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Review Article

Nanomaterials for Targeted Drug Delivery through Skin to Treat Various Diseases: Recent Trends and Future Perspective

Nazish Mumtaz,[1] Muhammad Imran,[1] Ayesha Javaid,[1] Shoomaila Latif,[2] Nazim Hussain,[3] and Liviu Mitu[4]

[1]*Centre for Inorganic Chemistry, School of Chemistry, University of the Punjab, Lahore 54000, Pakistan*
[2]*School of Physical Sciences, University of the Punjab, Lahore 54000, Pakistan*
[3]*Center for Applied Molecular Biology (CAMB), University of the Punjab, Lahore 54000, Pakistan*
[4]*DIMSIA Department, University of Pitesti, Pitesti 110040, Romania*

Correspondence should be addressed to Muhammad Imran; imran.hons@pu.edu.pk and Liviu Mitu; ktm7ro@yahoo.com

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There is an increased trend of drug delivery via skin due to its convenience and affordability. To accomplish this task in a better way and more successfully, nanotechnology has opened the door to transport drugs for the treatment of acute diseases in unique ways. For partially solvable drugs especially, designing new drug transportation systems is always challenging. However, it has been fixed by utilizing nanomaterials as effective carriers for drugs. These carriers allow the controlled and continuous drug release at the specific spotted site and have been successfully manipulated for the creation of innovative drug-delivery systems. These innovative systems are applied to overcome the challenge of reduced water solubility that may improve the drug accessibility, sustained release, and high metabolic stability. The prime emphasis of this review is particularly on the universal routes of drug administration through the skin, limitations of conventional drug delivery systems (DDS), and types and properties of nanomaterials (NMs) used. Recent advancements in NMs such as carbon-based NMs, inorganic-/metal-based NMs, polymeric NMs, and hybrid NMs for drug delivery and their mode of action have been summarized. This review further discusses existing constraints and difficulties that impede the integration of nanomaterials from research to practice, as well as recommendations for more efficient use of nanomaterials in a number of diseases.

1. Introduction

Skin is regarded as the principal organ that enables the human body to be defensive against external stimuli such as ultraviolet radiations, infectious pathogens, and mechano-chemical stress [1]. Over the past few decades, human health has been severely affected due to rapid urbanization, increased pollution, and climatic changes. The prevailing environmental deteriorating conditions have caused several infectious diseases and skin cancer [2]. It is reported that in the United States, skin cancer affects approximately 3 million individuals each year. That is why, skin cancer (melanoma) is 5th most commonly affecting type of cancer in the United States of America (USA). Certain skin treatment protocols cause harm to the unaffected cells. Therefore, some efficient therapeutic methods with fewer side effects are high in demand [3]. Skin typically includes 200–250 sweat ducts cm^{-2} and 10–70 hair follicles that allows for medication distribution through the skin [4]. But at the same time, the excellent insulating feature of the skin is a fundamental impediment to successful medication delivery via this channel. The outer covering of the skin (stratum corneum) is mechanical, anatomical, and chemical in nature and causes resistance due to tightness in this regard [5]. Therefore, innovation is highly needed in drug delivery systems through the skin.

Nanotechnology has opened new horizons due to the unique properties of nanoscale materials. An appropriate

drug delivery system is necessary for attaining the benefits of pharmaceutically active compounds at targeted sites with reduced side effects. There are several problems such as poor solubility, less absorption of the drug by intestinal mechanism, and inefficient delivery of drug at the diseased site, which has been associated with conventional drug delivery systems. These problems have been overcome by nanotechnology-based drug delivery systems [6]. Generally, a drug delivery system consists of a drug, its carrier, targeting agents to target cells [7]. Materials whose diameter is in the range of 1–100 nm are nanomaterials [8] and are being used in promoting fitness and illness prevention. These nanomaterials have been well recognized as having the capability to be used in the treatment of long-term disorders such as cancer and cardiovascular diseases (CVDs) [9]. The pharmacokinetics of medication administration through nanomaterials offers the transportation of drugs with fewer side effects due to controlled release at specific sites only [10]. Moreover, it also increases the bioavailability of the drug and protects it from degradation before reaching the site of action [11]. Pharmaceutical drug can be delivered to any part of the body by dissolving, entrapping, encapsulating, or absorbing it with nanomaterials [12]. It is established in literature that nanomaterials have been successfully used to deliver various drugs (hydrophobic/hydrophilic), biopolymers, and even vaccines [13].

Nanomaterials are defined as materials that possess one or more external dimensions or internal structures at the nanoscale. Materials with nanoscale structures often have distinct optical, thermal conductivity, mechanical, or electronic properties compared to their bulk counterparts [14]. Nanomaterials have distinctive properties, for example, a great number of surface atoms that confer outstanding surface chemistry, permitting numerous biomolecules/drug inhibitor molecules to be involved, while demonstrating quantum-size effects and distinctive electronic structures [15]. Nanomaterials (NMs) have enticed extreme research benefits due to their application potential in several fields of science and technology for instance health care, food, textile, and electronics [16].

Herein, in this article, we discuss the routes of drug delivery through the skin along with drawbacks associated with the conventional DDS. The principal importance of this review is based on various types of updated nanomaterials employed for drug delivery and their mode of action to treat various skin diseases. Furthermore, challenges related to their practical applications are mentioned and future recommendations are also given for further research.

2. General Routes of Drug Delivery through Skin

From a biopharmaceutical point of view, the skin is reported to be an interesting route for drug delivery. Nanoparticles being smaller in size have been employed to improve the penetration of drug through the skin and to broaden the variety of compounds available for therapeutic use [17]. Some of the generally used drug delivery routes are as follows.

2.1. Topical Drug Delivery. Topical administration of drugs is a strategy of localized drug delivery that utilizes ophthalmic, rectal, vaginal, and cutaneous channels as topical routes. Topically applied antiseptic, antifungal, anti-inflammatory, and skin emollients provide protective properties [18]. The pilosebaceous unit is the site of unique biochemical, metabolical, and immunological events and is comprised of hair follicles, hair shafts, and sebaceous glands. The drugs applied topically may diffuse through this pilosebaceous unit by permeation [19]. This drug system is advantageous because of greater patient concordance, wider interface area for drug administration, rapid completion of treatment, and avoidance of first-pass metabolism. These remarkable features allure the drug industries to manufacture topical therapeutics for the cure of epidermis disorders [20, 21]. Solid nanomaterials containing lipids such as solid lipid nanomaterials (SLNs) have already been described as a new lipid-based medication procurement route for the topical administration of a variety of medicinal drugs [22]. The fundamental difficulty in constructing a pharmacotherapy method is achieving an optimum concentration of a given medicine at its action site during certain intervals of time [23].

2.2. Dermal Drug Delivery. Dermal drug administration includes delivery of the drug through the dermal skin layer for targeted medication action [24] and is noninvasive [25]. This type of delivery also entails the administration of medicines to diseased spots inside the skin with little systemic absorption [26]. It is reported that dermal drug delivery through nanoemulsions is promising for chronic and autoimmune diseases [27, 28]. With lipid nanoparticles, this delivery of drug is of particular interest in hair follicle diseases due to enhanced bioavailability of active pharmaceutical ingredients (API) at their drug target [29].

2.3. Transdermal Drug Delivery. Transdermal drug distribution methods sometimes referred to as "patches" distribute drugs via the skin in a regulated manner. Transdermal drug delivery system (TDDS) has attained significant attention because of its inherent benefits, such as extended therapeutic efficacy, prevention with the first metabolism, or ease of treatment completion [30]. This administration strategy recently has been investigated extensively over the previous few centuries because of greater patient adherence, the better release of drugs, tissue targeting, and prevention of presystemic breakdown in the liver [31]. This technique releases pharmaceuticals at a predefined and regulated pace, hence, enhancing treatment effectiveness and pharmacovigilance [32, 33]. TDDS has enhanced bioavailability and extended the number of medicines, in which transdermal and topical distribution is employed [34–36].

The transdermal method has several benefits over traditional medication delivery systems, for example, prevention of first-pass consequence, simplicity of implementation, biodistribution, minimally invasive procedures, comfortable drug administration, stable plasma

drug concentration, and convenience of patch replacement if toxicity occurs [4]. Figure 1 illustrates the pathways for the delivery of drug via the transdermal route and dermal route.

