The applications of nano-medicine in the breast cancer therapy

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Abstract. Breast cancer (BC) is the commonest malignancy in women worldwide. Triple-negative breast cancer (TNBC) with three main-receptors which is estrogen-receptor, progesterone-receptor, and human-epidermal-growth factor receptor-2, Absent hormonal-receptor in cells of breast cancer familiar to expression an aggressive phenotypes as well as increasing the metastasis that leading to develop the resistance for chemotherapies. Different types of treatment and therapies currently can stop the spreading of BC and TNBC but with side-effects for healthy cells or tissues. Nanotechnologies present many unique efficient alternatives to designs and synthesis of small-size nanomaterial which target both active and passive and can be used to attached multi-targeting moiety by controlled cellular uptakes with a minimum amount of nanometric carriers. Which are able to carry drug, tracking-probes, and ligands, designing on same pathway, which specifically targets each cell of BC on sites. Indicating the targeted deliver-system by highly functional molecules with multi specificity, tracking, diagnosing, and treating emerge as theranostic-approach. Particularly, carbon nanomaterial such as fullerenes, nanotube and graphenes, is scientific interesting regarding the chemical functions, biological and physical characteristics. The latest scientific guide offers the possibility usage of carbon nanomaterial to be a therapeutically factors, Systematic agents to control drug releasing as well as contracting factors to diagnostic the tumor. producing new potentials to developing innovatively orders to detecting BC on the beginning and treatment period. In this review, we shed the light on traditional drugs therapy, unique therapy to providing the current nanotechnology applied for approaching metastatic BC treatment and diagnosing by using carbon nanomaterials.

Keywords: Nanotechnology, breast cancer, triple-negative-breast cancer, carbon, nanomaterial

1. Introduction

Cancers are the major cause of death and the main health problem globally [1, 2]. Cancers mean the uncontrollable-growth of cells and spreading. That can infect any part of the body while the cells accumulating to make the mutation [3, 4]. Growing can promote the genes at normal-cell and duplicate many times on cancer-cell and turn to unsteady gaining fatal character like its propagation [5].

Breast cancer is the commonest kind cancer type in females worldwide[6]. The international occurrence of BC is increment more than 25% before ten years ago. Closes to 1.6 million new patients with BC documented every year, reaching around 30% in whole cancers. Meanwhile, BC is a second lethal cause after lung-cancers, and in women, it constitutes the top-one cause of cancer mortality [7]. Breast cancer is a highly heterogeneous disease, that’s why it is completely complex-classification [8,9]. Recently, BC is often
the first classification according to the histopathologically type. Most BC cases are invasive-ductal carcinomas, followed by other subtypes that still make attentions towards aggression and occurrence on many patient sub populations [10]. The second major concerning is the tumor stage generally. The progression of the disease, primary tumor in the breast which is known as stage-1, then spreading to other tissue and lymph node that nearby stage-2, 3 and the distant organ distant-metastasis, stage-4.

