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REVOLUTIONIZING BREAST CANCER THERAPY: NANOCARRIERS CUTTING-EDGE ROLE AND PROGRESS

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Abstract : Breast cancer is a pervasive and unfortunately, one of the deadliest cancers affecting women globally, second only to lung cancer. However, there has been a notable improvement in survival rates, especially among younger female patients. The progress in cancer treatment has been significantly influenced by the development of advanced nanomaterials and nanocarriers. One breakthrough in cancer research involves the creation of nanoparticles tailored to target metastasized breast cancer. These nanoparticles possess distinct characteristics, such as their small size and unique coating, which enable more effective drug delivery. Particularly, they enhance the distribution of hydrophobic anticancer drugs to specific locations within the body while evading the body's natural defense mechanisms, a process known as opsonization. This review delves into recent approaches and developments in the realm of breast cancer treatment. It covers various types of nanoparticles designed for targeting metastasized breast cancer, shedding light on the promising advancements in drug delivery. Furthermore, the review explores the different causes of breast cancer and discusses therapeutic approaches. By examining conventional therapies in-depth, the goal is to provide breast cancer patients with more reliable and effective treatment options. Overall, the focus is on presenting a comprehensive understanding of the current landscape of breast cancer treatment, incorporating the latest innovations and therapeutic findings.

Key words: Breast cancer, Nanomaterials and Nanocarriers

I.INTRODUCTION

Breast cancer is characterized by the development of malignant tumors in breast tissue, predominantly originating from the lobules that supply milk ducts or the inner lining of these ducts. It represents a widespread malignancy affecting a significant number of women globally, with an annual incidence ranging between 2 to 2.5 million cases. The gravity of the situation is underscored by the fact that in 2018 alone, an estimated 627,000 women lost their lives to breast cancer worldwide. This prevalence is starkly evident in the United States, where one out of every eight women is projected to face invasive breast cancer during their lifetime, and an anticipated 280,000 new cases are expected to be reported in 2020.The impact of breast cancer is not confined to the Western world; the World Health Organization (WHO) estimates that 170,000 women in India are poised to receive a breast cancer diagnosis, representing 14% of the country's total cancer cases. Globally, breast cancer stands out as the most common cancer among women, contributing to over 2.05 million new cases in 2018 and securing its position as the second most prevalent cancer overall according to GLOBOCAN.A myriad of risk factors is associated with the development of breast cancer, encompassing environmental and lifestyle elements, gender (with a 100% likelihood in females compared to males), genetic predisposition, advancing age, familial history, hormonal influences, and factors such as early breast development, menstrual frequency, and age at menopause. Despite considerable strides in research and medical advancements, the repertoire of available treatments for breast cancer remains relatively limited. Surgical interventions, including mastectomy and lumpectomy, radiation therapy, chemotherapy, and immunotherapy stand as the primary options. However, challenges leading to treatment failures persist, rooted in pharmacologic complexities, toxicological issues, and the emergence of drug-resistant strains. In the pursuit of more effective treatment modalities, nanotechnology emerges as a promising avenue. Defined by the American Society for Testing and Materials (ASTM), nanotechnology involves manipulating systems and devices at the nanometric range (1 to 100 nm) in two or three dimensions. Within the context of breast cancer treatment, nanotechnology unfolds through the utilization of nanocarriers and nanomaterials. Nanocarriers play a pivotal role in improving drug delivery efficacy by augmenting the therapeutic index and concentrations of drugs specifically within tumor tissues. Their contribution extends to offering superior pharmacokinetic features, such as prolonged blood circulation time, enhanced cellular uptake, increased volume of distribution, and prolonged half-life. These attributes collectively contribute to establishing an improved therapeutic window, thereby enhancing the potential for clinical success in the treatment of breast cancer.

II. CAUSES

Understanding the origins or causes (etiology) of this disease, referring to breast cancer based on the context provided, is a complex task due to three key factors:

i)Function of Childbearing

The link between childbearing and the risk of breast cancer has been a topic of investigation for many years. Historical observations have revealed a notable connection between childbirth and breast cancer risk, evident in the higher rates among nuns, who typically do not have children, and the comparatively lower rates among married women as opposed to single women. The prevailing understanding is that the act of having children itself appears to confer a protective effect against breast cancer. This observation aligns with the concept of parity, where a higher number of childbirths is associated with a reduced risk of breast cancer. Married women, who often have more opportunities for childbearing, exhibit lower rates of breast cancer compared to their single counterparts, supporting the idea that the experience of pregnancy and childbirth may have a mitigating effect on breast cancer risk. Additionally, the practice of breastfeeding has been considered as a potential factor influencing breast cancer risk. Regions where extended breastfeeding is common demonstrate lower rates of breast cancer, suggesting a potential preventive effect associated with nursing. Conversely, in the Western world, where breastfeeding rates have sometimes declined, higher rates of breast cancer have been observed. This observation has led to the hypothesis that the duration and intensity of breastfeeding may play a role in modulating breast cancer risk. The intricate relationship between childbearing, breastfeeding practices, and breast cancer risk highlights the complex interplay between reproductive factors and the development of breast cancer. While the protective effects of having children and breastfeeding are acknowledged, ongoing research aims to unravel the precise mechanisms behind these associations. This deeper understanding contributes to the knowledge of factors influencing breast cancer risk and may inform preventive strategies and interventions for at-risk populations.