The natural function of the skin is to protect the body from unwanted influences from the environment. The main barrier of the skin is located in the outermost layer of the skin, the stratum corneum. Since the lipid regions in the stratum corneum form the only continuous structure, substances applied onto the skin always have to pass these regions [38]. Transdermal drug delivery has many potential advantages, but the skin's poorly permeable stratum corneum blocks the delivery of most drugs at therapeutic levels [39]. Skin is an intact barrier that serves as a primary defense mechanism to preclude any foreign particle's entry into the body. Owing to the unique anatomical framework, *i.e.*, compact packing of stratum corneum with tight junction and fast anti-inflammatory responses, it emerged as a critical physiological barrier for TDDS. Fusion with other novel approaches, such as nanocarriers, specially designed transdermal delivery devices, and permeation enhancers, can overcome the limitations [40].

2.4. Limitations of Conventional Drug Delivery Systems (DDS). Various methodologies, such as salting out (salting-out agent requisite), supercritical liquid technique (capillary injector as well as a supercritical liquid needed), dialysis (capillary impeller or a supercritical liquid demanded), solvent vaporization (surfactant desired), and nanoscale precipitate formation (nonsolvent for the polymer required), have been used in traditional medication techniques. This approach has now been linked to a number of flaws, including decreased patient adherence and reduced medicine half-lives among others [41]. Similarly, getting medicinal compounds to the appropriate spot is a critical issue for the cure of various illnesses. Consequently, traditional medication application results in inappropriate bio-distribution, inadequate efficacy, and insufficient selectivity [42]. Traditional dosage formulations also have numerous limitations, including a smaller half-life of repeated drugs, poorer therapeutic response, a sharp peak, and characteristic maximum plasma concentration-time pattern [43]. Often, this system requires multiple administrations leading to irregular systemic drug distribution [44].

The advancement in medical sciences and the aforementioned limitations of conventional drug delivery systems have attracted the attention of researchers towards nanomedicine [42, 45]. In this context, scientists have created a variety of multipurpose nanocarrier structures that might deliver medications in a directed, regulated, and sustainable manner [46]. The therapeutic efficiencies of these drugs are increased while unfavorable side effects are reduced because of the nanocarriers ability to deliver the active drug component to the target site [47, 48]. Nanotherapeutics is quickly progressing to overcome the limitations of conventional drug delivery systems [49].

3. Types and Properties of Nanomaterials (NMs) Used in DDS

Materials produced having sizes in the range of 1–100 nm in one dimension (1D) are known as nanomaterials (NMs). The physical characteristics of NMs are directly related to their diameters, morphology, and composition. Similar to this, the extraordinary qualities of NMs are because of their larger ratio of surface area to volume. These NMs also have enhanced catalytic efficiency for chemical reactions because of their extremely large surface area [50]. These materials also show unique electronic properties, good mechanical strength, high chemical stability, wide electrochemical window, and excellent support substrate [8, 51]. By virtue of these properties and many other properties, nanomaterials (NMs) have drawn the extreme interest of researchers having versatile applications in various fields such as pharmaceuticals, food and nutrition, fabric, and electronics [16, 52]. The usage of nanomaterials in both pharmaceutical fields especially in drug delivery systems (DDS) receives enormous attention nowadays and are being utilized extensively in biomedical applications such as antibiotic efficacy, cancer diagnostics, bio-imaging, target-specific, drug administration, diagnostic devices (sensors), tissue regeneration, oral treatment, and skin treatments [6, 53]. Some notable examples of nanocarriers for drug delivery through skin as depicted in Figure 2 are solid lipid nanoparticles (SLNs) [55], which are at the forefront of the rapidly developing field of nanotechnology with several potential applications in drug delivery, in clinical medicine and research, and in other varied sciences. Due to their unique size-dependent properties, lipid nanoparticles offer the possibility to develop new therapeutics. The ability to incorporate drugs into nanocarriers offers a new prototype in drug delivery that could be used for secondary and tertiary levels of drug targeting. Hence, solid lipid nanoparticles hold great promise for reaching the goal of controlled and site-specific drug delivery and hence have attracted wide attention from researchers [56]. Nanostructured lipid carriers (NLCs) [57], consisting of solid lipid and liquid lipid, are a new type of colloidal drug delivery system, which offer the advantage of improved drug loading capacity and release properties [58], such as nanospheres [59], nanocapsules [60], micelles [61], dendrimers [62], microemulsion [63], ethosomes [64], nanoemulsion [65], and liposomes [66, 67]. These nanoparticles show numerous capabilities in treatment and diagnosis of stubborn diseases such as cancer and neurodegenerative diseases, emerging as novel drug carriers or therapeutic agents in future [68].

4. Recent Advancements in Nanomaterials for the Drug Delivery

For simplification and demonstration of their role in drug delivery, NMs are classified and discussed as follows:

(i) Carbon-based nanomaterials
(ii) Inorganic-/metal-based nanomaterials
(iii) Polymeric nanomaterials
(iv) Hybrid nanomaterials

Recently, it has been reported that transdermal drug delivery systems (TDDS) through these nanomaterials as narrated above exhibit high drug discharge and deeper medicine diffusion. In addition, unlike nanocarriers, these

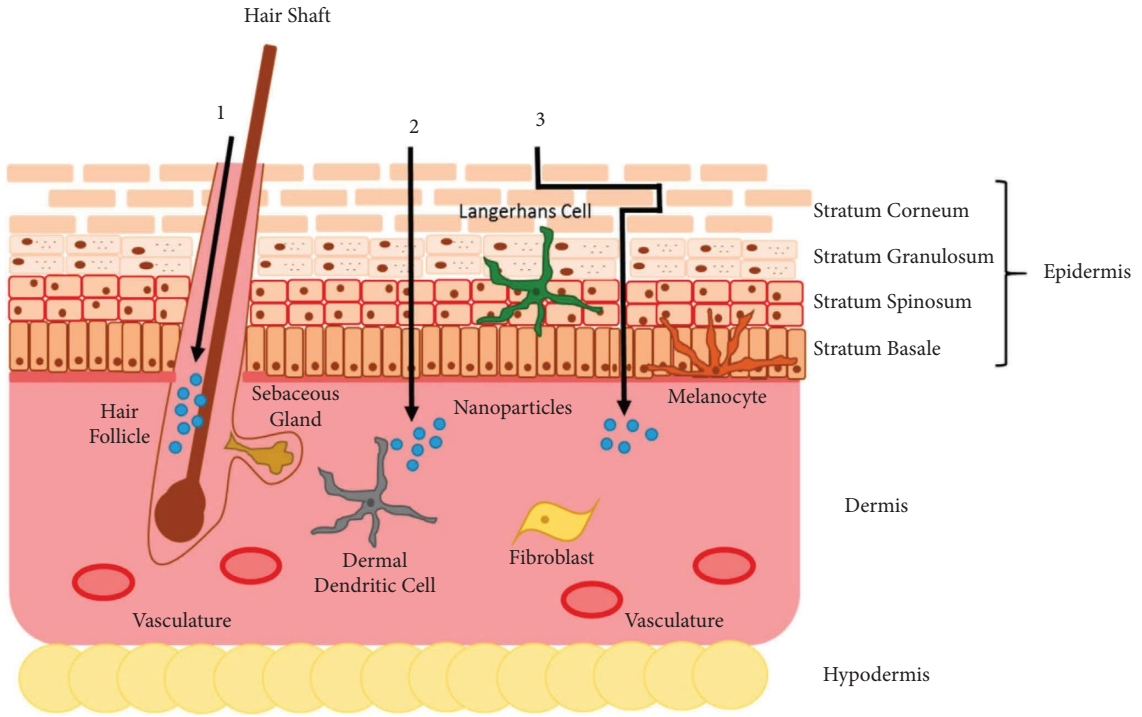

Figure 1: Schematic illustration differentiating the dermal drug delivery system (DDDS) and transdermal drug delivery system (TDDS), reproduced from [37]; this article is an open access article distributed under the terms and conditions of the creative commons attribution (CC-BY) license (https://creativecommons.org/licenses/by/4.0/).

