



Nano-biotechnology, an applicable approach for sustainable future

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Received: 28 July 2021 / Accepted: 30 December 2021 / Published online: 9 February 2022
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Abstract

Nanotechnology is one of the most emerging fields of research within recent decades and is based upon the exploitation of nano-sized materials (e.g., nanoparticles, nanotubes, nanomembranes, nanowires, nanofibers and so on) in various operational fields. Nanomaterials have multiple advantages, including high stability, target selectivity, and plasticity. Diverse biotic (e.g., Capsid of viruses and algae) and abiotic (e.g., Carbon, silver, gold and etc.) materials can be utilized in the synthesis process of nanomaterials. “Nanobiotechnology” is the combination of nanotechnology and biotechnology disciplines. Nano-based approaches are developed to improve the traditional biotechnological methods and overcome their limitations, such as the side effects caused by conventional therapies. Several studies have reported that nanobiotechnology has remarkably enhanced the efficiency of various techniques, including drug delivery, water and soil remediation, and enzymatic processes. In this review, techniques that benefit the most from nano-biotechnological approaches, are categorized into four major fields: medical, industrial, agricultural, and environmental.

Keywords Nanotechnology · Nano-biotechnology · Nanomaterial · Nano-therapies

Introduction

The development process of a sustainable future generally consists of methods that ensure the satisfaction of future needs, while fulfills the current generation’s requirements (Raghav et al. 2020). To obtain a proper overview of

upcoming demands in the future, it is important to anticipate future stressors (e.g., climate change) (Iwaniec et al. 2020). Since nanotechnology is applicable in various majors, it is expected that nano-based techniques will take a key role in a sustainable future (Raghav et al. 2020), along with making substantial impacts on the universal economic situation due to their wide range of applications in variant industries (Adam and Youssef 2019). The unification of diverse fields in science, Inspired by the oneness of nature, is one of the most noticeable subject matters now in the early twenty-first century. Merging four massively operational fields of science has received great attention in recent decades: nanotechnology, biotechnology, information technology, and cognitive sciences (NBIC), which are known as “convergent technologies” (Roco and Bainbridge 2013). Non-renewable sources don’t seem efficient for providing large amounts of energy required in various industrial technologies. Convergent technologies are considered as a remedy for this issue. For instance, several nano-based technologies, which consume biological-renewable energy sources, have been introduced (Zhironkin et al. 2019). The unification of material on nanoscale makes the mentioned combination of multiple technologies possible. Hence, nanotechnology plays a critical role in NBIC advancement (Roco and Bainbridge 2013). According to the definition set by National Nanotechnology

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Initiatives in 1999, Nanotechnology is an advanced area of research that allows for the production of a wide class of materials in the nanoscale range (less than 100 nm) to make use of size- and structure-dependent properties and phenomena (Luo et al. 2020). Although “nano” is defined as that which is less than 100 nm in size, the use of this definition in the biomedical field is less strict and instead may encompass particles up to 1000 nm in size (Landowski et al. 2020). Nanotechnology has a wide range of applications, including Agricultural usages (Ndlovu et al. 2020), biofuel production (Zahed et al. 2021a), cancer Immunotherapy (Goracci et al. 2020), carbon capture (Zahed et al. 2021b) and biomarker detection like nanobiochips, nanoelectrodes, or nanobiosensors (Bayda et al. 2020). Nanomaterials (NMs) are chemical substances or materials that are manufactured and used at a very small scale, i.e., 1–100 nm in at least one dimension. NMs are categorized according to their dimensionality, morphology, state, and chemical composition (Saleh 2020). NMs can be used for rapid extraction of RNA of the novel coronavirus (Kailasa et al. 2021). Expanding nanoscience through various branches can eventually enhance the intelligence and capability of individuals, solve various social issues, cure numerous diseases, and generally improve the quality of mankind's life in the long term (Roco and Bainbridge 2013). Deploying nanotechnology into biotechnology will help the commercialization process of nano-based techniques and make them more practical in the industry (Maine et al. 2014). The idea of developing interdisciplinary research (IDR) (Jang et al. 2018) in science presents a promising landscape of the future, in which human intelligence has reached such high levels that the term “superhuman” would be more proper for mankind. According to the Israeli philosopher Harari, with the appearance of a highly technologically advanced society, only individuals with great intelligence and technological advancements can survive through natural selection in society. He states that superhumans will be produced by society eventually, considering the logic of social Darwinism, and this will be a remarkable phenomenon of the twenty-first century (Mantatov et al. 2019). One massive application of nanobiotechnology is enhancing the efficiency of various therapies (Table 1). The application of nanobiotechnology in delivering chemical drugs or gene modifying agents to their target cells will increase the efficiency of the treatments and reduce the side effects remarkably. Within the previous two decades, RNA-based therapeutic methods, including messenger RNA (mRNA), microRNA, and small interfering RNA (siRNA), have been supremely developed. These therapeutic approaches are expected to be operative in the treatment and prevention of various diseases, such as cancers, genetic disorders, diabetes, inflammatory diseases, and neurodegenerative diseases (Lin et al. 2020). In the case of cancers, conventional therapies (surgery, chemotherapy,

and irradiation) may cause severe side effects to patients, plus they are often inefficient for disease treatment (Hager et al. 2020). Loading anti-cancer drugs into nanomaterials provides a nano-based drug delivery system that detracts the side effects. Platinum (Pt) compounds are one of the most common anti-cancer drugs since 1978. Pt drugs directly aim at the DNA of the targeted cells, thus covering up the defects of the malformed DNA repair mechanisms in cancerous cells. Encapsulating Pt drugs into liposomes constructs a nano-based drug delivery system for treating cancers (Rottenberg et al. 2021). Gold nanoparticles (AuNPs) are advantageous options for cancer treatment and diagnosis. AuNPs are created in the size range between 1 and 150 nm and in various shapes, including nanorods (AuNRs), nanocages, nanostars, and nanoshells (AuNSs). AuNPs consist of high rates of biocompatibility and exhibit controlled patterns of medicine release in the drug delivery process. AuNPs consist of conduction electrons on their surfaces which get excited by certain wavelengths of light. This feature enables AuNPs to adsorb light and produce heat that is fatal to cells. Destroying the cancerous cells with the heat released under irradiation is called photothermal therapy (PTT) or photodynamic therapy (PDT) (D'Acunto et al. 2021).

On the other hand, RNA-based therapies can regulate the expression of immune-relevant genes, therefore increasing anti-tumor immune responses directly. Several nanomaterials have been introduced that can deliver nucleic acid therapeutics to tumors and immune cells (Lin et al. 2020). There are biomimetic strategies for providing a co-delivery system that is capable of supporting both chemical and RNA-based therapies (Liu et al. 2019). Considering RNAs as therapeutic agents or drug targets requires precise knowledge about the 3D structure of specific RNAs. There are reliable algorithms for pronging the second structure of RNAs, but the tertiary architecture which determines the RNA's functions is quite challenging to anticipate. Bioinformatics provides several methods for predicting the tertiary structures of RNAs such as Vfold, iFoldRNA, 3DRNA, and RNAComposer. They all face particular hurdles, but it should be noted that the field of computational RNA structure anticipation, has a bright future (Biesiada et al. 2016). RNA-based vaccines are quite impressive immunotherapeutic tools in cancer therapies. However, the *in vivo* delivery of synthesized mRNAs could face some obstacles. Encrusting mRNAs with a lipid-polyethylene glycol (lipid-PEG) shell increases the mRNA delivery rate up to 95% more than the conventional nanoparticle-free mRNA vaccines (Islam et al. 2021).

In RNA-based nano-techniques, utilizing large-sized RNAs faces several difficulties. Wang et al. have reported an interesting method of using gold nanoparticles (enriched by expanded genetic alphabet transcriptions) to increase the effectiveness of detecting the large natural or artificially synthesized RNAs through an RNA nano-based labeling

