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An Exhaustive Review on Nanowire: An Ascendance of Emerging Nanoconveyor as Theranostic Approach

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Anusha K*, Suganya M, Ramesh Kumar K, Chandru B S, Dhanesh Kumar M R

**Department of pharmaceutics, College of Pharmacy, Madras Medical College, Chennai, Tamil Nadu, India.*

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ABSTRACT

Nanotechnology transformed advancement in the contemporary healthcare industry with Massive Improvement in the Pharmaceutical & Biotechnological Field. In the field of biosensing, nanowires (NWs) provide multiple advantages for the identification of diverse biological compounds linked to illnesses and disorders. With NWs, sensing technologies' adaptability, resilience, and dynamic nature have been increased. It has some advantages over conventional nanoparticles in the pharmaceutical field. The most important of them is its higher surface area, which enables high drug loading capacity and target molecule attachment, making it useful in cancer therapies and diagnosis (Theranostic approach). Greater drug delivery and therapeutic platforms, particularly in the areas of magnetic drug targeting, magnetic hyperthermia, and magnetic actuation used in cancer treatment, are consequently produced by larger net magnetic moment compared to nanoparticles. In addition, drug-loaded nanoparticles coated with NWs exhibit greater bio-adhesion than single nanoparticles. This review focuses on the design consideration, fabrication, and future potential of NWs systems for the diagnosis of various biological compound & with the emphasis on improving patient chemotherapeutic outcomes in cancer treatment.

INTRODUCTION:

Among various nanoparticle and nanocarrier, NWs are unique in nature due to their shape anisotropy & large surface area. NWs are immensely small wires of rod shaped, sometimes as small as 1 nanometer in diameter. NWs, which are solid crystalline fibres & due to their length, it can connect with other macroscopic devices and the outside world .Using a vapour deposition technique, NWs can be "grown" on a range of substrates from a variety of materials. Tiny beads of melted gold or other metals are placed on a surface; the material from the NWs is finally absorbed by the molten gold in vapour and grows as a thin column from the bottom of that bead. The size of can be precisely controlled. The apparatus needed for this kind of vapour deposition is frequently used in the semiconductor sector and is easily adaptable for the creation of NWs. Because of their special qualities and cutting-edge uses, 1D structure NWs have drawn a lot of interest lately. In order to fully understand NWs, scanning electron microscopy, or SEM, has become essential. NWs will exist in crystalline or amorphous forms and will selectively activate mammalian cells via optical and electrical means.

OPTICAL PROPERTIES:

In the medical sector, detecting the symptoms of various diseases such as cancer, stimulating nerves, targeting stem cell growth and so on can be done by NWs. (2)

BIOLOGICAL PROPERTIES:

In reality, the two protein strands that make up an organism's DNA molecule have a diameter of two nanometers. This molecule is used extensively in nanotechnology nowadays and serves as a model for the creation of various nanostructured materials.(2**)**

NANOWIRE IN BIOSENSING: The high surface area-to-volume ratio of the NW boosted sensitivity. Their uses in drug development as well as biomarker, virus, and DNA detection. Neurotransmitters, protease, DNA and RNA, various bacteria and diseases, and chemical substances can all be detected by NWs acting as biosensors. The usage of NWs in biosensors has significantly advanced biosensing technologies. This is the outcome of novel biorecognition components and transducers being used, as well as advancements in the production, engineering, and micron-scale downsizing of nanostructured devices and novel methods for synthesizing NWs. The application of NWs has enhanced the sensing technologies' resilience, dynamic nature, and versatility. (3)

Highly adjustable parameters that can be found in NWs include optical performance, electrical characteristics, chemical composition, and topographies (3). Different surface functionalization on different NWs can be used to achieve a range of biochemical sensing approaches, significantly expanding the applications for chemical and biomolecular (H2O2, nucleic acids, glucose, and proteins) sensing. (3) High-throughput, high-spatiotemporal resolution cell sensing is possible with NWs. Biophysical signals that are extracellular, like contraction force and mechanical transmission of cells, are analyzed by neural workers. Notably, NWs-based sensing platforms have been used to create devices that sense and activate cells. They may present chances for the simultaneous detection of multiple biological materials.(3)

The challenge of finding more intracellular signals as well as the gathering of long-term, high throughput signals may be aided by patterning neural networks. NWs' high specific surface area, which provides a multitude of attaching sites for identifying chemicals, cells, or receptors, is a contributing factor to their exceptional sensitivity [57,58]. However, the 3D sensing matrix also guarantees multichannel bio-signal detection that is reliant on space or is weak [59, 60]. However, the remarkable selectivity of NWs should be partially explained by their precise shape and multi-level structure, which facilitates simple attachment to certain cell structures like tentacles and synapses. A synergistic contribution to the tunable selectivity of NWs is also provided by the adaptable bio-recognition layer. (3)

The identification of biological and chemical species is essential in the fields of healthcare and the life sciences that deal with illness diagnosis, development, and screening of novel therapeutic compounds [25–26]. Thus, the development of novel instruments that provide an expeditious, sensitive, and direct assessment of these species holds significant potential implications for humans [26–28]. In order to directly detect biological and chemical species, NWs-based devices are developing into a powerful and adaptable class of electrical sensors with exceptional sensitivity [62,63,64,]. Biosensors have been essential in the creation of testing kits, vaccines, and antiviral drugs to detect, prevent, and treat disease. Their high sensitivity and poor specificity, rapid and continuous testing, inexpensive reagent requirements, and other advantages have led to their widespread usage as immuno-sensors for the identification of target biomolecules in body fluids [65]. However, the biosensor's detection limit is insufficient for a clinical treatment. The incredibly low likelihood of false-positive results in the low concentration range can have an impact on the sensitivity of

sensors. Therefore, in order to identify clinically meaningful signs, it is imperative to develop a highly sensitive sensor system with a broad dynamic range (3).