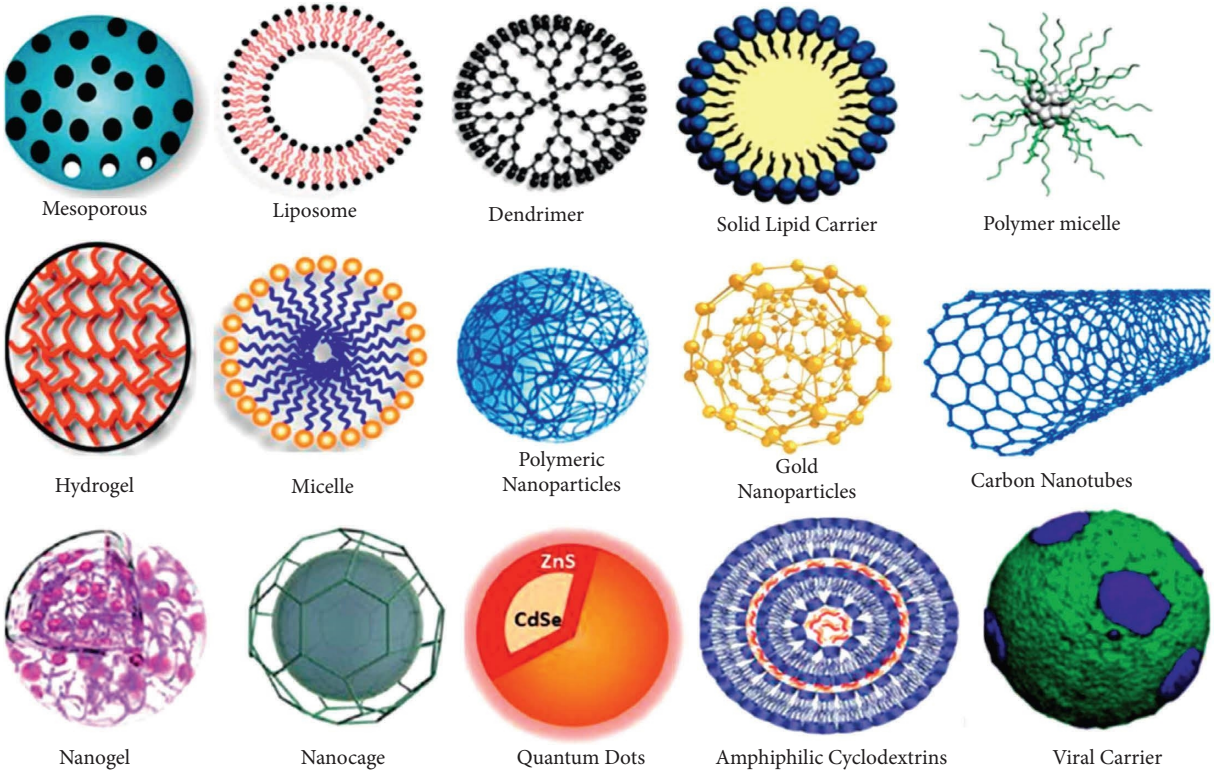

Figure 2: Different types of nanocarriers (nanoparticle) for drug delivery via skin, reproduced from [54]; this is an open access article under the creative commons attribution license (CC-BY-4.0), https://creativecommons.org/licenses/by/4.0/.

materials encapsulate hydrophobic as well as hydrophilic parts of medicinal moieties [31]. In order to target deadly malignancies, nanotechnology is a revolutionary drug-delivery technique that holds significant promise for effectiveness and precision. For tailored administration of drugs in this scenario, nanoparticles (NPs) are derivatized with various biological macromolecules, proteins, and antibody ligands, including protein-binding sites [69]. These systems comprise a target-focused biocompatible external membrane, a center hydrophobic base, and a center hydrophilic core [70].

4.1. Carbon-Based NMs. Carbon nanomaterials are quite emerging porous materials with great applications [71] and include zero-dimensional carbonaceous materials fullerenes, one-dimensional carbon nanotubes, two-dimensional nanodiamonds, graphene oxide, and derivatives of graphene [72]. These materials have been recognized for exceptional mechanical, electrochemical, thermodynamic, optical, or chemical capabilities, as well as their distinctive structural dimensions [73]. Low toxicity and anti-inflammatory have been reported when these carbon nanomaterials (CNMs) have been combined with different drugs, proteins, nucleic acids, and bioactive peptides [74]. Novel functionalized CNMs are characterized by biocompatibility, effective drug loading, and the absence of immunogenicity [75]. CNMs carry drugs via π-π (Pi) stacking interaction which does not change the structural/functional characteristics of medicines, a dynamic factor in stacking medications into supply systems [74]. Summarily, because of their physiochemical characteristics and large surface area to be used in biomedical activities such as antibacterial activities, tumor diagnosis, bio-imaging, target-specific, therapeutic agents, biosensing materials, tissue engineering, oral treatment, and skin care products, carbon-based nanostructured materials have drawn research attention from all over the world [53]. For a further and better overview, we have tabulated various carbon-based nanomaterials with comparative parameters for targeted drug delivery as shown in Table 1.

4.1.1. Carbon Nanotubes (CNTs). Carbon nanotubes (CNTs) have gained prominent interest in the biological field during recent decades. For example, site-specific medication administration and targeted are made possible by surface modification of CNTs by covalent and noncovalent adjustments [103]. CNTs have unique physicochemical properties and make it easier for medications to enter the brain through the olfactory pathway, which helps to restore appropriate autophagy and stop the clearance of autophagic substances [104, 105]. The two different kinds of carbon nanotubes (CNTs) include single-walled carbon nanotubes (SWCNT) and multiwalled carbon nanotubes (MWCNT). CNTs are represented as tubular cylinders made of graphene sheets [106]. These CNTs exhibit improved chemical, physical, electrical characteristics, remarkable cell membrane penetration, higher drug loading capability, and pH-dependent medicinal unloading capabilities, thermal characteristics, a wide surface area, and ease of molecular manipulation. The CNTs have now been discovered to offer tremendous potency in a number of biological sectors because of these characteristics, notably in nanodrug administration and therapeutic targeted applications [107]. As an example, to point out the use of CNTs, doxorubicin (DOX)-loaded SWCNTs coupled with folic acid plus polyethylene glycol biofunctionalized was used in a site-specific DDS to specifically destroy breast carcinoma cells. Because of the tumor's acidic pH, it was discovered that doxorubicin (DOX) was discharged at the location in a regulated manner. The combined action of site-specific drug-loaded DOX-FA-PEG-SWCNTs resulted in the rapid death of about 95% of tumor cells [108]. More examples can be evaluated from Table 1.

4.1.2. Graphene and Graphene Oxides. Graphene is based on the sp^2 hybridized layered carbon atoms packed into a planar structure, and it has a long history owing to its unique intrinsic properties [109, 110]. Surface-enhanced Raman scattering (SERS), superior ease of processing, amphiphilicity, and surface functional capacity make graphene oxide a potential product for biomedical application [111, 112]. For example, a unique nanomedicine based on GE11 peptide-functionalized GO (Ori@GE11-GO) was designed for site-specific administration of oridonin for the recognition of cancer cells and enhanced anticancer efficiency [113]. Similarly, dopamine (DA) active receptor-positive in human breast cancer cell line methotrexate (MTX) administration using a dopamine-associated nanographene oxide (DA-nGO) has already been described [114]. For integrated photothermal treatment (PTT) and photodynamic treatment (PDT) of the tumor, one more nanohybrid (rGO-Ru-PEG; where rGO = reduced nanographene oxide sheet and Ru-PEG = a phosphorescent polyethylene glycol-modified Ru (II) complex) is used. It has been demonstrated that exposure to radiations can accelerate the discharge of Ru-PEG out of the surface of rGO, which is pH-dependent [115]. An innovative medication administration method based on arginine-glycine-aspartic acid RGD-conjugated graphene quantum dots (GQDs) has been described to load the anticancer medicine doxorubicin (DOX) for site-specific tumor fluorescence imaging. The fluorescence spectroscopic technique was used to investigate the emission of DOX from GQDs-RGD in buffer solution with different pH values (*i.e.*, 5.0, 6.0, and 7.4) [116]. A nice pictorial representation to demonstrate the role of graphene oxide as a drug carrier is shown in Figure 3. Some more examples illustrating the importance of graphene-based nanomaterials in drug delivery have been added in Table 1.

4.1.3. Nanodiamonds. Nanodiamonds (NDs) were accidentally produced as a result of nuclear blasts utilizing carbon-based activated explosives in 1963 [55]. The dimension, form, and configuration of NDs are dependent upon the nature of production procedures, generally explosion as well as extraordinary high pressure/high temperature (HPHT) method [118]. Nanodiamonds are

Table 1: Various carbon-based nanomaterials for targeted drug delivery.