BC can be classified according to the tumor-grades and molecular-subtype, involving luminal-A, luminal-B, HER-2 as well as triple-negative BC [8]. The tumor with high-grade but lack expression hormonal receptor is more aggressive and leads to metastasize [11,12]. Triple-negative-breast-cancer (TNBC) constitutes 22% of whole invasive-subtype of BC [13] characterization with absence of expressed an estrogen-receptors (ER), progesterone-receptor (PR) and human-epidermal-growth-factor-receptor type2(HER-2) in tumor cells membranous. According to the biologically networks-driven approaching, researchers have recognized six TNBC sub groups, while, others recognized four stable-TNBC sub groups regarding the mRNA expression as well as profiling DNA-genome [14]. The absence of hormonal receptors on TNBC throws out the interest of endocrine-therapies or treatments, and then mostly depends on chemotherapies [15]. Also the systematic chemotherapies with clinical approved drug reflected poor responses, highly-toxicity, and developing multi-drug resistant, in addition to the molecular-heterogeneity and high-risk of metastasizes [16]. To earlier therapeutically involvement, an accurate diagnostic is critical. Yet palpations, mammographic, ultrasonographic, ultrasounds, MRI, and IHC are preferable for TNBC diagnosis at clinical based. Whereas, inaccurately diagnostic when used nonspecific contrasted agent, false-positive results and exam-experience were limited and critical factors for validate TNBC diagnostic. Because of the therapeutic involvement is limited for surgeries, radiotherapy is using for cytotoxic chemotherapies by taxanes and anthracyclines. This limitation avoids improvement of a current availability diagnosis and therapies to explorer a novel method and approach [17]. Recent researches reported that the nanotechnology progress explorer biomedical sciences for cancer therapeutic due to a contrasted agent as well as drugs delivery carrier, it is really great emerged thing to studying sciences and engineering for their designs, creating, synthesizes, characterizing, manipulations, as well as applications, all these can occur among controlling the matters in nanoscales, which is the scales of atoms or molecules [18]. Presently, nanocarriers is known to be more accurate to the target and co-delivery for diagnosis and therapy agent. Availables of wide types of nanocarriers were made of polymers, lipids, nucleic acids, proteins, carbons, and metals included micelles, dendrimers, liposomes, nanoparticles-tubes, so as DNA-tetrahedral-pyramids [19]. Those bright Nano-particles encapsulated anti-tumors drugs (arsenals), and surfaces coating by specific-ligands (keys) which finally binding to the receptors (locks) expression in the breast cancer sites (targets) and destroying all cells and molecular-imaging (tracer-agents) allows for both diagnosis and treatment BC. In the last decade, the theranostic process is turning very clear to promote efficiently drug delivering orders that will be eligible to pass biological-barriers to deliver the correct amounts of drugs at a specific sites at a suitable time and eventually reducing the side-effect and upgrade therapeutic efficiently [20]. Because there is no FDA approved theranostic to TNBC, currently approach in conjugations and novel therapeutic-modules as yet essential at clinical order. Due to the therapeutical preferences of TNBC are restricted, applications of cancer immune-therapy are effective to treat different types of malignancies. To date, the FDA approved the atezolizumab as the first immunotherapeutic to treating TNBC. It worthily to explorer immunotherapeutic and performance studies for treating patients of TNBC by immunotherapy [21]. Carbon nanomaterials have unique chemical and biological characters. Different characters of carbon nano materials like size, shape, structure, and charging of the surfaces, chemical components, soluble property, can directly impact the interactional with bio-cells and molecules. The carbon nano-material produces specific forms of tumor-sites [22]. The prospect of highly efficient delivery carriers for drug and biomolecule within the cell is impressive [23].
2. Traditional diagnostic and therapeutic of BC and TNBC

Clinically order, radiological, and pathologically exam are the major diagnosis accession of breast cancer. More closely applying radiological-exam is mammographic by using x-rays, loss of abnormal featured on TNBC, and results for an incorrect diagnostic. To get over the mammographic limitation, Ultrasonographic represents high sensitivities >90% must be considered [24], otherwise, confined nicety of benign-tumor, enclose the usage to the TNBC detections. MRI is very sensitive and highly positivity prophetic amounts on TNBC diagnostic [25]. Precision for TNBC detections via radiologically exams needs practice and specialty to developing radiographic techniques and different new forms of benign and early-stages. The Immunohistochemical technique (IHC) and onco-pathologists are decisive on the clinical specification of TNBC. The IHC method of TNBC depends on the special characteristic of the absence of the hormonal-receptor (ER, PR and HER2) in tissue of patient [26]. After a convenient diagnostic of BC and consideration the other aspects of metastasis and drug-resistance, poorly prognosis as well as therapy interference were completed. Treating BC is the first way to avoid mastectomies in both BC and TNBC. The highly occurrence repetition even after radiation treating squeak patients to do mastectomy to radiotherapies [27]. Hormonal therapies may be effective in some BC subtypes but not applicable when there is a lacks in HER-2, ER, and PR receptors, herewith requires a chemotherapies treatment that is actually the mainstays for systemic treatment [28]. Anthracyclin and taxanes are the most common drugs used as a chemotherapeutic treatment for BC. While, the hereditary cytotoxic-effect and present non-targetable strategies of drugs direction needs to be determined by a novel technology. Frequent chemo-cycle with high dosage of cytotoxic-drug pull down the cancerous cells as well as healthy cells in the nearness. Avoidable of the incorrect targeted, the chemo-side effects as well, the nanotechnology based-on drugs delivering system are committed tools. Recently evolution of nanotechnologies and expression of diagnosis with therapies in the theranostic process as the co-delivery prescript, it is allowing specifically targeted cancer cells, in addition to ignoring the drug cytotoxicity to the other organs [29].

