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Mini Review

Nanotechnology-based Strategies in Breast Cancer Diagnosis and Therapy: A Mini-review

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Abstract

Breast cancer (BCA) is one of the most common cancers worldwide, with a high rate of mortality and morbidity in women. This review focuses on the applications of nanotechnology, nanomaterials, and nanoparticles (NPs) in BCA, encompassing diagnosis and therapy. Nanotechnologies, nanocarriers, and nano-encapsulations versus their corresponding counterparts for BCA diagnosis and therapy have been discussed. Various drug formulations into different nanocarriers (lipid NPs, nanoemulsions, polymeric NPs, and metal-based NPs) enhanced their bioavailability and therapeutic efficacy, overcoming the limitations of conventional formulations. Additionally, clinical specialists have achieved improved outcomes in the detection and monitoring of BCA at various stages using nanotechnology, ultimately leading to an improved quality of life for patients.

Introduction

According to estimates from the World Health Organization in 2019,[1] cancer is the first or second leading cause of death before the age of 70 years in 112 of 183 countries and ranks third or fourth in a further 23 countries. The rising prominence of cancer partly reflects marked declines in mortality rates of stroke and coronary heart disease, relative to cancer, in many countries.[2–4] Despite the continuous rise in the number of diagnostic cases, the overall cancer mortality rate has been steadily decreasing since the early 1990s.[4] This trend may be attributed to the implementation of advanced technologies and nanotechnology across various medical fields.

Breast cancer (BCA) is the most common type of cancer, predominantly impacting women, and ranks as the second most common cancer type following lung cancer, contributing to a significant number of fatalities globally, irrespective of gender. It represents 30% of all cancer cases and 15% of cancer-related deaths in women.[1,4–7] Scientific research has demonstrated that the intracellular signaling pathway (PI3K/AKT/mTOR) is crucial in the development and progression of BCA, influencing essential cellular functions such as cell growth, proliferation, angiogenesis, and metastasis. BCA cases also have significant hereditary implications.[8,9] Nanomedicine is a branch of medicine that deals with applications of nanomaterials (NMs), nanoparticles (NPs), or nanodevices in medicine. Nanoscience and nanotechnology are growing in various sectors of medicine, resulting in significant changes in the quality and duration of life. Different research subjects, including preparation, properties, characterization, and applications of NMs *in vitro* and *in vivo*, have been under investigation since 2000.[10–12] Nanotechnology could be used in prevention, diagnostics, and various types of treatment for BCA.[13] Abbreviations along with their full names are provided prior to the reference list.

The innovation presented in this manuscript addresses the following: (a) the issues and challenges of coarse-sized materials and conventional technology in the treatment of BCA; (b) the advantages of NMs over bulk materials and nanotechnology over conventional approaches; and (c) the solutions that overcome the limitations, achieving adequate efficacy using NMs and nanotechnology in BCA treatments. The present review aims to discuss applications of nanotechnology and NMs in BCA, encompassing diagnosis and therapy, including *in vitro* and *in vivo* (pre-clinical and clinical) studies.

General aspects of NMs and NPs

Characteristics and properties of NMs and NPs

NMs exhibit the following characteristics: (i) one dimension in the nanometer-length scale (1–100 nm); and (ii) a large surface area per volume, giving rise to novel properties and phenomena that differ from the corresponding counterparts for bulk materials with the same composition.[14] The most defining feature of NMs is their

Keywords: Breast cancer; Nanotechnology; Nanomaterial; Therapy; Stage; Quality of life; Challenge; Nanomedicine; Health care.

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Table 1. Comparison between conventional and nanotechnologies for cancer treatments

Item	Advantages	Disadvantages	References
Conventional	Surgery, chemotherapy, and radiotherapy have improved survival compared with no treatment.. A major advantage of conventional therapies over innovative therapies is that they are relatively easy to perform	Conventional therapies are often limited by: (i) lack of target specificity; (ii) nonspecific drug delivery; (iii) development of drug resistance; (iv) high adverse effect; (v) collateral damage to healthy tissues; (vi) systemic toxicity; and (vii) the need for separate imaging and monitoring procedures	19,20
Innovative technology based on nanotechnology	improve bioavailability; (b) enhance drug targeting; (c) facilitate controlled release; (d) deliver higher drug concentration at target sites; (e) can combine different therapies; (f) reduce adverse effects; (g) combat drug resistance; and (h) enhance treatment outcomes	Nano-sized particles can penetrate cell membranes. Their safety *in vitro* and *in vivo* should be confirmed before clinical practices	19,20

size. The shape and architecture of NMs also significantly influence their properties. Nano-sized materials demonstrate superior chemical, biological, physical, and mechanical properties when compared to their bulk counterparts, leading to notable interactions and effects.