Carbon-based nanomaterials (NMs)	Material type	NMs composition	Drug loaded	Disease treated	Technique name	Method applied for drug-releasing ability	pH value	Functionalized with	References
Mesoporous carbon	Uniform mesoporous carbon spheres	VER/DOX/HA-UMCS	Doxorubicin (DOX) and verapamil (VER)	Cell apoptosis and cell cytotoxicity, antitumor efficacy	Conjugation	*In Vitro* and *In Vivo*	7.4	Hyaluronic acid	[76]
	Hollow mesoporous carbon nanospheres	HMCNs@D	Doxorubicin	HeLa cancer cell treatment	Amine functionalization	*In vitro*	5 and 7.4	Poly (epichlorohydrin) and calcium chloride	[77]
	Hierarchical porous carbon	HPC–GAL	Galantamine	Human liver hepatocellular carcinoma (HepG2) cells Alzheimer's illness therapy	Adsorption	*In vitro* plus *In vivo*	7.4	Poly (L-lactic acid) and poly (L-coglycolide)	[78]
Carbon nanotubes	SWCNT (single-walled carbon nanotubes)	PTX–SWCNT	Paclitaxel	Inhibit cancer cell growth	Conjugation	Nil		Paclitaxel and SWCNTs	[79]
	SWCNT	SWNT–CR–DOX	Doxorubicin	Effective targeted anticancer drug delivery	Chemical interaction	*In Vitro*	5 and 7.4	Congo red	[80]
	SWCNT	ISN-SWCNT	Isoniazid	More effective drug delivery of isoniazid for tuberculosis treatment	Conjugation	Nil	6	Sulphuric acid and nitric acid	[81]
	MWCNT	PTX-MWCNT	Paclitaxel	Over-expression in colon cancer cells	Catalytic chemical vapor deposition technique	*In vitro*	6.8	Phenylboronic acid and ethylene diamine	[82]
	MWCNT	MWCNTs/DOX/TC	Doxorubicin	Enhanced antitumor efficacy	Conjugation	*In Vitro* and *In Vivo*	5.5 and 7.4	TAT peptide and chitosan	[83]
	MWCNT	GF-CNT, SMZ-CNT	Griseofulvin and sulfamethoxazole	Improve entrapment of hydrophobic interaction	Carboxylation	Nil	5.2	Sulphuric acid and nitric acid	[84]
	MWCNT	PEG-CNT-ABT737	ABT737	Enhanced the mitochondrial targeting against lung carcinoma cells	PEGylation	*In Vitro*	5 and 7.2	PEG amine	[85]
Graphene and graphene oxides	Graphene oxide-ferroferric oxide	GO/Fe_3O_4-TMZ	Temozolomide	Inhibit proliferation of cancer cells	Conjugation	*In Vitro*	5 and 6.8	Folic acid	[86]
	Graphene oxide	TFGP * DOX	Doxorubicin	Treatment of hepatocellular carcinoma	Conjugation	*In Vitro*	5.5 and 7.4	Transferrin and folic acid	[87]
	Planar polymer graphene oxide	TA-PEI-GO-Fu	5-fluorouracil	Improve chemotherapy efficacy	Conjugation	*In Vitro*	5.8 and 7.4	Poly (ethyleneimine) and tannic acid	[88]
	Graphene oxide	RGO-PDA-BSA-DTPA-Mn (II)/MTX	Methotrexate	Higher affinity for 4T1 cells	Immobilization	*In Vitro*	7.4	1-Ethyl-3 (3 dimethylaminopropyl) carbamide and *n*-(hydroxysuccinimide)	[89]
	Graphene oxide	PTX-GO-HSA-PEG-VEGF	Paclitaxel	Specific tumor suppression effects	Coating and conjugation	*In Vitro* and *In Vivo*	6.5 and 7.4	Human serum albumin and monoclonal antibodies	[90]
	Magnetic graphene oxide	MGO-PEG-CET/DOX	Cetuximab and doxorubicin	Effective tumor growth inhibitor	Conjugation	*In Vitro* and *In Vivo*	5.5 and 7.4	Folic acid	[91]
	Graphene oxide	GA-GO@DOX	Doxorubicin	Mitochondria-mediated apoptosis (MMA) for tumor treatment	Conjugation	*In Vitro* and *In Vivo*	7.4 to 5.4	Glycyrrhetinic acid	[92]
	Reduced graphene oxide	DOX-rGO/dopa-MAL-c (RGDfC)	Doxorubicin	Capable of destroying and directing MDA-MB-231 cells	Conjugation	Nil	7.4	Maleimide-containing dopamine	[93]
	Graphene oxide	(CA-GO)	Chlorogenic acid	Efficient against the cervical cancer cells line HeLa, the human lung adenocarcinoma A549, and the human liver hepatocellular carcinoma HepG2	Hummer's method	*In Vitro*	7.4 and 4.8	Chlorogenic acid	[94]

Table 1: Continued.

Carbon-based nanomaterials (NMs)	Material type	NMs composition	Drug loaded	Disease treated	Technique name	Method applied for drug-releasing ability	pH value	Functionalized with	References
Nano diamonds	Nanodiamonds	PEG-ND-SO-NH-DOX (ND-P-D)	Doxorubicin	Potential contenders for tumor therapy or regulated intracellular medicine administration	Conjugation by thiol-ene click reaction	*In Vitro*	5.4 and 7.2	Dicumyl peroxide and methyl 3-mercaptopropionate	[95]
	Nanodiamonds	PTX@050GS–C8–ND–SP and PTX@8Arm–C12–ND–SP	Paclitaxel	Innovative nanomedicine for antitumor treatment and a passive medicine distribution strategy	Detonation and PEG conjugation	Nil	Nil	Sodium octanoate, sodium laurate, and sodium oleate, HNO_3	[96]
	Nanodiamonds	Cetuximab-NDs-cisplatin	Cetuximab and cisplatin	Inhibit growth of human liver hepatocellular carcinoma	Conjugation	*In Vitro*	Nil	N-Hydroxy-succinimide and 1–(3-dimethylamino propyl)-3-ethylcarbodiimide hydrochloride	[97]
Fullerenes	Fullerenes (C_{60}, C_{59})	HU-C_{60}, HU-BC_{59}, and HU-SiC_{59}	Hydroxyurea	BC_{59}, SiC_{59}, and AlC_{59} are potential candidates for HU drug delivery	Conjugation	Nil	Nil	Pristine C_{60} and heterofullerenes	[98]
	Fullerenes C_{55}	Ibp/TMN4C55	Ibuprofen	Promising vehicles for Ibp medication distribution in the field of nanomedicine	Conjugation	Nil	Nil	Transition metal–N4-clusters such as porphyrin	[99]
	Fullerenes C_{60}		Chloroquine	An effective drug in the control of COVID-19 infection	Chemical interaction	Nil	Nil	Pristine fullerene and chloroquine	[100]
	Fullerenes	*C_{60}-Dox*	Doxorubicin	A promising synergetic approach to cancer treatment	Complexation	*In Vitro*	Nil	Toluene	[101]
	Fullerenes	C_{60}-Dox	Doxorubicin	Potential for optimization of doxorubicin efficiency against leukemic cells	Complexation	*In Vitro*	Nil	Toluene	[102]

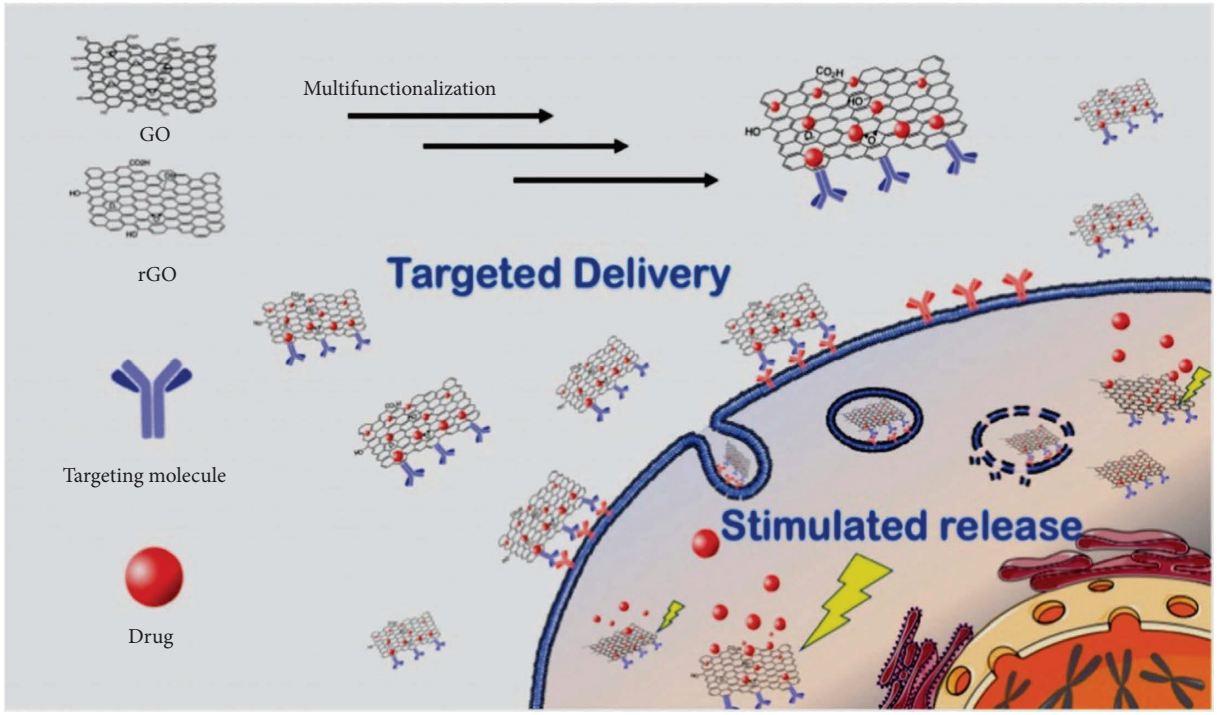

Figure 3: Graphene oxide as a drug carrier to deliver the drug molecule at the targeted site, reproduced from [117]; this is an open access article licensed under the creative commons attribution 3.0 unported license (CC BY 3.0), https://creativecommons.org/licenses/by/3.0/.