Table 1 Medical applications of nanobiotechnology

Nanomaterials	Biotechnological application	Utilized therapeutic or diagnostic agents	References
Smart nanoparticles synthesizes from organic, inorganic, and hybrid nanomaterials	smart drug delivery-based cancer therapies/ radiation therapies/ tissue engineering	Anti-cancer medicines/Targeting ligands(antibodies, peptides, aptamers, and small molecules)	(Lombardo et al. 2019; Doroudian et al. 2021; Samrot et al. 2020)
Viral capsid-based nanoparticles	Producing Vaccines and biosensor/ medical imaging/ gene therapy/enzyme delivery/ antigen delivery/Can get exploited as protein supplements	Antibodies/ enzymes or aptamers/ drugs/ Proteins	(Jeevanandam et al. 2019; Lyu et al. 2019; Selivanovitch and Douglas 2019)
Protein-based nanomaterials	Cancer therapy	Anti-cancer medicines/ Oxali-palladium (OX) and iron nanoparticles (NP)	(Tavakoli et al. 2021; Azarakhsh et al. 2021)
Liposome-based nanomaterials	Cancer therapy/Producing viral, DNA-based, and bacterial vaccines	Platinum (Pt) compounds/ Antigens/ Specific gene sequences	(Rottenberg et al. 2021; Evelyn Roopngam 2019)
Magnetic nanoparticles	SARS-CoV 2 Diagnosis/Drug delivery/Tissue engineering	Specific anti-bodies/Nano-medicines	(Abdelhamid and Badr 2021; Cardoso et al. 2018)
Graphene/Carbon-based nanomaterials	SARS-CoV 2 Diagnosis/ Alzheimer's Disease Therapy/ Nano-bio detection of biomarker of woodsmoke exposure/ Drug delivery/ bio-imaging/ photothermal therapy nanocapacitors/ Designing scaffolds	Specific anti-bodies/Acrine and physostigmine/ Tetracycline (TC)	(Abdelhamid and Badr 2021; Nawaz et al. 2021; Ruan et al. 2019; Karimzadeh et al. 2019; Patel et al. 2020)
Metallic nanomaterials	Alzheimer's Disease Therapy/ bio-imaging, photothermal therapy nanocapacitors/ Drug delivery/ Inhibition of procine epidemic diarrhea virus (PECV) / probably efficient in inhibiting the coronavirus/ Magnetic devices, nanowires battery, nanogenerator, semiconductor/ Prosthodontics (Increase the wear resistance,the hardness and toughness of the ceramic)/ Nanodiagnosis and Biosensors (FRET: fluorescence resonance energy transfer)/ Large RNAs labeling/ Nanodiagnosis and Nanotherapeutic approaches(viruses)/ Cancer therapy and diagnosis/ Designing nano-bioreactors for enhancing the maturation of cultured cells (in-vitro maturation of heart tissue)	Acrine and physostigmine/ Virus/Protein/ DNA/ expanded genetic alphabet transcriptions/ Therapeutic agents/ providing the photothermal therapy (PTT) or photodynamic therapy (PDT)	(Nawaz et al. 2021; Patel et al. 2020; Du et al. 2020; Rabiee et al. 2020; Wang et al. 2020; Fouad 2021; D'Acunto et al. 2021; Jeong et al. 2021)
Resin-based nanomaterials	Prosthodontics (Provide greater hardness) / Improve tribological and mechanical features)/ oral chronic disease therapy	Triggers anti-bacterial mechanism	(Patel et al. 2020; Chen et al. 2020)
Ceramic-based nanomaterials	Prosthodontics /considerable anti-microbial and anti-fungal activities against C.Albicans/ Drug delivery/Biomedical imaging/bacterial infections, glaucoma, and cancer therapies	Bio-imaging operators/drugs/genes/proteins	(Patel et al. 2020; Thomas et al. 2015)

Table 1 (continued)

Nanomaterials	Biotechnological application	Utilized therapeutic or diagnostic agents	References
Algae-based nanomaterials	Cancer, bacterial, and fungal diseases therapies/Exhibits antioxidant, free radical scavenging, and biocompatibility characteristics/ could be synthesized with other nanomaterials(e.g. Gold)	Nano-medicines	(AlNadhari et al. 2021; González-Ballesteros et al. 2017)
Nanoemulsions	conveying needed nutrients to gastroectomy patients/ Chronic periodontics therapy, wound healing(soft tissue wounds in the oral cavity)/ Increasing the viability and resistance against oxidative stress in the sperm samples	Food components/ Vitamin C, E, and Propolis	(Razavi et al. 2020; Fidoski et al. 2020; Sánchez-Rubio et al. 2020)
MOF-based nanomaterials	cancer therapy/ biomedical imaging/ Nano-bio detection of biomarker of woodsmoke exposure/ Drug delivery/ Efficient delivery of protein into the cells	Oxidoreductase family(POD, oxidase (OXD),superoxide dismutase (SOD),catalase (CAT))/ Tetracycline (TC)/ Insulin	(Ding et al. 2020; Ruan et al. 2019; Karimzadeh et al. 2019; Wang et al. 2019)
Poly hydroxyl alkanooates (PHAs)-based nanomaterials	Electrospun nanofibers: efficient in drug-delivery and bone tissue engineering/ PHA nanofibers: exploited in tissue engineering/anti-tumor therapies	Nano-medicines	(Chai et al. 2021; Korde and Kandasubramanian 2020)
Polyethylenimine (PEI)-based nanomaterials	Producing DNA vaccines/Drug Delivery	Specific gene sequences/CRISPR/Cas9 system/ chemical drugs or gene modifying agent	(Lim et al. 2020; Lin et al. 2020; Deng et al. 2019)

technique. These techniques are highly dependent on the conjugation between nanoparticles and RNAs (Wang et al. 2020). Since gene sequencing is of great importance, multiple biotechnology-based diagnostic tools, including quantitative PCR, DNA barcoding, next-generation sequencing, and imaging techniques are commonly currently used. These methods are considered economically advantageous, along with providing a reliable diagnosis. Incorporating nano-based sensors with mentioned tools increases the sensitivity and spatiotemporal resolution, which are two fundamental features of the gene sequencing process (Kumar et al. 2020). Designing nano-based devices for diagnosis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) has been promoted recently. Nanomaterials such as gold nanoparticles, magnetic nanoparticles, and graphene (G) significantly increase the accuracy and decrease the required time and costs. Hence, render beneficial tools for viral detection more effective compared to the traditional techniques. Nanoparticles are specified via anti-bodies to identify particular antigens on the surface of the virus. Suspected samples from the patient, air, and surface can get examined by nano-based serological or molecular diagnosis methods (Abdelhamid and Badr 2021).

Nanomaterials can be utilized in the form of membranes. Chemically or physically synthesized nanomembranes remarkably advance the conventional water purification techniques (Lohrasebi and Koslowski 2019; Kim et al. 2020). Incorporating nanomembranes with bioreactors is the basis of the membrane bioreactor (MBR) technique, which is exploited in wastewater reclamation (Ma et al. 2018). Eliminating pollutant components from the environment is one of the main purposes of nanobiotechnology (Table 2). In the agricultural fields, nano-bio technologically modified pesticides and fertilizers notably prevent crop loss. Nano-based bioremediation processes have been developed to reduce soil pollutions and are expected to improve both environmental and agricultural approaches (Usman et al. 2020). Several studies are expanding the idea of producing nano plants that show better biological performances (e.g., photosynthesis) compared to natural plants (Marchiol 2018) (Table 3). Enzymes empowered by nanomaterials have rendered higher recovery and productivity rates and thus are potentially able to act spotless in different industrial techniques (Adeel et al. 2018; Zhang et al. 2021) (Table 4).

The objective of this study is to review the applications of nanoscience in enhancing the efficiency of biotechnological methods (Fig. 1).

Application of nano-based materials for drug delivery, therapeutic and diagnostic processes

One recently promoted technique in the gene therapy field is the application of the CRISPR/Cas9 systems, which has

been indicated to be highly effective in the treatment of monogenic disorders, non-monogenic disorders, and infectious diseases. Emerging studies have suggested that nanocarriers, which are created from Polymer polyethyleneimine (PEI), are more efficient in delivering CRISPR/Cas9 systems to targeted cells compared to the viral carriers (Deng et al. 2019). Gene mutation-related diseases such as cancers and human immunodeficiency viruses are potentially treated by DNA-based vaccines. This type of vaccine enhances disease symptoms by delivering specific gene sequences-which are embedded in plasmids- to targeted cells. Despite having clinical utilization, DNA vaccines face limitations in delivering their genetic cargos to the target cells. Designing efficient nano-delivery systems will eliminate such deficiencies PEI (Lim et al. 2020). Virus-like nanoparticles (Jeevanandam et al. 2019) seem to form applicable nanocarriers for this purpose (Fig. 2).

Nanomaterials used in cancer diagnosis can be mainly divided into contrasting agents (magnetic, iron oxide and gold nanoparticles) and fluorescent agents (quantum dots). Some nanocarriers have inherent optical properties (such as carbon nanotubes, gold and magnetic nanoparticles) that can be converted into high energy to cells for destruction and can serve as nanotheranostics (Barani et al. 2021).

Nanomaterials used in smart drug delivery-based cancer therapies are categorized as organic and inorganic materials. Micelles, vesicles, multilamellar liposomes, and solid lipid nanoparticles are some examples of self-assembled organic nanomaterials. Other organic materials are not capable of self-assembling and need to be synthesized, such as nanotubes and dendrimers. Gold nanoparticles, quantum dots, mesoporous silica nanoparticles, and superparamagnetic iron oxide nanoparticles (SPIONs) are classified as inorganic nanomaterials (Lombardo et al. 2019). SPIONs are vastly utilized in therapeutic approaches, including cancer therapy, radiation therapy, and tissue engineering. SPIONs are synthesized through different physical, chemical, and biological methods. Bacteria and plants are the biomaterials upon which the biological method is based (Samrot et al. 2020). Nanoparticles containing both organic and inorganic materials (hybrid nanoparticles) have been indicated to be highly efficient, as well (Lombardo et al. 2019). Embedding targeting ligands (e.g., antibodies, peptides, aptamers, and small molecules) on the surface of nanoparticles assures the delivery of medicines to specific sites in the body, such as tumor tissues. The mentioned process is called: “targeted drug delivery system” (Doroudian et al. 2021). There are two types of targeting delivery: passive targeting and active targeting. In the passive form, the high aggregations of medicines at the tumor sites are related to the nano-scaled size of the nanocarriers. The tight junctions between epithelial cells of the vessel tissues prevent the nanoparticles from exiting the vessel. The cancerous cells loosen the tight junctions

