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Development and Characterization of Phytoconstituent Loaded Niosomal Formulation as Targeted Delivery System in Breast Cancer Treatment

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ABSTRACT

The present work aims to comprehensively examine and analyze Niosomal formulations, with a special focus on their potential use as a targeted delivery approach for the treatment of breast cancer. The objective of this study is to get in-depth understanding of the dynamic field of cancer therapeutics by conducting a thorough examination of formulation parameters and characterization techniques. The research aims to address the pressing need for novel treatment options in light of breast cancer's increasing prevalence and impact on women's health in India. This disease has now surpassed cervical cancer as a major cause of morbidity and death among women in the country. Niosomes, which are vesicles composed of lipids, have shown the capacity to augment the sustained release of drugs, so enabling a controlled and prolonged therapeutic effect. By using the mechanism of endocytosis, these formulations effectively promote the internalization of medicines into cellular structures, so permitting precise delivery to specific intracellular locations. The investigation of niosomal formulations as precise delivery methods in the context of breast cancer treatment signifies a notable development in the field of cancer therapies. Niosomes has distinctive characteristics that render them very promising vehicles for drug delivery, since they have the capacity to be customized for precise targeting of cancer cells while minimizing detrimental impacts on healthy organs. Therefore, the use of niosomal formulations as a precise delivery strategy in the treatment of breast cancer has potential in enhancing the therapeutic efficacy of anticancer medications while mitigating undesired adverse reactions. Ongoing scholarly research activities are focused on further investigating and improving these formulations, with the objective of maximizing their efficacy in clinical environments.

Keywords: *Breast Cancer, Niosomes, Targeted Drug Delivery, Drug Release, Niosomal Formulations, Cancer Therapies*

1. INTRODUCTION

Cancer is an extremely dangerous disease that affects people all over the world. It is characterized by the uncontrolled multiplication and dispersion of cells across the body, and it has the potential to affect almost every tissue in the body. Based on the findings of a study conducted by the World Health Organization, it was anticipated that there would be 14.1 million instances of cancer cases worldwide in the year 2012. It was determined that males were responsible for 7.4 million of the overall number of cases, while females were responsible for 6.7 million of those, respectively. It is expected that the aforementioned number would see a significant growth, reaching an astounding 24 million by the time the year 2035 comes to a close. A substantial amount of attention has been drawn to the growing worldwide concern over cancer, which has resulted in the field of research being more popular in recent years [1].

1.1 Background of Study

It is generally acknowledged that breast cancer, which is caused by the growth of breast tissue, is the most common kind of cancer that affects women all over the globe that is diagnosed [2]. According to the statistics from 2012, breast cancer

accounted for one-fourth of the total number of newly diagnosed cases of cancer. Breast cancer, like other forms of cancer such as skin, lung, liver, and bone cancer, has the capacity to infect neighboring organs in the body. This is a characteristic that other types of cancer also share. In the latter stages of the illness, it is also possible for it to spread to other organs, infiltrate the circulation, and move through the lymph nodes with the progression of the disease. Radiation therapy, hormone therapy, chemotherapy, combination chemotherapy, and surgical removal of malignant tissue are the components that make up the modern approach to the treatment of breast cancer. Chemotherapy is the systemic treatment for breast cancer that is used the most often. This treatment method includes the delivery of anti-cancer drugs to the patient. Some of these treatments include anthracyclines, gemcitabine, alkylating agents, capecitabine, 5-fluorouracil, eribulin, taxane, and vinorelbine. The necessity to develop delivery techniques that are both effective and accurate in the treatment of breast cancer has been a driving force behind the development and characterization of niosomal formulations that are loaded with phytoconstituents [3]. An additional facet of potential therapeutic efficacy is brought into play by the use of bioactive compounds that are derived from plants. The purpose of this study is to analyze the intricate process of investigating and analyzing niosomal formulations, with a particular focus on the possibility of these formulations as a targeted delivery strategy for breast cancer treatment. A comprehensive analysis of formulation parameters and characterization processes is going to be carried out as part of this research project with the intention of providing substantial insights into the developing landscape of different cancer medicines [4].

