CHAPTER

1

Bioactive hybrid nanowires: a new in trend for site-specific drug delivery and targeting

A.R. Fernandes[1], *J. Dias-Ferreira*[1], *M.C. Teixeira*[1], *A.A.M. Shimojo*[2], *Patrícia Severino*[3,4], *A.M. Silva*[5,6], *Ranjita Shegokar*[7], *Eliana B. Souto*[1,8]

[1]Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra (FFUC), Pólo das Ciências da Saúde, Azinhaga de Santa Comba, Coimbra, Portugal; [2]Department of Materials Engineering and Bioprocesses, School of Chemical Engineering, State University of Campinas (UNICAMP), Cidade Universitária Zeferino Vaz – Barão Geraldo, Campinas, São Paulo, Brazil; [3]Universidade Tiradentes (UNIT), Aracaju, Sergipe, Brazil; [4]Instituto de Tecnologia e Pesquisa (ITP), Aracaju, Sergipe, Brazil; [5]Department of Biology and Environment, School of Life and Environmental Sciences, University of Trás-os-Montes and Alto Douro, Vila Real, Portugal; [6]Centre for the Research and Technology of Agro-Environmental and Biological Sciences, University of Trás-os-Montes and Alto Douro, Vila Real, Portugal; [7]Capnomed GmbH, Zimmern, Germany; [8]CEB – Centre of Biological Engineering, University of Minho, Campus de Gualtar, Braga, Portugal

1. Introduction

Hyperthermia ("hyper" and "therme", meaning "rise" and "heat") is a therapeutic approach to cancer treatment. Some researchers have related that a sarcoma disappeared after a very high fever. This finding is due to the reaction of immune systems with bacterial infection [1]. Cancer cells are recognized as being vulnerable to high temperatures. The growth of these cells can be terminated at temperatures ranging from 41 to 46°C or below 47°C for at least 20–60 min [2,3]. Hyperthermia is therefore used locally to prevent disease by exposing the whole body to high temperatures to overcome adverse side effects and to increase treatment efficiency [4].

The introduction of magnetic nanoparticles in cancer hyperthermia has been developed and grown significantly during the last decade.

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The special features of these particles are related to their capacity to efficiently accumulate at the tumor cells through the increased permeability of the tumor vessels and by cancer-specific binding agents, making the treatment more selective and effective [5]. The application of an alternating magnetic field (AMF) with the introduction of magnetic nanoparticles generates local heat in the tissues that contain these nanoparticles due to magnetic relaxation and hysteresis loss [6]. Particle characteristics such as size distribution, shape, crystal structure, particle magnetic anisotropy and its temperature dependence on magnetization, fluid viscosity, amplitude and frequency of the AMF directly affect the generation of heat, which in turn depends on the absorption efficiency of the magnetic particles [1,7].

A significant number of magnetic nanoparticles have been studied over the last few decades. Examples of well-known hyperthermic agents include iron oxide-based nanomaterials such as magnetite (Fe_3O_4) and maghemite (γ-Fe_2O), which continue attracting attention due to their lack of toxicity and excellent biocompatibility [8]. Ferrite nanoparticles (XFe_2O_4, where X can be Co, Mn, Ni, Li, or mixes of these metals), metallic nanoparticles, such as Mn, Co, Ni, Zn, Gd, Mg, and their oxides, or metal alloys (FeCo, CoPd, FePt, NiPd, NiPt, NiCu) have also been studied as possible candidates for hyperthermia treatments [9–11].

There are new designs of magnetic nanomaterials based on a core/shell approach that have started to gain prominence due to their versatility to tailor properties of both core and shell and to offer multifunctionality, such as core protection, biofunctionalization platform, toxicity reduction, and increase in biocompatibility. Examples of these particles are gold- or silica-coated ferromagnetic particles [12]. Magnetic nanoparticles also hold great promise for drug delivery by heating the tissues. The drug can be released using two strategies. In the first approach, the drug molecules are attached to the particles through a linker, which breaks with the heat generated by the presence of AMF, with the consequent release of the drug. In the second approach, the release of drugs takes place from a polymeric matrix with magnetic material [5,13]. The heat created by the magnetic field produces crevices or cracks inside the polymeric matrix, which releases the encapsulated drugs [5].