Table 2 Environmental applications of nanobiotechnology

Nanomaterials	Biotechnological application	Biological agent (if existed)	References
Nanoparticles synthesized from nanoscale zero-valent iron (nZVI), Magnetite (Fe ₃ O ₄), Maghemite (γ -Fe ₂ O ₃), Iron oxide, Silver (AgNPs), nZVI/Cu, and biochar	Elimination of toxic components from environment /Water remediation/Nano-bioremediation/ Waste water treatment(enhances the growth of the microbial populations in the waste water)/Nanocomposites utilized for nano-bioremediation	Effective microorganisms (EM), such as lactic acid/phototropic bacteria, Streptomyces sp. Z38, and yeast are used during Nano-bio-based water remediation	(Vázquez-Núñez et al. 2020; Lincy et al. 2020; Patra Shahi et al. 2021; Costa et al. 2020; Bensaïda et al. 2021; Al-Gheethi et al. 2020)
Nanocatalysts synthesized from Cs/Al/Fe ₃ O ₄ /Mg/Al/ ZrO ₂ loaded with C ₄ H ₄ O ₆ HK/ Lithium impregnated calcium oxide (Li-Cao)/ Magnetic solid base catalysts CaO- / KF/CaO/TiO ₂ /ZnO/ Al ₂ O ₃	Optimizing the bioenergy generation/Water purification/Optimizing the biodiesel production		(Ahmadi et al. 2019; Nasrollahzadeh et al. 2020; Mofijur et al. 2020)
All the mentioned materials are recruited from biomass			
Membrane bioreactors (MBRs), supplemented from O ₃ , O ₃ /Fe ₂ +, O ₃ /nZVI (nano zero valent iron),	Designing nano-bioreactors for waste water reclamation		(Ma et al. 2018; Jiang et al. 2019; Abass and Zhang 2020; Malik et al. 2019)
Nanomembranes synthesized from Graphene-based nano-channels, 3D printed finger-sized units(FSU) with prepared wheat straw (WS)/ Nano-scaled zinc oxide, or through a top-down approach using biomass(wood tissue)	water purification		(Lohrasebi and Koslowski 2019; Li et al. 2019; Kim et al. 2020)
Nanoadsorbents synthesized from silica gel, activated alumina, clays, limestone, chitosan, activated carbon, zeolite, liquid ammonia (AlCl ₃ ·6H ₂ O), and metal/metal oxide based nanocomposites	Removing contaminations in the water purification process/Elimination of toxic dyes (by alumina nanoparticles)/Eliminating arsenic from water		(Ali et al. 2020; Banerjee et al. 2019; Ashraf et al. 2019)

Table 3 Agricultural applications of nanobiotechnology

Nanomaterials	Biotechnological application	Biological agent (If existed)	References
Nanomaterials synthesized from Silver, zinc, iron, titanium, phosphorus, molybdenum, and polymer	Designing nanofertilizers, nanopesticides, and nanobiosensors to Increase the crop value and decrease crop loss caused by agricultural pests		(Usman et al. 2020; Chhipa 2019)
Nanoparticles covered with garlic essential oil/ Nanotubes containing aluminosilicate	Designing nanopesticides, nanofungicides, and nanoherbicides that are Utilized in horticulture; to reduce diverse types of herbal pests		(Thangadurai et al. 2020)
Nanomaterials synthesized from quantum dots, magnetic, carbonaceous, noble metals, organic (carbon, graphene, chitosan, and onion membrane) and inorganic (silver, gold, silica, and titania)	Designing nanobiosensors for Monitoring the interactions in soil–plant-air and Detecting the dichlorvos	Antibodies/aptamers/proteins/enzymes/ Acetylcholinesterase (AChE)/ tyrosinase enzymes	(Usman et al. 2020; Mishra et al. 2021)
Single-walled carbon nanotubes (SWNT)/carbon, graphene-based nanomaterials	plant nanobionics: designing engineered artificial photosynthetic systems, enhancing the growth rate of this new type of plants		(Marchiol 2018; Lew et al. 2020)
Pd/Fe0 bimetallic nanoparticles	Triggers dechlorination/dehalogenation process in organic pollutants and neutralize them, therefore enhances the remediation process of contaminated soils (Bioremediation)/Spiked soil remediation/Decomposing a soil polluting agent named Hexabromocyclododecane (HBCD)	Living organisms (bacteria, fungi, plants etc.)	(Usman et al. 2020; Singh et al. 2012; Le et al. 2019)

Table 4 Industrial applications of nanobiotechnology

Nanomaterials	Biotechnological application	Biological agent (If existed)	References
Nanocarriers synthesized from silver, titanium dioxide, zinc oxide, Metal oxide (calcium, magnesium oxide, and strontium oxide), and magnetic material	Increasing the shelf life of food and prevent its spoilage(delivery of nutritional or antimicrobial components such as, polyphenols)/ optimizing the biodiesel production process		(Bhuyan et al. 2019; Nizami and Rehan 2018)
Graphene- immobilized nano-bio-catalysts	Providing a proper environment for enzymatic immobilization process (Nanomaterial-based nano catalysts)		(Adeel et al. 2018; Zhang et al. 2021)
MOF-based nanozymes	biosensors, biocatalysis, and biomedical imaging / biosensors for evaluating the food safety in the food industry	Antibodies/aptamers/proteins/enzymes/ Acetylcholinesterase (AChE)/tyrosinase enzymes/mycotoxins/antibiotics/pathogens	(Ding et al. 2020; Zhang et al. 2019b)
lipid-based, polymeric-based, metal-based nanosystems, micelles, hydrogels, dendrimers, TiO ₂ , ZnO, silica, and carbon black nanoparticles	Improve the supplementation of skin, hair or teeth with active cosmetic ingredients (ACIs)(Cosmetic industry)		(Santos et al. 2019; Chiari-Andréo et al. 2019; Manikanika and Jaswal 2021; Yadwade et al. 2021)
Nanomaterials synthesized from Carbon, Nitrogen, Graphite, and Silver/Graphene oxide (Ag-GO)	In the structure of nano-bio fuel cells: nanotube forests (NTFs), nanotubes (NTs), Nitrogen-doped hollow nanospheres with large pores (pNHCSs), and Ag-GO or graphite nanoparticles Nanofluids, Nanocatalysts, and Nanomembranes in oil exploration /production, recovering the oilfield, oil purification, and purification of gas and waste water produced in oil industry carbon nanotubes, carbon nanofibers, graphene oxide, and biochar in optimizing the biodiesel production process	Glucose oxidase (GOx)/Glucose oxidase and Laccase/Fructose dehydrogenase and laccase/Glucose oxidase and laccase/NADH dehydrogenase	(Sharma et al. 2021; Hajiabadi et al. 2020; Nizami and Rehan 2018)

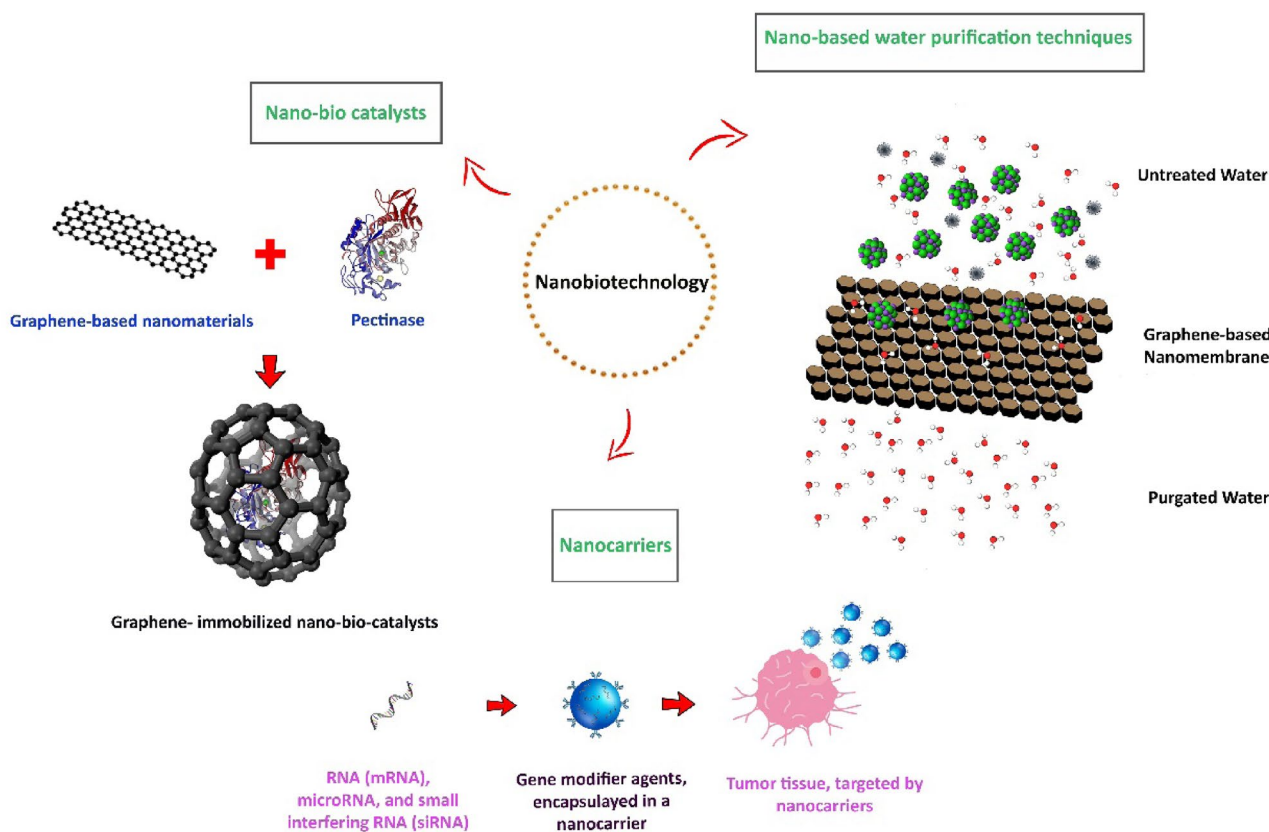
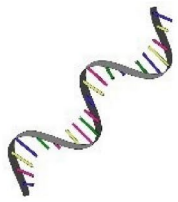


