities

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Abstract: During recent years, the development of suitable green chemistry methods for the synthesis of metallic nanoparticles has become the main focus of researchers. The investigations are under process for the creation of standardized nanoparticles (NPs). One of the most frequent ways for NPs synthesis is using plants that are ideally suited for nanoparticle production. The nanoparticles created from various organisms vary in physical appearance, and the plant-based NPs enable the researchers to explore the plant mechanisms for the uptake and creation of metallic NPs. Nanotechnology is emerging as a crucial discipline of science and technology that examines the cell-level interaction between synthetic and biological materials. The use of this technology is rising worldwide due of its advantages and simplicity. Organisms from primitive prokaryotes to complex eukaryotes and angiosperm plants are used for the production of NPs. Further investigation and study are required in this field to enhance the biological synthesis of nanoparticles. This book chapter discussed the plants employed in NPs synthesis. It also represents the many biological systems that create the art of fabrication of NPs and the development of this advanced technology.

Keywords: Applications, Biological based nanoparticles, Characterization, Metallic Nanoparticles, Nanotechnology, Physiochemical Properties, Toxicity.

1. INTRODUCTION

The newly created field of nanobiotechnology in recent years is focused on using nanotechnologies for the creation of nanometer-size particles *via* biological resources. Nanoparticles (NPs) are of immense importance because of their

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magnetic, electro-optic, and physicochemical properties which are determined by their morphology [1 - 3]. Due to the large surface area to volume ratio and extremely small size, the differences in their properties is very significant *i.e.* catalytic activity, biological activity, optical immersion, heat and electrical conduction, mechanical properties, melting point, as compared to the substances that are present in bulk or at large scales [4 - 7]. Due to the uniquely extensive range of physicochemical characteristics, NPs play a part in various techniques, including medical diagnosis and imaging, medical treatment protocols, pharmaceutical products, chemical sensors, *etc*. For example, inert metals like gold (Au), silver (Ag), palladium (Pd), and platinum (Pt) are being widely used in medical and pharmaceutical products. As Ag NPs are used in anti-inflammatory and antibacterial activities, along with that, they are also used in dressing wounds and medical implant coating [8, 9]. Similarly, the gold NPs are also used in biomedical applications such as disease diagnosis and pharmaceutics [10, 11]. The palladium NPs are used in chemical sensors, catalysis, and electrocatalysis applications [12, 13]. The platinum is either used as a pure form or its alloy is made with other NPs and universally used in NPs applications. In addition to those, the non-metallic NPs comprising Cu, ZnO, Se, and iron are involved in medical treatment, cosmetics, and pharmaceuticals. These NPs are synthesized and stabilized by various techniques, including lithography, laser ablation, and high-energy irradiation, *etc* [14]. Studies have shown that many variables (such as concentration, temperature, *etc*) affect the production of NPs [15]. So, consequently, during the synthesis of the NPs, the physicochemical properties, stability, and morphology of NPs are to be effectively monitored. With the wide range of applications of NPs, there comes a slight drawback as the conventional synthesis of NPs often uses toxic materials that have potential hazards for instance, carcinogenicity, cytotoxicity and environmental toxicity. But luckily these hazards can be controlled by the biological monitored production of the NPs. And therefore the outcome will be an ecofriendly process *i.e*., the biotic production of NPs [16, 17]. This method is now highly efficient, reliable, and biologically compatible with the traditional method for the synthesis of the NPs. The biological synthesis eventually resulted in the use of green chemistry comprising of unicellular and multicellular biological organizations including actinomycetes, bacteria, viruses, algae, bryophytes, *etc.* The biosynthesis of NPs may result in the creation of a wide variety of NPs based on their shape, size, stability, compositions, and physicochemical properties. The production of NPs through biological objects such as plants is an advantageous approach as compared to micro-organisms or other entities as it does not require difficult steps and stages for its production. It is a faster method and especially cost-effective and also used in the synthesis of NPs at a large scale.

2. CHARACTERIZATION TECHNIQUES

The production of NPs is initiated by many methods. But all those methods and techniques fall under two major approaches, including the bottom-up approach and the top-down approach [18, 19]. In either of these approaches, the NPs produced are used in various techniques and their characterized properties are determined such as their shape, size, *etc*. In a bottom-up approach [20], the NPs are simply made from their monomers, while in the top-down approach [21], the material of interest is selected and it undergoes the side reduction by various physical or chemical methods to produce NPs. Due to their significantly high dependency on their size, shape, and surface structures, there is a possible risk of producing surface imperfections by these techniques [22 - 25]. For a particular application, the NPs need to be homogeneous. During the biological synthesis of the NPs, the appearance of the color changes in the action combination is the primary positive indication that NPs are present afterward, the Tyndall effect is used for detection of the NPs in the solution in which a colloidal solution is present. A laser beam is passed through it [26]. After this, a high-speed centrifugation process is applied in which the NPs separate from the colloidal solution and then various characterization techniques are applied for their examination. Some of the commonly used characterization techniques, including spectroscopy and microscopy are, Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Powder X-Ray Diffraction (XRD), UV-visible spectroscopy (UV-vis), Dynamic Light Scattering (DLS), Fourier Transform Infrared Spectroscopy (FT-IR), Energy Dispersive Spectroscopy (EDS), *etc*. The techniques based on microscopy including SEM, AFM, and TEM are the direct method to obtain the images of NPs, which are then applied to find the size and structural features of NPs. In comparison to that, the techniques based on spectroscopy are the indirect methods such as UV-vis, DLS, EDS, FT-IR that are used to find out the composition, period, and characteristics of the NPs. UV-vis uses a wide range to determine the interaction of radiation with matter and also used to determine the electronic transitions of the particles from the low to high energy states. The XRD technique uses special diffraction patterns to conclude the structural information of the constituent part while the DLS method is used to plot the size spreading and evaluate the surface charge on NPs in a liquid suspension.

3. SYNTHESIS OF NPS

3.1. Biological Synthesis of NPs

In recent times, various researches have reported that the NPs produced by micro-

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