1.2 Breast Cancer and Epidemiology of Breast Cancer

The clinical disease known as breast cancer is defined by the abnormal cellular functioning of breast tissue cells, which leads to the cells' continued growth via the avoidance of apoptosis, also known as programmed cell death [5]. It is common for abnormal cellular proliferation to lead to the accumulation of cells into clusters, which eventually culminates in the development of a tumor. Malignant tumors, also known as cancerous tumors, are characterized by the presence of abnormal cells that have spread to neighboring areas of the breast. Similar to the phenomena described above, the term "metastatic breast cancer" refers to the process by which cancerous cells spread from the breast to other parts of the body via the lymphatic system or the circulation [6].

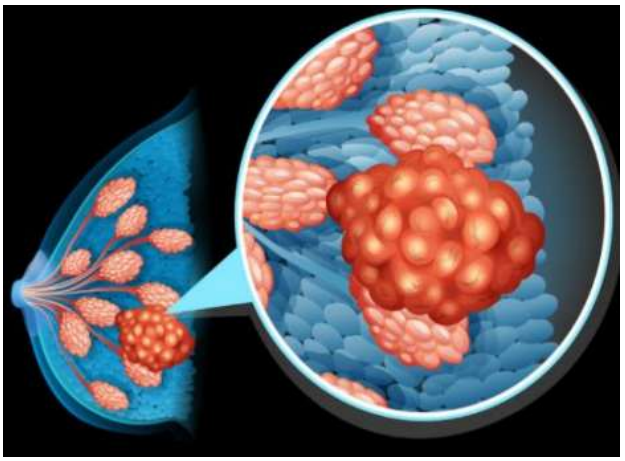

Figure 1: Breast Cancer [26]

It is estimated that around twenty-five percent of all cancer cases that have been documented are breast cancer, making it the second most frequent type of cancer worldwide (Figure 2). It is projected that 1.67 million instances of breast cancer were detected in women in 2012. Breast cancer is the form of cancer that is diagnosed the most commonly among this population. It was anticipated that industrialized nations will have a lower incidence of breast cancer cases in 2012 (7, 94,000) compared to poor countries (8,833,000) [7]. This was based on the findings of the research. Breast cancer is ranked as the fifth most dangerous kind of cancer when mortality is taken into consideration. It is responsible for roughly 522,000 deaths per year resulting from the disease. Among women living in poor nations, breast cancer is the most dangerous form of the disease. It is responsible for 14.3 percent of all deaths that are attributed to cancer, which amounts to 324 thousand deaths. Breast cancer, on the other hand, is the second highest cause of mortality in developed countries, accounting for 198,000 deaths, which is equivalent to 15.4% of the total number of deaths that are attributed to cancer [8].

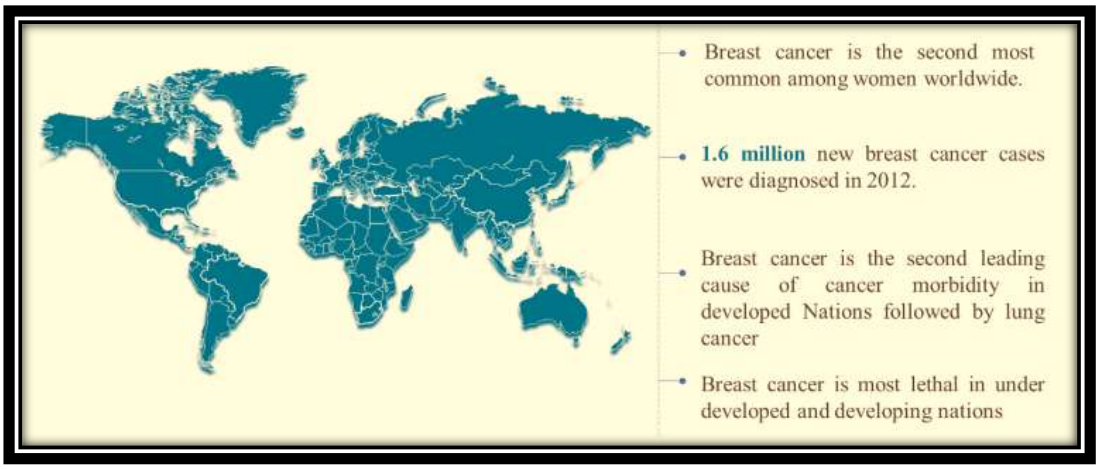

Figure 2: Incidence of breast cancer worldwide [30]

Breast cancer has emerged as a predominant source of cancer-related morbidity and death among women in India, surpassing cervical cancer (Figure 3). Similarly, breast cancer accounts for 32% of all cancer cases in India [9]. In 2012, it was predicted that there were 1.28 lakh new instances of breast cancer, and it is expected that this number would increase to 1.9 lakh by 2020. According to the Globocan-2012 study, there has been an 11.54% rise in the prevalence of breast cancer in India between 2008 and 2012. During the same time period, there was a notable increase of 13.82% in the death rate attributed to breast cancer. The increase in morbidity may be attributed to the lack of accessibility to breast cancer screening facilities, inadequate awareness among women, late-stage diagnoses, and inadequate medical resources [10].