Fig. 1 Diverse Applications of Nanobiotechnology: multiple techniques, including Drug delivery-based therapies, remediating processes, and industrial nano-bio catalysts benefit from nano-scaled particles

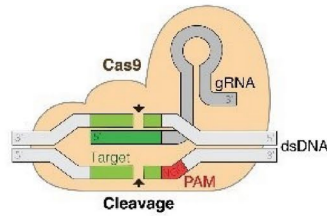
of the adjacent vessels. Therefore, nanocarriers can pass through the vessel and get into the tumor site. The targeting ligands incorporated with nanoparticles are not responsible for the passive targeting action. The binding between the targeting ligands and the particular receptors on the cancerous cells-which are exclusively found on the surface of the tumor cells- causes a more precise drug delivery, which is known as active targeting (Doroudian et al. 2019). Although drug-loaded nanoparticles efficiently carry the medicines to target sites, according to the in-vivo studies, these nanoparticles might not be quite biodegradable. Hence using such nanoparticles could lead to toxicities and side effects. It is worth mentioning that Zhou et al. have developed biodegradable nanoparticles using poly (aspartic acid) (PASP) microtube, a thin Fe intermediate layer, and a core of Zn (Zhou et al. 2019).

Nano-based drug delivery systems provide highly promising prospects for treating neurodegenerative disorders. It is reasonable to assume that treating neurological diseases by conventional drug delivery systems is extremely challenging due to the presence of the blood–brain barrier (BBB). The blood–brain barrier prevents the entrance of therapeutical agents to the central nervous system (CNS),

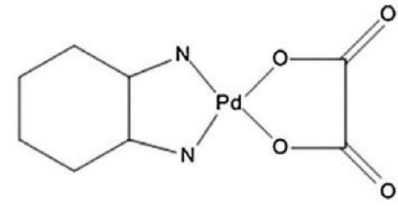
therefore, making the conventional therapies inadequate. The blood–brain barrier provides a stable environment for the CNS and regulates the cell-to-cell interactions, which take place in the CNS. The dysfunction of the blood–brain barrier leads to severe neurodegenerative disorders (e.g., Parkinson’s disease (PD), Alzheimer’s disease (AD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS)). The blood–brain barrier is responsible for the proper functioning of the CNS, so naturally, it has a super-sensitive permeability. This feature of the blood–brain barrier is highly related to the tight junctions between the barrier’s cells. Only 1–4 percent of most CNS medicines succeed in passing the blood–brain barrier. Nanoparticles are more likely to pass the barrier because of their nano-scaled size. Encapsulating drugs in nanoparticles can significantly increase the drug transmission rate through the blood–brain barrier (Furtado et al. 2018). For instance, graphene, metals, carbon-nanotubes, and metal-oxides are the nanomaterials that can get exploited in the treatment procedure of patients with Alzheimer’s disease (AD). AD is caused by different genetic and environmental cues. Chemical and electrical malformations are observed in the brain of an AD patient. Acrine and physostigmine, which are conventional medicines for AD, have



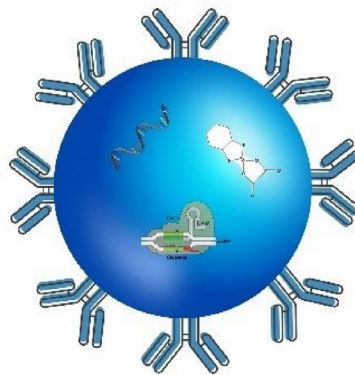
Therapeutic RNAs



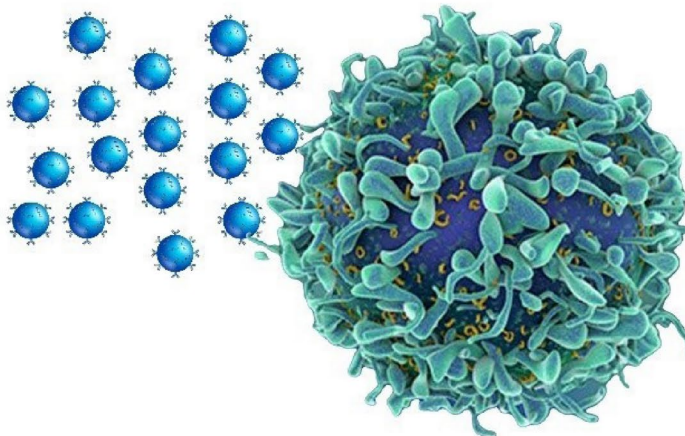
Crisper/Cas9 Systems



Oxali-palladium (OX), an anti-cancer medicine



Nanoparticles can get loaded by diverse therapeutic agents



Nanoparticles target the cancerous tumor

Fig. 2 Encapsulating therapeutic agents within nanoparticles: embedding medicine or gene-modifying agents into the nanoparticles remarkably enhances the therapeutic efficiency along with diminishing potential side effects

been proved to stimuli severe effects on the gastrointestinal tract and nervous system. Therefore, attention is drawn to nano-based therapies (Nawaz et al. 2021). Marcos-Contreras et al. have proposed that the augmentation of VCAM-1 ligands to the drug-loaded nanocarriers can significantly improve the cerebral accumulation rate of nanoparticles in inflamed brains (Marcos-Contreras et al. 2020) (Fig. 3).

Although nano-based medications of neurodegenerative disorders seem spotless theoretically, the internal

environment of the body puts out several obstacles on the path of the medicine nano-delivering. For instance, lipid nanoparticles (LNPs) may safely carry their therapeutic cargos to the targeted cells, but if the drug needs to reach the cytoplasm, lipid nanoparticles are not capable of efficiently crossing the cell membrane. Small interfering RNAs (siRNAs) are delivered to hepatocytes via lipid nanoparticles, but only 2% of them accomplish reaching to the cytoplasm. It should be mentioned that big data and computational

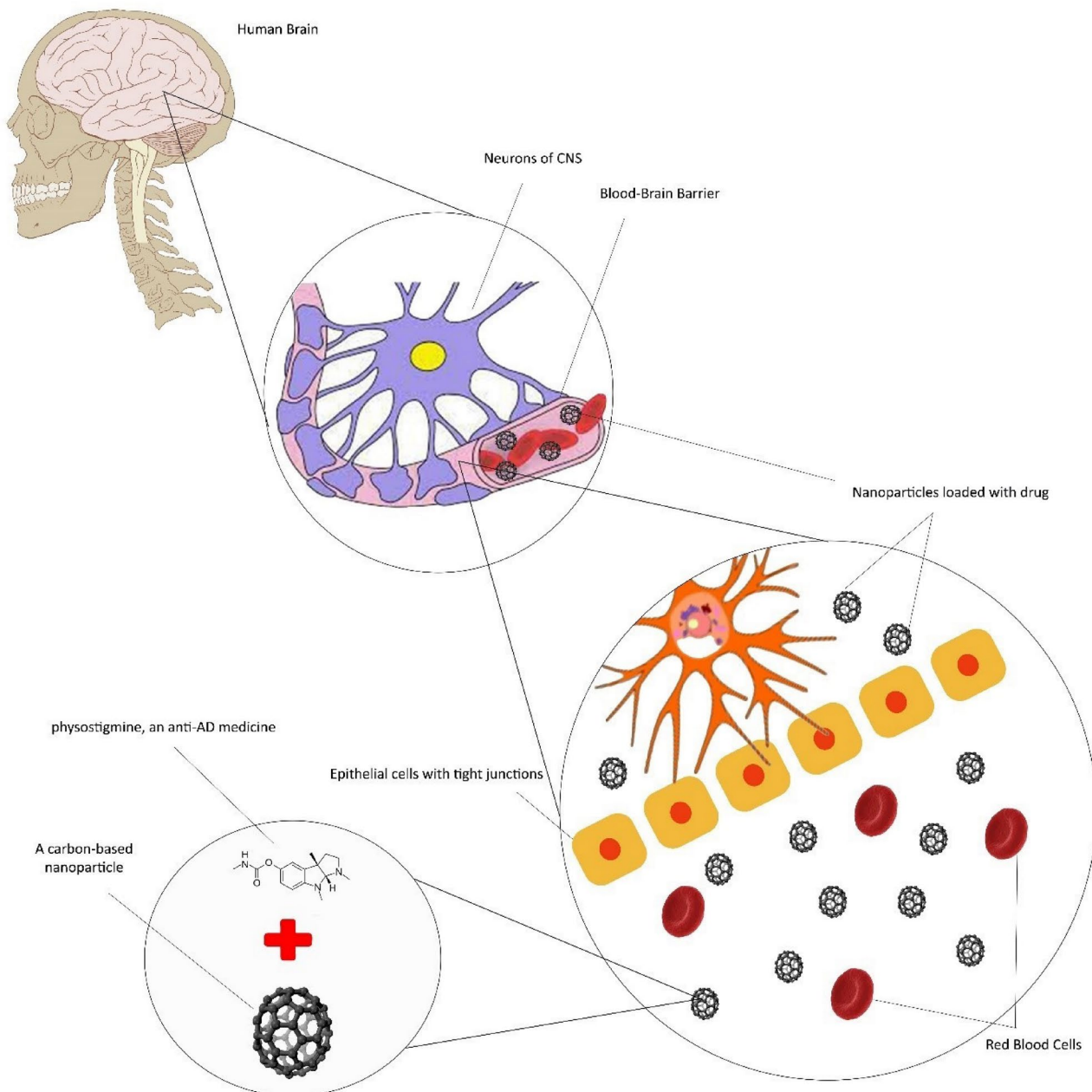


Fig. 3 Nano-based drug delivery in the therapies of neurodegenerative disorders: blood–brain barrier (BBB) is a noticeable obstacle for conventional medicines; however, drugs encapsulated within nano-