Nanowires, nanowhiskers, nanofibers, nanotubes, and other one-dimensional nanostructures have demonstrated huge abilities for improving the electrical, optical, thermal, and mechanical properties of a broad range of functional materials and composites [14]. These enhancements substantially exceed those offered by micro- or nanosized particles. Most of the methods used for their synthesis are relatively expensive and difficult to scale up [15]. The underlying principles for the synthesis of one-dimensional materials offer significant challenges in the control of diameter, structure, and composition in the axial and radial coordinates, which are essential for the synthesis of materials with designed and tunable functionality [16].

Nanowires, besides their magnetic performance, also have aso an interest in developing intrinsic mobility triggered by a photochemical reaction. Examples of applications of magnetic segmented nanowires are:

1. Magnetic alignment and wireless manipulation (Au/polypyrrole/Ni) [17]
2. Magnetic field sensors and spintronic nanodevices (Co/Cu and FeCoNi/Cu) [18]
3. Photochemical conversion and hydrogen generation (Ag/ZnO) [19]
4. Detection of DNA molecules (CdTe/Au/CdTe) [20]
5. Magnetic control of biomolecule desorption (FeCo/Cu) [21]
6. Exchange-coupled patterned media (Ni/CoPt) [22]
7. Nanosensors (Au/Co) [23]
8. Catalytic activities (Pt/Ni) [24]
9. Higher oxygen reduction reaction activity (Co/Pt) [25,26]
10. Drug delivery

Magnetic nanoparticles (including nanowires) are recognized as nanoparticles with unique physicochemical properties and are mostly different from those of conventional materials, specifically the electromagnetic properties. Magnetic nanoparticles show good magnetic orientation, small size, biodegradability, and reactive functional groups [27]. The biocompatibility of magnetic nanoparticles can be improved by combining them with a variety of functional molecules such as enzymes, antibodies, cells, DNA, or RNA. The coating of other materials such as polyethylene glycol (PEG), chitosan, lipids, and proteins with good biocompatibility can stabilize magnetic nanoparticles in physiological fluids and provide chemical functionality for additional modifications [28].

2. Types of nanowires

In the last few years, magnetic hybrid nanowires have been intensively studied for many applications, such as optics and medicine. There are two types of morphologies in hybrid nanowires:

1. Radial structures (core/shell type); and
2. Axial structures (segmented or layered type).

The nanowires that present a core/shell structure explain many physical characteristics in the magnetism of the nanoparticles. The hard/soft core/shell nanoparticles have been studied and reveal interesting magnetic properties, i.e., reversible tuning of the blocking temperature [29], improved microwave absorption [30], optimized hyperthermia [31], and enhanced coercivity [32]. The magnetic segmented nanowires have multifunctional and structural advantages compared to their counterparts, single-component nanowires. The literature reports that magnetic segmented nanowires are composed of alternating structures of ferromagnetic/ferromagnetic or ferromagnetic/nonmagnetic materials, such as Ni/Cu [33], Ni/Au [34], Co/Cu [35], NiFe/Cu [36], CoNi/Cu [37], FeCoNi/Cu [38], FeGa/Cu [39], Co/Pt [40], NiFe/Pt [41], and NiCoCu/Cu [42], among others.

3. Production methods

The properties of many systems are basically dependent of the material type used in production; however, in the case of nanowires the material geometry is also important. Thus to produce and maximize all the properties of nanowires requires reliable and controlled syntheses. The synthesis methods can be grouped into two categories: (1) top-down and (2) bottom-up synthesis.

3.1 Top-down method

The most conventional top-down method in the fabrication of nanowires is lithography. Lithography is based on the deposition of a resistant material, for example, poly(methylmethacrylate), that has the function to act as a photographic film for the production of a pattern after exposure and development using a patterned mask. The resolution of this technique is dependent on the wavelength of light used in photolithography and sometimes is not suitable for small nanowires [43]. To obtain patterns with a higher resolution, normally electron-beam lithography is the method used, which does not use a mask and has direct-write exposure [44]. Thus nanowires can be obtained by etching the extraneous material from the wafer. Resistance can be applied directly because the etch mask can serve as the template for the deposition of a much more stable mask material, for example, gold. Material that can be used to

etch a pattern is, for example, potassium hydroxide (a wet chemical etchant) or another electrochemical etchant. With these materials it is possible to produce tapered cylindrical wires once the etching is underneath the mask [45]. One way to obtain cylindrical vertical wires is to change the wet chemical etch with a highly anisotropic deep reactive ion etch [46]. Nanosphere lithography is another approach that promises higher resolution by combining the self-assembly of a monolayer of nanospheres of polystyrene, for example, onto a substrate in a close-packed lattice [47]. The nanospheres serve as a model for the deposition of a metal or another material and are removed after deposition. Nanoscale patterns can be produced by mechanical transfer using nanoimprint lithography [48,49].