ii) Breast conditions

Breast density, as identified through mammography, stands out as a significant determinant of breast cancer risk. Studies indicate a strong connection, revealing that women with breast densities exceeding 75% are four times more likely to develop breast cancer compared to those with lower breast density. The relevance of this correlation is highlighted by the central role of mammography in breast cancer screening. Mammograms provide a visual assessment of breast density by gauging the ratio of glandular and connective tissue to fatty tissue. Higher percentages of breast density signify an increased presence of these non-fatty components, linking them to an elevated risk of breast cancer. Understanding the impact of heightened breast density on breast cancer risk has implications for tailoring more precise screening and prevention approaches. Integrating breast density evaluations into routine screening procedures enables a more nuanced evaluation of individual risk profiles, empowering healthcare professionals to offer personalized guidance and interventions. Ultimately, this awareness has the potential to refine early detection strategies and preventive measures, optimizing the management of breast cancer risk in women.

iii)International Variance in Risks, Especially Age-Specific Risks

Age plays a crucial role in determining the risk of female breast cancer, as highlighted by research conducted by Newcomb and Wernli. The study underscores that postmenopausal women exhibit the highest degree of increased susceptibility to breast cancer. Moreover, this risk follows a distinctive pattern, doubling at each successive decade until reaching the age of 80. The observed connection between age and breast cancer risk underscores the necessity of accounting for life stages when evaluating the likelihood of developing the disease. The heightened risk in postmenopausal women suggests a complex interplay of hormonal shifts and other age-related factors contributing to breast cancer development. The progressive doubling of risk with each decade underscores the cumulative impact of age on breast cancer vulnerability, emphasizing the importance of age-specific considerations in both preventive measures and screening strategies. Grasping the intricate relationship between age and breast cancer risk is pivotal for tailoring effective interventions and healthcare approaches that address the unique needs of women at different phases of life.

III. OTHER RISK FACTORS

i) Physical activity

Physical activity has been identified as a protective factor against breast cancer in postmenopausal women, but the evidence supporting this protective effect in premenopausal women remains inconclusive. Studies suggest that engaging in regular physical activity may contribute to a reduced risk of breast cancer in women after menopause. However, the relationship between physical activity and breast cancer risk in premenopausal women lacks sufficient substantiation. The observed protective effect in postmenopausal women is thought to be linked to the potential influence of physical activity on hormonal and metabolic factors associated with breast cancer development. Regular exercise is believed to contribute to hormonal balance and weight management, both of which play roles in the postmenopausal breast cancer risk equation. Furthermore, the significance of physical activity in the context of breast cancer mortality is underscored by predictions that 10% of breast cancer-related deaths can be attributed to physical inactivity. This highlights the potential impact of sedentary lifestyles on disease outcomes, emphasizing the importance of promoting physical activity as a crucial component of breast cancer prevention and overall health.

ii) Alcohol

The International Agency for Research on Cancer (IARC) has reached a significant conclusion regarding the association between alcohol use and breast cancer. According to their findings, alcohol consumption is identified as a causal factor in approximately 5.0% of breast cancer-related fatalities. This conclusion underscores the substantial impact of alcohol use on breast cancer mortality, highlighting the role of lifestyle choices in influencing disease outcomes. The link between alcohol consumption and breast cancer has been established through epidemiological research, with evidence suggesting that even moderate alcohol intake can contribute to an increased risk of developing breast cancer. The 5.0% estimate emphasizes the proportion of breast cancer-related deaths that

can be attributed to alcohol use, shedding light on the preventable nature of a certain percentage of breast cancer cases. It also serves as a critical piece of information for public health initiatives and awareness campaigns, emphasizing the importance of alcohol moderation as a measure to reduce breast cancer risk and associated fatalities. In essence, the IARC's conclusion regarding the contribution of alcohol use to breast cancer-related fatalities provides valuable insights into the modifiable factors influencing breast cancer outcomes. It reinforces the need for public health interventions aimed at promoting awareness about the impact of alcohol consumption on breast health and encouraging responsible drinking behaviors to reduce the associated risks.