A key physicochemical property of a drug for clinical use is its solubility in water. The solubility of numerous promising drugs in water is insufficient. It is estimated that over half of all drugs exhibit poor water solubility. Most drugs have been discarded due to their inadequate water solubility. Poor water solubility of a drug requires the use of higher amounts, which in turn may result in higher adverse effects.[12,15,16] Reducing particle size results in enhanced surface interactions and increased solubility.[17]

Applications of NMs and nanotechnology in the cancer sector

Nanoscience and nanotechnology have been used in various branches of cancer practice, including prevention, detection, diagnosis, and treatment of cancers. The applications of nanotechnology in the cancer sector result in: (a) NMs remain in the body for a longer duration than larger-sized materials, facilitating sustained therapeutic effects. Thus, the use of NMs improves pharmacokinetic effects; (b) NPs can penetrate the animal or human body through essential organs (such as the skin, lungs, and gastrointestinal tract) more easily and rapidly than larger particles. Generally, the skin serves as an effective barrier against foreign substances, while the lungs and gastrointestinal tract are more vulnerable; (c) NPs enhance the proportion of the administered dose that successfully reaches the tumors, facilitating targeted delivery and absorption, which ultimately reduces the required dosage; and (d) NMs serve as effective agents for the prevention of cancer through chemotherapy, attributed to their enhanced permeability and retention effects. These effects refer to the ability of NPs to preferentially accumulate in tumor tissues rather than in normal tissues.[13,17] The targeted delivery of drugs delivers more anticancer drugs to cancer cells than non-targeted ones.[18] Table 1 describes the advantages and disadvantages of conventional and nanotechnologies in cancer treatment.

Different aspects of BCA

Statistical data on BCA

The global incidence and mortality of BCA in 2022 were presented in Table 2. The data were collected from GLOBOCAN 2022, including new incidence and mortality cases (the age-standardized incidence rate and the age-standardized mortality rate) of BCA across 21 United Nations regions and 185 countries. The incidence and mortality rates of BCA differ considerably between countries.[4,21–23]

Molecular subtypes of BCA

In 1994 and 1995, two genes linked to hereditary BCA (BRCA1, BRCA2), found on human chromosomes 13 and 17, were discovered. The clinical implications of mutations in BRCA1 and BRCA2, along with the crucial role of DNA repair in BCA susceptibility, were examined from 1994 to 2004 and documented in a report.[24] These two genes play a significant role in maintaining genomic integrity and facilitate DNA repair. Mutations in these genes are correlated with aggressive forms of both breast and ovarian cancers.

Clinically, BCA is categorized into three primary subtypes based on the status of progesterone receptor, estrogen receptor, and human epidermal growth factor receptor 2 (HER2).[8,9] Molecular subtypes of BCA are presented in Table 3. Major subtypes of BCA are classified by hormone receptors and HER2. BCA tumors that overexpress the protein HER2 are associated with the epidermal growth factor receptor. Triple-negative breast cancer (TNBCA) tends to occur in younger women, with a mortality rate as high as 40% in advanced stages within the first five years after diagnosis.[25–27] Approximately 45% of patients diagnosed with advanced TNBCA will experience distant metastasis to the brain, with a median survival time of 13.3 months.[28] Due to the lack of expression of targetable proteins, TNBCA patients, who have poorer prognoses than other BCA types, primarily rely on surgery, radiotherapy, and chemotherapy.[29] TNBCA has a recurrence rate of up to 25%, and the presence of residual micrometastatic disease after neoad-

Table 2. The incidence and mortality of breast cancer worldwide in 2022

Age range	Incidence		Mortality	
	Case (number)	ASIR (per 10^5 person)	Case (number)	ASMR (per 10^5 person)
All ages	2,296,840	46.80	666,103	12.70
<40 years	246,060	8.10	48,700	1.60

ASIR, age-standardized incidence rate; ASMR, age-standardized mortality rate.