3.2 Bottom-up method

In contrast to top-down techniques, bottom-up synthesis offers the opportunity to control nanowire composition during growth.

In this technique of the production of nanowires, the anisotropic growth of nanowires is normally done using nanoparticle catalysts and gas-phase precursors. The most used method of production is vapor/liquid/solid growth. In this method, gaseous precursors are used to obtain the desired nanowires and these precursors are dissolved into a liquid-metal catalyst, for example, in the case of silicon nanowires the precursor used is $SiCl_4$. After the catalyst is supersaturated, solid nanowire crystallization from the liquid catalyst begins [50,51]. In this process, the metal should form a droplet in the liquid state that will serve as the catalyst. This droplet, in some cases, will melt at a lower temperature when compared to pure metal, due to its eutectic composition. In the case of the synthesis of binary or ternary compounds, which are metals with low melting points, the vapor/liquid/solid system can be self-catalyzed [52]. The solution/liquid/solid method is another technique of nanowire production similar to the vapor/liquid/solid method; however, in this case nanowire precursors are dissolved in a high-boiling liquid and the catalysts are suspended in this liquid [53]. Substrates, such as anodic aluminum oxide, can be used as template solution for nanowire growth, using electrochemical deposition and after filling the channels in the template [54]. Control of growth along the axes of nanowires is necessary for the introduction of surfactants capable of changing the surface energy of crystal facets, for example, hexadecyltrimethylammonium bromide. Anisotropy of nanowires is easy to achieve by the control of surface chemistry [55] (Tables 1.1 and 1.2 and Fig. 1.1).

4. Applications of nanowires

Nanowire biosensors consist of typical field-effect transistor-based devices, made up of three electrodes that are very sensitive to the variation in the charge density that promotes changes in the electric field at the external surface of the nanowires [64].

Nanowires have a high surface-to-volume ratio and well-defined geometry; they have high sensitivity and short response time. These characteristics offer applications in biology and chemistry. Applications of nanowires can be categorized into two methodologies: electrical detection and optical detection [49].

4.1 Nanowires in bioanalytical chemistry

One of the bioapplications of nanowires is biomolecule analysis. This application includes the study of mechanical cell lysis. Cellular lysis is a fundamental process in the study of intracellular components. There are a number of well-established methods that can analyze the cell components, such as chemical, electrical, and mechanical methods. In the case of chemical cell lysis many steps are necessary and it is an expensive process, consuming many reagents aimed at the purification of biomolecule samples. Another disadvantage is the high probability of the occurrence of harmful effects on