3. Nanotechnology progression for BC, TNBC Targeted-Theranostics

During nanoscience, developing the committed nanoparticles inheritance in many physiochemical, biologically or efficient properties of biomedical usage. The size is the first importance; nanoparticles desire size is about 1 to 200 nm, the modulation decides the dynamical pathway of particle that is decisive of nanomedicine formula. In advance, the key operator of the accurate target drug delivery is the charging surfaces and encapsulated capacities of the nanoparticles, which uses special conjugate ligands with targeted receptors at cancerous cells. Any other characteristics as the higher drugs loaded performance, long half-life on circulations and minimal systematic toxicity, selectively localized, high adherence at the tumorous environments, enhancement internalizing within tumors through endocytosis, sustaining and controlling releases of image-agent so as cytotoxicity of drugs with the period of time and to safe bio removal of the body is significant to nanoparticles to be like theranostic on diagnostic and therapeutic of cancers. Nano-delivering orders count on the enhancement permeations and retention impact for target drug deliver. Technically, the highly recovers and control drug loaded with released as well as financing stabilization of a large scales producing, while determines the successful and researches in cancer nano medicine. Whereas, applied to nano medicine in limits with BC and TNBC according to the absence of high expression of tumors targeted and ligand [30].

4. Standard treating of BC and possibility of implication nanomedicine

Presently, breast cancer patients who are newly diagnosed, predominating had taken multi-model treating which includes a standard model like surgery, drugs, and radiotherapies. As well as to optional
complement measuring between acupuncturists and dietary [32,33]. Firstly, the two models using mostly for eradication of the primary tumor and localize the tissue cancer. Drug therapeutic of BC mainly contains the hormonal therapies that used hormone or hormones like a drug for cancer cell proliferating suppression, chemotherapy that mostly depends on killing cancerous cells by cytotoxic complexes [32]. Recently, in both molecular-biology and immunotherapeutic, the target of therapy tailoring for special pathophysiologic of various types of breast cancer which increasing involved. That mainly includes drugs of small-molecules or monoclonal-Ab, which targets a specific molecular pathway, thereafter, cancer proliferating, progressing, spreading or drug resistant, may be blocked and controllable [33]. Trastuzumab (Herceptin) is a very famous therapeutic targeting, it humanizes anti HER2 monoclonal-Ab. To date, adjuvants drug therapeutics in general dependent on the essential subtype of breast cancer. The optional standard of drug therapeutically is shown in Table 1. Even the drug therapies can realize systemic treating, the present successful rate is perfectly sub-optimal. Many obstacles limit the efficiency [34,35] as shown in (Table2). The challenge in fact falls within 3-major classes. From 1-4, the cases derive from sub-optimal bio distributions in the drugs of the body, which is, very little drug of tumor-tissue (as sub-optimal activity) and very much on healthy-tissue (as highly toxic). From 5-7 relations to poor responses for the drugs although it reached the tumors, whereas, 8-9 correlated with attendant properties of the drugs and drug-combination. The nanomedicines have the possibility to get-over at a minimum of two of these restrictions. The ratio of largest surfaces zone: volume of nanocarriers providing the chance to manipulates these surfaces properties to amended treating, just like, cancers-targeting, circulation-extending, increasing-endocytosis and transcytosis, in addition to get more efficiently accesses in tumors site, metastatic site as well as cancer cells. While, via engaging with nanocarriers, the therapeutic-factors also can get more stabilization, increasing the solubility and control releasing kinetics. Drug-combination has also co-delivering to increase synergists and the additional impact of anticancer [31] using those advantages to tackles the restrictions of BC drug therapeutic. Many kinds of nanomaterials mostly using, for example: solid–lipids, liposomes, and polymers. The nanocarrier helps to improving the water-solubility for anticancer drugs, increasing the activity of drug delivering to tumor-site as well as enabling target-site to deliver of anticancer-drug. Besides these advantages, the nanocarriers also have some restrictions, that including toxic potency, immunogenic possibility, as well as excreting mechanisms. The nanomaterial advantages and restrictions on targeting cancer therapy and drug-delivery have been shown in (Table 3), [36].

