

Nanotechnology: Modern Advances for the delivery of Anti-Cancer drugs in the treatment of Breast Cancer

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Abstract: Now a days, one of the most common type of cancer is breast cancer which can be mostly seen high natality rate in women worldwide. There are many types of treatment option for most cancers i.e., surgery, chemotherapy and radiology but most efficient and effective treatment is done by using nanotechnology. The centre of attention in this review is on various nanoparticles such as liposomes, polymeric nanoparticles, solid lipid nanoparticles as well as their applications in the treatment of breast cancer. In recent studies nanotechnology has been developed and having advance methods have been applied for the treatment various types of cancer. Currently this nanotechnology plays a vital role in the targeted drug delivery for the treatment of cancer. This nanoparticles mostly plays on tumors and involves the sustained release of drug to precise on particular sites so far it will improves the therapeutic efficiency of the relevant drug and decreases the toxicity in the particular site of tissues or organs and turn them into normal condition by activate the immune cells against the tumours. So these nanoparticles are promising advance tool for the cancer research & treatment.

Keywords: Breast cancer - Anti cancer drugs – Nanoparticles - Drug delivery – Advance method- Immune cells.

❖ INTRODUCTION :

People around the world mostly suffering from many types of cancer but the most efficient type of cancer is breast cancer. So in simple words one of the leading causes of natality rate in world wide is cancer which can be defined as a disease that set about when there is a uncontrollable growth in normal cells . It may develops in any site of body parts either lungs, breast or liver or tissue region .The WHO predicted that cancer will be burden as it increase day by day to 23.6 million annually.Thus the cancer treatment has become most prominent issue over the past several years. But one of the most hectic type of cancer is breast cancer globally. This kind of breast cancer is due to on the basis of particular type of overgrowth of receptors present on the cancer cell membrane including progesterone & estrogen hormone receptors and HER2 receptors. If the PR-ER-HER2 shows positive breast cancer it can be said to have triple positive breast cancer. In Europe alone, ferlay et al. recently estimated that 1.7 million cancer deaths occurred and 3.2 million cancer cases were diagnosed .So the triple negative breast cancer can be determined by having neither PR/ER positivity nor HER2 positive. This has been reported that the primary cause for natality rate due to breast cancer is the result of its own potential metastasis to distant organs viz., liver ,lungs, lymph nodes, bones and brain.(carty et al.1995; grobmyer et al 2012)

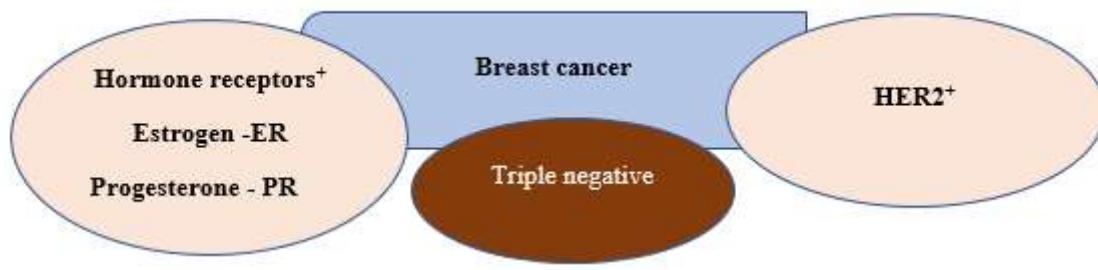
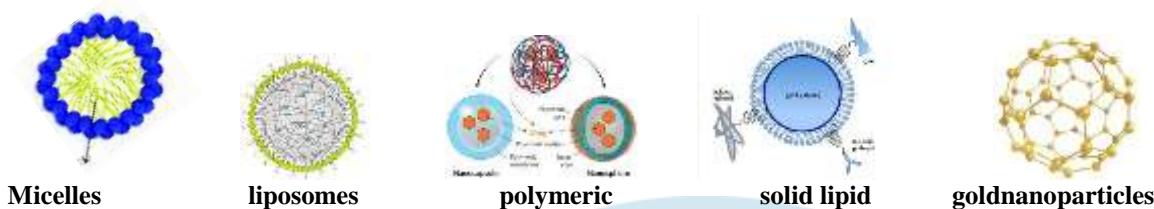