considered to be superior to any other nanomaterials in biomedical applications due to the characteristics small size, scalable manufacturing, less side effects, high stability of the diamond interior, and surface chemistry [119]. NDs have also been reported as biocomposites with biopolymers having a lot of usage in the administration of chemotherapy drugs, injury recovery, and bone tissue regeneration [120]. Cetuximab-NDs-cisplatinbio-conjugated material was manufactured which improved the inhibition of human liver hepatocellular carcinoma (HepG2) cells [97]. Another composite, i.e., doxorubicin hydrochloride (DOX)-loaded ND, was produced with the help of a hydrophilic polymer called CHO-PEG and had excellent targeted and sustained release properties for the transport of DOX to HepG2 cells [95]. Some more examples of nanodiamonds used for drug-loading system have been given in Table 1.

4.1.4. Mesoporous Carbon. Various initiatives to investigate composites with mesostructures (2–50 nm) were conducted in 1990s. Mesoporous carbon compounds have been designed to provide innovative materials with exceptional functionality in a diverse range of applications. A class of porous materials having consistent pore channels as well as large surface area is known as ordered mesoporous carbons (OMCs) [121]. Due to the certain physical and chemical properties possessed by mesoporous carbon materials such as exceptional access to binding sites, a very well-arranged porous architecture, outstanding particular surface areas, electrical or chemical conductivity, and improved mass transfer and diffusion make them versatile and eligible for numerous applications. Mesoporous carbon nanocomposites (MCNs) stand out between them because of their lower density, a greater number of pores, and better adsorption potential, giving them a better drug-loading potency that is crucial for chemical therapies that acquire significant dosages to fulfill therapeutic demands [122]. For instance, an inorganic/organic medication administration method centered on regular mesoporous carbon spheres (MCS) was created to enhance its existing good capabilities through the synergistic advantageous interaction of uniform mesoporous carbon spheres (UMCS) and hyaluronic acid (HA). The physiological distribution consistency of UMCS is enhanced by HA, enhancing its suitability for intravascular infusion. Verapamil (VER) and doxorubicin (DOX) were incorporated for co-treatment at high dose concentrations (25% for each medication) in the mesopores core of MCS. To obtain in vivo anticancer activity, human intestinal carcinoma HCT-116 cells were injected into BALB/c nude mice, and these turned out to be successful [76]. A unique mesoporous carbon synthesized hydrothermally was used as a carrier for doxorubicin anticancer drug that released through cleavage of the pH-sensitive coordination bonding. Hence, results showed that nanocarrier is less toxic than doxorubicin molecules and is effective to carry and release DOX and calcium ions in cancer cells [77]. Mesoporous carbons are becoming an increasingly popular multidisciplinary issue in the fields of analytical chemistry, inorganic chemistry, catalysis,

adsorption, membrane science, physical chemistry, and material science [123].

4.1.5. Fullerenes. Fullerenes are segmental structures of porous carbon frameworks with multiple orifices and are synthetic targets of interest [124]. These nanomaterials have remarkable applications that are useful in the realm of bioscience. Fullerene C_{60} is well recognized and promising therapeutic mediator because of its antioxidant, anti-inflammatory, and other characteristics [125]. Some magnetic composites of fullerenes have been reported by attaching iron oxide nanocomposites on the outer layer of fullerene followed by polyethylene glycation resulting C60-IONP-PEG nanocomposite, and the resulting nanocomposites have high photothermal treatment capability and superparamagnetism ability. For instance, a novel photodynamic antitumor medication called hematoporphyrin monomethyl ether (HMME) was coupled to C60-IONP-PEG to create a medicine administration method called C60-IONP-PEG/HMME that showed exceptional magnetic focusing capabilities in the carcinoma treatment [126]. Doxorubicin used in cardiomyopathy has also been conjugated with fullerene. The result showed 100% medicine discharge at pH 5.25, and this conjugation was used to decrease side effects and provide targeted drug delivery. Due to the fact that fullerene proved hydrophobic (water insoluble) but doxorubicin was water soluble, in this situation, ethylene glycol (EG) intermediates were utilized to increase the dissolution rate of this coupling [127]. Hexamethonium was administered as a fullerene complex which blocked the 40 times effects of nicotine upon intraperitoneal administration compared to hexamethonium alone. The hexamethonium alone has partial penetration into the central nervous system thus causing nicotine effect [128]. Some more examples of fullerene used in DDS have been presented in Table 1.

4.2. Inorganic-/Metal-Based NMs. Inorganic nanomaterials when contrasted with organic substances are thought to be harmless and biocompatible [129]. Their increased ability to carry drugs with minimal adverse impacts has been identified for imaging and therapy [130]. Among various inorganic materials, nanoparticles have special features due to their simplicity in manufacturing, intrinsic functionalization, and capacity to carry a variety of biological components, including tiny pharmacological compounds, peptides, proteins, nucleic acids, and nanomaterials [131]. They are versatile representatives for prospective biological uses, notably in the therapy of tumors since their surface area can be altered with various aiming and functional substances. In cutting-edge treatments, bifunctional gold nanomaterials have high biocompatibility and controlled bioavailability tendencies [132, 133]. According to reports, their inherent properties—including electro-optic, physicochemical, and surface plasmon resonance (SPR)—may be changed depending on a material's configuration, magnitude, aspect ratio, or surroundings. These properties can then be used in a variety of biomedical applications, including sensors, site-specific medicine administration, tomography, photodynamic treatment, and phototherapy [134, 135]. Methotrexate is an anticancer drug, whose carboxylic groups can combine to the surface of gold nano-particles (AuNPs) upon overnight incubation. In Lewis lung cancer mice concepts, the conjugated configuration showed 7 times greater destruction of cells more effectively than free methotrexate [136]. Another case involved spherical nanomaterials coupled to many antibacterial drugs, including streptomycin, ampicillin, and kanamycin, which demonstrated better consistency and bacteria growth suppression than the unconjugated versions of the particles [137]. Iron oxide NPs have "superparamagnetic" properties and have been proved in abundant applications. For example, in site-specific medication administration methods, with the use of an externally applied magnetic field, drug-loaded iron oxide NPs can gather in the tumor area where they can be discharged to destroy cancerous cells without affecting normal cells [138]. Due to their extraordinary biological and magnetic characteristics, they might attain significant medicine loading and have targeting qualities [139]. A multifunctional Mn_3O_4@PAA/MTX NPs composite containing manganese oxide (Mn_3O_4) nanoparticles (NPs) in combination with polyacrylic acid (PAA) has been reported for the target drug delivery of methotrexate (MTX). The drug release capacity of the Mn_3O_4@PAA/MTX NPs at specific pH values of 5.4 and 7.4 was studied and exhibited effective controlled release [140]. Many metal oxides, in particular titanium dioxide, are known to be highly biocompatible, at least when photochemical oxidation processes are prevented [141]. Figure 4 indicates the *in vivo* delivery of doxorubicin at the targeted site using magnetic gold nanoparticles. Some more examples of inorganic/metal drug-loaded nanocarriers are given in Table 2 for comparison.

4.3. Polymeric NMs. Polymer nanomaterials have several attractive properties such as the simplicity of administration, the capacity to functionalize and modify the surface using various ligands, biocompatible, and biodegradable and are viable competitors in drug administration system [179]. These nanoparticles play a key role to improve drug bioavailability or specific delivery at the site of action. Polymers are particularly appropriate for satisfying the demands of each unique medication distribution strategy because of their inherent plasticity (Figure 5).