Table 1. Molecular-subtype of BC related to their standard drug-therapeutic [69].

| Molecular-subtypes | another condition | Hormonal therapeutic | Chemotherapeutic | Anti/HER2 |
|--------------------|-------------------|----------------------|------------------|-----------|
| Luminal-A          | Lower tumor burdens | +                    | _                | _         |
|                    | Higher tumor burdens/ Grade-III | + | + | _ |
| Luminal-B          | HER2+ve           | +                    | +                | +         |
|                    | HER2−ve           | +                    | +                | _         |
| HER2+ve            | Not viable        | _                    | +                | +         |
| TNBC               | Not viable        | _                    | +                | +         |
Table 2. The key-challenge of BC- drug therapies in the way nanomedicines using to tackles that challenge [69].

| Challenge to BC drug-therapeutic                                      | Nanomedicine can assistant in                                                                                                                                 |
|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BC Insufficiency specificities                                      | Passively targeted or actively targeted via nanomedicines to increasing tumor-drug levels or decreasing noncancer-drug levels                                |
| Inefficiently accesses of a drug for metastasis sites (brain/bones) | Lots of nanomedicines formula innately can modulate brain/bone penetrations                                                                               |
| Unwanted pharmacokinetics (quickly clearances or short-half-life)   | Usage of the strategies (PEGlyation to extended circulation times)                                                                                         |
| Dosage limitation toxicities of anti-cancerous drug or excipient    | Increasing tumor specificities like above: controlling drug releases for nanocarrier, solvents, surface-free nanoformulation                              |
| or excipient (surfaces or organic-co-solvent)                       |                                                                                                                                                               |
| Drugs resistant in cellular-levels( increasing drug outflow         | Passively and actively target both can enhancing endocytosis and nanoformulation that inhibits drug outflow mechanism, co-deliveries of factors which targeted drug-resistant mechanism |
| transportation)                                                    |                                                                                                                                                               |
| Drug-resistant on tumor-microenvironments levels (low-pH, hypoxia,  | Target the tumor-microenvironments, using stimulation-reactive nanoformulation (pH responsively device)                                                      |
| cancer-microenvironments)                                           |                                                                                                                                                               |
| Difficult eradicable cancer-stem-cells                              | Targeted cancer-stem-cell                                                                                                                                     |
| Unwanted pharmaceutical characteristics of a drug (lower aqueous-  | Lots of nanocarriers may ascertain drugs solubility or may be protecting unstable drug                                                                       |
| solubility or poorly invivo stabilization)                          |                                                                                                                                                               |
| Suboptimal dosage table and sequences, chiefly after combine with   | Carefully optimizing of dosage time and sequences, using nanocarriers for co-delivery multiple-drugs                                                             |
| multiple-drugs involving                                             |                                                                                                                                                               |
Table 3. Advantages and disadvantages of various nanomaterials BC treating with clinically trials status [69].

| Nanocarriers               | Targeting drug therapeutic                                                                 | Clinically trial for BC treating                                                      |
|----------------------------|-------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| Solid-lipids nanoparticle  | Well-solubility/bio-availability according to organic makeups                             | Lower loaded drugs capacitae                                                          |
|                            | Best controlling of drugs releases kinetics                                                | Possible contains some colloidal structure and compounds physical-status               |
|                            |                                                                                           | Not viable                                                                              |
| Liposomes                  | Wide-range of drugs delivering usage                                                      | Cationic lipid causes toxic effects                                                   |
|                            | Able to increasing drug-loaded or minimizing unwanted activities of drugs                  | Rapidly degeneration of nanocarriers by mononuclear phagocytosis order                 |
|                            |                                                                                           | Liposomes-anamycin Phase I-II (anamycin on lipids structure of “Distearoyl-sn-glycero-3-phosphocholine”, istearoyl-sn-glycero-3-phospho-1’-rac-glycerol” and Tweeny for intravenously administrations) |
| Polymeric                  | Versatile in term of chemical structure                                                   | regression of the carriers                                                             |
|                            |                                                                                           | Nanoxel Phase-1 (paclitaxel on polymeric micelles)                                      |
| Magnetics-nanoparticles    | Affected by external magnetics area of guide therapeutic, images and drugs delivering     | Possibility of materials toxicity                                                      |
|                            |                                                                                           | Not viable                                                                              |
| Quantity-dots              | Fluorescence characteristics of images and drugs tracking                                  | Possibility of materials toxicity                                                      |
|                            |                                                                                           | Not viable                                                                              |
| Carbon-nanotubes           | can penetration or localization on cellular levels for delivering of chemotherapeutical and factor images | Possibility of materials toxicity                                                      |
|                            |                                                                                           | Not viable                                                                              |
5. Carbons-Nanomaterial