Fig.1 classification of breast cancer based on receptors

Breast cancer is the most malignancy in women and this is the second leading cause of cancer related deaths among women and a brief account of the clinical development of inhibitors of poly(ADP-RIBOSE) POLYMERASE,CYCLINE dependent kinases 4 and 6 phosphatidylinositol 3 kinase target of rapamycin pathway. Four major molecular subtypes viz., (i) luminal A [HR⁺/HER2⁻] ; (ii) HER2⁺ ; (iii) luminal B [HR⁺/HER2+] ; (iv) Triple negative [TNBC ; HR-/HER2-] also overlap with the basal like subtype. Nanotechnology has been broadly used over last decades however the nanoparticle drug delivery is believed as a promising tool for the delivery of drugs in cancer treatment due to its high loading capacity, efficacy, reduced toxicity and tolerability of drug loaded nanoparticles compared to standard chemotherapy drugs.The anti-cancer drugs loaded in nanoparticles can be widely used to actively or else passively to delivered the drugs near the site of tumors during breast cancer treatments (singh et al.2017).This review mostly focuses on the ability of nanoparticles while inject near the site of tumors in the treatment of breast cancer.

❖ Various types of nanoparticles have been used in the treatment of breast cancer :

In brief, nanotechnology has widely developed to show their activity during the cancer treatment and it plays a vital role in the treatment strategies however some of the nanoparticles are used in the treatment of breast cancer viz., liposomes, micelles, polymeric nanoparticles, Solid Lipid nanoparticles & gold nanoparticles.



❖ **Micelles :**

Micelles are colloidal particles, size around 10-100 nm which are currently under investigation as carriers for hydrophobic drugs in anti-cancer therapy and this micelles consists of two distinct regions hydrophilic head group and hydrophobic tail. The unique advantages of micelles are prolonged blood circulation flow, low toxicity & enhanced tumour aggregation. Many cancer drugs are encapsulated in micelles for insertion of drugs into breast cancer cells. For the first time, Batrakova et al. denoted that the exposure of cells to pluronic P85 resulted in a substantial decrease in ATP level selectivity in multidrug resistant (MDR) [Batrakova et al. 2001]



Fig 2. Schematic diagram of micelles

Anti-cancer drug	Results	References
Dasatinib	Dasatinib micelle exhibited 1.35 fold increase invitro cytotoxicity against triple negative human breast cancer cell line (MDA-MB-231)	Sabra et al. (2019)
Paclitaxel/cisplatin	This micelles showed more active than either of the single drug IC ₅₀ of cisplatin micelle was about 0.25µg/mL	Wan et al. (2019)
Docetaxel	The therapeutic effects of docetaxel could be enhanced by micelle formulation which were 205.	Kutty and feng (2013)
Doxorubicin	The IC ₅₀ value were found to be 0.13 µg/ML for encapsulated doxorubicin.	Rosch et al. (2019)

Tab.1 Anti-cancer drug delivery in Breast cancer by micelles

❖ **Liposomes :**

Liposome based chemotherapeutics used in the treatment of breast cancer. Liposomal preparation composed of relatively high phase transition temperature phospholipid hydrogenated soy phosphatidylcholine (HSPC) and cholesterol resulting in a stable DDS with enhanced bilayer rigidity. A paclitaxel nanoliposome formulation was prepared using phosphatidylcholine and cholesterol, the cytotoxicity of this liposome was evaluated in MCF-7 breast cancer cells.



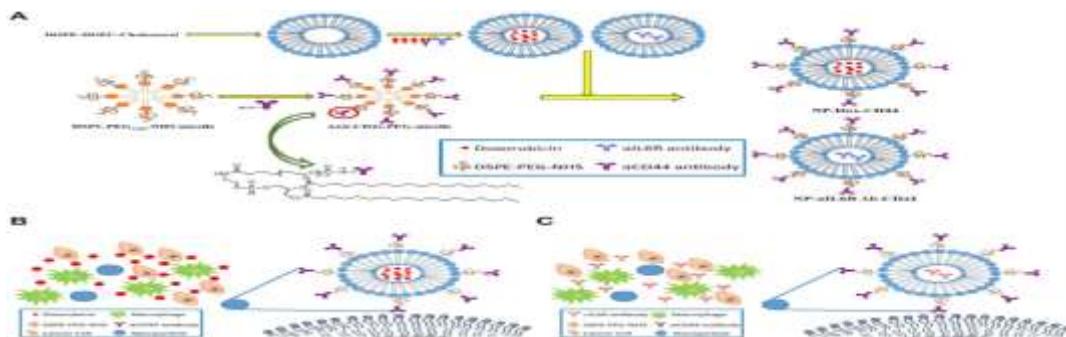


Fig.3 Schematic diagram of liposomes

Anti-cancer drug	Results	References
Doxorubicin	The liposome nanoparticle of doxorubicin provided 1500- fold higher plasma and 20 fold higher intracranial tumor.	Anders et al. (2013)
Paclitaxel	Liposomes were more cytotoxic to the 4T1 breast cancer cell than the free and co-encapsulated of two drugs in liposomes .	Franco et al. (2019)
Quercetin	Liposomes formulation were physically stable and enhance quercetin solubility.	Wong and chiu (2010)