NANOWIRE IN CANCER THERAPEUTICS:

Design Consideration: Magnetic nanowire applications need to be customized to target the right microenvironment of the cancer in order to create effective cancer therapy systems. The rationale behind integrating magnetic nanowire technology (NW) into a multifunctional system needs to be supported by the synergistic combination of its promising applications.

The distribution and biological impact of nanosystems are significantly influenced by tumor microenvironments [66]. Fernandez et al. summarize that in order for nanosystems to be effective as cancer therapies, they must achieve a homogenous distribution and overcome the obstacles present in the tumor microenvironment [67]. To be effective, improved permeability and retention effect help nanosystems extravasate intratumorally; nevertheless, they must first overcome high interstitial pressure, aberrant tumour vasculature, and dense stroma. The design of ideal nanosystems must take into account the pathophysiological circumstances of the targeted tumor, including endogenous components of the tumor microenvironment and functional proteins and amino acid levels. Acidosis, hypoxia, hyperthermia, oxidative stress, redox potential, enzyme activity, and high interstitial fluid pressure are some of these variables,That must be utilized in the design of nanosystems for drug delivery.

The acidic environment of tumors, which is different from physiological pH, can be utilized by nanosystems to start medication release. The medicine can be bonded to the nanosystems utilizing covalent bonds that are sensitive to acid hydrolysis in order to do this [68]. The pathophysiological circumstances of the targeted tumor can also be used to accomplish active targeting. Certain antibodies that bind to receptors expressed on the tumor cell are bound. For example, anti-Her2/neu antibody is attached to the nanosystem and binds to Her2/neureceptors on the tumor cell membrane. Wnts inhibitor attachment is a promising potential use of magnetic NWs drug delivery devices. Wnts inhibitors have always been limited by their high toxicity and effective drug delivery methods [69]. These restrictions, however, can be addressed by a targeted and stimuli-release drug delivery system, which is possible thanks to nanotechnology and magnetic nanowires in particular.

The inorganic core of the NW is represented by the surface coatings, which impart a range of biomedical properties. To improve treatment outcomes and lessen side effects associated with therapy, these surface coatings use a variety of stimuli to elicit reactions in a way that enables

the systems to become targeted, selective, and trigger drug release. Because of its special advantages, this combination is useful in the creation of drug delivery systems for the treatment of cancer. By battling various medication resistance in malignancies, it can improve therapeutic results or offer a synergistic combination of therapeutic effects. Additionally, this combination permits medication accumulation at the targeted tumor locations, hence mitigating treatment-related side effects [70–75].

Chemotherapeutic Drug Loading:

Large surface area has a positive influence on the drug loading capacity of nanosystems. Thus, NW morphology has a direct impact on drug loading capacity. Although NWs inherently have large surface areas, their surface area can be increased further by changing their morphology to include rough surfaces [38-39] or by synthesizing porous NWs [40-41]. Guo and co-workers achieved a high drug loading of 2000 mg/g using porous NW while Zhu and co-workers achieved a high drug loading capacity of 992.91 mg/g with their Co NW, which had a rough morphology. The GO in the functionalized Co NW of Zhu and research group provided attachment points for DOX or other therapeutic agents as it is decorated with many functional groups on its surface such as hydroxide radicals. In the case of DOX, it is hypothesized that it is also able to absorb directly onto the GO via-interactions. Their NW system also exhibited a higher drug release profile in acidic environments and after near infrared radiation when compared to the control [42]. The decrease in pH made the DOX more hydrophilic and soluble due to the protonation of the NH2 group on it, thus causing the release from the Co NW-GO. They also proved a direct correlation between drug release and laser power intensity.

TYPES:

1)Superconducting

2) Metallic (Au, Ag, Ni, and Pt) [1–4]

3) Semi conducting

4)Insulating ones (TiO_2, SiO_2).

ADVANTAGE (2)(15)

1) Small size
2) Low weight

3) Low cost for mass production
4) Self-powering(3)
5) High Drug loading capacity
6) Stronger adhersion with biological tissue
7) The ability to increase the permeation of drugs across the epithelial lining of the gut wall
8) Increase half-life
9) Increase solubility of hydrophobic drugs.
10) Selectively release drug at targeted site
11) Reusability
12) Sensitivity in high ionic strength solvents, and long-term stability
13) Fe NW also have good cell internalization.

DISADVANTAGE:

1)Expensive to produce

2)It is very small, difficult to work

3)Difficulty to implement

4)Ni NW despite Ni's known cytotoxicity, carcinogenicity, and genotoxicity.

5)NW suffers an inherent disadvantage when compared to spherical nanoparticles in terms of cell internalization, different curvatures between the two shapes have a direct effect on cell binding, thus reducing cell internalization.

METHODS:

1 Spontaneous growth

A) Evaporation (or dissolution) - condensate;

B) Vapor growth (or solution) - liquid - solid (VLS or SLS);

C) Recrystallization.

2 Methods based on template (Template, templateless)

A) Electroplating

B) Filling with melt or colloidal nanoparticles or solution

C) Conversion with chemical reaction.

FABRICATION:

These include electrodeposition, electroless deposition, chemical techniques, and physical methods [54], all of which combine top-down and bottom-up strategies. The NW is revealed through material carving of a larger initial material block in the top-down manner, a subtractive process. However, the bottom-up method uses an additive synthesis wherein smaller particles are joined to create NWs [55]. Atop-down strategy divides huge material pieces into smaller ones using processes like lithography, milling, or thermal oxidation. The NWs are created by combining adatoms using a bottom up approach. Most synthesis techniques have a bottom-up approach. It is common practice to follow initial synthesis using either method with a fine-tuning step to adjust the structures' aspect ratio and size.
heat treatment phase.