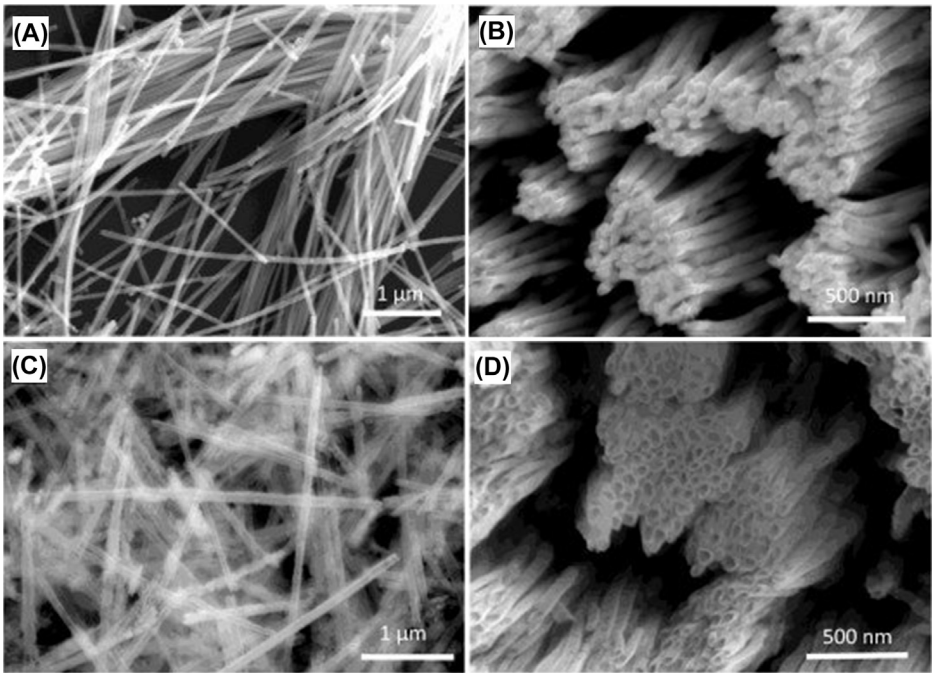

FIGURE 1.1 Scanning electron microscopy images of CuS nanowires: (A) array; (B) copper oxide (CuO) nanotubes; (C) array; (D) fabrication using anodic aluminum oxide template. *Image copied from Mu C, He J, Confined conversion of CuS nanowires to CuO nanotubes by annealing-induced diffusion in nanochannels. vol. 6. 2011. p. 150. Available via license: CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/).*

TABLE 1.1 Advantages and disadvantages of top-down and bottom-up methods [56–58].

Methods	Advantages	Disadvantages
Top-down	Easy to construct order arrays of nanowires. This order facilitates electrical contact with the nanowires and their integration into large-scale devices	The applicability of the photolithography method decreases as the desired length scale diminishes, which requires the use of more advanced methods, for example, extreme ultraviolet lithography, electron-beam and scanning probe lithographies
	Compatibility of production methods with standard microelectronics industry processes. Easy scale-up	Nanowires formed by top-down methods frequently lack complex electronic characteristics. All the codifications after growth greatly increase the material cost of nanowire
Bottom-up	Provides the opportunity for the control of the composition of nanowires during growth, which permits the production of complex superlattice structures	The major challenge of these methods is their integration into large-scale devices

microorganisms [65,66]. The solution to this problems is the use of electrical cell lysis, which is less harmful than the aforementioned method; however, it still an expensive method and has a low throughput [67]. The ultimate discovery was the use of nanowires because of their small size (smaller than the cells) and the critical advantage is that the nanowire tip can penetrate and

TABLE 1.2 Drugs incorporated in nanowires.

Active pharmaceutical ingredient (API)	Type of system	Aim	Production methods	References
Paclitaxel	Cu nanowires	To target the spleen	Bottom up	[59]
Dexamethasone	Polypyrrole nanowires	For ulcerations, deep bone injuries, or tumors; avoids the side effects of systemic treatment with steroids or chemotherapy	Bottom up	[60]
Curcumin	Silver nanowires	Cancer treatment	Bottom up	[61]
Doxorubicin	Silver nanowires	Cancer treatment	Bottom up	[62]
Cerebrolysin	Hydrogen titanate nanowires	Reduction of brain edema	Top down	[63]

disrupt the function of cellular membranes [68]. Nanowires eliminate microorganisms in cells much faster than the previously described methods.

In analytical and biological processes, the development of biomolecule separation and analysis is essential. In the separation of long DNA molecules, conventional gel electrophoresis has a disadvantage: it is necessary to analyze biomolecules for several hours. The combination of nanostructures produced by top-down approaches and microfluidic systems is usually proposed to overcome the problem. However, difficulty in their production using an electron-beam lithography process makes it a very expensive and sophisticated system [69,70]. On the other hand, nanostructures produced by bottom-up approaches offer easy fabrication and separation of biomolecules; however, size limitation causes difficulty in their development. To overcome all these problems, self-assembled nanowire structures of metal oxides have been investigated due to their rigidity and the possibility of reusability [49] (Table 1.3).