Nanofillers assist polymers and offer improved properties in polymeric nanoparticles, which are made up of both polymers and nanofillers. These polymeric nanoparticles may be divided into two categories based on their nanofillers: CNTs and layered silicates [181]. The distinctive properties of polymeric nanomaterials include their notable consistency in body fluids, easily accessible, and selectively release the encapsulated constituents in response to particular stimuli [182, 183]. The polymeric nanorevolution in the field of medicine is an exciting project which is efficiently replacing the existing difficulties of the therapeutic/diagnostic remedies. Some updated and recent examples of

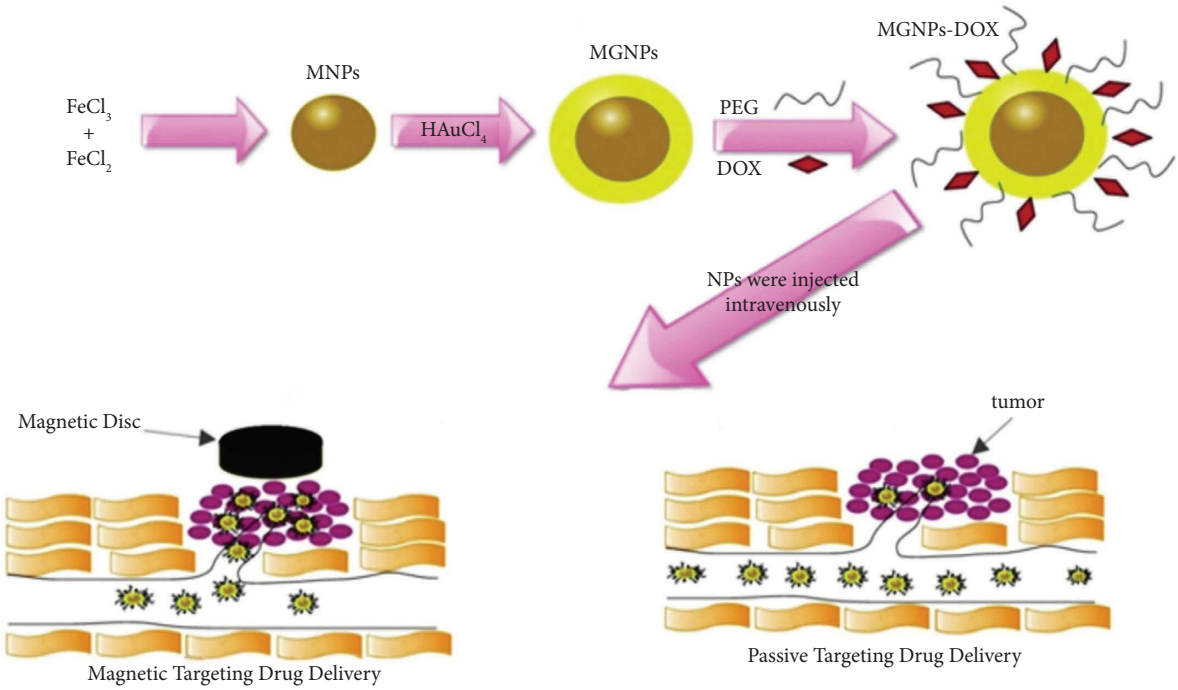

Figure 4: Schematic representation of the targeted drug delivery via magnetic gold nanoparticles loaded with doxorubicin drug, reproduced from [142] with permission from Elsevier, license no. 5398260598801.

polymeric nanomaterials used in DDS have been tabulated in Table 2 to get an idea about polymeric nanorevolution in the field of medicine.

4.4. Hybrid Nanomaterials. The construction of organic-inorganic mixed nanostructures is of tremendous significance in the domain of nanobioengineering. The composites developed from the blending of organic and inorganic components at the molecular or nanoscale stage provide a vast array of adaptability [184]. In order to create supramolecular architects of hybrid inorganic nanomaterials, which are thought of as blazing hybrid nanostructures, macrocyclic organic compounds and the supramolecules are anchored to inorganic nanoscaffolds [185]. Due to the high surface-area-to-volume ratio as well as intricate surface characteristics, the varied alteration of hybrid nanomaterials may be readily accomplished [186]. These hybrid composites can exhibit superior qualities to their respective equivalents, resulting in the contribution of specialized electromagnetic, oxidation-reduction, electrochemical, or chemical capabilities or the creation of approachable and interlinked porosity architecture for catalysts or sensors [187]. These materials due to increased surface area permit more reactions to take place on their interface [188]. Through a simple one-pot technique, Zhou et al. synthesized disulfide-bridged silsesquioxane (SSQ) with an organic-inorganic mixed porous architecture. After polyethylene glycol treatment, the resultant hybrid composites showed increased durability and biocompatibility. These SSQ-based hybrid composites revealed the release of doxorubicin triggered by characteristic pH and glutathione and had a significant potential for the packing of doxorubicin. Hybrid nanostructures with SSQ have been shown to offer an excellent role as nanocarriers for DDS and therapeutic/diagnostic applications [173]. Spherical cellulose nanocrystal-based hybrids grafted with titania nanoparticles were successfully produced for topical drug delivery. Triclosan was selected as a model drug for complexation with titania and further introduction into the nanocellulose-based composite. Thus, the developed hybrid patches are highly promising candidates for potential application as antibacterial agents [174]. New efficient drug delivery systems based on cellulose nanofiber–titania nanocomposites grafted with three different types of model drugs such as diclofenac sodium, penicillamine-D, and phosphomycin were successfully synthesized and displayed distinctly different controlled long-term release profiles. The drug release kinetics was studied *in vitro* for diclofenac sodium and penicillamine-D spectrophotometrically and for phosphomycin using a radio-labeling analysis with ^{33}P-marked ATP as a model phosphate-anchored biomolecule. The obtained nanocomposites could potentially be applied in transdermal drug delivery for anesthetics, analgesics, and antibiotics [175]. Two new nanocomposites of cellulose nanofibers grafted with titania nanoparticles loaded with antibiotic tetracycline (TC) and phosphomycin (Phos) were successfully synthesized which exhibits antimicrobial properties against *Escherichia coli* and *Staphylococcus aureus* [176, 189].

5. Mode of Action of NMs for Drug Delivery

The chief purpose of nanomaterials in the medication administration is to assure that the drug has been carried to their specific action sites. Moreover, these materials are used to enhance the pharmacological impact of therapies to cope their side effects which may obstruct the efficiency of drug [190]. Recently, it has been reported that TDD involves the use of nanomaterials (NMs) having a fantastic opportunity

Table 2: Various inorganic/metal-based nanomaterials and polymeric nanomaterials for targeted drug delivery.

Nanomaterials	Material type	NMs composition	Drug loaded	Disease treated	Functionalized with	Method applied for drug-releasing ability	pH value	NMs diameter (nm)	References
Inorganic/metal based nano-materials	Magnetite (Fe_3O_4) nanoparticles	(Fe_3O_4/GO-DOX)	Doxorubicin	Antitumor efficacy	Graphene oxide	Nil	7.4 to 5.4	14	[143]
	Manganese oxide (Mn_3O_4) nanoparticles (NPs)	Mn_3O_4@PAA/MTX	Methotrexate (MTX)	Effective against cancer cells	Polyacrylic acid	*In vitro*	5.4 and 7.4	Nil	[140]
	Gold nanoparticles	MTX–AuNP	Methotrexate (MTX)	Cancer treatment	Gold nanoparticles and methotrexate	*In vitro* and *in vivo*	5.5 and 7.4	13	[144]
	Magnetic gold nanoparticles	MGNPs-DOX	Doxorubicin	Antitumor activity	Thiol-terminated polyethylene glycol	*In vivo*	7.4	22	[142]
	Gold nanoparticles	AuNPs-DOX	Doxorubicin	Cancer treatment	Polyethylene glycol	*In vitro* and *in vivo*	4.6	Nil	[145]
	Gold nanoparticles (AuNPs)	Doxorubicin-oligomer-AuNP, DOA	Doxorubicin	Colorectal cancer therapy	Oligonucleotides (ONTs)	*In vitro* and *in vivo*	Nil	13	[146]
	Gold nanoparticles (AuNPs)	AS1411-g-DOX-g-PEI-g-PEG@ AuNPs	Doxorubicin (DOX)	Proved excellent platform for targeted DDS in tumor treatment	Polyethylenimine and polyethylene glycol	*In vitro*	Nil	39.9	[147]
	Hybrid chitosan silver nanoparticles	Ch-AgNPs-Dox	Doxorubicin (Dox)	Effective against human breast cancer cells and intravenous tumors	Acetic acid and chitosan	*In vitro* and *in vivo*	Nil	48	[148]
	Silver nanoparticles (AgNPs)	DOX-PEG/AgNPs	Doxorubicin (DOX)	Controlled release and efficient carrier for DOX, showed greater synergistic cytotoxicity	Polyethylene glycol	*In vitro* and *in vivo*	5.0 and 7.4	19.1	[149]
	Silver nanoparticles	AgNPs-PVA-Dox AgNPs-PVA-Cur	Doxorubicin and curcumin	Anticancer activity Antibacterial activity	Polyvinyl alcohol (PVA) and sodium borohydride	Nil	7.4	46.7	[150]
	Silver nanoparticles	AgNPs-MTX	Methotrexate (MTX)	Used in chemotherapy against human cancers (lung cancers)	Borohydride and citrate	*In vitro* and *in vivo*	7.4	13	[151]

Table 2: Continued.