iii) Diet

Research has consistently pointed to a connection between a high-fat diet and an elevated risk of developing breast cancer, particularly in postmenopausal women. This association underscores the potential impact of dietary choices on breast cancer susceptibility. High-fat diets are often characterized by an increased intake of saturated fats, which are commonly found in animal products such as red meat and full-fat dairy. These dietary patterns can contribute to weight gain and obesity, and excess body fat has been identified as a risk factor for breast cancer, especially after menopause. The mechanism behind the heightened risk is multifaceted. Adipose tissue, or fat cells, is capable of producing estrogen. After menopause, when the ovaries produce less estrogen, the hormone is still generated in fat tissue. Elevated levels of estrogen have been linked to an increased risk of hormone receptor-positive breast cancers, which are more common in postmenopausal women. Furthermore, high-fat diets may influence the insulin-like growth factor (IGF) pathway, which plays a role in cell growth and proliferation. Dysregulation of this pathway has been associated with an increased risk of breast cancer. It's crucial to note that while the link between a high-fat diet and breast cancer risk is more evident in postmenopausal women, the relationship is complex, and additional factors such as genetics, overall dietary patterns, and lifestyle choices contribute to an individual's overall risk profile. Nonetheless, dietary modifications, including reducing the intake of saturated fats and promoting a balanced and healthy diet, can be a part of comprehensive preventive strategies against breast cancer, particularly in postmenopausal women.

iv) Stress

The belief that stress may play a role in the progression of breast cancer is a common assumption among many patients and survivors. There is a growing recognition of the mind-body connection in the context of cancer, with a positive outlook and psychological well-being being considered important factors in influencing health outcomes. An optimistic outlook is often viewed as crucial in preventing cancer recurrence. Numerous studies and anecdotal evidence suggest that maintaining a positive mindset can contribute to overall well-being and potentially influence the course of the disease. This positive approach is often reflected in the choices made by breast cancer patients and survivors, with many opting to engage in activities and practices that promote relaxation and emotional balance. Participation in retreats, yoga, and meditation are examples of such activities. Retreats offer individuals an opportunity to step away from the stresses of daily life, providing a supportive environment for emotional healing and reflection. Yoga and meditation, on the other hand, are practices known for their stress-relieving and mindfulness-promoting benefits. Engaging in these activities can not only alleviate the psychological burden associated with a cancer diagnosis but may also contribute to a sense of empowerment and control over one's well-being. While the exact role of stress in cancer progression remains a complex and evolving area of research, the emphasis on psychological well-being and positive lifestyle choices is increasingly recognized as a valuable component of comprehensive cancer care. It is essential to note that individual responses to stress and coping mechanisms can vary, and what works for one person may not be the same for another. Nevertheless, the integration of practices that foster a positive outlook and emotional resilience is an integral aspect of the holistic approach to supporting breast cancer patients and survivors.

v) Hormones

The intricate involvement of sex hormones in the etiology of breast cancer is a well-established aspect of breast cancer research. The interplay between endogenous hormones, which are naturally produced within the body, and exogenous hormones, those introduced from external sources, significantly contributes to the initiation and progression of breast cancer.

Endogenous Hormones:

Estrogen:

Role in Normal Breast Development: Estrogen, a key endogenous sex hormone, plays a pivotal role in the normal development and functioning of the breast tissue. It stimulates the growth and differentiation of breast cells.

Lifetime Exposure: Prolonged exposure to estrogen over a woman's lifetime, due to factors such as early onset of menstruation and late menopause, is associated with an increased risk of breast cancer. This is because estrogen promotes cell proliferation, and extended exposure heightens the chances of genetic mutations leading to cancer.

Progesterone:

Influence on Breast Tissue: Progesterone, another endogenous sex hormone, influences the breast tissue in coordination with estrogen. Its role in the menstrual cycle and pregnancy affects the dynamics of breast cell growth and differentiation.

Hormone Replacement Therapy (HRT): Postmenopausal women undergoing hormone replacement therapy (HRT) that includes both estrogen and progesterone have been found to face an elevated risk of breast cancer.

Exogenous Hormones:

HRT and Breast Cancer Risk: Exogenous hormones, introduced through therapies like HRT after menopause, can significantly impact breast cancer risk. Long-term use of combined HRI, which includes both estrogen and progesterone, has been associated with an increased risk of breast cancer.

Oral Contraceptives:

Impact of Birth Control Pills: The use of oral contraceptives, a form of exogenous hormones, has been a subject of study in relation to breast cancer risk. While the association is generally modest, some research suggests a slight increase in breast cancer risk among women using oral contraceptives.