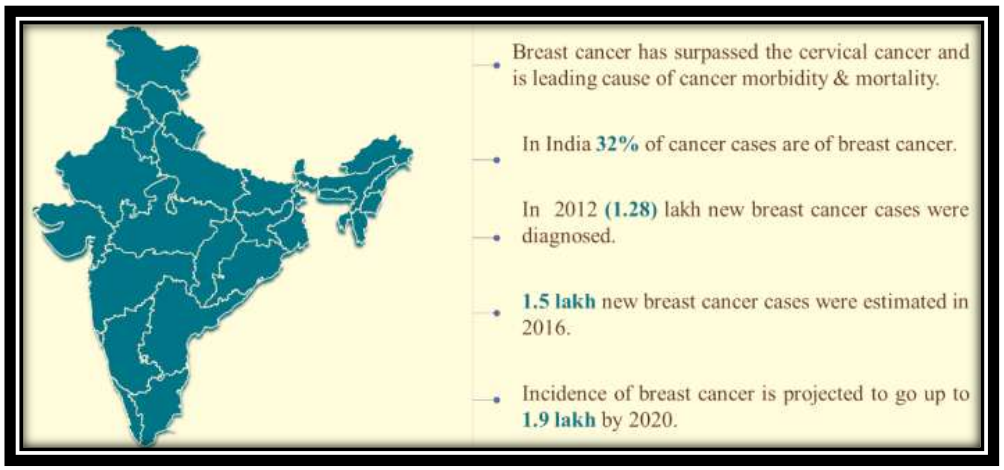

Figure 3: Incidence of breast cancer in India [30]

1.3 Types of Breast Cancer

Breast cancer may arise from several anatomical sites inside the breast, such as the ducts, lobules, and, in rare cases, the interstitial tissue located between the breast components (Figure 4). Breast cancer may be classified according to its degree of invasiveness [11]. Non-invasive and invasive carcinoma represent two separate classifications of malignant neoplastic formations. A more appropriate methodology for regularly identifying or classifying breast cancer is via the assessment of biological markers that play a significant role in its development [12]. These variables include the presence or absence of hormone receptors, namely progesterone or estrogen receptors (HR+/HR-), as well as the quantity of a growth-promoting protein known as human epidermal growth factor receptor-2 (HER2+/HER2-) [13]. There are four primary intrinsic molecular subgroups of breast cancer, as seen in Figure 5.

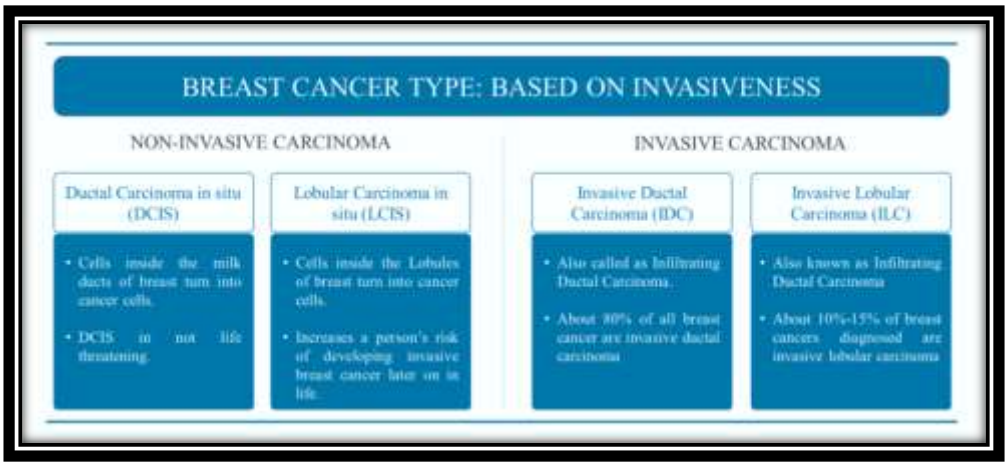

Figure 4: Breast Cancer Subtypes Predicated on Invasiveness [30]