Table 1: Showing different fabrication technique.

Fabrication Technique	Top Down/Bottom Up	Remarks on Technique	References
Electrodeposition	Bottom up	Reasonable cost of, Accurate dimensions and complex structure synthesis.	27-30
Atomic Layer deposition	Bottom-up	Reasonable Cost, complex structure synthesis, Slow deposition rate	30-31
Chemical vapor deposition	Bottom-up	Reasonable Cost, Complex structure synthesis,Difficult to deposit multicomponent constituents	30-32
Pulsed laser deposition	Bottom-up	Reasonable Cost, complex structure synthesis Difficult to control dimensions of NW	30-33
Focused Electron Beam Induced Deposition	Bottom-up	Reasonable Cost, complex structure synthesis,Lack of control in final composition of NW	30-34
Chemical reduction	Bottom-up	Reasonable Cost, Sternuous to control NW dimensions and morphology	30-35

Solvothermal	Bottom-up	Strenuous to control NW dimensions and morphology ,Requires high temperatures and pressures	30-35
Hydrothermal	Bottom-up	One step synthesis, Sternuous to control NW dimensions and morphology	30-35
Sol-Gel	Bottom-up	Reasonable Cost ,Can form defects in products	30-36
Lithography Techniques	Top-down	Adaptable in designing nanoparticles low resolution high cost	30-37

Electrodeposition of Magnetic NWs:

The most popular technique for creating NWs is electron deposition. It can be applied to create nanoparticles with a single or multiple composition and has been used historically as a standard surface modification technique to modify surface morphology and properties [43–46]. Solids are formed and deposited via electrochemical processes, a process known as electrodeposition. Usually, the formation of these solids results from the application of a voltage that reduces an electroactive species present in an electrolyte.

Electrodeposition of NWs: template-based and template-less deposition methods [30]. Templates come in two varieties: soft templates and hard templates. Non-rigid structures called soft templates are employed to regulate the direction of growth and, consequently, the final morphologies of the nanoparticles that are created. Surfactant aggregates, micelles, and co-block polymers are examples of soft templates that can be utilized to control the porosity and texture of the resulting NW. Hard templates are inflexible, conducting objects with one end that control the size and shape of the produced nanoparticles by virtue of the template's shape. The concept of creating small diameter NW in porous membranes was initially illustrated by Possin's groundbreaking work [47]. Hard templates are frequently utilized in the synthesis of since they are incredibly convenient and adaptable. Synthesis of NWs. The most widely used hard templates include mesoporous materials, polycarbonate membranes, and anodized alumina [48].

Hard templates enable the synthesis of both orientated and non-orientated NWs, as well as free-standing NWs. Additionally, they make the synthesis of intricate one-dimensional NWs easier [30]. Diffusion of the electroactive species through the small diameter pore channels,

difficulties in upscaling due to the challenge of generating large templates with uniform pore distribution, and template removal, which may impact the NW, are the drawbacks of employing hard templates.

Precise control of the NW dimensions can be achieved a necessary condition for positive cell contact, regulation of magnetic ability, and drug loading electrodeposition has the potential to produce NW for efficient drug delivery systems. In a convenient, scalable, and reproducible manner, this technique can produce a range of non-toxic, biocompatible NWs, such as iron oxide, iron, and iron palladium NWs, as well as segmented NWs. This provides a stable platform upon which drug delivery systems can be engineered, while retaining the inherent benefits of a NW for multifunctional systems.

Pulsed Laser Deposition of Magnetic NWs:

An alternative technique for producing NWs is pulsed laser deposition (PLD) [76–79]. An expelled plume is created by exciting the surface energies of a target substrate in a regulated environment with a pulsed, high-power laser beam. After that, the vapor is applied to a sample stage, creating thin films or nanoparticles that are identical in composition to the intended target. PLD enables the synthesis of nanoparticles with few flaws, high purity, and monocrystalline structure. PLD also has the benefit of being scalable and having a quick rate of production. In an effort to comprehend the mechanism underlying the formation of the NWs, Shkurmanov and colleagues examined the growth of zinc oxide (ZnO).NWs by PLD [80]. They noticed that the growth of the NW was non-linear, and this could be explained by the quantity of laser pulses used and how they interacted with four different particle fluxes. The second flow is in charge of the NWs' vertical expansion, whereas the first flow creates the nuclei from which the NWs will grow. It was discovered that the third f low caused a backflow, shortening the NW. The fourth flow, which was ultimately accountable for the NW's lateral expansion, was Cancers 2019, 11, 1956 12 of 23. This demonstrated that geometric parameters may be managed with PLD.

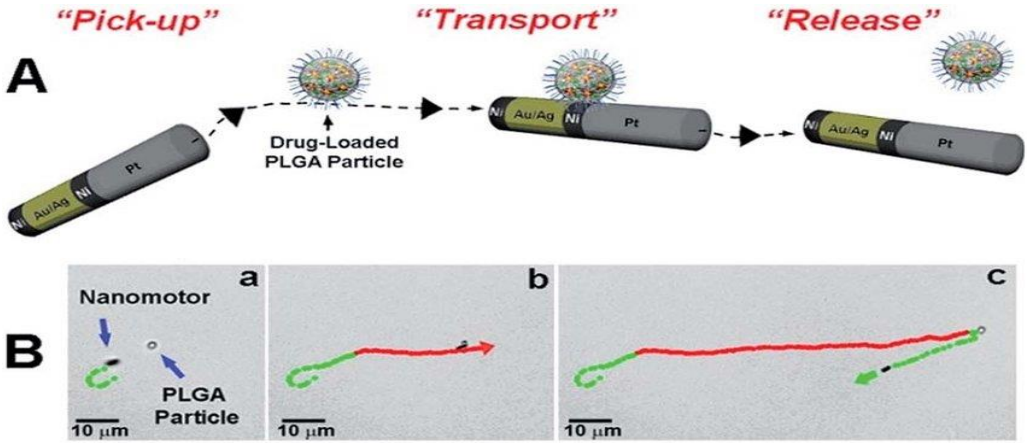
Electrospinning: An electric field is used in the electrospinning technique to spin nanofibers out of a polymer solution. After that, the threads are collected to form a network of NWs on a substrate. from a solution of polymers. After that, the threads are collected to form a network of NWs on a substrate.