Table 3. Subtypes of breast cancer cell lines

Breast cancer subtype (Percent, %)	Cell lines	References
TNBCA (~15-20%) HR- (ER-, PR-), HER2-	MDA-MB-231 MDA-MB-468; BT-549	20,25,32,33
Luminal A (~40%) HR + (ER+, PR+), HER2-	MCF-7, T-47D	25,34–37
Luminal B (~20%) HR + (ER+, PR+), HER2+/−	BT-47, ZR-75-1	25,32,37,38
HER2-enriched (~10-15%) HR − (ER-, PR-), HER2+/−	HCCC-1954, SK-BR-3	25,32,37,38

ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; PR, progesterone receptor; TNBCA, triple-negative breast cancer.

juvant chemotherapy is associated with an increased risk of tumor recurrence and mortality, while options for routine postoperative adjuvant chemotherapy are limited.[30,31] Various risk factors have been associated with the incidence of BCA, including obesity, diabetes, age, increased hormone production, genetic predisposition, and familial history of BCA.[32]

Challenges in BCA after diagnosis

Challenges in BCA after diagnosis and subsequent treatment include: (a) treatment resistance; (b) recurrence; and (c) persistence of adverse effects.[39] Traditional cancer therapies have challenges such as low cellular absorption, multidrug resistance, and limited bioavailability. Therefore, many patients seek complementary and alternative therapies that can enhance treatment efficacy, alleviate adverse effects, and improve overall quality of life.[40] Surgery is an effective treatment; however, it is associated with certain limitations, such as metastasis and recurrence, which restrict its utilization in the clinical setting.[41] Current innovations in nanotechnology, such as nanocarriers for drug delivery systems (DDSs), provide a promising approach to address some of these limitations.[10,42–44]

Various therapies for BCA treatment

Among various treatment options available for BCA (surgery, chemotherapy, radiotherapy, chemoradiotherapy, and immunotherapy), chemotherapy stands out as one of the most effective approaches. It has primarily been utilized in the early stages of BCA treatment.[45,46] Multiple therapeutic strategies are available for the management of BCA. Clinically, BCA treatment is managed through a combination of chemotherapy, radiation therapy, hormonal therapy, and surgery.[47] Figure 1 illustrates conventional therapies versus innovative therapies utilizing nanotechnology and NMs.

Carriers and nanocarriers for delivery of drugs to different cancers, including BCA

Conventional carriers exhibit a limited response to tumors and can adversely affect normal cells.[30,40,48] Table 4 describes major nanocarriers for delivery of drugs to different cancer types, including BCA. Figure 2 shows different carriers for conventional and innovative BCA treatments. The latter carriers were developed using nanotechnology.

Oral delivery of a nanoemulsion (NE) formulation is beneficial due to the direct delivery of a medication to a targeted organ and its associated cells. NEs are utilized across a wide array of biomedical fields, including the development of pharmaceutical formulations for topical, ocular, intravenous drug delivery (DD), as well as biomedical aids and vehicles that demonstrate significant potential for diagnostics, drug therapies, and biotechnologies. Additionally, NE formulations can enhance the oral delivery of poorly soluble drugs. NEs act as a framework to generate hydrophobic active pharmaceutical ingredients for biomedical use.[13,64] The toxicity of drugs is minimized by their encapsulation in NEs, and their delivery to targeted tumors is improved. General information on the applications of emulsions, NEs, and micelles in different aspects of medicine, including various cancers, can be found in elsewhere.[65]

Nanocarriers for delivery of drugs to BCA cells

A detailed description of nanocarriers for delivery of drugs to BCA cells, both *in vitro* and *in vivo* (pre-clinical and clinical trials), is provided in Table 5. The content of Table 5 differs from Table 4 as follows: (1) Table 4 describes nanocarriers for DD for all types of cancers, including BCA, whereas Table 5 describes nanocarriers specifically for BCA; and (2) Table 5 presents reported experimental results from pre-clinical and clinical trials of nanocarriers for DD to BCA cells.