Understanding the role of sex hormones in breast cancer etiology is essential for several reasons. It guides risk assessment for individuals, informs decisions regarding hormonal therapies and contraceptives, and emphasizes the importance of lifestyle factors that can modulate hormonal influences. This nuanced understanding contributes to the development of personalized prevention and treatment strategies in the context of breast cancer.

IV. SYMPTOMS OBSERVED IN BREAST CANCER

- Breast lump Nipple abnormalities
- Axillary lump Breast ulceration
- Breathlessness
- Breast rash
- Neck lump or lymph node abnormalities
- Other breast abnormalities: Chest pain
- Fatigue or weakness
- Weight Loss

V. STAGES OF DEVELOPMENT OF THE CANCER

The following stages of breast cancer can be found.

Stage 0:

Ductal Carcinoma *In Situ* (DCIS):

Description:

Aberrant cells are found in the breast duct's lining, but they have not invaded surrounding tissues.

It is non invasive.

Spread: The unusual cells have not extended beyond the breast duct.

Lobular Carcinoma In Situ (LCIS):

Description:

Aberrant cells are present in the breast's lobules but are noninvasive.

Risk Increase: While not invasive, the presence of aberrant cells increases the risk of developing invasive breast cancer.

Nipple Paget Disease:

Description: Aberrant cells are found only in the nipple.

Spread: Limited to the nipple area.

Stage I:

Stage la:

Tumor Size: Tumors are less than 2 cm in diameter and are confined to the breast.

Lymph Nodes: No involvement of lymph nodes.

Stage Ib:

Tumor Size: Tumors are either not present in the breast or are 2 cm or smaller.

Lymph Nodes: Small clusters of cancer cells may be found in the lymph nodes.

Stage II:

Stage IIa:

Tumor Size: Tumor is larger than 2 cm but not more than 5 cm, with no new cancer in lymph nodes.

Stage IIb:

Tumor Size: Tumors are larger than 2 cm but not over 5 cm.

Lymph Nodes: Cancer has spread to 1-3 axillary lymph nodes or nearby nodes near the sternum.

Stage IlI:

Description: Tumors of any size causing growth or ulceration spreading to the chest wall.

Lymph Nodes: Cancer has spread to ten or more axillary lymph nodes.

Treatment Perspective: Further divided into operational and non-operational groups.

Stage IV (Cancerous):

Description: The disease has spread to other body parts, commonly to the liver, bones, or lungs.

VI. TREATMENT

Early-stage breast cancers, often identified through screening mammography, are generally highly treatable with local or regional interventions. In some cases, breast cancer may be localized without spreading to distant areas.

The optimal treatment for women diagnosed with primary breast cancer encompasses a comprehensive approach that incorporates various techniques, including systemic hormone therapy, combination chemotherapy, or a combination of both.

i. Local or Regional Treatment

Surgery: The primary approach for early-stage breast cancer often involves surgical interventions. This may include lumpectomy (removing the tumor and a small margin of surrounding tissue) or mastectomy (complete removal of the breast).

Radiation Therapy: Radiation therapy stands as a critical element in the comprehensive treatment of breast cancer. It entails the precise application of high-energy radiation to eradicate cancer cells. The specific utilization of radiation hinges on the surgical method employed, whether it be a lumpectomy (partial removal of the breast) or a mastectomy (complete removal of the breast).

Standard practice includes post-lumpectomy whole-breast radiation in breast-conserving therapy. For mastectomy recipients, radiation may be directed at the chest wall and local lymph nodes. Recent research has indicated that administering chemotherapy before radiotherapy, particularly in the postoperative phase, can yield improved survival rates.

ii. Systemic Hormone Therapy

Hormone Receptor-Positive Breast Cancer: For cancers that express hormone receptors (estrogen or progesterone receptors), hormone therapy is a key component. This may involve drugs like tamoxifen or aromatase inhibitors, which block the effects of hormones that fuel certain types of breast cancer.
Duration: Hormone therapy may be recommended for several years to reduce the risk of cancer recurrence.

iii. Combination Chemotherapy

The emergence of drug resistance is a formidable challenge in chemotherapy, especially when patients are consistently exposed to a single medication. A promising solution to this predicament is the adoption of combination therapy, incorporating various treatment modalities, which has proven to be effective in enhancing treatment outcomes over several cycles. Unlike the limitations associated with relying on a single agent, combination therapy offers the advantage of achieving heightened efficacy with lower dosages of individual drugs, thereby mitigating adverse side effects. The synergy created by combining different chemotherapeutic agents contributes to an additive therapeutic effect, amplifying the overall effectiveness of the treatment. A compelling illustration of the benefits of combination therapy is seen in the utilization of tamoxifen, particularly when paired with chemotherapy or ovarian ablation for premenopausal women. The combined approach of tamoxifen and chemotherapy surpasses the efficacy of either treatment in isolation, demonstrating its significance, especially for women at a high risk of recurrent disease. The recommendation to combine chemotherapy and tamoxifen, particularly in high-risk scenarios, underscores the importance of a comprehensive and integrated approach to breast cancer treatment. Consensus on the selection of optimal adjuvant therapy becomes crucial once it is established that a woman is poised to benefit from such interventions. This collaborative and multifaceted strategy reflects the evolving landscape of breast cancer treatment, aiming to address challenges like drug resistance and optimize positive outcomes for patients (Table 1).