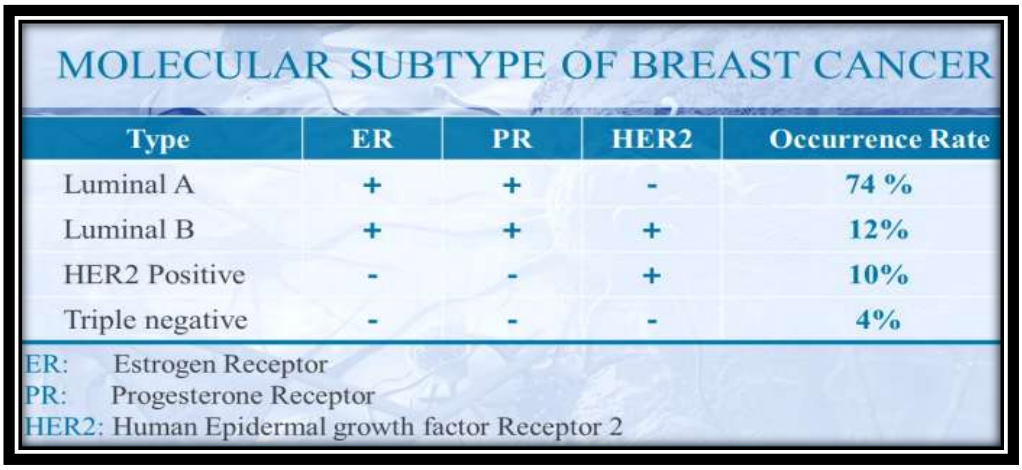

Figure 5: An examination of the molecular subtypes of breast cancer [30]

1.3.1 Other Types of Rare Breast Cancer

- **Tubular carcinoma in Breast:** This is the invasive manifestation of breast cancer, which arises from the lactiferous ducts of the breast and infiltrates the adjacent tissue. Tubular carcinomas are often characterized by their very diminutive size, generally measuring around 1 cm or less, and their resemblance to tubular structures. These particular carcinomas have a lower level of aggressiveness and are responsive to cancer therapy interventions. According to reports, tubular carcinoma is often detected in women in their early fifties [14].
- **Medullary carcinoma in Breast:** This is an infrequent variant of invasive ductal carcinoma, constituting around 3-5% of all cases of breast cancer. The tumor has a shape and appearance that closely mimic the medulla of the brain, therefore leading to its identification as medullary breast cancer. Medullary carcinoma is often seen in women who possess the BRCA-1 mutation, with diagnoses occurring across all age groups. However, women in their late 40s and early 50s have an elevated risk of developing this kind of cancer. This particular carcinoma has a moderate growth rate and lacks the ability to spread beyond the breast to the lymphatic system. Consequently, it is comparatively more manageable to treat when compared to other forms of breast cancer [15].
- **Mucinous Carcinoma in Breast:** This particular kind of cancer is also recognized as colloid carcinoma and is classified as a variant of invasive ductal carcinoma, exhibiting a notably low incidence rate. Mucinous carcinoma is capable of being detected in women of any age, however it mostly affects postmenopausal women, with the typical age of onset occurring in the late 60s to early 70s. This particular kind of cancer has favorable treatment outcomes due to its non-aggressive behavior and absence of metastasis to other regions of the breast [16].
- **Papillary carcinoma in Breast:** The uncommon variant of invasive carcinoma is a minority, comprising less than 1-2% of the overall occurrences of breast cancer. The aberrant cells possess short finger-like extensions and have a distinct demarcation line, indicating their boundaries. Furthermore, these cells demonstrate rapid proliferative ability. This particular kind of cancer is often seen in elderly women [17].