Nanocarriers transport chemotherapeutic agents, increase cytotoxicity towards BCA cells, and inhibit the emergence of drug resistance. Additionally, nanocarriers enhance the effectiveness of gene therapy and support regulation of gene expression. The simultaneous delivery of drugs and genes by nanocarriers can produce a synergistic impact on BCA cells and alter the tumor microenvironment.[30]

Natural polymers such as chitosan present significant potential as versatile and effective materials in the creation of DDSs, provid-

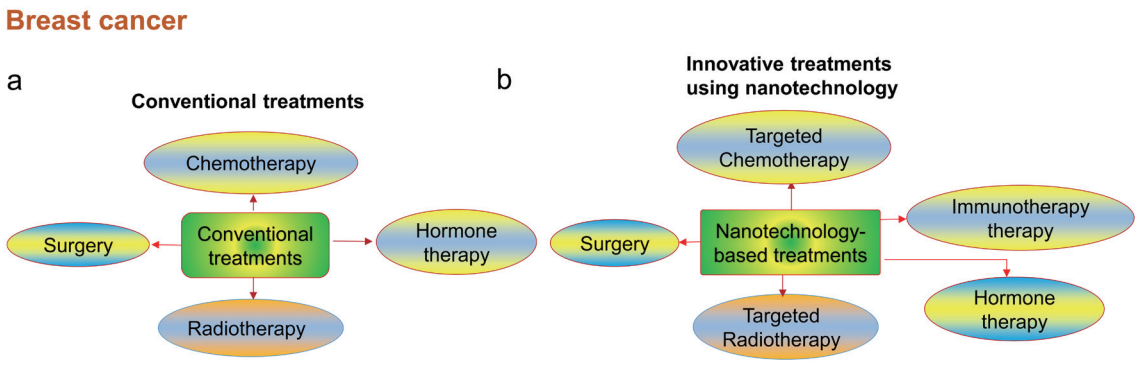

Fig. 1. Conventional therapies versus innovative therapies utilizing nanotechnology and nanomaterials. (a) Conventional therapies; (b) Innovative therapies utilizing nanotechnology.

Table 4. Major nanocarriers for delivery of drugs to different cancer types, including breast cancer

Nanocarriers	Functions and applications	References
NPs	The addition of a small amount of functionalized NPs leads to a major change in the properties of final pharmaceutical formulations or commercial medical products	13,17
LNPs	(a) LNPs enhanced drug stability, drug absorption and encapsulation efficiency for hydrophobic and hydrophilic drugs; (b) chemotherapeutic agents encapsulated in LNPs serve as optimal delivery systems for cancer treatments, particularly beneficial for chronic patients or patients are under short-term metronomic treatment; and (c) LNPs can be designed to deliver both hydrophilic and hydrophobic drugs concurrently in cancer therapies	49–51
Nanoemulsions	NE formulations present numerous advantages over CEs as follows: (a) increase absorption; (b) improve clinical efficacy, (c) NE formulations are more effective than that of CEs for cancer therapy.; (d) NEs can be delivered in the deepest of tissues; (e) NEs serve as good carrier systems for chemotherapeutic drugs; and (f) NEs can be used in target cancer therapy to deliver active ingredients	52–55
Polymer-based NMs	Enhanced penetration and bioavailability, reduced toxicity, and extended duration of drug releasing	13,42,56–62
Metallic NPs	The metallic NPs have potential for diagnosis of cancers and monitoring cancer therapies	10,13,48,63

CEs, conventional emulsions; LNPs, lipid nanoparticles; NEs, nanoemulsions; NMs, nanomaterials; NPs, nanoparticles.