Template-assisted synthesis: "Template-assisted synthesis" refers to the process of directing the creation of NWs using a template. The template can be either a porous membrane or a

self-assembling monolayer. "Template-assisted synthesis" refers to the process of directing the production of NWs with the use of a template. The template might be either a porous membrane or a self-assembling monolayer.

Vapor–liquid–solid (VLS) growth: In this technique, NWs are grown from a vapor-phase precursor using a metal catalyst.

Transport and release of PLGA drug carriers by catalytic nanowire motor:



APPLICATION OF NANOWIRES:

(A) NANOWIRE INCORPORATED IN CONDUCTOR FOR CANCER TREATMENT AND DIAGNOSIS (13)

Silver nanowires, or AgNWs, have very high electric conductivity (27), can transfer electricity efficiently when incorporated in elastic conductors (28), and therefore, like gold NWs (29), may find use in the production of cardiac patches. Preclinical studies have also been conducted to evaluate the use of silver nanomaterials for cancer treatment (30–32) and/or diagnosis. Once their biocompatibility has been established, AgNWs may be used as theranostic, nano-enabled drug delivery platforms for the treatment of lung cancer.

(B) NWS IN MAGNETIC DRUG TARGETING IN CANCER TREATMENT (1)

Magnetic drug targeting utilized for Locoregional cancer therapy. Modifying the shape of carrier particles enhancing magnetic force. It has been mathematically proved that exerting much stronger magnetic dipoles to NWs are more possible than to spheres with the same volume.

Getting medication to the precise disease tissues is a top priority for researchers these days. Chemotherapy, for example, is a modern therapy in which 99.9% of the medication impacts healthy cells and less than 0.1% is absorbed by the tumor cells.[81-82] One of the most recent innovations in the treatment of confined diseases, including malignant tumors, is magnetic drug targeting (MDT). The ideal MDT treatment consists of injecting magnetic particles into the bloodstream at the proper site after the drug has been bound to the magnetic particle or linked to the magnetic nanoparticles using a similar technique. The disease tissues are the focus of careers. Magnetic forces employed externally drive the careers to separate from streams and penetrate the tumor tissues. These professions are triggered by pH, temperature, enzymes, or magnetic triggers[83], which call for magnetic actuators to regulate the migration of magnetic particles within the body.

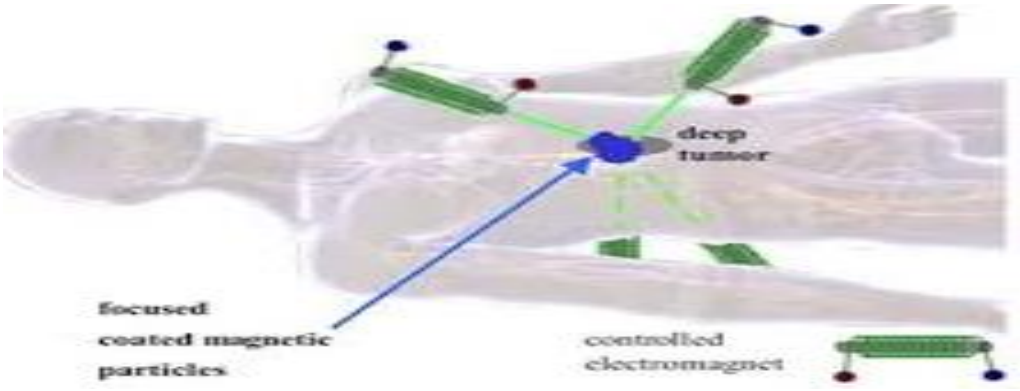


FIG 1: Perspective on using magnets to guide MNPs within the human body.

Since the human body can only target to a maximum depth of 5 cm [84–85], deepening magnetic targeting remains a difficult goal for tumor treatments[52–54] The main objective is to increase the magnetic drug-catching depths and relevant magnetic forces. Behzad et al.'s study shown that magnetic nanowires (NWs) can produce magnetic forces and magnetic targeting depths significantly greater than those of spherical particles.

(a) Utilizing Magnetic NWs as Magnetic Drug Targeting Agents in cancer therapeutics :(15)

Magnetically active, drug-loaded nanoparticles are drawn out of the circulatory system and trapped there by an external magnetic field, drug accumulation can occur at particular tumor sites. Its ability to raise drug saturation at the necessary location while lowering saturation in healthy tissue makes it seem promising. decreasing side effects and improving therapeutic

results. Thus, a magnetic field gradient and a magnetically responsive nanocarrier are required for magnetic targeting [86]. There are two types of magnet systems used in magnetic targeting: those that use an external magnet and those that combine an external magnet with an implanted magnet close to the target area [86]. When injected into the bloodstream, magnetic NW systems must overcome the viscous drag force of the blood stream. As a result, the external magnet may be able to draw the magnetic NW systems from the capillary blood flow and deliver them to the desired location. The field gradient needed to capture the NW is lessened by the enormous magnetic moments of magnetic NW [87]. There are presently two types of magnet systems: changing field magnet systems and static field magnet systems, which give the magnetic field and magnetic field gradient. While varying field magnet systems have high targeting accuracy and allow for three-dimensional (3-D) precise targeting, they are more energy-intensive, require complex hardware systems and precise calculations, and are less convenient, low-cost, and simple [30]. Because of its anisotropy, magnetic nanowires (NWs) have a better medication loading capacity and can target deeper tumors than spherical nanoparticles such super paramagnetic iron oxide nanoparticles [88,89].