particles efficiently penetrate through the BBB and reach the central nervous system (CNS)

methods can help scientists to predict the in-vivo challenges of nano-drug delivery to design proper techniques to overcome them (Paunovska et al. 2019). Besides, bioinformatics provides tools for measuring the interaction rate between exploited nanomaterials and drug targets (Nawaz et al. 2021). Designing efficient nanomaterials is fundamental for nanotechnological approaches. Carbon nanotubes (CNTs) and graphene-based nanomaterials have been vastly utilized in nanotechnology during the last two decades (Kinloch et al. 2018). As a case in point, Single-walled carbon nanotubes (SWCNTs) are considered as excellent options for designing nano-based biomedical approaches, including but not limited to drug delivery systems. The most noticeable features of SWCNTs are their great photophysical properties (Farrera et al. 2017). Even though Carbon nanotubes (CNTs) and graphene-based nanomaterials have unique qualities such as high flexibility, they face some challenges in their load transfer capability, dispersion, and viscosity. Hence, creating more applicable and eco-friendly nanomaterials has drawn intense attention (Kinloch et al. 2018). AlNadhari et al. have introduced algae as a green and eco-friendly source of materials that can be used in nanoparticles. Algae-based nanoparticles in the biomedical field consist of therapeutical characteristics, such as antibacterial, anti-fungal, and anti-cancer features (AlNadhari et al. 2021). Milk-derived proteins such as β -lactoglobulin (β -LG), lactoferrin (LF), and the caseins (CN) are other biological alternatives for synthesizing nanocarriers. Anti-cancer medicines have been embedded into protein-based nanocarriers and successfully deteriorated cancerous tumors (Tavakoli et al. 2021). Azarakhsh et al. have demonstrated specific binding sites for the anti-cancer drug, Oxali-palladium (OX) and iron nanoparticles (NP) on the Beta-Casein (β -CN). Hence, the Beta-Casein can perform as an efficient carrier for both agents (Azarakhsh et al. 2021). One common strategy in designing nanocarriers for cancer therapies is to create nanoparticles that can detect the vitamin or growth factor receptors on target cells. Cancerous cells usually over-express the receptors for such nutrients so that they can keep their high proliferation rate (Peer et al. 2020). Reprogramming the nutrient signaling and micropinocytosis of the cancer cells seriously affects the efficacy of Nano-particulate albumin-bound paclitaxel (nab-paclitaxel, nab-PTX); which is one of the most commonly prescribed nanomedicines (Li et al. 2021).

Antimicrobial peptides (AMPs) are short-chain, often cationic, peptides possessing several attributes which make them attractive alternatives to conventional antibiotics with a low likelihood of resistance developing in target organisms (Meikle et al. 2021). Conjugation and functionalization of nanoparticles with potentially active antimicrobial peptides has added advantages that widen their applications in the field of drug discovery as well as a delivery system, including imaging and diagnostics (Mohid and Bhunia 2021).

Silver nanoparticles coated with zinc oxide (Ag@ZnO), can stimulate proliferation and migration of human keratinocytes, HaCaT, with increased expression of Ki67 and vinculin at the leading edge of wounds. Interestingly, Ag@ZnO stimulates keratinocytes to produce the antimicrobial peptides hBD2 and RNase7, promoting antibacterial activity against both extracellular and intracellular *Staphylococcus aureus* isolated from wounds (Majhi et al. 2021).

Wound dressing is an important action against an injury. In recent years, nanotechnology has been combined with wound dressing techniques, and there are several new materials and techniques available for this action. The nanoparticles' dimensions make them suitable for penetrating into the wound. Thus, bioactive agents and drugs can be released locally (De Luca et al. 2021). Numerous synthetic and natural materials have been applied for wound healing; Hyaluronic Acid, as an illustration, is one of the most-used materials (Ahire and Dicks 2016).

In 2017 Polyethylene Oxide (PEO)-hyaluronic acid (HA) nanofibers as an inhibitor of *Listeria monocytogenes* infection (Ahire et al. 2017a). Gauze is a traditional wound dressing used to protect dermal wounds from bacterial infection. In a study in 2021, an antibacterial gauze was prepared by the combined use of antimicrobial peptides and AgNPs. The prepared antibacterial gauze showed excellent antibacterial activity against *E.coli*, *S. enteritidis*, *S. aureus*, and *B. cereus* and also exhibited good biocompatibility (Chen et al. 2021a, b). In 2014, Ahire and Dicks introduced 2,3-Dihydroxybenzoic Acid-Containing Nanofiber as a suitable nanomaterial for wound dressing as it prevents *Pseudomonas aeruginosa* infection (Ahire and Dicks 2014). To inhibit the growth of this microorganism, Copper-Containing Anti-Biofilm Nanofiber Scaffolds can be used too. Copper-containing nanoparticles have the potential of inhibiting *Escherichia coli* growth either (Ahire et al. 2016). Surfactin-loaded nanofibers are also a great candidate to be used in wound dressings or in the coating of prosthetic devices to prevent biofilm formation and secondary infections (Ahire et al. 2017b). In addition to nano-therapies, nano-diagnostic agents- metal nanoparticles- have been indicated to be highly applicable in the detection of viruses, including covid-19 (Fouad 2021). Several biotic [e.g., algae (AlNadhari et al. 2021) and viral capsid (Jeevanandam et al. 2019)] and abiotic [e.g., gold, silver, graphene oxide, and zinc oxide (Fouad 2021)] nanomaterials have been reported to be applicable in biomedical processes. The combination of biotic and abiotic sources provides efficient nanomaterials as well. For example, the highly effective graphene-starch nanocomposites, are resulted from embedding graphene-based nanomaterials into the starch biopolymers (Mishra and Manral 2021). The delivery of therapeutics via nanoemulsions (NE) has shown striking results. Sánchez-Rubio et al. have successfully defeated deficiencies of vitamin E (e.g., hydrophobicity and

low stability) by creating nanoemulsions comprising vitamin E. The sperm samples derived from the red deer's epididymal tissue were treated with the mentioned nanoemulsions and the sperm's viability and resistance against oxidative stress, was increased (Sánchez-Rubio et al., 2020). Jeong et al. have reported another growth-promoting method that elevates the maturation process of cultured cells. The mentioned technique aims to develop an extremely operational and cost-effective bioreactor that enables in-vitro maturation of heart tissue. Next-generation stage-top incubator (STI) containing nano grooves patterned PDMS diaphragm (NGPPD) was designed to boost cell maturation and myogenic differentiation. The surface of NGPPD was covered with a slim layer of gold (Au) (Jeong et al. 2021). Microfluidic systems are proven to have applications in biological analysis, tissue engineering, etc. Embedding nanolitre volumes into micro-sized fluidic channels is the basis of the aforementioned technique (Valencia et al. 2020).

Application of nanoparticles on bioreactors as contributory agents

Since wastewater reclamation is a universal challenge and plays a major role in providing clean water for many people across the world, various techniques have been developed for this purpose. Among them, the application of membrane bioreactors (MBRs) in water purification has attracted great attention recently. In the MBR technique, the conventional activated sludge (CAS) process is incorporated with a filtration process provided by a physicochemical membrane (Ma et al. 2018). It has been shown that treating the mentioned membrane with nanoparticles in different types of MBR techniques can significantly improve the efficiency of the process (Abass and Zhang 2020; Jiang et al. 2019). The pharmaceutical industry produces one of the most pollutant wastewaters; which contains various amounts of organic compounds, including benzene, polynuclear aromatic hydrocarbons (PAHs), and heterocyclic, etc. these compounds have high Chemical Oxygen Demand (COD) and low degradability; which makes conventional biological treatments inefficient for treating them. However, applying O_3 , O_3/Fe^{2+} , $O_3/nZVI$ (nano zerovalent iron) processes in wastewater purification has made noticeable signs of progress. Nano catalytic ozonation process ($O_3/nZVI$) in a semi-batch reactor has the highest effect on advancing degradation amongst all (Malik et al. 2019). An experiment conducted in southern Tehran succeeded in removing the Methyl Tertio Butyl Ether (MTBE) and benzene from groundwater, using Fenton's chemical oxidation with stabilized nano zerovalent iron particles (S-NZVI) as a catalyst. The removal efficiency of MTBE and benzene were increased to 90% and 96%, respectively, by reducing the pH of the reaction environment down

to 3.2. Acidification of the environment decreased iron consumption as well (Beryani et al. 2017).