Interestingness the chemically and biologically characters of nanomaterials depends on the structure properties. There is different usage for several biomedical applicable [37], the developments of innovating orders for treating BC. There are many different nanomaterials synthesized and presently studying in biology, while, scientific communities are partially interesting in carbon nanomaterials because of its physical-characters, chemical-functions, as well as biocompatible [38]. Though the diamond and graphite features are widely analyzed, other allotropic shapes of carbon like fullerenes, carbon nanotube (CNT), or graphenes are recently interesting. The first carbon nano-structure is fullerenes which are spherical shaped and the third more stable carbon type after the diamond and graphite [39], carbon nanotubes discovered decades-ago but not surly assumed till the fullerene discovered [39] and theoretic study of probable similarly nanostructure. CNT has a geometrical structure that could be generated through graphite sheet. Graphene is known as a single-graphite-layer (bi-dimensional) of limited size, constitutes via carbon-atoms existing on vertices of a hexagonal nets. CNT structure formational can be conceptualizing as one layer of enveloped graphite (graphene), which results in a single wall CNT. Multiplied roll layers of graphene results on Multi-Wall-CNT (Figure 1). The diameters, internal-geometric, physico-chemical characteristic of CNT depends on the graphite-layers that in rolled (chirality-vectors-dependent) [40] (Figure 2). Presently, graphene is theorized as a structure based on allotropic types of carbon [28]. Regarding to the studies of carbon nanomaterial on BC, physico-chemical characteristics and special technique of synthesized the fullerenes, that aims to studying and treating cancers with the carbon nanomaterial (figure3), [23]. Different reports toward the applications on carbon nanomaterial for breast cancer diagnostic and therapeutic are performed.

Figure 1. allotropic forms of carbon [70].

Figure 2. the chirality vector [70].
Inside the body, chemotherapies and hormonal-therapies are the major treating plan for all cancers by destroying and controlling cells [41,42]. Drugs of chemotherapies can take intravenously and orally but they are not specifically for cancer-cell, so, different side-effect can occur through the treating period, including hair-loss, nausea, vomits, fatigue, as well as infectious development [43]. Anthracyclin (doxorubicin/epirubicin) and taxanes (paclitaxel/docetaxel) are the commonest drugs of chemotherapies [41]. About more than 65% of breast cancers patients receiving hormonal-therapeutic, that mentions the blockage of hormone, which promotes cancer cells growing, that’s known as pharmaceutical [42] like, estrogen (ER). This kind of therapeutic depends on biological-properties of cases and hormones-receptor positivity (ER+). Tamoxifen aromatase-inhibitors, and fulvestrant [41, 43] is the commonest pharmaceutical. Tamoxifen is the anti-estrogen, which is, a selective-estrogen receptor modulator (SERM) binding to an estrogen-receptors in BC cells, blockage the actions of thus hormone. Widely BC/ER+ is treating with Tamoxifen which efficient and testing among an initially as well as advanced-stages on all ages women [43]. With a big problem of association between tamoxifen and traditional-drugs for BC treating is the unfavorably soluble pharmacokinetic and limited bio-distribution. It could be avoiding these things by placement the drug or reducing the dose of the drug, concentrating on sites is not interested, in addition to the side-effects correlated to chemotherapies and hormonal therapies [44]. Regarding that, carbon nano-materials potentially usage to administrational drugs versus cancers and BC which is analyzing [45,46] it is considered like advantageously systematic for controlling drugs releases on the organism increasing an efficient treatment as well as reducing the toxicity [45, 47]. Carbon nano-materials come with few disadvantages involving the soluble lacking and lower reproductive rate during the chemical-function and structural-properties. Otherwise, using medicines in wide range tests according to the toxic potentials [47]. Carbon nano-materials possess the lowest solubility on biological-medias while there are on native-way or on not chemical-functionalize. In this way, nano-materials lack their molecular-aggregation (simples and complexes) which supply its specified activity. Insolubleness is very relevant to toxicological researches like excessively accumulations at traditional medicines within the biological circumstances, over the high stableness of enzymatic oxidations, hindered the eliminations for the bodies. Thereafter, increasing chemical functionalization of carbon nano-materials (fullerenes, CNT, graphene) favored solubilizing and reducing the toxic effects on the organisms, increase the viability of administrational and delivery of medicine [48, 49]. CNT is essentially in scientific interest regarding the chemical-stabilization, mechanical-resistance, highly electric and thermal-conductivities, higher surface zone, the tubule structures, and ability to cross among the endothelium membrane, and tumor-cells [47, 50]. Highly electric, thermo accessibility of surfaces of CNT allows drugs, nucleic acid, peptides and another molecules to attack to their walls. CNT is