ing numerous benefits.[56,59.60] The interactions between positively charged groups of chitosan and negatively charged groups of cancer cells facilitate the targeted delivery of chemotherapeutic agents encapsulated in chitosan. These interactions enhance the cellular uptake of the nano-micelles, resulting in a higher rate of internalization of drug-loaded nano-micelles into cancer cells.[58,62] The electrostatic interactions of chitosan-based DDSs can open tight junctions in cancer cell membranes, thereby promoting the entry of chemotherapeutic agents into the cells.[73] The mechanisms associated with chitosan can be enhanced by increasing the positive charge groups on the native chitosan backbone through the formation of quaternary ammonium chitosan. The additional positive charge groups present in quaternary ammonium chitosan derivatives render them more favorable than the original chitosan for the delivery of chemotherapeutic agents. Quaternary ammonium chitosan improves penetration and permeability into cancer cells, along with enhanced biocompatibility, mucoadhesive properties, and controlled release of drugs.[74,75] Chitosan nanocarriers can also induce phototherapy-mediated tumor ablation. Smart and multifunctional types of chitosan NPs, including pH-, light-, and redox-responsive NPs, can be used to improve the potential for BCA tumor removal. Additionally, the acceleration of immunotherapy has been achieved by employing chitosan NPs. Chitosan-NPs in hydrogel forms can also be used to suppress tumorigenesis.[42] In conclusion, chitosan-based NPs can be used: (a) to deliver genes, drugs, and natural bioactive compounds (like curcumin, ellagic acid, and phenolic antioxidants possessing pro-apoptotic effects) in BCA treatment; (b) to induce phototherapy-mediated tumor ablation; (c) to fight against BCA tumor cells; (d) to mediate combination therapy of phototherapy with either chemotherapy or immunotherapy; and (e) to participate synergistically in BCA therapy.[57]

Major metallic nanocarriers for delivery of drugs to BCA cells

A detailed description of major metallic nanocarriers [gold (Au) NPs, silver (Ag) NPs, copper (Cu) NPs, and iron oxide (Fe_3O_4) NPs] for DD to BCA cells, both *in vitro* and *in vivo* (pre-clinical and clinical trials), is provided in Table 6.

Clinical results for BCA treatment using nanotechnology

Numerous clinical trials have compared the utilization of existing and registered medications within various combination regimens, occasionally yielding improved treatment outcomes. The introduction of NPs as a DDS has demonstrated significant potential

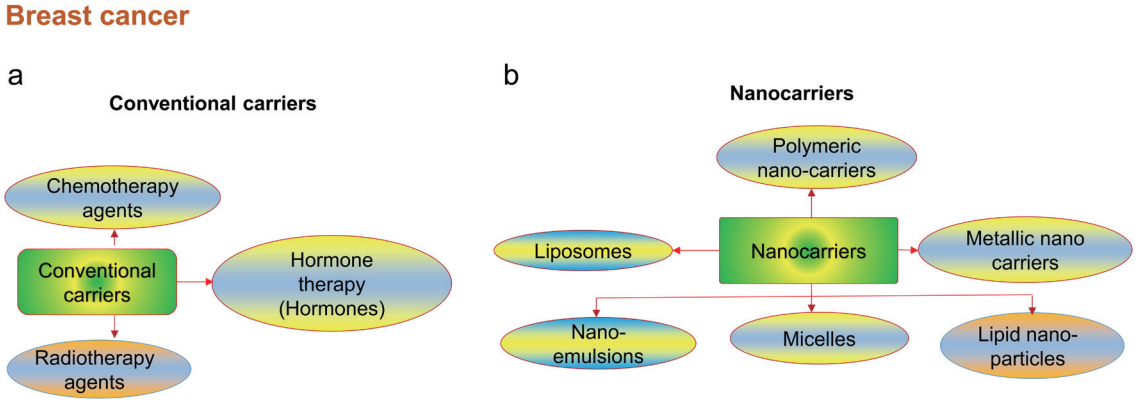

Fig. 2. Conventional and innovative carriers for breast cancer treatments. (a) Conventional carriers; (b) Innovative carriers employing nanotechnology (nanocarriers).