Tab.2 Anti-cancer drug delivery in Breast cancer by Liposomes

❖ Polymeric Nanoparticles :

Polymeric nanoparticles are solid colloidal system, particle size less than 200 nm in which Anti-cancer drugs are dissolved, entrapped, encapsulated or adsorbed into the composition of the polymer matrix (joshi et al. 2015). To enhance the solubility and bio-availability of psoralen which is a promising anticancer drug that is limited by its poor aqueous solubility and bio-availability. Polymeric nanoparticles containing tamoxifen nanoparticles and in vivo biodistribution was evaluated in NU/NU (Shenoy and Amiji)

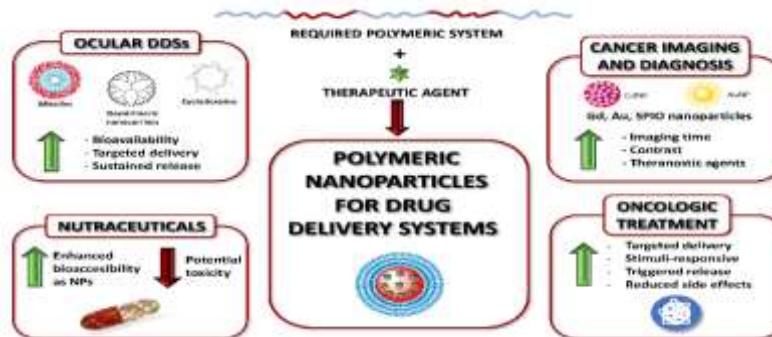


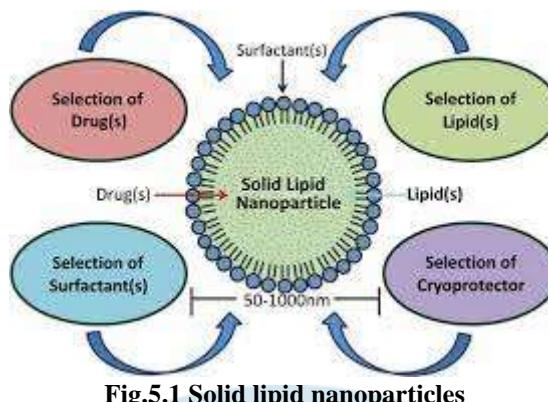
Fig.4 schematic diagram of polymeric nanoparticles

Anti-cancer drug	Results	References
Psoralen	The tumor weight after administration of psoralen polymeric nanoparticles(<1g) indicates decreasing with control group(~4g)	Du et al.(2019)
Tamoxifen	Nanoparticles exhibited significantly increased drug aggregation levels within tumors.	Shenoy and amiji (2005)

Tab.3 Anti-cancer drug delivery in Breast cancer by polymeric nanoparticle

❖ Solid lipid Nanoparticles :

Solid lipid nanoparticles are composed of lipids, emulsifier and water/solvent. They are a novel drug delivery system and a novel formulation. The most common ingredients used to formulate SLNs are solid lipid(s), surfactants/co-surfactant(s) or emulsifier/co emulsifier(s), solvents or co-solvents and active ingredients. The selection of emulsifier depends on the type and route of delivery. The SLNs accumulation can be reduced by inclusion of cryoprotectants and facilitates to redisperse freeze dried nanoparticles.



Guney Eskiler et al. made tamoxifen SLNs using stearic acid and tween 80 to evaluated the SLNs in MCf-7 tam resistant breast cancer cells .The addition of 2-hydroxypropyl- β -cyclodextrin in SLNs for improving the bioavailability, cellular uptake and anti-cancer activity of paclitaxel in MCF-7 breast cancer cells via modification of the paclitaxel (cho et al.2015).

Anticancer drugs	Results	References
Tamoxifen	The maximum cytotoxicity against R<-> Cells was 72.6 % whereas the highest cytotoxicity on R cells was 81.8%.	Guney Eskiler et al. (2018)
Doxorubicin	This type of SLNs reduced cytotoxicity, arrested cell cycle progression in the G2/M stage and persuade more apoptosis in MCF-7 cells at a low dose compared to the control.	Kang et al.(2010)
Paclitaxel	Paclitaxel SLNs showed remarkably enhanced anticancer activity in MCF-7/ADR compared to paclitaxel delivered in dimethyl sulfoxide.	Xu et al. (2018)

Tab.4 Anti-cancer drug delivery in Breast cancer by solid lipid nanoparticles.