4.2 Nanowires as biosensors in medical diagnosis

There are many challenges ahead that must be addressed before nanowires can be successfully used for biomedical applications. Major challenges include

1. advanced techniques and easy methods (needed to increase the sensitivity of nanowire-based electrochemical cytosensors in signal amplification),
2. further research into nanowires to promote cell adhesion, sensitivity, and selectivity,
3. more specialized coatings to decrease non-specific bonding,
4. protocols and further experiments to determine the exact nature of the nanotoxicity of nanowires and their constituents,
5. innovative solutions to reduce fabrication and running costs of nanowire-based micro/nanofluidic devices to make them economically viable,
6. with every emerging technology, standards to avoid doubts about the lack of reproducibility, repeatability, and compatibility across platforms and laboratories, and
7. an opportunity for further advances and developments of cytosensing devices based on electrochemical methods [73].

Circulating tumor cells play an essential role in cancer metastasis, and knowledge of their presence in blood samples of cancer patients is needed to understand more about the type of cancer. Hosokawa et al. have shown an array

TABLE 1.3 Nanowires in bioanalytical analyses.

	Nanowire type	Production method	Results	References
Mechanical cell lysis	ZnO nanowires (diameter: 100 nm) on the surface of a pillar array in a microchannel	Method of low-temperature hydrothermal reaction	Higher extraction efficiency for nucleic acids and proteins than using chemical cell lysis methods	[71]
	ZnO nanowires were synthesized on the Si membrane (average pore diameter: 75 nm)	Method of low-temperature hydrothermal reaction	Easy and rapid mechanical cell lysis Higher extraction efficiency for proteins and nucleic acids than that obtained for commercially available kits	[72]
Biomolecule separation and filtration	SnO_2 nanowires produced into fused silica microchannels	Photolithography process and vapor/liquid/solid technique	Nanowire structure controlled the pore size (20−400 nm) by varying the number of nanowire growth times Highly dense nanowires, used as a molecular filter, could provide high-throughput filtration of DNA molecules	[49]

of microcavities to perform size-selective capture of circulating tumor cells [74]. Another study reported that a herringbone chip captured and isolated clusters of circulating tumor cells from the patient's blood, which had a capture efficiency of more than 80% [75]. Tseng et al. developed silicon nanowires, which they called a NanoVelcro chip, to capture and release circulating tumor cells from blood samples with high selectivity [76,77]. Si nanowires were produced based on substrates by a standard photolithography and chemical wet etching process, and they were then bonded to a chaotic mixture of microfluidic channels to fabricate the NanoVelcro chip. This procedure of surface modification with cell surface markers of anti-EpCAM increased the capturing efficiency of circulating tumor cells or of anti-CD45-depleted white blood cells on the nanowires [78,79]. The NanoVelcro chip with nanowires has been developed for single-circulating tumor cell isolation by depositing thermoresponsive polymer brushes, poly(*N*-isopropylacrylamide), on silicon nanowires [78]. NanoVelcro chips are promising tools in diagnosis, because they capture and purify circulating tumor cells rapidly prior to circulating tumor cell molecular analysis [49,76].

A silicon nanowire-based electrical cell impedance sensor has been developed for the detection of cancerous cultured living lung cells by monitoring their spreading state at which the cells stretched and became extended on nanowires [80]. The diagnosis was carried out by penetration into the extended membrane of malignant cells with respect to healthy cells.

Silicon nanowire biosensors have advantages in molecular detection because of their high sensitivity and fast response. A polycrystalline silicon nanowire field-effect transistor device was developed to achieve specific and ultrasensitive detection of microRNAs without labeling and amplification, showing that the diagnostic and prognostic value of microRNAs in a variety of diseases is promising. Thus the polysilicon nanowire biosensor device is promising for microRNA detection [81].

In short, semiconductor nanowires are emerging as promising biosensors enabling

TABLE 1.4 List of biosensors in the literature based on nanowires.