Nanomaterials	Material type	NMs composition	Drug loaded	Disease treated	Functionalized with	Method applied for drug-releasing ability	pH value	NMs diameter (nm)	References
		Albuminated-PLGA-NPs containing bevacizumab	Bevacizumab	Choroidal and retinal neovascularization	Poly vinyl alcohol	*In vitro* and *in vivo*	7.4	219	[152]
		PLGA/PVA	Dexamethasone	Ocular inflammation	Alginate, lactic acid, and glycolic acid	*In vitro* and *in vivo*	7.4	341	[153]
		PLGA/PVA	Fenofibrate	Dysfunctions in the retina, leukostasis in the retina, vascular leakage in the retina, overexpression of VEGF, and choroidal neovascularization	Fenofibrate	*In vitro* and *in vivo*	7.2	236	[154]
		PLGA/PVA/PEI	Bevacizumab and dexamethasone	Choroidal neovascularization	Polyethylenimine	*In vitro*	8	200	[155]
		PLGA/Tween 80, poloxamer 188 or Brij®	Brinzolamide	Effective against ophthalmic stress	Potassium dihydrogen phosphate and disodium hydrogen phosphate	*In vitro*	7.4	74.38	[156]
		PLGA/Pluronic F127	Dexamethasone	Immunologic graft rejection	Triethanolamine and tetrahydrofuran	*In vitro*	7.4	200	[157]
		PLGA/PVP	Bevacizumab	Age-related macular degeneration	Poly (ethylene glycol)-b-poly (D,L-lactic acid) and poly (DL-lactide-co-glycolide)	*In vitro* and *in vivo*	7.4	200	[158]
		CH/sodium tripolyphosphate	Levofloxacin	Ocular infections	Acetic acid	*In vitro* and *in vivo*	Nil	311	[159]
		CH/sodium tripolyphosphate/ hyaluronic acid	Ceftazidime	Ocular infections	Sodium tripolyphosphate/hyaluronic acid	*In vitro*	Nil	78.5	[160]
		CH/PVA/sodium deoxycholate	Prednisolone	Ocular inflammation	Sodium deoxycholate	*In vitro*	Nil	350	[161]
Polymric nanomaterials	Polymeric micelles	Valylvaline with stearate functionalized CH	Dexamethasone	VEGF upregulation, conjunctival neovascularization, ocular disorder, retinal leukostasis, retinal vascular spillages, and infection of the eye	Stearic acid and valylvaline	*In vivo*	7.4	480–976	[162]
		Methoxy poly (ethylene glycol)-poly (-caprolactone) bonded cationic CH	Diclofenac	Ophthalmic infection	Hydrogenated castor oil-40/octoxynol-40	*In vitro* and *in vivo*	6.8	37.85	[163]
		Block copolymer of methyl poly (ethylene glycol) and poly (lactide)	Cyclosporin A	Dry eye disease	Sodium chloride	*In vitro*	Nil	105	[164]
		Tween80/polyoxyethylene stearic acid	Everolimus	Corneal neovascularization, immune-mediated rejection, noninfectious uveitis, and autoimmune uveoretinitis	Glucose, sucrose, L-glutamic acid, sorbitol, mannitol, and mPEG2000	*In vitro* and *in vivo*	Nil	50	[165]
		PVA/poloxamer P407/ hydroxypropyl methylcellulose	Everolimus	Corneal neovascularization, immune-mediated rejection, noninfectious uveitis, and autoimmune uveoretinitis	Tween-80 (P80) and polyoxyethylene stearate	*In vitro* and *in vivo*	5.5 to 7.8	156	[166]
		PEG–PCL–PEG	Triamcinolone acetonide	Ocular inflammation	Succinated triamcinolone acetonide (TA-SA)	*In vitro* and *in vivo*	7.4	36	[167]
		NPs made of lecithin encapsulated in poloxamer gels (P188 and P407)	Dexamethasone	Ocular inflammation	Poloxamer gels	*In vitro* and *in vivo*	Nil	274	[168]
		PEG-PLGA-PEG gel with PLGA-PEG NPs embedded	Triamcinolone acetonide	Macular aging and degradation	Polyethylene glycol	*In vitro*	Nil	208	[169]
		PLGA nanoparticles encapsulate bevacizumab-coated PLA nanoparticles	Bevacizumab	Age-related macular degeneration	poly (lactic acid-*co*-glycolate (PLGA)	*In vitro* and *in vivo*	7.4	265	[170]

Table 2: Continued.

Nanomaterials	Material type	NMs composition	Drug loaded	Disease treated	Functionalized with		Method applied for drug-releasing ability	pH value	NMs diameter (nm)	References
Hybrid nano-materials	Nanohybrids of Fe_3O_4 and poly (glycidyl methacrylate) chains with hydrazine		Fe_3O_4@GMA@Hy@DOX	Doxorubicin (DOX)	Effective cytotoxicity against HeLa cells	Epoxy rings and hydrazine molecule	*In vitro*	7.4 and 5.4	147	[171]
	Transition metal dichalcogenides (TMDC) and 5 phosphocholine DOPC/WS_2 hybrid material		WS_2DOX/DOPC	Doxorubicin (DOX)	Effective cytotoxicity against cancer cells	Grapheneoxide	*In vitro*	7.6	200	[172]
	S-nitroso polysilsesquioxane hybrid nanomaterials		SNO-DOX NPs	Doxorubicin (DOX)	Effective in anticancer therapy	Silsesquioxane	*In vitro*	7.4 and 5.7	172	[173]
	Disulfide-bridged silsesquioxane nanoparticles		HSNs-4S-FITC/PEG@DOX	Doxorubicin (DOX)	Nano-carriers for theranostic applications	Polyethylene glycol	*In vitro*	5.0 and 7.4	180	[173]
	Nanocellulose and titania nanocrystals		(CNC-TiO_2-TR)	Triclosan (TR)	Antibacterial activity against *Escherichia coli,* and *Staphylococcus aureus*	Titanium oxide	*In vitro*	5.5	300	[174]
	Cellulose nanofibers titania nanocomposites		CNF-TiO_2_-DS-M, CNF-TiO_2-PCA-D-M, CNF-TiO_2-Phos-M	Diclofenac, pencillamine-D, phosphomycin	Transdermal drug delivery for anesthetics, analgesics and antibiotics	Titania	*In vitro*	Nil	278	[175]
	Cellulose nanofibers titania nanocomposites		CNF-TiO_2-TC -M, CNF-TiO_2-Phos-M	Tetracycline phosphomycin	Antibacterial activity against *Escherichia coli,* and *Staphylococcus aureus*	Titania	*In vitro*	6	375	[176]
	Nanotitania-nanocellulose hybrid materials		CNF_PEG_TiO_2, CNF_PEG_CaptiGel, and CNF_PEG_TiBALDH		Induced activation of the platelets. Beneficial for efficient healing	Polyethylene glycol	*In vitro*	7	Nil	[177]
	Nanoceria–nanocellulose hybrid materials		CNC/PEG/BTCA/CeO_2/ ampicillin, CNC/PEG/BTCA/ CeO_2/triclosan, CNC/PEG/ BTCA/CeO_2/diclofenac	Triclosan and ampicillin and diclofenac	Antibacterial activity against, and potential new materials for controlled drug delivery in wound-dressings	Polyethylene glycol	Nil	—	200	[178]