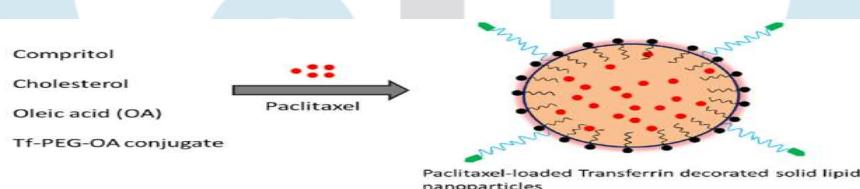


Fig. 5.2 schematic diagram of solid lipid nanoparticles

❖ Gold Nanoparticles :

Gold nanoparticles are developed by a synthetic method for creating AuNPs in 1951 by tending hydrogen tetra-chloroaurate with citric acid in boiling water where the citrate acts as both reducing and stabilizing agent.This nanoparticles are in wine red colour and are inert,non-toxic contains a gold core which are below 150 nm in size.

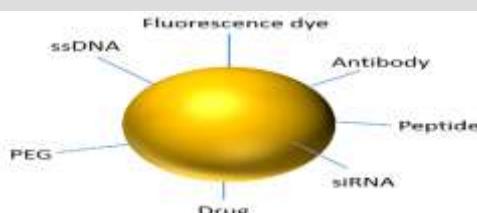
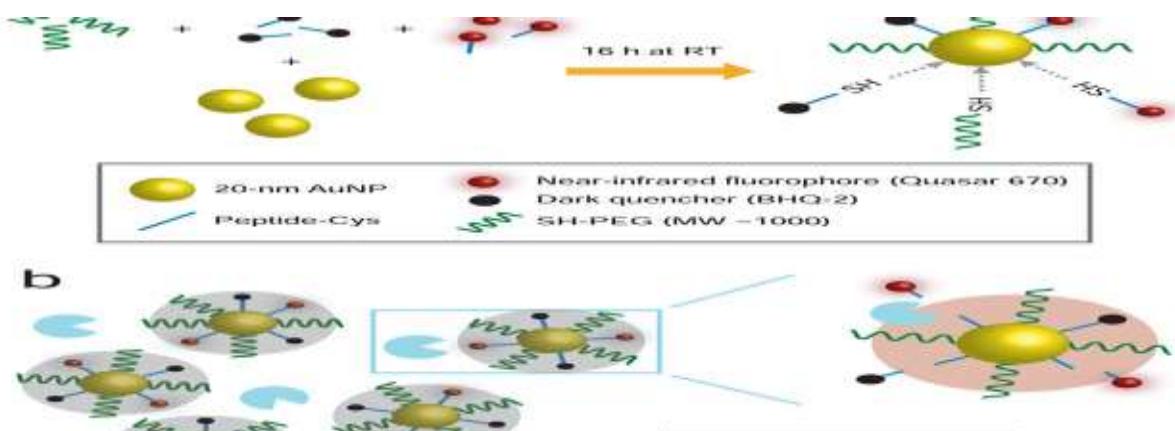


Fig.6.1 Gold nanoparticles

These nanoparticles were prepared and functionalized with a mixed monolayer of a zinc phthalocyanine and a lactose derivatives .(Gracia calavia et al. 2018). At a lower pH , the release of chloro-quine from gold nanoparticles are suggested that the lysosomal uptake of chloro-quine will shows the cytotoxicity of nanoparticles in MCF-7 breast cancer cells which depends mostly on concentration.(Joshi et al.2012), However the anticancer activity towards MCF-7 breast cancer cells increased .

Anticancer drugs	Results	References
Chloro-quine	This gold particles exhibits the concentration dependent cytotoxicity in MCF-7 breast cancer .	Joshi et al.(2012)
Docetaxel	This gold nanoparticles were found to be 2.5 fold more efficient than docetaxel alone against MCF -7 .	Fracois et al.(2011)

Tab.5 Anti-cancer drug delivery in Breast cancer by gold particles

**Fig 6.2 Schematic diagram of gold nanoparticles**

❖ Conclusion :

At present, this nanotechnology is widely used. The nanoparticle research also widely increased for the treatment of breast cancer and has been priorly focused on using targeted ligands so far to achieve high accumulation with the tumors. This plays a best and vital role as cell surface receptor on breast cancer cells and HER2 receptor which can be moderately used as an effective target for traditional anticancer drugs such as paclitaxel, docetaxel and doxorubicin. The preparation of nanoparticles mostly by using targeting ligands and this can be based on their treatment efficiency and to avoid toxicity in normal cells. Finally these nanoparticles are promising tools for the treatment of various types of cancer around the world.

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