- **Cribriform carcinoma in Breast:** This particular kind of breast cancer is characterized by the invasion of aberrant cells into the stroma, which is the connective tissue of the breast. Nest-like formations are seen inside the interstitial space between the ducts and lobules of the breast, posing challenges in their identification due to the cells exhibiting typical shape of breast cells [18].
- **Paget's Disease of the Nipple:** This particular kind of breast cancer is characterized by the accumulation of abnormal cells in the vicinity of or inside the nipple. This particular kind of cancer primarily targets the ductal area of the nipple, subsequently spreading to the surface of the nipple and the areolar region of the breast. This progression leads to symptoms such as irritation and inflammation [19].
- **Phyllodes tumors in Breast:** This particular kind of breast cancer is classified as a rare subtype, representing a minority, specifically less than 1%, of the total cases of breast cancer. The name "Phyllodes" originates from Greek and refers to a leaf-like structure. In the context of tumors, the proliferation of cells in these tumors mimics the structure of a leaf. This particular carcinoma variant has a proclivity for rapid growth and seldom demonstrates invasive behavior outside the confines of the breast [20].
- **Male breast cancer:** Male breast cancer is a relatively uncommon manifestation of an epidemic illness. There is a scarcity of reported instances or cases that are accessible for research purposes. The primary factor contributing to the development of this particular cancer is an elevated concentration of estrogen, while a significant familial predisposition may be attributed to genetic mutations in the BRCA-1 and BRCA-2 genes [21].

1.3.2 Metastatic Breast Cancer

Metastatic breast cancer, usually referred to as stage IV cancer, is characterized by the migration of cells from the primary location (breast) to other regions of the body, commonly include the bones, brain, liver, or lungs. This particular stage is often referred to as "De-novo-metastatic" breast cancer. The dissemination of cancer cells to different organs is facilitated by the lymphatic system and circulation. Around 30% of breast cancer patients progress to the metastatic stage. The diagnosis of metastatic breast cancer may be a distressing circumstance, but, with appropriate medical oversight and intervention, significant improvement in this disease can be achieved [22].

1.4 Niosomes and its Constituents

Niosomes, which are Nano carriers in the form of vesicles, have garnered significant interest as promising transdermal drug delivery systems. This is primarily attributed to their advantageous characteristics, including improved drug penetration, the ability to serve as a local depot for sustained drug release, and the capacity to act as a rate-limiting membrane for regulating the systemic absorption of drugs through the skin. Niosomal carriers have shown suitability for facilitating the transdermal administration of a wide range of pharmacological drugs, including antioxidant, anticancer, anti-inflammatory, antimicrobial, and antibacterial compounds [23].

Composition of Niosomes: The lamellar structures under consideration consist of amphiphilic molecules arranged in a bilayer configuration, with an aqueous compartment around them. The molecules referred to as surfactants are classified as amphiphilic due to their possession of both hydrophobic tails and hydrophilic heads. These molecules have the ability to self-assemble, resulting in the formation of various structures such as micelles or planar lamellar bilayers. Potential drug delivery systems include a range of surfactants, including sorbitan esters and analogs, sugar-based surfactants, polyoxyethylene-based surfactants, polyglycerol surfactants, and crown ether-based surfactants. These surfactants may be used in conjunction with membrane additives, such as cholesterol or its derivatives [24].

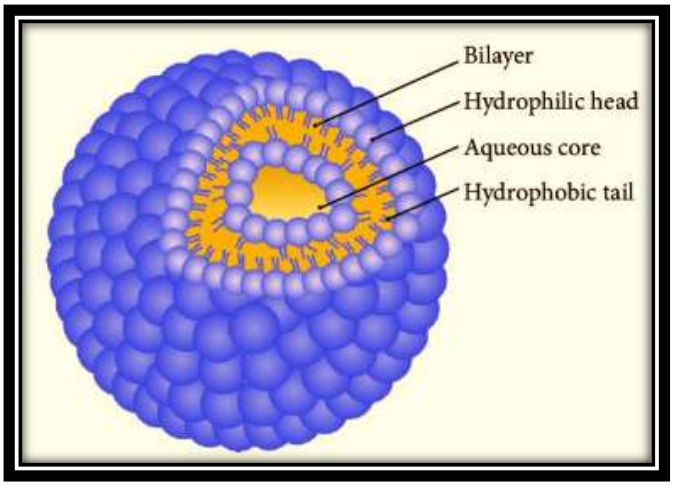

Figure 6: Structure of Niosomes [26]