Figure 3. The graphene sheet with chemotherapy [70].

6. Carbon nanomaterial applications in the treatment of BC and drug-releasing
considering as viably alternate for administrating and delivering drug. The chemical functionalize can increase the solubility of extremely insolubleness and hydrophobic-fullerenes. Instancing, cationic functionalizing fullerene has a settled solubility, has an ability to binding anionic-residue for cancer-cells that can be targeting and controlling drug delivering [51]. Graphenes are bi-dimensional carbon nano-materials characterizing by the simple synthesis [54]. It is readily functionalizing regarding the high surface zone and has highly electric and thermo-conductivity as well as highly flexible and mechanically resistant [52]. Recently researchers reported that graphenes are hardly nanomaterial that manipulates and synthesize on controllable pathway. While, in the case of biomedical-application, graphenes has lower toxicity than CNT and fullerene [53]. Lately, researches of nano-medicine concluding that fullerene, CNT, and graphen are favorable characteristics of the transport, target, and control delivery of chemotherapeutic drugs, taxol (paclitaxel), docetaxel (DTX), doxorubicin (DOX),[47,55]. The fullerenes system (C60/DTX) showed the ability to improve up to 4.2 times than bioavailability of DTX and decreasing DTX about 50%. In addition, C60/DTX order showing the effective control that releases more than 83% of DTX within/120hours. Otherwise, in-vitro cytotoxic method reveals that compared to the free-DTX, C60/DTX order exhibits significance increasing cytotoxic in the human BC cell-line [58]. Development of multifunctioning tumor targeted drugs delivering systems for an in vitro treating of BC-cells, meaning that hyaluronic-acid functionalize multi-walled carbon nanotubes (MWCNT) as drug-carriers, and transferrin like a target ligand with artemisinin as a drug, showing synergists antitumor effectiveness according to enhancing intracellular accumulates of artemisinin on cancer-cells and the simultaneously delivering of transferrin and artemisinin. Whereas, under-radiation, the nano-materials improved the inhibition against tumors. Otherwise, though experiment guide of the pharmacokinetic and toxic profile that is favorable when carbon nano material is functionalizing [51,57]. Carbon nanomaterials with biochemical properties which allowing them to cross among cell-membranes and releasing drugs on special tissues (Figure 4), [51, 56].