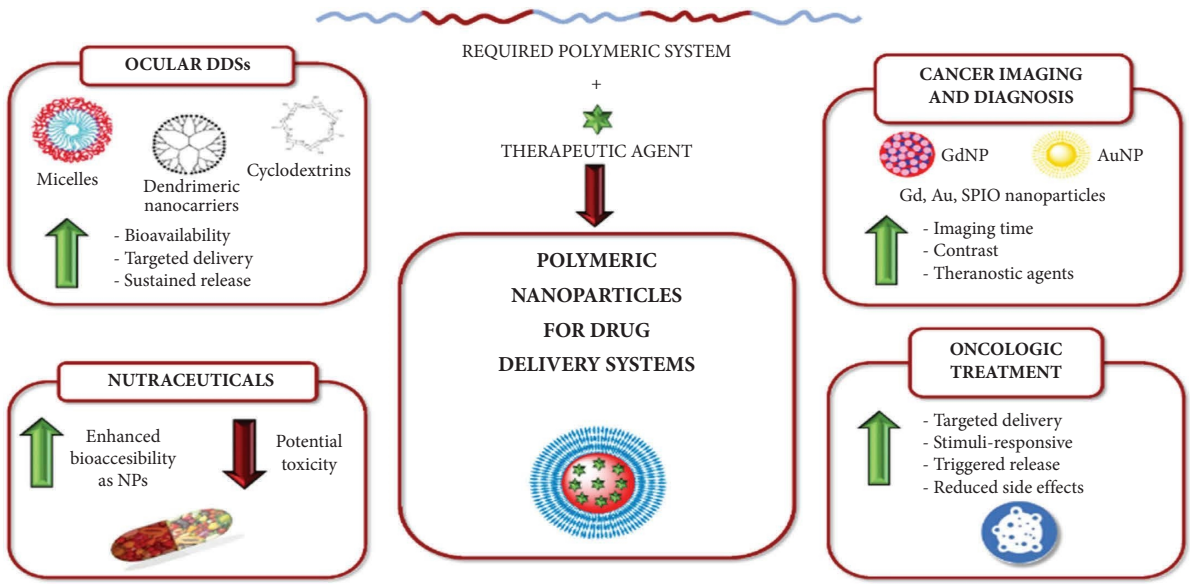

Figure 5: Polymeric nanoparticles for diagnosis and treatment of various diseases, reproduced from [180]; this is an open access article under the creative commons attribution license (CC-BY-4.0), https://creativecommons.org/licenses/by/4.0/.

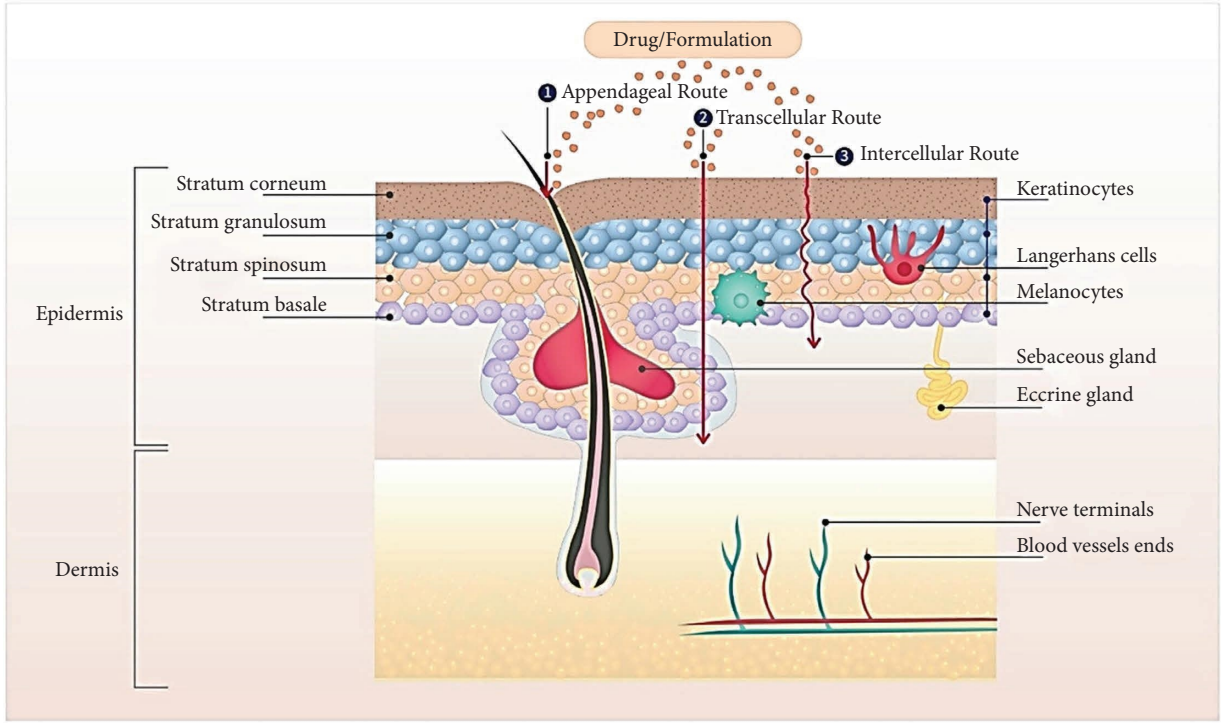

Figure 6: Mechanism of drug delivery through skin penetration, reproduced from [194]; this is an open access article under the creative commons attribution license (CC-BY-4.0), https://creativecommons.org/licenses/by/4.0/.

to improve medication absorption via the skin and also give regulated release [191]. The benefit of avoiding medication first-pass degradation is the delivery of drugs through the skin via the *stratum corneum* (SC). The medicine passes through the layers of the skin before entering systemic blood flow and finally arriving at the specific organ. Among the several techniques used to deliver drugs via the skin, nanoscale systems have drawn interest as pharmacological carriers for transdermal medication administration [192].

The skin is the body's biggest organ and can serve as a painless and accommodating medication administration interface [193]. The action of drug administration mechanism utilized by these systems has different steps such as disturbing the *Stratum Corneum*, rupture the tight

connections, disturbing the cell membrane assembly, and thus assisting drug penetration (Figure 6).

6. Future Challenges and Recommendations

Apparently, the innovative collection of biocompatible and biodegradable nanomaterials appears as promising candidates for the drug delivery applications. Keeping in view the advancement in nano-based drug delivery till now and their shortcomings opens the new perspectives for future research. Because of the covalent bonding, the drug-loaded CNT is persistent, and the cellular atmosphere does not support persistent drug release in cancerous cells. Contrarily, noncovalent association lacks stability at ambient pH levels while facilitating the medication's sustained release in the acidic environment of tumor sites. The prime challenges in the field of nanodiamonds are associated with their commercial-scale applications. Generally, nanomaterial-based targeted drug delivery systems offer good avenues to develop diagnostic and personalized administration methods with promising roles in the future. Nanomaterials are at the forefront of the rapidly developing field of nanotechnology with several potential applications in drug delivery, in clinical medicine and research, and in other varied sciences. Although huge amount of efforts and resources have been utilized in research and development of drug delivery nanoparticles, there is still a long way to the clinical use of these novel-designed nanoparticles, with many impedances in the way. For instance, multiple kinds of nanomaterials used in the administration of diseases and various biological disorders are rather constrained due to concerns of the hazardous residues of solvents as well as legal concerns about its cellular distribution and biodegradability. Therefore, future studies should focus on the materials having more uniform consistency, drug loading, or targeted/controlled drug release capability.

7. Conclusions

Nanomaterial-mediated drug delivery is a great innovation in the field of science, particularly to cope with the challenges of conventional drug delivery. The nanocomposites and nanoarchitectures are fabricated in such a way that the response and interaction with the targeted cells or tissues take place under controlled conditions. It is concluded that the promising biological efficacy can be achieved by nanodrug delivery with a number of novel approaches. The targeted medication is incorporated into the nanocomposite matrices by dissolving, encasing, adsorbing, attaching, or encapsulating it. Due to their tiny size, nanomaterials can efficiently accumulate drugs at the target areas by being absorbed by cells and passing via smaller capillaries. The utilization of biodegradable composites for the synthesis of nanomaterials allows controlled drug discharge within specific sites over a specified time period. In the future, nanotechnology is expected to grow at a much faster pace with promising and fruitful outcomes. The continuous technological developments in the nano-based drug delivery system can be beneficial to treat lethal diseases whose treatments are difficult.

Data Availability

All related data are mentioned in the manuscript with references.

Conflicts of Interest

The authors declare that they have no conflicts of interest regarding the publications of this paper.

Authors' Contributions

All listed authors have made a significant scientific contribution to the manuscript.

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