Type of biosensor	Aim	References
Silicon nanowire field-effect transistors	Detection of proteins, DNA sequences, small molecules, cancer biomarkers, and viruses	[83]
NanoVelcro chip with nanowires	Developed for single-circulating tumor cell isolation	[78]
Silicon nanowire-based electrical cell impedance sensor	Detection of cancerous cultured living lung cells	[80]
Nanowire-based field-effect sensor devices (which can be modified with specific surface receptors)	Used as a powerful detection device for a broad range of biological and chemical species in solution	[84]

direct electrical detection of various biomolecules. A comparative analysis of biofunctionalization strategies needs to be discussed to design and develop optimum memristive biosensors to be implemented in label-free sensing applications. The surface of the device is modified with a specific antigen–antibody via: (1) direct adsorption on the device surface, (2) a bioaffinity approach using the appropriate combination, and (3) the optimum memristive biosensor, which is defined via the calibration and comparative study of biosensors' electrical response under controlled environmental conditions, such as humidity and temperature, aiming to maximize the performance of the biosensor. This modified system shows potential for general application in molecular diagnostics, and, in particular, for the early detection of cancer, namely, prostate [82] (Table 1.4).

Some investigators of the University of San Diego have been developing nanowires with the purpose of recording the electrical activity of neurons in fine detail. The ambition of the group is that one day this new nanowire technology could serve as a method to screen drugs used specifically in neurological diseases, which could help researchers to understand the mechanism of how single cells can communicate in complex neuronal networks. The main objective is to allow the scientific community to delve deeper into how the brain works. In the future, the goal of researchers is to implant this new nanowire technology into the brain [85].

4.3 Nanowires for delivery of chemotherapeutics

Sharma et al. developed noncytotoxic, magnetic, Arg-Gly-Asp (RGD)-functionalized nickel nanowires (RGD nanowires) that could trigger specific cellular responses via integrin transmembrane receptors, resulting in the dispersal of nanowires [86]. Their results showed that dispersal of 3 μm long nanowires increased considerably with functionalization by RGD when compared to PEG, through integrin-specific binding, internalization, and proliferation in osteosarcoma cells. Additional results showed that a 35.5% increase in cell density was observed in the presence of RGD nanowires when compared to an increase of only 15.6% with PEG nanowires. These results are very promising to advance applications of magnetic nanoparticles in drug delivery, hyperthermia, and cell separation where uniformity and high efficiency in cell targeting are desirable.

Contreras et al. showed that magnetic nanowires with weak magnetic fields and low frequencies could induce cell death via a mechanism that does not involve heat production [87]. The low-power field exerted a force on the magnetic nanowires, causing a mechanical disturbance to the cells. In their results, cell viability studies showed that the magnetic field and the nanowires had separately decreased deleterious effects on the cells. On the other hand, when combined, the magnetic field and nanowires

caused cell viability values to drop by up to 39%, depending on the strength of the magnetic field and the concentration of the nanowires. Cell membrane leakage experiments showed membrane leakage of 20%, which proved that cell death mechanisms induced by nanowires and magnetic fields involve cell membrane rupture. Thus these results suggested that magnetic nanowires can kill cancer cells. The advantages of this process are the use of simple and low-cost equipment with exposure to only very weak magnetic fields for brief time periods.

Another alternative is ultrasound-powered nanowire motors based on nanoporous gold segments that are developed for increasing drug loading capacity. These nanowire porous motors are characterized by a tunable pore size, high surface area, and high capacity for the drug payload. These highly porous nanomotors are prepared by template membrane deposition of a silver/gold alloy segment followed by dealloying the silver component. The chemotherapeutic drug doxorubicin was loaded within the nanopores via electrostatic interactions with an anionic polymeric coating. The nanoporous gold structure facilitates near-infrared light-controlled release of the drug through photothermal effects, which is a great advantage. Incorporation of the nanoporous gold segment leads to a nearly 20-fold increase in the active surface area compared to common gold nanowire motors [88].

The latter work offers very important information for the treatment of cancer patients at a patient-specific level based on specific drug responses of circulating tumor cells. So, platforms for high capture efficiency of circulating tumor cells are essential for clinical evaluation of patient-specific drug responses of circulating tumor cells. Recently, nanostructure-based platforms have been developed. In the Kim et al. study, the breast carcinoma cell-line with an ultralow abundance range was captured by streptavidin-functionalized silicon nanowire platforms for evaluation of capture efficiency [89]. In this case, a capture efficiency of more than 90% was achieved. Specific drug responses of breast carcinoma cell-line cells captured on these platforms were analyzed using tamoxifen or docetaxel as a function of incubation time and dose. In addition, circulating tumor cells were successfully captured, and this study suggests that this platform is adaptable for clinical use in the evaluation of circulating tumor cells and drug response tests.