Chemotherapy Agents: In cases where the risk of cancer spreading is higher, or if the cancer is more aggressive, combination chemotherapy may be recommended. Chemotherapy involves the use of drugs that target and destroy rapidly dividing cancer cells. Chemotherapy is a systemic therapeutic approach utilizing anti-cancer medications to combat malignant cells. Tailoring a specific chemotherapy regimen considers various factors such as overall health, medical history, age, cancer type, and stage. Despite regional therapy, residual risk often persists for women with primary breast cancer, necessitating systemic interventions like chemotherapy. Recent studies underscore that hormone therapy may not be the most suitable approach for tumors lacking estrogen receptor expression.

Adjuvant Chemotherapy: It may be administered after surgery to eliminate any remaining cancer cells and reduce the risk of recurrence.

Table 1: Adjuvant Systemic Therapy Selection and Adjuvant Treatment Indications for women with operable primary breast cancer

Characteristics of Patient and Tumor		**Level of Risk**	**Adjuvant Systemic Therapy**
Age	**Estrogen Receptor Status**		
<50 yr	Negative	Any	Chemotherapy
	Positive	Low	Hormonal therapy Or Chemotherapy Or Chemotherapy& Hormonal therapy
	Positive	Moderate or high	Chemotherapy & Hormonal therapy Or Investigational therapies
	Unknown	Any	Chemotherapy and hormonal therapy

≥ 50 yr	Negative Positive Positive Unknown	Any Low Moderate or high Any	Chemotherapy Tamoxifen Or Chemotherapy and hormonal therapy Chemotherapy and hormonal therapy Investigational therapies Chemotherapy and hormonal therapy

iv. Targeted Therapies

HER2-Positive Breast Cancer: For cancers that overexpress the HER2 protein, targeted therapies like trastuzumab (Herceptin) may be employed to specifically target and inhibit the HER2 pathway.

Personalized Medicine: Advancements in understanding the molecular characteristics of breast cancer allow for more personalized and targeted treatment approaches.

v. Immunotherapy

Emerging Role: Immunotherapy is an evolving area of breast cancer treatment. Some ongoing research and clinical trials explore the use of immunotherapeutic agents to stimulate the body's immune system to recognize and attack cancer cells.

vi. Follow-up Care

Monitoring: Regular follow-up appointments and imaging studies are crucial to monitor for any signs of recurrence or new developments.

vii. Psychosocial Support

Comprehensive Care: Beyond medical interventions, psychosocial support, counseling, and survivorship care are integral components of a holistic approach to breast cancer treatment.

The choice of treatment modalities is individualized, taking into account factors such as the specific characteristics of the cancer, the patient's overall health, and personal preferences. A multidisciplinary team, including surgeons, oncologists, and other specialists, collaborates to design a tailored treatment plan for each woman diagnosed with breast cancer. Advances in research and personalized medicine continue to enhance the effectiveness and precision of breast cancer treatment strategies.

Other Novel treatment Options:

a) Nanocarriers

A significant stride in breast cancer treatment comes from nanocarriers, an innovation in nanotechnology aimed at transforming drug delivery. Nanomedicine, leveraging nanocarriers, offers distinct advantages over traditional treatments, including reduced drug degradation during transport, enhanced biocompatibility, and targeted drug delivery. Nanocarriers have demonstrated efficacy in addressing breast cancer stem cells, which play a pivotal role in development, recurrence, and resistance to chemo-radiotherapy. The application of nanocarriers follows two primary routes—passive and active. The passive approach relies on increased permeability and retention (EPR), capitalizing on the specific characteristics of the cancer type and stage to enhance drug delivery.