Table 5. Preclinical and clinical results for the effects of various nanocarriers for delivery of drugs to breast cancer cells

Nanocarriers	Results in BCA	Remarks	References
Nanocarriers for BCA clinical trial	Nanocarriers enhanced both the effectiveness of drug delivery, and overall outcomes for BCA treatment	They overcame the limitation of traditional therapy	19
Photothermal nanomaterials	Preclinical and early clinical trials showed that the nanomaterial-assisted photothermal therapy (PTT) improved therapeutic efficacy against metastatic BCA. The PTT facilitated the targeted ablation of tumor tissues, reduced damage to adjacent healthy cells. Additionally, the combination of PTT with chemotherapy, immunotherapy, gene therapy, or imaging techniques has shown to produce synergistic therapeutic benefits in preclinical models of BCA metastasis. The efficiency, targeting specificity, and safety were significantly improved using nanotechnology and PTT-based methods, either alone or in combination with other treatments, by facilitating deep tissue penetration, and inducing immunogenic cell death	The combination of nanotechnology and PTT has potential to eliminate primary tumors and control or eradicate metastases	66–70
Nanoemulsions (NEs)	(a) 7,12-dimethylbenzanthracene (DMBA) was encapsulated into cyclophosphamide NEs. *In vivo,* breast organ of rats was treated with the developed encapsulated drug system. The results demonstrated remarkable tumor reduction; and surpassed the results of conventional lyophilized cyclophosphamide injection; and (b) these therapeutic results can be attributed to improved bioavailability, sustained release, and targeted intracellular delivery, and facilitated by the nano-carrier system	(a) The results signified a notable progress in utilizing nanocarrier systems for effective BCA treatment; and (b) the results confirmed the efficacy of NEs for drug delivery, offered a clinically viable approach to enhance cyclophosphamide effectiveness, while reduced systemic toxicity	44
Metallic NPs	Metallic NPs enhanced drug delivery to the tumor cells via penetration to the tumor cells, reduced systemic toxicity; improved target specificity with both active and passive therapies; and reduced adverse effect	Drug delivery by various metallic (Au, Ag, Cu) NPs enhanced the efficacy of treatment by destroying tumor cells	10,20
Polymer-lipid hybrid nanoparticles (PLHNPs)	Exemestane is an irreversible aromatase inhibitor for estrogen receptor-positive BCA therapy with a limit of both its oral bioavailability (<10%) and anti-breast cancer efficacy in free form. It was encapsulated in PLHNPs as a nanocarrier in the presence of an emulsifier/ stabilizer, alpha-tocopheryl polyethylene glycol succinate (TPGS). In the animal clinical model (Balb/c mice), the oral bioavailability, safety, and anti-BCA efficacy of exemestane were improved in the encapsulated system. The encapsulated exemestane in the hybrid nanocarrier showed significantly superior intestinal permeation in comparison to the free form. The oral bioavailability of the encapsulated exemestane in Wistar rat was at least 3.5 times greater than that of the conventional suspension. The results of the toxicity experiment suggested that the developed nanocarrier system was safe for oral administration. The exemestane-PLHNPs system represented much better anti-breast cancer activity in Balb/c mice, The tumor (in MCF-7 cells) inhibition rate was 62%, after 21 days of oral chemotherapy, whereas in the conventional exemestane suspension was 31%	The encapsulation of exemestane in PLHNPs can be a promising approach for oral chemotherapy of BCA	71,72

Ag, silver; Au, gold; BCA, breast cancer; Cu, copper; LNPs, lipid nanoparticles; NMs, nanomaterials; NPs, nanoparticles.

to serve as a foundation for diagnosis and treatment due to their distinctive properties that ensure enhanced efficacy and patient safety.[83] NPs occupy a crucial role in TNBCA therapy, particularly in advanced and metastatic stages, where conventional treatment regimens often fail to deliver satisfactory results. Exemestane drug was encapsulated in polymer-lipid hybrid nanoparticles. Alpha-tocopheryl polyethylene glycol succinate was used as an emulsifier/ stabilizer for polymer-lipid hybrid nanoparticles. Oral administration of the encapsulated drug to Balb/c mice was evaluated as a function of time course. Clinical experimental results demonstrated that DD was targeted to MCF-7 BCA cells. Tumor volume was significantly reduced after 21 days of treatment.[71]

Summary of findings in this study

A schematic of conventional findings versus innovative findings *in vitro* and clinical practice is presented in Figure 3.