Magnetic silica core/shell nanovehicles presenting atherosclerotic plaque-specific peptide-1 as a targeting ligand have been prepared through a double-emulsion method and surface modification with magnetic iron oxide (Fe_3O_4) nanoparticles. The results demonstrated that under a high-frequency magnetic field, magnetic carriers incorporating the anticancer drug doxorubicin collapsed, releasing approximately 80% of the drug payload, due to the heat generated by the rapidly rotating Fe_3O_4 nanoparticles, thereby realizing rapid and accurate controlled drug release. At the same time, the magnetic Fe_3O_4 could also kill the tumor cells through a hyperthermia effect, i.e., inductive heating. The combination of remote control, targeted dosing, drug-loading flexibility, and thermotherapy and chemotherapy suggests that these magnetic nanovehicles have great potential for application in cancer therapy [90].

Another study showed that an electroresponsive drug release system based on polypyrrole nanowires was developed to induce the local delivery of the anticancer drug doxorubicin, according to the applied electric field. These nanowires were initially prepared by electrochemical deposition of a mixture of pyrrole monomers and biotin as dopants in the anodic alumina oxide membrane as a sacrificial template. Additionally, the antitumor efficacy of doxorubicin released from these nanowires in response to the external electric field using two kinds of cancer cell lines, human oral squamous carcinoma cells and human breast cancer cells, was investigated. An advantage of these

particles is the strong photothermal effect as a result of the near-infrared absorbing ability of polypyrrole synergistically that, as a consequence, maximizes chemotherapeutic efficacy, which is very promising for many therapeutic applications, including cancer [91].

To detect specific mRNA sequences, essential in the treatment of cancer, molecular beacons have been widely employed as sensing probes. Kim et al. developed a nanowire-incorporated and pneumatic pressure-driven microdevice for rapid, high-throughput, and direct molecular beacon delivery to human breast cancer MCF-7 cells to monitor survivin mRNA expression [92]. This microdevice is composed of three layers: (1) a pump-associated glass manifold layer, (2) a monolithic polydimethylsiloxane membrane, and (3) a ZnO nanowire-patterned microchannel layer. The molecular beacons are immobilized using the ZnO nanowires by disulfide bonding, and the glass manifold and monolithic polydimethylsiloxane membrane serve as a microvalve. The cellular attachment and detachment on the molecular beacon-coated nanowire array can be easily manipulated. All these procedures enable the transfer of molecular beacons into the cells in a controllable way with high cell viability and are useful to detect survivin mRNA expression quantitatively after docetaxel treatment [92].

Combination therapy is a promising cancer treatment strategy that is usually based on the utilization of complex nanostructures with multiple components. Ultrathin tungsten oxide nanowires ($W_{18}O_{49}$) were synthesized using a solvothermal approach and were examined as a multifunctional theragnostic nanoplatform [93]. In vitro and in vivo analyses demonstrated that these nanowires could induce extensive heat- and singlet oxygen-mediated damage to cancer cells under 980 nm near-infrared laser excitation. The comparison of near infrared-induced photothermal therapy/photodynamic therapy and radiation therapy alone showed that $W_{18}O_{49}$-based synergistic trimodal therapy eradicated xenograft tumors, and no recurrence was observed. In conclusion, these nanowires have shown significant potential for cancer therapy with inherent image guidance and synergistic effects from phototherapy and radiation therapy, which warrants further investigation [94].

5. Conclusions

This chapter summarizes the critical results obtained using nanowire structures as a platform useful in bioanalytical chemistry and medical diagnostics. Nowadays, there are various technical approaches to develop nanowires for bioapplications in molecular to cellular levels. Nanowires have been integrated with microchannels, providing a novel pathway from the macroscale to the nanoscale that will allow researchers to observe and analyze target molecules such as DNA, RNA, proteins, and circulating tumor cells. Another benefit of nanowires is their very small diameter size with high aspect ratio; this can allow researchers to use nanowires as a probe tip to stimulate and record changes in electrical signals in living cells. Nanowires were also used as biological optical sensors. These improvements in nanowire structures will allow the development of new bioanalytical chemistry and medical diagnostics tools that will open a new age of nanotechnology with the widespread use of nanowires for bioapplications.

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