b) Liposomes

Discovered in 1965 by Bangham and colleagues, liposomes have rapidly become a sophisticated drug delivery system of considerable significance. These enclosed, spherical vesicles consist of cholesterol, synthetic dimyristyl phosphatidylcholine (semisynthetic DMPC), and natural phospholipids such as soybean and egg yolk lecithin. Characterized by a central aqueous cavity, liposomes provide a versatile platform for drug encapsulation, and their formulation is highly adaptable, allowing for easy modification using various phospholipids and excipients. The creation of liposomes involves diverse methods, including stirring, extrusion, freezing, freeze-thaw processing, reverse phase evaporation, ether/ethanol injection, emulsification procedures, and a transmembrane pH gradient-driven encapsulation approach. Each method contributes to the customization of liposomal characteristics, such as permeability, stability, size, and lamellarity. Liposomes can be categorized into three types based on lamellarity and size: small unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles. To address limitations in breast carcinoma research studies, hybrid systems and nanocarriers are incorporated into liposomal formulations. Pioneering the field of drug delivery are three anthracycline-based nanoformulations: liposomal daunorubicin (DaunoXome), nonpegylated liposomal doxorubicin (Myocet), and pegylated liposomal doxorubicin (Doxil in the USA and Caelyx in other countries). While liposomal daunorubicin is widely approved for the primary treatment of AIDS-related Kaposi sarcoma, its role in metastatic breast cancer (MBC) is less explored in available literature.Significantly, pegylation in pegylated liposomal doxorubicin plays a crucial role by shielding liposomes from uptake by the mononuclear phagocyte system. This modification alters drug pharmacokinetics, extending the circulation time of liposomes in the bloodstream. Notably, Doxil exhibits an extended half-life compared to other anthracycline-based nanoformulations (55 hours) and displays a distinct biodistribution profile, resulting in a higher tumor concentration even at lower dosages. These advancements underscore the intricate and evolving landscape of liposomal formulations in drug delivery, offering tailored solutions for various medical applications, including breast cancer treatment.

c) Solid lipid nanocarriers

In the early 1990s, a versatile group of colloidal drug carriers called solid lipid nanoparticles (SLNs) was introduced, offering a range of clinical applications for drug delivery. These SLNs, representing the initial generation of in vivo systems capable of sustaining solid lipid matrices at the nanometric scale, are characterized by aqueous colloidal dispersions with solid lipid matrices composed of biodegradable lipids. The solid lipids include diverse substances such as palmitic palmitate, cetyl palmitate, beeswax PEG-8, alba wax, carnauba wax, saturated glycerol esters, and glyceryl Di behenate. The distinctive feature of SLNs lies in their ability to regulate drug release, enhance drug solubility, minimize dosage requirements, improve stability by protecting chemically unstable compounds, and facilitate uptake with an affinity for malignant cells. Moreover, the active targeting capacity of SLNs contributes to their dispersion throughout tumor blood vessels and enhances their penetration into multidrug-resistant cells. This active targeting mechanism holds promise for optimizing drug delivery to specific sites, improving therapeutic outcomes, and addressing challenges associated with chemically unstable drugs or drug resistance. The development of SLNs marks a significant stride in drug delivery systems, offering a multifaceted approach to enhance the precision and efficacy of drug administration in clinical contexts.

d)Breast cancer screening using gold nanoparticle

In recent times, a groundbreaking therapeutic approach has emerged, centered around the use of metallic nanoparticles, particularly gold nanoparticles (AuNPs), for the treatment of cancer. This innovative method has found versatile applications in clinical diagnosis, biomedical imaging, and the targeted treatment of solid breast tumors. Gold nanoparticles, owing to their unique properties, are being explored for their roles as contrast agents, photothermal agents, drug carriers, and radiosensitizers in the realm of cancer therapy. One notable application involves the creation of multivalent radiopharmaceuticals by utilizing radiolabeled gold nanoparticles. This opens avenues for advanced diagnostic capabilities and targeted therapeutic interventions. Conjugating different peptides to a single AuNP enhances stability, biocompatibility, and the ability to precisely target specific areas within the body. The high atomic number of AuNPs is pivotal, as it enables efficient absorption of X-rays (kilovoltage) and the generation of heat when exposed to microwaves, ultrasound, or radiofrequency waves. Gold nanoparticles can exist in various forms, including aurous compounds, auric compounds, and a nonoxidized state. In practical applications, these nanoparticles are often formulated as suspensions containing submicrometer-sized particles of gold in water or other solvents.

The historical roots of gold nanoparticle synthesis trace back to 1856 when Michael Faraday published the first scientific paper on the subject. In this seminal work, he described the synthesis of colloidal gold from aurochloric acid (HAuCl4) using phosphorous reduction. The principle behind this synthesis is based on the rapid stirring of an HAuCl4 solution containing gold particles in the presence of reducing agents, resulting in the formation of neutral gold atoms with a uniform size in the subnanometer range. The exploration of gold nanoparticles in cancer therapy not only reflects cutting-edge advancements but also builds upon a rich history of scientific inquiry. The potential applications of these nanoparticles in medical research underscore their significance in pushing the boundaries of diagnostic precision, targeted drug delivery, and overall therapeutic efficacy in the context of cancer treatment.

e) Drug-printed (anticancer and antiviral) bioadhesive films

Making of drug-printed films:

The successful creation of ink loaded with anticancer and antiviral drugs using an inkjet printer depends on the chosen template. The precise matching of ink is evident when considering the timing of droplet generation during the printing process. Specifically, when printing the (paclitaxel) PCX HpCD (cyclodextrin) inclusion complex, there were no observed faults in droplet formation, as evidenced by visual inspection. Our previous work detailed ink formulations that proved satisfactory and stable, facilitating the production of printed films containing anticancer and antiviral drugs.To assess the mechanical characteristics of inkjet printer film compositions, equal-sized samples of both unprinted and printed HPC films were obtained using a manual cutting press. Subsequently, these film samples underwent testing in a universal testing machine to measure parameters such as force at break (F break), displacement at break (dL (F break)), maximum force (Fmax), and displacement at break (dL (Fmax)). Statistical analysis of the Fmax values revealed a significant difference ($p < 0.05$) among various film preparations. Unprinted films exhibited minimal stress and strain, whereas the stress and strain values increased after printing on HPC film for both ink formulations. This study aimed to compare the characteristics of films produced on an inkjet printer with different ink formulations to films that had not undergone the printing process. The results of these investigations suggest that both polymers and the printing technique significantly influenced the mechanical and biological adhesive properties of the film samples. Characterization research unequivocally demonstrated that the printing procedure enhanced both the mechanical and biological adhesive qualities, despite not resulting in a thicker film sample. Overall, the study highlights the successful integration of inkjet printing for the production of films with improved mechanical and biological characteristics for drug delivery applications.

Cisplatin-loaded nanofibers for Breast cancer
Preparation of cisplatin-loaded nanofibers:

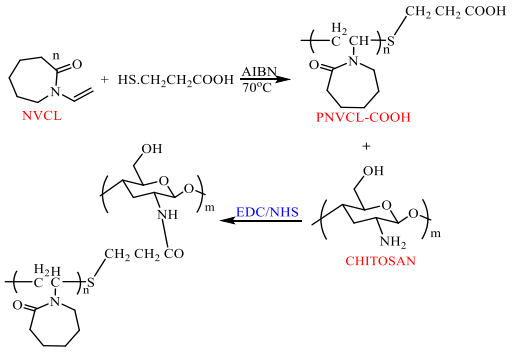

Fig 1: Schematic Synthesis of chitosan-g-PNVCL copolymer

The synthesis of chitosan-g-PNVCL copolymer involves grafting poly(N-vinylcaprolactam) (PNVCL) onto chitosan, resulting in a copolymer with improved properties. Above is a general overview of the synthesis process:

Materials: Chitosan, N-vinylcaprolactam (NVCL), Initiator (e.g., potassium persulfate), Solvent (e.g., water or another suitable solvent)

Procedure:
Activation of Chitosan:
Chitosan is typically activated to provide sites for grafting. This is often done by reacting chitosan with a suitable activating agent, such as epichlorohydrin. The activation step introduces reactive functional groups onto the chitosan backbone.

Preparation of NVCL Solution:
N-vinylcaprolactam (NVCL) is dissolved in an appropriate solvent. The solvent choice depends on the solubility of NVCL and the compatibility with the reaction conditions.

Grafting Reaction:
The activated chitosan is then mixed with the NVCL solution.A suitable initiator, such as potassium persulfate, is added to initiate the grafting reaction. Initiators generate free radicals that initiate the polymerization of NVCL.

Polymerization and Grafting:
The reaction mixture is heated or exposed to the desired polymerization conditions.NVCL undergoes polymerization, and the growing polymer chains graft onto the activated chitosan backbone, forming the chitosan-g-PNVCL copolymer.

Purification:
The resulting copolymer is usually purified to remove any unreacted monomers, initiators, or by-products. This can be achieved through precipitation, dialysis, or other suitable purification methods.

Characterization:
The synthesized chitosan-g-PNVCL copolymer is characterized using various analytical techniques such as spectroscopy (e.g., FTIR), chromatography, and gel permeation chromatography (GPC) to confirm the successful grafting and determine the copolymer's molecular weight and composition.

Synthesis of electrospun chitosan-g-PNVCL nanofibers
In the process, three different concentrations of chitosan-g-PNVCL—5%, 10%, and 15% by weight—were dissolved in a solution of 0.5% acetic acid. The resulting solution underwent stirring for a duration of four hours to ensure thorough mixing and homogeneity. Subsequently, the well-mixed solution was loaded into a 5 mL plastic syringe equipped with a 19-gauge nozzle syringe needle. To fabricate consistent and homogeneous chitosan-g-PNVCL nanofibers, specific electrospinning parameters were carefully adjusted. The applied voltage during electrospinning was set within the range of 15–25 kV, while the tip-to-collector distance was maintained between 10 and 20 cm. These adjustments aimed to optimize the electrospinning process and achieve nanofibers with desired characteristics. Throughout the electrospinning procedure, the solution flow rate and the speed of the collector remained constant at 0.5 mL h~1 and 1000 rpm, respectively. These consistent settings were chosen to ensure stability and reproducibility in the nanofiber manufacturing process. The electrospinning technique, characterized by its high voltage, precise tip-to-collector distance, and controlled solution flow, played a crucial role in producing chitosan-g-PNVCL nanofibers with uniformity and reliability.