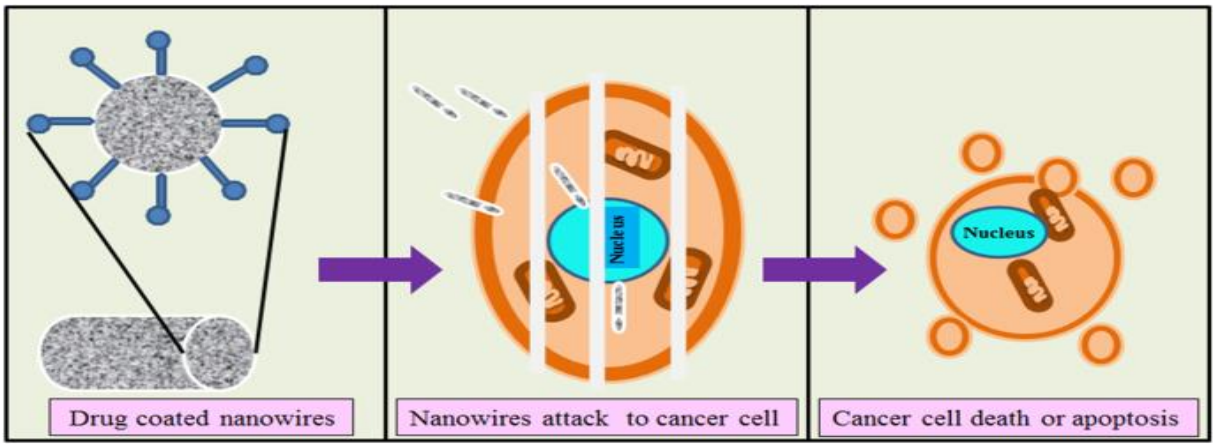


FIG 2: Illustration of how nanowires induce apoptosis in cancer cells. Vibration, heat, and medication delivery are the three ways that the nanowires target cancer cells, ultimately resulting in cell death.

(b) Utilizing Magnetic NWs as Hyperthermic Agents in Cancer Therapeutics:

With its ability to be appropriately organized to offer thermal response to stimuli like low-frequency alternating magnetic fields and near-infrared irradiation, NW shows promise for application as hyperthermic agents [34]. When malignant tumors experience hyperthermia, their cancer cells die as a result of energy injection. The temperature can be classified into three states: diathermy (above 41°C), apoptosis (between 42°C and 46°C), and

thermoablation (above 46°C). The optimal range for the death of cancer cells is apoptosis, thermoablation promotes heat-induced necrosis, and diathermy promotes tumor growth [35]. When an alternating magnetic field is present, there are two ways to cause magnetic hyperthermia. These two mechanisms are referred to as the Néel and Brownian relaxation mechanisms [36]. The rotation and vibration of the NW in the direction of the external magnetic field is a part of the Brownian mechanism. The magnetic NW in its suspended medium causes a mechanical friction as a result, which causes hyperthermia.

(c)Utilizing Magnetic NWs as Magnetic Actuation Agents in Cancer Therapeutics:

Magnetic NW can cause a magnetomechanical process that results in cell death without the need for a heat-dependent mechanism. Zablotskii et al. conducted the first investigation into the cytotoxic effects of magnetic actuation at low frequencies resulting from alternating magnetic fields [45]. Utilizing Magnetic Nanoparticles as Magnetic Actuation Agents in Cancer Therapy As shown in Figure 3, a magnetomechanical process using magnetic NW can cause cell death without the need for a heat-dependent mechanism [43, 44]. Zablotskii and colleagues [45] conducted the first investigation into the cytotoxic consequences of magnetic actuation resulting from alternating magnetic fields at low frequencies. They cultured mesenchymal stem cells to mechanical vibration and a high gradient magnetic field with a low frequency (1–10 Hz). Their findings revealed that the F-actin remodelling and subsequent down-regulation of the audiogenic genes were caused by both mechanical vibration and an alternating magnetic field.

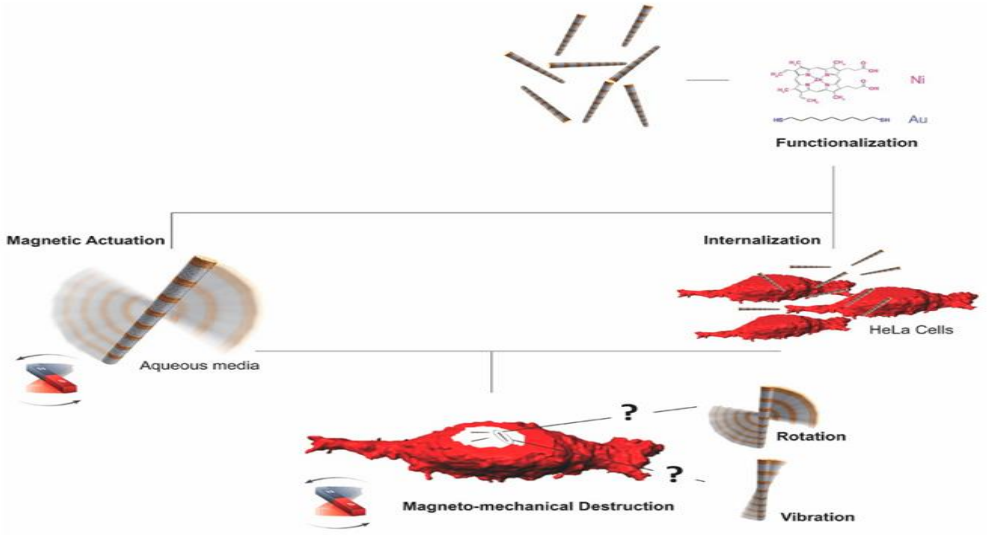


Fig 3: A magneto mechanical process using magnetic NW

(d) The Use of Magnetic NWs as a Theranostics System in Cancer:

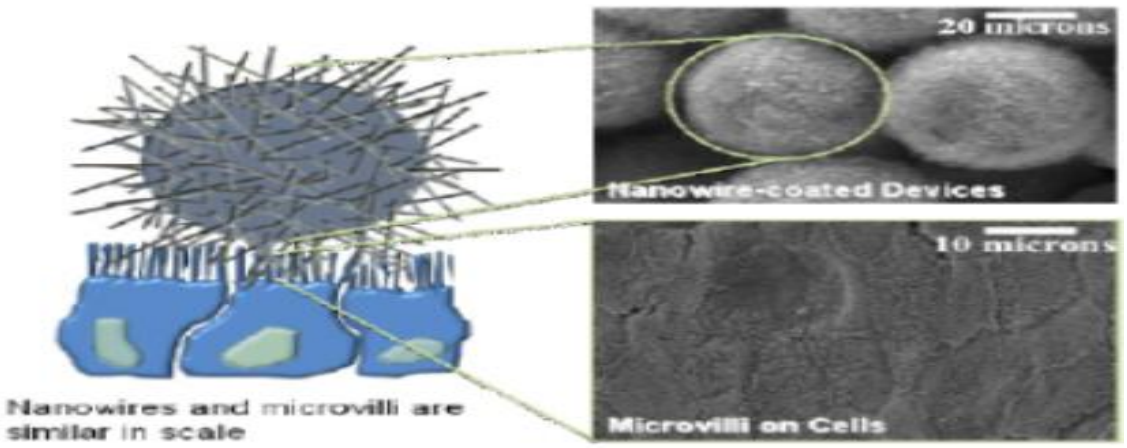
Magnetic NW's function in theranostics, which encourages treatment customisation by combining medicines and diagnostics. Photothermal therapy, magnetic actuation systems, and targeted and triggered release drug administration are all included in the therapeutic application of magnetic NW platforms. The huge surface area of NW improves the efficacy of fluorescent labelling in diagnostics, and its increased magnetic moment in magnetic NW makes it appealing for magnetic resonance imaging (MRI) and fluorescence imaging, respectively. There are two types of contrast compounds used in MRIs: T1 and T2. T1 is based on longitudinal magnetization recovery, whereas T2 is based on transverse magnetization degradation [60]. This is the key distinction between T1 and T2 agents.Fe and Ni NWs have been demonstrated to be effective T2 contrast agents in this sense, with Ni NWs being on par with commercial agents [61,62]. NWs and magnetic NWs are promising options for developing cancer theranostics systems due to their efficacy in both treatments and diagnostics.

(C) NANOWIRE ON MICROPATICLE OFFER BETTER BIOADHESION & DRUG DELIVERY:(23)

The creation of silicon NWs on microparticles in a conformal three-dimensional coating has been made possible by recent developments in nanotechnology, by Kathleen Elizabeth Fischer. It has been demonstrated that these coatings for NWs are resistant to acid and break down within a few weeks in physiological solutions. Microparticles coated with nanoscale cellular characteristics, including microvilli, can interact with NWs-coated microparticles to enhance their surface area of contact. Under extreme physiological circumstances, including shear exceeding 100 dynes/cm2, a simulated mucous layer, and several injuries to the cellular cytoskeleton, these devices cling firmly. They attach well to many types of tissue and are retained better than mucoadhesives because of their geometry-dependent processes of adhesion and direct interaction with the epithelial cells. The NWs coated devices withstand tensile tension by adhering to The NWs coated devices adhere up to 1000 times stronger under tensile strain than the corresponding uncoated devices. Surface area dependent forces are implicated in NWs-related adhesion, with charge and NWs shape having the most overall influence. The mouse and the dog are two different animal models in which the in vitro adhesion data have been verified. Stainless steel particles coated with NWs were at least ten times longer to remain in the stomach of beagles than comparable controls. Microspheres

coated with NWs in mice did not leave the stomach until at least five hours after administration.

The internalization of NWs and the cellular toxicity or systemic accumulation are avoided by attaching them to a microscale device. A reservoir between the NWs at their base and a template for spatially patterning chemical alterations are two other features that an adhesion system based on NWs offers. Reactive oxygen species, cytokine release, and monocyte activation all demonstrate a reduced inflammatory response in silicon NWs when compared to flat glass 60. Because of their unique combination of nano and microscale properties, NEMPs provide a means of preserving medicines from degradation, extending their duration at the mucosal surface, and enhancing concentration gradients near to cells all without compromising their high loading capacity or inducing inflammatory reactions.



(D) NANAOWIRE PARTCIPANT IN BIOSENSING (3)

(1) DETECTION OF VARIOUS NEUROTRANSMITTER & MOLECULAR:

Currently, biological molecules can be identified, including tiny molecules, neurotransmitters, and nucleic acids. A biosensor's ability to function depends on how the target analyte and biological recognition component interact. The signal that the target analyte emits when it attaches to the biological recognition element is converted into an electrical signal by the transducer. These biosensors are used in many industries, such as food safety, medical diagnostics, and environmental monitoring. Biosensors can be used to specifically detect dopamine as well as other compounds like glucose, cholesterol, and others. To identify the GABA molecule, Lee et al. created an immunosensor based on a silicon NWs

field-effect transistor (FET) device. The optimal immobilizing condition for the antibody against the GABA molecule was determined by evaluating the fluorescence signal.