Future perspectives

Traditional technologies with low efficacy result in inconvenience and difficulties for patients who suffer from BCA, whereas many potential benefits are expected from nanotechnology and NMs. Their major advantages are summarized in the conclusion section. Despite these benefits, NMs and NPs may induce potential toxicity

Table 6. The effects of major metallic nanocarriers for delivery of drugs to breast cancer cells

Item	General characteristics	Advantages	Remarks	References
Au NPs	Biocompatible; Stable structurally; Easy for surface modification; Possess adequate colloidal, optical, quantum, magnetic, mechanical, and electrical properties.; The high atomic number of Au provides advantages for diagnosis and (photothermal-, radio-) therapies	a) Effective in treating TNBCA; (b) Au NPs enhanced treatment efficacy by destroying tumor cells; (c) Au NPs-Rad6 conjugated system significantly inhibited TNBCA cells by inducing mitochondrial dysfunction and PARP-1 hyperactivation; The conjugated system exhibited cytotoxicity against all TNBCA cells. while preserving normal cells. However, the therapeutic effectiveness of the system is hindered by its low solubility. The chemically modified molecule improved its solubility and facilitated its conjugation and process of hydrolysis	Although preclinical and clinical data are promising for Au NPs, their clinical translation is restricted by toxicity signs in major organs (liver, kidneys and spleen)	10,13,48,63,76–79
Ag NPs	The high atomic number and high significant photon attenuation provide advantages for diagnosis and therapies	Ag NPs coated by ethyl cellulose inhibited tumor necrosis factor-α (TNF-α) in human BCA cell lines. The nano- formulations of ethyl cellulose- Ag NPs had an inhibitory effect on protein expression and cytokine messenger ribonucleic acid (mRNA). Ag NPs enhanced treatment efficacy by destroying tumor cells Ag NPs-ethyl cellulose were spherical with an average size of 150 ± 5.1 nm and a zeta-potential of −41.4 ± 0.98 mV		10,76,80
Cu NPs	Similar to Au NPs and Ag NPs, Cu NPs provide advantages for diagnosis and therapies. Cu NPs are bioactive agents	5-Fluorouracil encapsulated in β-Cyclodextrin-Cu NPs demonstrated anticancer activity against TNBCA (MDA-MB-231) cell lines. The encapsulation efficiency of 5-fluorouracil, into β-cyclodextrin-citrate-Cu NPs was 94%. The nanocarrier (β-cyclodextrin-citrate-Cu NPs) represents a low-toxicity and sustained-release drug delivery agent. The 5-fluorouracil-loaded nanocarrier released slowly		81
Magnetic Fe_3O_4 NPs	Fe_3O_4 NPs with various characteristics and properties can be a part of nanocarriers	Fe_3O_4-poly(N-isopropylacrylamide) grafted with chitosan was a nanocarrier for methotrexate as an anticancer drug. The nanocarrier exhibited 94% drug entrapment efficiency and 32% drug loading capacity for methotrexate as an anticancer drug. The nanocarrier enhanced antitumor activity against MCF7 BCA cell line compared to free form of methotrexate *in vitro* cytotoxicity assay. The highest methotrexate release was observed at 40 °C and pH 5.5. The conditions were similar to those of cancerous cells. The core-shell structure and size of final NPs were determined by transmission electron microscopy (TEM) as 85 nm		82

Ag, silver; Au, gold; Cu, copper; NMs, nanomaterials; NPs, nanoparticles; TNBCA, triple-negative breast cancer.

in humans. There exists a critical knowledge gap regarding their safety. The toxicity of NMs should be experimentally determined both *in vitro* and *in vivo.* The results can lead to the identification of safe dosage levels, a defined range of safety, and the potential risks linked to the application of certain nano-sized NMs. Thus, the range of safety for each component should be confirmed *in vitro* and in pre-clinical trials before clinical trials. Therefore, toxicity assessment, risk evaluation of NMs, and the migration of nano-sized materials into specific human organs are needed to ensure that these materials can be safely utilized in clinical practice. Additionally, there is a gap and a lack of knowledge regarding the potential interactions of NMs and NPs with each body organ.