Cisplatin loading into nanofibers with gold nanoparticle coating
The preparation of drug-loaded nanofibers involved mixing the chitosan-g-PNVCL solution with varying concentrations of cisplatin (1 µg/mL, 10 µg/mL, and 50 µg/mL) before initiating the electrospinning process. This step aimed to incorporate cisplatin uniformly into the nanofibers. The electrospinning parameters considered ideal for manufacturing these drug-loaded nanofibers included a chitosan-g-PNVCL concentration of 10%, an applied voltage set at 20 kV, a tip-to-collector distance of 15 cm, a consistent flow

rate of 0.5 mL/h, and a collector speed of 1000 rpm. In a subsequent step, 100 milligrams of the resulting electrospun chitosan-g-PNVCL nanofibers were introduced into a ten-milliliter mixture of gold-gold sulfide. This mixture was stirred for twenty-four hours, ensuring the coating of the nanofiber surface with nanoparticles. Following this, a 20-minute centrifugation at 15,000 rpm was carried out, and the resultant product underwent a thorough cleaning process using distilled water. To determine the concentration of gold nanoparticles deposited on the nanofiber surface, an atomic absorption spectrophotometer was employed, providing accurate quantification. This comprehensive procedure aimed to achieve drug-loaded nanofibers with a controlled cisplatin concentration and a surface coating of gold nanoparticles for potential therapeutic applications.

vi. Nanotubes in breast cancer treatment

Nanotubes, members of the fullerene structural family, are characterized by their elongated, hollow structure and one-atom-thick carbon walls, resembling graphene. The specific properties of nanotubes, including their chiral angles, radius, and rolling angles, contribute to their unique characteristics. The term "chiral" pertains to the tube's orientation or handedness, adding to the diversity of nanotube features. The classification of nanotubes is based on the number of walls they possess, with single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs) being the primary categories. Single-walled nanotubes consist of a single layer of graphene, forming a seamless cylinder. In contrast, multi-walled nanotubes comprise multiple concentric layers of graphene, resembling nested cylinders. The distinctive geometric and structural attributes of nanotubes underpin their remarkable electrical, mechanical, and thermal properties. The ability to manipulate these properties by adjusting parameters like chiral angles and wall count makes nanotubes a versatile material with promising applications in fields such as nanotechnology and materials science.

VII.CONCLUSION

In conclusion, the imperative for innovative Breast Cancer treatments becomes evident, given its substantial contribution to cancer incidences. Conventional pharmacological therapies face challenges posed by drug resistance, underscoring the necessity for novel approaches. Advanced drug delivery technologies, particularly nanocarriers, emerge as promising solutions to overcome these resistance issues.The pivotal role of nanocarriers in breast cancer treatment lies in their capacity to enhance drug solubility, reduce required dosages, ensure drug stability, and regulate drug release. Their targeted approach to tumor cells, facilitated by a favorable volume-surface ratio susceptible to enzymatic activity, adds to their efficacy. The adaptability of nanocarriers to combination therapies further enhances their utility.Looking ahead, extensive pre-clinical studies, especially employing representative animal models of breast cancer, are essential. These studies should focus on exploring nanocarrier-based formulations, offering valuable insights into medication efficacy, safety, and optimal distribution. Additionally, comprehensive toxicological assessments will contribute to a nuanced understanding of the potential benefits and risks associated with these innovative treatment modalities.

VIII. FUTURE PROSPECTS

The primary aim of investigating the causes of a disease is to gain control, ideally through the development of effective preventive measures. Alternatively, if prevention proves challenging, the emphasis shifts to early detection and treatment, with a focus on identifying high-risk groups. In the context of breast cancer, substantial strides have been made, especially with the introduction of targeted nanoparticles. Recent research indicates a decline in the occurrence of breast cancer, accompanied by a significant decrease in morbidity and mortality rates. This positive trend is credited to the adoption of innovative systems, where targeted nanoparticles play a crucial role. The incorporation of potent anticancer medications into nanoparticles has notably enhanced the therapeutic index. As a result, breast solid tumors exhibit heightened responsiveness to treatment, marking promising progress in effectively managing and treating breast cancer.

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