Nano-bioremediation

One green and cost-effective approach for treating the pollutant soils to reduce their toxicity is applying living organisms (bacteria, fungi, plants, etc.) through a process named: "bioremediation." Integrating bioremediation with nanoparticles increases the efficiency of the process (Usman et al. 2020). The technology of nano-remediation is a sustainable method to reduce the contaminants of the soil by various means (Yue et al. 2021; Sajjadi et al. 2021; Lian et al. 2021). As an example, the reduction of Cr (VI) levels using this technology is known to be worthwhile in many aspects (Azeez et al. 2020; He et al. 2020). Chemically active nanoparticles can trigger the dechlorination/dehalogenation process in organic pollutants and neutralize them, consequently. Even the toughest pollutants are targeted in this nano-bio-based remediation method. The time needed for the purgation of highly contaminated soils will be minimized by virtue of the mentioned technique (Usman et al. 2020). Iron oxide nanoparticles (NP) and Fe_3O_4 /bio-char nanocomposites are vastly exploited in the synthesis of nanoparticles of nano-bioremediation (Patra Shahi et al. 2021). It is worth noting that nano zerovalent iron (nZVI) is an effective technology in the case of remediation that has been applied broadly in recent years due to high levels of reactivity for contaminants (Luo et al. 2021; Visentin et al. 2020; Ken and Sinha 2020; Hou et al. 2019; Zhu et al. 2019).

The bioremediation process can be used in water purification as well. Separating solid components from liquid waste is a necessary stage in the water remediation process. The fresh market waste may contain infectious components, which can seriously harm humans and plants. Hence, it is important to develop methods to collect, separate, and treat these adverse agents. Solid wastes in the wastewater contain high amounts of carbohydrates and proteins, and they provide matrices for the colonization of infectious organisms. Altogether, the presence of solid wastes improves the growth rate of pathogenic organisms. After solid matters got collected, they should be stored and treated immediately. The treatment process must not be delayed because the enriched environment of the solid wastes can easily get corrupted. One way to treat them is through triggering the fermentation and composting processes. Adding effective microorganisms (EM), such as lactic acid/phototropic bacteria and yeast, accelerates the conventional fermentation and composting processes used for the solid waste treatment (Al-Gheethi et al. 2020). Costa et al. have sequenced the whole genome of the strain *Streptomyces* sp. Z38, and detected growth-promoting, heavy metal-eliminating, and anti-microbial features within specific biosynthetic genes. *Streptomyces* sp.

Z38 seems to be a suitable agent for bioremediation due to its ability to decompose heavy metals such as Cr (VI) and Cd (II). Costa et al. have supplemented the bioactive water (BW) extracted from *Streptomyces* sp. Z38 with AgNO₃ additives and produced silver nanoparticles (AgNPs) that are capable of performing the bioremediation process (Costa et al. 2020). There are other effective nanomaterials exploited to reduce many pollutants from soil and wastewater. For instance, utilization of nano-manganese oxide to eliminate ZnII/CoII from water (Mahmoud et al. 2020), application of nano-semiconductors on water and their Photocatalytic effectiveness (Oliveira et al. 2021), nano-scaled Iron (II) sulfide exploited to reduce hexavalent chromium from soil (Tan et al. 2020), production of nanocomposite for eliminating viruses (Al-Attabi et al. 2019), and successful application of nano biosurfactants which cause no toxicity for the environment (Debnath et al. 2021). Nano-bioremediation as an emergent approach causes some concerns and benefits at the same time. It is possible that nanomaterials exploited in this method would be a threat to the organism populations that exist naturally in water bodies. On the other hand, new living organisms would be introduced through bioremediation. The mentioned two scenarios can potentially put the anthropogenic features of ecosystems in danger (Weijie et al. 2020). Concerning this problem, however, scientists are trying to apply new methods to remove nanoparticles from marine ecosystems via other technologies (Ebrahimbabaie et al. 2020).

Designing nano-based water purification techniques, to overcome the problem of lack of clean water, across the world

Waterborne diseases that cause almost 10–20 million deaths annually are considered crucial health-related issues. According to the World Health Organization and environmental protection agencies, the pollution level of several water bodies has long crossed the defined limitations. Thus, developing methods for purging water from adverse components is of great concern (Sahu et al. 2021). The water purification process profits extremely from nanobiotechnology. Nanoparticles are extremely efficient in eliminating pollutants (e.g., dye components) due to their nano-scaled size and increased surface areas. In the case of dye removal, magnetic nanoparticles have been proved to be proper candidates (Lohrasebi and Koslowski 2019). Nanoadsorbents such as silica gel, activated alumina, clays, limestone, chitosan, activated carbon, and zeolite are cost-effective and profitable options for eliminating the contaminating agents during water purification process (Ali et al. 2020).

Copper and copper compounds are potent biocides and have been utilized as a disinfectant for centuries due to their anti-microbial properties. It becomes more functional

in its nano form and exhibits outstanding synergist, anti-fungal, and anti-bacterial effects (Bashir et al. 2021).

Copper nanoparticles have the potential of combination with other materials like Polyacrylonitrile (PAN) nanofibres and Polyethylene Terephthalate Filters to act more beneficial (Ahire and Neveling 2018; Nguyen et al. 2021).

Metallic nanomaterials, carbon-based nanomaterials, nanocomposites, and dendrimers are four major types of nanomaterials that can be applied in wastewater purgation (Murshid et al. 2021). Graphene-based nano-channels, which are inspired by aquaporin channels, have been utilized as water filters and are expected to enhance the water permeability and the salt rejection rate. It is worth noting that the efficiency of these filters can be affected by various factors. For example, it has been indicated that increasing the charges on the channel will decrease the water flow through the channel but, on the other hand, increase the ion rejection rate (Lohrasebi and Koslowski 2019). Carbon nanotubes (CNTs) have rendered noticeable results in eliminating the water contaminants, as well (Kutara et al. 2016).

The biosafety of water purification via finger-sized unit (FSU) has been certified by cellular and animal tests. In one study, Li et al. loaded 3D printed finger-sized units with prepared wheat straw (WS). To prepare WS for mentioned technique, the carbonized wheat straw (CWS) was adjusted with nano-scaled zinc oxide during an in-situ surface-modification process (CWS/ZnO). The resulted FSU was able to reduce bacteria, organic dyes, and heavy metal ions; therefore, elevating the purification efficiency. Since WS is one of the major agricultural wastes worldwide, applying it in water purification will not only cost very low but will reduce the air pollution which is caused by burning WS in many countries. The WS has a hollow, flexible, and electrical conductor structure. These features make WS a great candidate for enhancing water purification performance (Li et al. 2019).

For designing a nano-based filtering membrane, nanoparticles don't always have to be chemically synthesized or externally applied on the membrane. An emerging study has suggested a top-down approach that uses biomass to provide a functional membrane for the purification of the emulsions. This method can be used massively in cleaning oily waters resulting from industrial or domestic activities. The biomass used in the mentioned technique is wood tissue. The lignin and hemicellulose fractions are removed sectionally, and therefore, a highly porous, flexible, and durable membrane is provided. Since the lignin is removed and there is no hydrophobia left, the resulting wood membrane consists of outstanding water-absorbing and anti-oil properties. The wood-nanotechnology-based membrane shows significant efficiency due to its numerous advantages, including being green, economical, easy to produce, durable, and having selective wettability (Kim et al. 2020).

Rezaei et al. have synthesized a flower-shaped ZnO/GO/Fe₃O₄ ternary nanocomposite through the co-precipitation method, which is considered a rather fast and easy synthesis approach. The mentioned nanocomposite improves the ZnO degradation through a performance with an efficiency that is more than two times greater than the efficiency of the methods using ZnO particles alone. Hence, the ZnO/GO/Fe₃O₄ ternary nanocomposite seems to be an economical and time-saving approach for wastewater remediation (Rezaei et al. 2021).

It is worth noting that the vast uses of nanoparticles in different industrial products increase the risk of the inevitable release of nanoparticles into the environment, and therefore cause some concerns about the potential damages of nanobiotechnology. The urban wastewater seems to be highly exposed to industrial nanoparticles. The high concentrations of nanoparticles in the urban wastewater contaminate the sewage sludge, consequently. Wastewater treatment plants (WWTPs) are currently exploited to remove nanoparticles from wastewater and sewage sludge (Wang and Chen 2016). Nanoparticles synthesized and utilized in the industry can end up in marine ecosystems. Nanoparticles are developed from various chemical components such as carbon, silver, gold, and copper, which are potentially hazardous to live organisms. Since nanoparticles are extremely small in size, likely, they will easily enter the bodies of aquatic animals. It has been demonstrated that the accumulation of nanoparticles in the animal's body can cause severe morphological and behavioral deformities. Genetic materials of cells may undergo various changes as well (Gökçe 2021).