Materials	Mechanism	Target	Concentration	Range Limit of Detection	Ref
Silicon NWs	Fluorescent signal	Aminobutyric acid (GABA)	970 fM to 9.7Mm	9.7 Mm	[90]
Ru@V2O4	Colorimetric sensor	Cysteine	300–240 μM	41.2 μA μM $1cm^{-2}$, 26.4 μA μM $1cm^{-2}$	[92]
Pt-Au NWs	Cyclic voltammetry (CV)	Penicillin and tetracycline	3–50μ M	0.139 M	[91]
Cu2O/Cu@C core–shell NWs	Amperometry	Uric acid	0.05 to 1.15 mM	330.5 advantage μ A μmM $1cm^{-2}$	[93]
Rutile/anatase TiO2 (R/A-TiO2)	Photoelectrochemical biosensor	Glucose	1–20 mM	0.019 mM	[94]
Mo-W-ONWs intercalated graphene	Electrochemical sensor (CV, Differential pulse voltammetry (DPV))	Dopamine and Tyrosine	0.001–448.0 μM, 0.001–478.0 μM	0.8 nM, 1.4 nM	[95]
CuO/Cu2ONWs	Photoelectrochemical	Tyrosinase	0.05–10 U/mL	0.016 U/mL	[96]

(2) DETECTION OF DNA & RNA:

A great deal of interest has been shown in DNA and RNA detection techniques which include the identification of clinical diagnoses, the recognition of DNA-based gene sequences, nano-bioengineering, and the food industry. The single stranded hepatitis B virus DNA (SS-DNA) was immobilized and used as a probe in the Au-modified NWs. The DNA targets have a linear concentration range of 1 fM to 10 M. The detection limit of the DNAbiosensor is 1fM. It took 90 minutes for the hybridization process to complete for a single strand. The biosensor's ratio of switching between the on and off states was 1.1 105. For biosensor sensitivity, DNA oligonucleotide sequences that belong to complementary, non-complementary, and mismatched groups were easily distinguished. The extremely pleasing specificity for differentiating between complementary and non complementary sequences mismatched oligonucleotides was proven using the HBV sensor.

(3) DETECTION OF PROTEIN:

There are essentially two stages to the identification of protein markers linked to oncological disorders reported in the literature. In the first step, the potential of DL detectors based on Si-NW sensors in the early detection of illnesses is determined by evaluating them in a model solution. It should be mentioned that the detection limit must be lower than the femtomolar concentration threshold in order to enable earlier disease identification. With very few exceptions, nearly all of the works listed below have made it feasible to use silicon nanowire detectors to achieve such low detection limits. This demonstrates the technology's great potential for early disease identification. In the second phase of the study, these technologies are modified to detect protein markers in the biological fluid of the patient, which typically consists of serum and, to a lesser extent, urine and other biomaterials. The following provides more thorough assessments of the application of Si-NW for the identification of protein markers in pure solutions and biological material. SI-NW sensors can use aptamers or antibodies as sensitive components to detect proteins in a biospecific manner. Initially, antibodies-based biospecific Si-NW sensors will be taken into consideration. Examine the use of Si-NW-sensors, which are highly responsive to proteins and nucleic acids linked to the advancement of disease. Personalized treatment begins with the use of Si-NW sensors as the disease advances. However, their incorporation into portable devices has the potential to transform cancer diagnostics by enabling the monitoring of a patient's bodily response to medication.(6)

DETECTION OF PROTEIN ASSOCIATED WITH ONCOLOGY:

ANALYTE	MEDIUM	DETECTION LIMIT	REF
Prostate-specific antigen (PSA)	Buffer	1.7×10^{-15} M	[15]
	Serum	3.13×10^{-14} M	
	Buffer	3.48×10^{-17} M	
	Serum	3.48×10^{-16} M	[31]
	Buffer	3.48×10^{-17} M	
	Serum	3.48×10^{-16} M	
Carcinoembryonic antigen (CEA)	Buffer	6.51×10^{-16} M	[15]
	Serum	1.17×10^{-14} M	
Mucin-1, a transmembrane glycoprotein (MUC1)	Buffer	4.09×10^{-16} M	[15]
	Serum	7.37×10^{-15} M	
APOA2	Urina	3.8×10^{-13} M	[37]
AFP	Buffer	1.46×10^{-13}M	[38]
	Serum	7.28×10^{-15}M	
D-NFATc1	Buffer	2.5×10^{-15}M	[5]
	Serum	2.5×10^{-14}M	
CYFRA21-1	Buffer	3.33×10^{-17}M	[31]
	Serum	3.33×10^{-16}M	
TumorM2-PK	Buffer	10^{-13}-10^{-15}M	[42]
ALCAM	Serum	2.38×10^{-13}M	[43]

(4) DETECTION OF VIRUSES & BACTERIA:

The tin-doped WO3/In2O3 heterojunction NWs photoelectrode-based sensitive DNA sensor for detection of hepatitis B virus relies on laser amplification.ThepresentCOVID-19 pandemic serves as an example of how the spread of viruses and bacteria has put the world's biosecurity at risk .Disease prevention and control have historically depended heavily on the early detection of bacterial and viral illnesses .Surface-enhanced Raman scattering (SERS),surface plasmon resonance, surface-enhanced fluorescence ,and surface enhanced infrared absorption spectroscopy are some examples of plasmonic phenomena that can be used to identify viruses. This finding and evaluation will help the audience accelerate the study and creation of a novel class of adaptable bacterium and virus biosensors.