Figure 4. application of nano-particles in cancer research

7. **Cancer therapy with Metal nanoparticles**

In addition to the carbon nanomaterial above, metallic nanoparticles like gold (Au)- silver (Ag)-platinum (Pt)- zinc (Zn)- titanium dioxide (TiO2) and many other materials using on cancer medicines. Those nanoparticles can offer a widely chances in therapies and diagnosis method regarding the magnets, optical, thermal as well as electrical characteristics. Modifications on the surface through conjugating many groups in metal nanoparticles expanded the usefulness of desirable clinical-outcomes. Various metal nanoparticles using different molecular-mechanisms as an intracellular product of reactive-oxygen-species (ROS), increase oxidative stresses, and special apoptotic death of tumor cells [59]. Nanoparticles of
transitional classes of metal prompts hyperthermia (non-invasive assay) for heating cells, via killings tumor cells during the modification of electro-magnetic radiation to heat. Little metals nanoparticles have an inherence strong anticancer going on due to the uniquely physiochemical characteristics. Gold nanoparticles are mostly extensive investigation and favorable nanoparticles metal familiar for delivering paclitaxel, a well-known anti-cancerous drug. Gold nanoparticles prepared and synthesized on various forms and arrangement as gold-nanoshell, gold-nanorod and gold-nanocage are now growing like multilateral nanovehicles in cancer therapies [60]. Sera coated gold-nanorods with inherence ability to down-regulate a capacity generating relation to gene-expressions. By reducing the energy, cancer cells immigration are inhibited on each of the in vitro and in vivo. Some researchers [61] reported that inhibitor or suppressor of BC and TNBC tumors/metastasis can use a combination of cisplatin which load gold-nanorod and NIR-laser. As the radio-sensitized factor, gold-nanorod reacting with acidic-environments on a cancer cells, increasing oxidative stresses via ROS products that finally stimulate the damages and apoptosis. A silver nanoparticle is familiar because of its anti-proliferative, proapoptotic, as well as the anti-angiogenic effect of a cancer cells. Previous study [62] showed committing result of silver nanoparticle treatments following by radiotherapies in gliomas. Those nanoparticles showed the inhabitation of endothelium growth factor in cancer cells, which limit the metastasis. Zinc-oxide (ZnO) nanoparticles function as genotoxic-drug for cancer therapeutic. The Zinc-oxide nanoparticle shape micronucleus within tumor cells, that eventually boosts mitotic and inter-phase apoptosis passing of cells [63]. Asparaginase is the familiar anticancer-enzyme using like a chemotherapy factor on another cancer treating, so Zinc-oxide nanoparticles loading asparaginase, also increase the specification and stabilization whereas offered in collection with paclitaxel/daunorubicin [64]. Although, Zinc-oxide nanoparticles in collection with drug paclitaxel and cisplatin showing reduction of the toxic effect and increment the activity on BC cells [65]. Another nanoparticles metal is Copper (CuO) nanoparticles, iron-oxide(Fe2O3), silica, cerium-oxide and titanium-oxide are explored and used with BC diagnostic and therapy. Copper-oxide nanoparticles are describing as green nanoparticles because of the synthesizing in Ficus religious and Acalypha-indica[66]. Double-modal therapy employs photo-dermal and radio-therapeutic with copper-sulfide (CuS) nanoparticles that showing the suppressor of a tumor growing on sub cutaneous BC sample and prolong the survival of mice firmness BC tumors. In vitro human BC cells with BC HER2+ are targeting specifically via antiHER2/Ab conjugate to silica-gold nanoshell on photothermal therapeutic. Cerium oxide(CNP) nanoparticles acting like radiosensitizing factor therapeutic which increasing an oxidative-stress and apoptotic tumor cells passing via follows biologically mechanisms for DNA-damage [67]. Likewise, cerium oxide nanoparticles complement the traditional chemotherapies via chemotherapy-deliver-drug that providing intelligent approaches to cancer therapies. While, platinum and titanium nanoparticles are a promising nominees nano carrier to cancer photodynamic therapies. Iron oxide nanoparticles explorer a magnetic characteristic of exacts diagnostic and therapeutic of SCC in mice models [68].

8. Conclusion

For more biological understanding of breast cancers, recent nanomedicine usage for treating breast cancer is applied. Previous discussion used, new protocols and many products entered the clinical-phase successfully. The current study, designs, creates, synthesizes, as well as applications for carbon nanomaterials are featuring technologically with hopeful applications on biomedicines, in particular for breast cancer diagnosis, detections and treatment. Until now, no carbon nanomaterial presenting completely the eligible stamps for treating usage in human. In addition, more researches are needed to avoid the side-effect potency. Actually, studying toxicology and biomedicine usage of carbon nanomaterial tends increase;
still these studies are indecisive for applications in humans. Some studies found the human part potential contributing to future applications at nanotechnology assistance resolutions for breast cancer treatment. Control the spreading and repetition of BC as well as reduce the toxicity of traditional treatment.

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