Conclusions

This review focused on applications of nanotechnology and NMs in BCA, encompassing diagnosis and therapy. Nanotechnologies, nanocarriers, and nano-encapsulations versus their corresponding conventional counterparts for BCA diagnosis and therapy have been discussed. Studies conducted *in vitro* and *in vivo* have demonstrated that diagnosis and treatment using nanotechnologies, NMs, nanocarriers, and nano-encapsulation techniques were more effective than traditional technologies and bulk materials. The DD targeting BCA cells and the release of medications within the cancer cells can be substantially enhanced by reducing drug particle size. The anticancer efficacy of the free form of drugs was improved by their encapsulation in nanocarriers. The kinetic release of drugs to cancer cells over a longer duration compared to conventional technology resulted in superior efficacy. Various formulations of drugs into different nanocarriers [lipid NPs, NEs, polymeric NPs, polymer-lipid hybrid NPs, and metal-based (Au, Ag, Cu, Fe) NPs] enhanced their bioavailability and efficiency, overcoming the obstacles presented by their conventional forms. Clinical specialists have achieved enhanced outcomes in detection and monitoring of

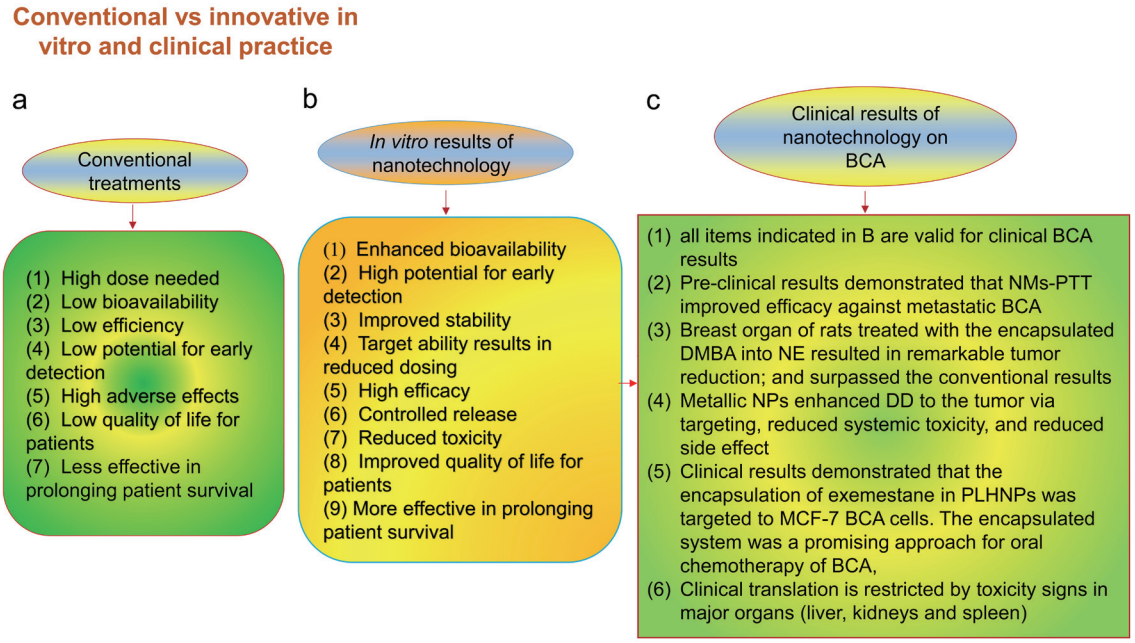

Fig. 3. A summary of conventional findings versus innovative findings *in vitro* and clinical practice. (a) Conventional treatments; (b) Innovative results *in vitro* using nanotechnology; (c) Clinical results on BCA using nanotechnology. BCA, breast cancer; DD, drug delivery; DMBA, 7,12-dimethylbenzanthracene; NEs, nanoemulsions; NMs, nanomaterials; PLHNPs, polymer-lipid hybrid nanoparticles; PTT, photothermal therapy.

BCA at various stages using nanotechnology and nanocarriers, ultimately leading to an improved quality of life for patients and more effective prolongation of patient survival. Based on *in vitro* and *in vivo* experimental results reported in this study, evidence suggests that TNBCA is more aggressive than other subtypes of BCA and occurs mostly in young women. Nanotechnology and nanocarriers are promising strategies for treating TNBCA using various therapies.

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Conflict of interest

The author declares that there are no conflicts of interest regarding the publication of this manuscript.

Author contributions

MRK is the sole author of the manuscript.

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