FeO ion, which is known as Nanoscale zerovalent iron particles (nZVI), is massively used in the synthesis of nanoparticles applied in wastewater nano-based treatments. Bensaida et al. have shown that combining nZVI with another metal (Cu) enhances the growth of the microbial populations in the wastewater treated with this nZVI\Cu bimetallic nanoparticles (Bensaida et al. 2021).

Exploiting nanobiotechnology-based methods in food industry

Nanotechnology-based pharmaceuticals were developed primarily, but wide applications of nanoscience in food and agricultural industries have been introduced as well (Sahani and Sharma 2020). Utilizing nanoscience in any stage of the food production process—either cultivation, production, post-harvest processing, or packaging—seems to be lucrative. The application of nano-based methods in the food industry has various advantages, but the most arguable of them would be its impact on shelf life augmentation and spoilage prevention (Bhuyan et al. 2019). Since Oxygen is known as an important cause of food spoilage in the food industry, scientists have developed the

technology of advanced coatings based on nanotechnology to prevent Oxygen from spoiling the product (Rovera et al. 2020). Multiple nanoparticles have the potential to deliver nutritional or antimicrobial components into food materials (Bhuyan et al. 2019). It has been reported that nanotechnology is a good option to deliver pesticides and nutrients successfully into the soil and improve the strength and tolerance of products in different stressful situations and reduce the probable contaminations (Ali et al. 2021). Among different nanoparticles such as silver, titanium dioxide, and zinc oxide, nanoliposomes are found to be small and have a large surface area which makes them more adhesive to biological tissues—therefore more bioavailable in comparison to others. Nanoliposomes are suitable candidates for creating a delivery system during food preparation. Food provided with the help of nanotechnology is called “Nano food” (Bhuyan et al. 2019). Nano foods can perform as therapeutic options. It is interesting to mention a recent study that has proposed exploiting nanoemulsions to convey needed nutrients to gastrectomy patients. These types of patients usually suffer from conditions like anorexia, energy deficit, and malnutrition, which can be treated by efficient nutrition delivery provided by nano food (Razavi et al. 2020). As mentioned earlier, in the food preparation process, antimicrobial components can be delivered along with nutritional components via a nano-based delivery system. Polyphenols are great examples of substantial antioxidant and antimicrobial agents in the food industry. Nevertheless, polyphenols have some limitations, including instability, low solubility, inefficient bioavailability, and being drastically susceptible to being degraded. There are several factors that reinforce degradation: Oxygen, light, pH, and interactions between polyphenols and other components in food. Polyphenol-loaded nanoparticles relatively overcome the mentioned obstacles due to their capacity to protect phenolic compounds against degrading processes (Milinčić et al. 2019). As a renewable and biodegradable source, starch is a useful polymer that has been applied in different fields such as the pharmaceutical and food industries. Nano-size starch is an advanced material with new abilities in the matter of hydrophobicity and stability (Wang and Zhang 2020). In the field of the food industry, there are also many other new methods based on nanotechnology, for instance, designing natural proteins as nano-architectures to deliver nutraceuticals (Tang 2021), new strategies for packaging food products by exploitation of the knowledge of nano-biotechnology, and nanomaterials (Reshmy et al. 2021; Jogee et al. 2021; Tiwari et al. 2021), utilization of the nano-delivery techniques to overcome the problems of consuming bioactive ingredients (Hosseini et al. 2021; Ozogul et al. 2021), producing nanoparticles in the shape of powder using the nanospray driers (Jafari et al. 2021),

detection of food contaminants by nano-Ag combinations (Yao et al. 2021), and even the application of nano-engineering in the field of the beverage industry (Saari and Chua 2020).

Nano-bio catalysts; an attempt to remove the barriers of enzymatic bioprocesses in the biotechnology industry

Organic enzymes, which are normally found in nature, have large applications in the biotechnology industry. Since organic enzymes are green and eco-friendly, they are usually preferred to commercially synthesized enzymes. Pectinase is considered to be extremely useful for manufacturing purposes. Pectinase application in industrial bioprocesses covers a large range from clarification of juice/ wine and tea/coffee fermentation to wastewater and industrial waste remediation. All enzymes- regardless of being organic or chemically synthesized- consist of limitations that make their usage challenging. Three major disadvantages of enzymes are inefficient recoverability, operational stability, and recyclability (Zhang et al. 2021). Functional nanomaterial-based bio-carriers render a proper environment for the enzymatic immobilization process, therefore facilitating recovery and recycling of enzymes and enhancing the efficiency of bioprocesses in the long run. Accordingly, designing nano-based carriers with these features has been attracted great attention. To achieve this aim, Graphene- immobilized nano-bio-catalysts have been proved to be greatly useful due to the Graphene's characteristics: electrical, optical, thermal, and mechanical high potency (Adeel et al. 2018; Zhang et al. 2021).

Nanomaterial-based nanocatalysts are useful in optimizing the biodiesel production process. This ability is related to the features of nano-scaled materials, including crystallisability, high adsorption and storage potential, having catalytic activities, and great stability and durability. Various materials can be used to create nanoparticles for this mean; some examples are metal oxide (calcium, magnesium oxide, and strontium oxide), Magnetic material, and Carbon. Carbon-based nanomaterials consist of multiple types, such as carbon nanotubes, carbon nanofibers, graphene oxide, and biochar.

All examples mentioned above have been proved to be highly effective in increasing the efficiency of the biodiesel synthesizing process and reducing the time and cost required for operating the process without utilizing nanotechnology (Nizami and Rehan 2018).

Replacing non-renewable energy sources with renewable ones is a great step in guaranteeing a sustainable future. Various devices, including solar and fuel cells, have been developed for this purpose. Conventional fuel cells are made from metal reactants instead of fossil fuels. They provide

an electron circulation, transfer electrons from the substrate to specific electrodes, and eventually produce sustainable energy. The metals used as catalysts in fuel cells (e.g., hydrogen, methane, and methanol) are usually expensive and non-durable. On the other hand, biofuel cells use cost-effective bio-catalysts (e.g., microbes and enzymes) instead of metal catalysts. Despite the mentioned advantages, biofuel cells have one major limitation: the low rate of electron transfer between substrate and electrodes, which is significantly enhanced by supplementing biofuel cells with nanomaterials. Nanomaterials are able to assemble the substrate (e.g., enzymes) with the electrodes. In other words, using them in the structure of electrodes, the electron absorption of electrodes improves- related to the high surface area rate of nanomaterials- therefore, a direct transition of electrons between enzymes and electrodes develops. Silver nanoparticles-Graphene oxide (Ag-GO), Graphite, Carbon-nanotube forest (CNTF), Carbon nanotube (CNT), and Nitrogen-doped hollow nanospheres with large pores (pNHCSs) are the nanomaterials applied in nano- biofuel cells. Respectively, Glucose oxidase (GO_x), Glucose oxidase and Laccase, Fructose dehydrogenase & laccase, Glucose oxidase and laccase, and NADH dehydrogenase form the enzymatic system of each nanomaterial (Sharma et al. 2021).

Metal-organic frameworks (MOFs); highly advantageous materials

Porous materials are known to be highly advantageous due to their high absorption and surface areas. Zeolites, activated carbons, and silicas are examples of this family, but the most eminent member among them are Metal-organic frameworks (MOFs). MOFs have features that make them unique for several applications. For example, MOFs show a high absorption rate, which is caused by their high surface areas. Another property of MOFs is their possession of several adjustable microporous channels, which makes it easy to produce different and changeable functional sites through them. The latest feature brings MOFs the shape and size selectivity. By controlling the starting materials and reaction parameters, it is possible to determine the morphology of MOFs (Kinik et al. 2020; Jun et al. 2020) into various shapes, including granule, pellet, thin-film, gel, foam, paper sheet, monolith, and hollow structures (Kinik et al. 2020).

There are two types of MOFs: (1) neutral MOFs and (2) ionic MOFs. Ionic MOFs are able to be used directly in anion purgation processes. For example, one approach for reducing the pollutant anions from the environment is synthesizing a cationic framework along with extra-framework anions. The synthesis of mentioned frameworks occurs by utilizing neutral nitrogen donors. The extra-framework anions will exchange with pollutant anions through an Ion exchange process called: "Anion trapping".

Anions are extremely abundant in nature. One of the most pollutant and hazardous anions is phosphates. These toxic anions are highly used in pesticides. Other examples of toxic anions, which are considerably frequent in industrial wastes, are the bulky anions. These are the dye molecules exploited in industry. Various diseases like cancers, lung/kidney dysfunction, and brain diseases, including Alzheimer's, are caused by dangerous anions like those mentioned above. Hence, creating methods that are able to recognize and delete the perilous anions from the environment is one of the most appreciated scientific approaches. MOFs have been proved to be functional for this mean (Desai et al. 2019).

Since MOFs have considerable surface areas and modifiable structure—different open metal sites and other functional groups can be introduced into their frameworks—they are suitable options for numerous applications which are generally related to detection and storage. In the case of storage, they exhibit acceptable physical adsorption for CO₂ (one of the major causes of global warming), H₂ (a clean energy source), and Methane (CH₄). The ability to adsorb variant components makes MOFs proper for water purification applications. Several toxic and harmful components which are responsible for water contamination, including organic pollutants (like dyes and oils) and heavy metal ions, can be detected, adsorbed, and removed by MOFs. Introducing different chemical groups into MOFs creates different internal interactions, which enable MOFs to detect target molecules functionally. Therefore, they can be used in active centers of catalysts, photocatalysts, and biosensors (Kinik et al. 2020).