When compared to a commercial immunoassay, an innovative serological test using the ZnO-NW MP is more sensitive, allowing for the early identification of anti-SARS-CoV-2 NP IgG antibodies in COVID-19 patients who are asymptomatic . This is the first assay as haemoglobin breaks down, bilirubin (BR), a byproduct that might signal liver problems and cause jaundice. When neonates' unconjugated BR concentrations rise quickly to fatal levels, it can result in brain damage . For sensitive label-free BR detection, Anna et al. suggest a novel technique for fabricating a SERS-active substrate using gold-decorated silicon NWs (Au@SiNWs). To create SiNWs, crystalline silicon wafers were chemically etched with the help of gold before being further embellished with gold. The model analyte 4-mercaptopyridine has a low detection limit down to a concentration of 10−8 M. Amino groups were added to the surface of the SiNWs to facilitate effective BR adsorption and SERS detection. The required sensitivity for clinical applications, 5 × 10−5 M for BR adsorption, was used to verify the signal stability for 7 days [16]. chemically etched with the help of gold before being further embellished with gold. The model analyte 4-mercaptopyridine has a low detection limit down to a concentration of 10 8 M. Amino groups were added to the surface of the SiNWs to facilitate effective BR adsorption and SERS detection. The required sensitivity for clinical applications, 5 10 5M for BR adsorption, was used to verify the signal stability for 7 days.

(5) In Vivo Sensing:

Injecting the NWs sensors into human body for long-term recording of bioelectric signals, such as neural activities in the brain [17,18]. The in vivo environment presents a lot of challenges to the properties of NWs. On the one hand, the in vivo microenvironment contains

many ions that can dissolve the passivation layer (silicon oxidation) of silicon NWs which naturally exist in air [19,20]. Early studies have reported the limited stability of NWs upon being used with cells [87,88]. Zhou et al. recently introduced a coating method to enhance the long-term stability of NWs [89]. Upon studying the protection of the 10 nm-thick Al2O3 shell, it was observed that the diameter of the NWs remained almost the same for at least 100 days in 1 PBS at 37 C, respectively, while the NWs without the shell disappeared. This coating strategy worked not only for Si NWs, but also for Si–Ge complex and InAs complex. However, the increment of shell thickness downregulated the sensitivity of NWs (4).

Summary of the salient features and the target application of NWs-based biosensors:

Features	**Application**	**Reference**
Top-down fabrication process using SCS wafer	Photodiode and FET for the retinal prosthetic systems	[49,50]
High sensitivity using PEG cross-linker	Detection of protein and DNA	[51]
Long-term stability using Al2O3 shell coating	In vivo sensing	[52]
Integrating NWs with disposable device	Glucose detection	[53]
Multivariable detection using machine learning	Multiple disease diagnosis	

6) NWs for detection of circulating tumor cells (CTCs) CTCs play an important role in cancer metastasis, and their presence in blood samples of cancer patients provides information about the type of cancer.(5) Tseng and his research team developed Si NWs, which they called a NanoVelcro chip, to capture and release CTCs from blood samples with high selectivity.73–76 Si nanowires were fabricated on substrates by a standard photolithography and chemical wet etching process, and then they were bonded on chaotic mixer microfluidic channels to fabri cate the NanoVelcro chip. Surface modification with cell

surface markers of anti-EpCAM enhanced the capturing efficiency of CTCs or of anti-CD45 depleted white blood cells on the NWs The Nano Velcro chip based on Si nano wires has been developed for single-CTC isolation by depositing thermoresponsive polymer brushes, polyIJN-isopropylacrylamide (PIPA Am), on Si NWs. This thermoresponsive Nano Velcro chip could capture and release CTCs at 37 °C and 4 °C, respectively. In addition, in the same study, biotin groups were introduced for conjugation of polymer brushes and anti-EpCAM to enhance the specific capture of CTCs. The efficiency of CTC release was nearly 90%. NanoVelcro chips are promising tools to capture and pu rify CTCs rapidly before CTC molecular analysis.(5)

CONCLUSION & FUTURE PROSPECTIVE:

Nanowire offer huge opportunistic potential in the field of diagnosis of various protein associated with illness & disorder.The future of nanowire seems promising especially with the rapid growth of technologies and materials which would enable large industrial scale production of NWs.It surface-to-volume ratio (interface phenomena), low defect density, excellent optical output, and adjustable n-type conductivity, which makes them suited and more sensitive for applications involving sensing. Over the past ten years, biosensing technology has dramatically increased due to the introduction of nanowires in biosensors . This is because of the use of new transducers and biorecognition components, improvements in the manufacture, design, and miniaturization of nanostructured devices at the micron scale, and innovative techniques for making nanowires . The versatility, robustness, and dynamic nature of sensing technologies have all increased with the usage of nanowires . The transduction process has been significantly enhanced by using many nanowires with different characteristics inside biosensors (such as better sensitivity, faster detection, shorter reaction time, and reproducibility). Enhancements in receptor binding techniques may address both the issue of increased sensitivity and simpler fabrication processing problems. Therefore, they could be modified to aid in the early medical diagnosis of infectious and cancerous disorders. Furthermore, a reduced cost of marketed items is made possible by the present top-down production processes' greater yield ratio. The versatile magnetic NWs platform can be used Wnt inhibitor delivery systems, ligand attachment to increase selectivity, and theranostic systems that include fluorescent compound attachment, chemotherapeutic drug attachment, and modifications to increase cancer cell selectivity. However, more research is needed to fully realize the potential of magnetic NW in drug delivery. For multifunctional NWs nano systems to advance into the pre-clinical stage, effective in vivo research is necessary. Further

study is necessary to optimize an approach involving the magnetic applications of NWs, such as .magnetic hyperthermia, magnetic actuation, and magnetic drug targeting, as they have demonstrated significant promise for enhancing cancer therapies.NWs coated nanoparticle offer better bioadhesion as compared to nanoparticle alone .NWs going to be boon in the Biotechnology and pharmaceutical field .

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