MOFs-based nanozymes

Nanozymes are classified into two types: (1) natural enzymes that are incorporated with nanomaterials and (2) nanomaterials that exhibit inherent enzymatic features. Exploiting MOFs as nanomaterials in nanozyme structures will produce an emergent form of nanozymes, called: “MOF-based nanozymes”; which have multiple advantages over conventional forms. MOFs provide more catalytic sites, simplify the entrance of small substrate molecules -due to their porous structure-, enhance the substrate exclusivity, and altogether improve the catalytic function of enzymes. MOF-based nanozymes are effective in designing biosensors, biocatalysis, and biomedical imaging techniques. A recent promising application of them is in cancer therapy which reduces side effects significantly (Ding et al. 2020).

Agricultural usages of nanobiotechnology

Applying nanobiotechnology in agriculture to improve the agricultural production rate has been of great importance recently. Achieving this purpose will solve several problems related to the universal hunger dilemma. Several

nanofertilizers, nano pesticides, and nano-bio sensors have been created, which are able to increase crop value and decrease crop loss caused by agricultural pests (Usman et al. 2020). Conventional chemical pesticides and fertilizers can be deteriorative for soil composition and fertility. This happens because chemical residues can target many molecules other than the ones that have been defined as their main targets (Chhipa 2019). Besides, pesticides can have ruinous impacts on the microorganisms that naturally exist in the environment and are required for the crop's growth (Nehra et al. 2021). Utilizing nanoparticles can considerably reduce such unwanted events due to the high exclusivity of these particles. Silver, zinc, iron, titanium, phosphorus, molybdenum, and polymer are suitable materials to be used in the structure of agricultural nanoparticles (Chhipa 2019). Nanoparticles containing nutrients, fertilizers, and pesticides, can be sprayed externally to the plant. The folium will adsorb the nanoparticles and send them to the soil (Chugh et al. 2021).

Another application of nanobiotechnology in diminishing the damages of some traditional pesticides is designing nano-bio sensors that can efficiently detect toxic pesticides. Dichlorvos is one of these toxic pesticides that accumulate in the air, soil, water, and crops; and therefore causes neural, genetical, respirational, and muscular disorders. Dichlorvos-sensitive Nano-biosensors comprise immobilized enzymes embedded in nanomaterials. Acetylcholinesterase (AChE), tyrosinase enzymes, and some others are options for the enzymatic part of the nanodevice. For the nano- matrix section, both organic (carbon, graphene, chitosan, and onion membrane) and inorganic (silver, gold, silica, and Titania) options are available (Mishra et al. 2021). Nanomaterials can enhance the remediation process of contaminated soils through distinct abiotic and biotic directions, including the nano-bioremediation process (Usman et al. 2020).

Other than improving the functions of existed plants, the possibility of introducing engineered plants with better performances has been discussed recently. The term “plant nano bionics” refers to a pioneering idea of involving nanoparticles in living plants to make their intrinsic functions adjustable. The landscape of this idea is designing engineered artificial photosynthetic systems, enhancing the growth rate of this new type of plant, and many other novel applications which are expected to grow extremely in the years ahead (Marchiol 2018).

It is necessary to mention that inorganic nanoparticles that may be found in consumer products, may alter the gut composition and could lead to various gut-related diseases. Thus, there have to be some limitations in nanoparticle agricultural usages (Gangadoo et al. 2021; Ghebretatios et al. 2021).

Using nanoparticles in cosmetic products

Nowadays, due to special and distinctive physicochemical characteristics, nanomaterials are being vastly used in different industries. Recent studies are focused on applying nano-based technologies to improve the quality of cosmetic products. Nanostructures are about to deliver active ingredients to the skin. For this reason, it is more suitable to use lipid particles that are better adaptable to dermal absorption. The high stability of the combination of nanomaterials and lipid particles with cosmetic components indicates high efficiency. However, the probable risks of this method should not be ignored (Benrabah et al. 2020; Khezri et al. 2018). Producing nanoparticles using plants (Phyto-metal nano-based particles) is another advantageous method to decrease the toxicity of nanomaterials and their hazardous effects on the body. For this reason, this material is suitable for dermal uses and cosmetic applications (Paiva-Santos et al. 2021). Chitosan nanoparticles with better penetrability (Ta et al. 2021; Sakulwech et al. 2018), Gold and silver nanoparticles with a higher ability to reduce microbial contaminants (Séby 2021), Titanium dioxide (TiO₂) nanoparticles deposited with yttrium oxide (Y₂O₃) with better attenuation of ultraviolet radiation and less cytotoxicity (Borrás et al. 2020), nanoparticles with high uptake of oily components (de Azevedo Stavale et al. 2019) are other examples of the efficient application of nanotechnology in the field of cosmetic products.

Since nanoparticles are small in size, they exhibit perfect penetrability through the skin. Hence, using nanoparticles in cosmetic productions improves the supplementation of skin, hair, or teeth with active cosmetic ingredients (APIs). It is important to note that utilizing nanoparticles for several applications, as an emerging field of science, causes various concerns about being toxic or harmful for the body or the environment. The cosmetic industry's products are commonly designed for skin, hair, nail, teeth, and therefore, are directly related to the health of the human body. Thus, it is reasonable to assume that there are even more concerns about using nanoparticles in this industry compared to others (Santos et al. 2019).

In addition to these cases, nanotechnology can be useful for the detection of harmful components in cosmetic ingredients. Therefore the application of methods like covered iron oxide nanoparticles with silver for detection of mercury contamination in cosmetics (Chen et al. 2021a, b), Quantitative assessment of the Triamcinolone acetonide (TCA) (which is a hazardous component in high doses) using nanoparticles with luminescence property (Zhang et al. 2019a), And detection of harmful N-nitrosamines with the utilization of magnetic nanoparticles (Miralles et al. 2019) are worth mentioning.

Oil industry benefits from multiple types of nanomaterials

Nanomaterials can play a major role in the advancement of the oil industry. Almost every form of nanomaterial—discussed in previous sections—has been exhibited to have numerous applications in the oil industry. Nanomaterial can be effectively exploited in various processes of this industry, including oil exploration/production and recovering the oil-field. Nanofluids (synthesized from nanomaterials) optimize the oil production process. Nanocatalysts have applications in petrochemical processes along with operating an efficient oil purgation function. Several applications of this technology are mentioned below.

There are nanomembranes designed to provide a proper matrix for separating water and oil from gas. They eventually purify the gas and delete redundant components from wastewater (Saleh 2018). Metal workings such as machining and stamping industry require some types of lubricants and coolants, which are mostly oil products. There has been produced an oil-based cutting fluid made up of Al₂O₃ nanoparticles to decrease the friction force between the object and snipping tool (Subhedhar et al. 2021). Encapsulation of extracted essential oil from hyssop in a nano-complex improves the antioxidant and antifungal efficiency of the oil (Hadidi et al. 2021). The application of nano-silica in the procedure of oil cementing enhances the resistance of the cement (Goyal et al. 2021; Thakkar et al. 2020). In the process of oil recovery, there is a high energy loss that imposes damages to the injection system and lowers the heat level. To keep the rate of temperature in a higher range and decrease the energy loss, scientists have applied nano-thermal insulators that are more economical (Afra et al. 2021; Zhao et al. 2021; Zhou et al. 2020). Gas and oil products can be cleaned from H₂S by applying nanomaterials (Agarwal and Sudharsan 2021). Utilizing starch nano coatings (Wang et al. 2021), Lignin and nano-silica (Gong et al. 2021), Lotus leaf coated with nano-SiO₂ (Yang et al. 2021), and nano zeolite membrane are new methods for the separation of oil and water due to their high hydrophobic property (Anis et al. 2021). Nanotechnology can be used to improve the quality of engine oil, which results in the better stability and lubricity power as well as a reduced rate of released carbon mono oxide (Tonk 2021; Saidi et al. 2021; Thirugnanam et al. 2021; Ardebili et al. 2020). Advanced nanoemulsions show high stability and benefits for the oil industry due to the larger surface and the ability to wet (Kumar et al. 2021). Encapsulation of essential oils in nanostructures indicates a better performance as a pesticide due to better maintenance of the oil (Campolo et al. 2020). Producing an oil-in-water emulsion by applying protein nanoparticles can protect unstable and active ingredients and benefit the medicine and food industry (Xu et al. 2020).

Conclusion

Combining diverse fields of science in a manner that they overcome each other's deficiencies indicates promising results. Within the last decades, biotechnology has made a lot of progress. Merging nanotechnology with biotechnological methods enables scientists to design less time taking, more economical, and more efficient techniques. This Nano-biotechnological approach influences multiple therapeutic, agricultural, environmental, and industrial methods. For instance, the effectiveness of the emergent crisper/cas9 systems increases noticeably by applying the nano-scaled additives at the process.

In this review, we investigated the current advancements and limitations of biotechnology, along with the nano-based alternatives rendered by nanotechnology. It seems highly probable that biotechnology will accomplish even more improvements in the future, and its incorporation with nanotechnology gets humankind one step closer to a sustainable future. Besides, the nano-based techniques are less costly compared to the conventional ones. Thus, with nano-biotechnology promoting, a revolution in the economic situation of the world is not implausible.

Author contributions All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version. This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue. The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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