The following table 1 below provides a comprehensive overview of the essential constituents of Niosomesand their corresponding functions within drug delivery systems. Nonionic surfactants are preferred over anionic, amphoteric, or cationic surfactants because to their capacity to improve stability, biocompatibility, and minimize toxicity in niosomal formulations. Cholesterol has a crucial role in determining the structural and physical properties of niosomes, which in turn affect several aspects such as the effectiveness of encapsulation, stability over time, release of the payload, and resistance to biological degradation. The existence of this entity contributes to the enhancement of both the structural integrity and stability. Furthermore, the table presents a comprehensive overview of the possible effects of charged molecules in niosome formulations. It acknowledges their capacity to modulate surface charge and interact with biological membranes, while also emphasizing the need for care due to their potential to hinder the synthesis process. The present analysis highlights the intricate factors involved in enhancing the effectiveness and safety of niosomal drug delivery systems across several medicinal contexts.

Table 1: Constituents of Niosomes [26]

Sr. No.	Components of Niosomes	Uses
1.	**Nonionic Surfactants**	In comparison to their anionic, amphoteric, or cationic counterparts, these substances exhibit enhanced stability, biocompatibility, and reduced toxicity.
2.	**Cholesterol**	The architectures of Niosomes are influenced by several factors, which in turn affect their physical characteristics. These qualities include entrapment efficiency, long-term stability, payload release, and bio-stability. Cholesterol enhances the structural integrity of vesicles and provides stability to Niosomes.
3.	**Charged Molecules**	The augmentation of charged molecules has the potential to impede the process of Niosome synthesis.

Niosomes, which are vesicular structures composed of lipids, exhibit a complex process in the context of drug administration. The encapsulation of hydrophilic and hydrophobic pharmaceuticals is achieved by the self-assembly of non-ionic surfactants, resulting in improved stability and solubility. Due to their biocompatible properties and little toxicity, these substances exhibit suitability for a wide range of applications. A crucial element is in their capacity to selectively target certain tissues or cells via surface changes, hence reducing the occurrence of off-target effects. Niosomes have been shown to enhance the sustained release of drugs, so enabling a regulated and extended therapeutic impact. The process of endocytosis facilitates the internalization of medicines into cells, allowing for targeted delivery to intracellular sites. In general, the multi-functionality of Niosomes in the encapsulation, protection, and transportation of pharmaceuticals, combined with their compatibility with biological systems and ability to selectively target specific sites, establishes them as promising carriers for sophisticated drug delivery systems. Particularly, their potential in the management of diseases such as breast cancer is noteworthy [25].

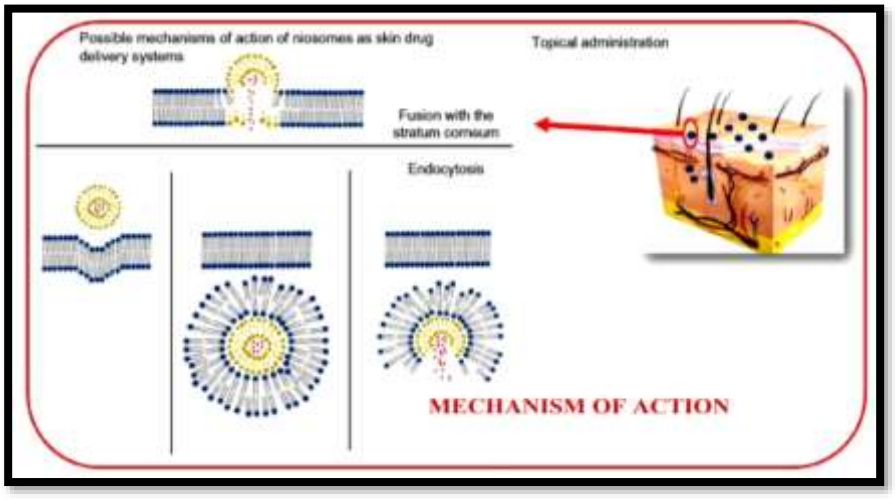

Figure 7: Mechanism of action of Niosomes [26]

1.5 Niosomal Formulation as Targeted Delivery System in Breast Cancer Treatment

The examination of niosomal formulations as precise delivery modalities in the realm of breast cancer therapy represents a significant advancement in the domain of cancer therapeutics. Niosomes, lipid-based vesicles, have unique characteristics that render them very advantageous as promising carriers for drug delivery. In the context of breast cancer, it is feasible to tailor these formulations with the aim of selectively targeting cancerous cells, therefore mitigating the potential adverse effects on healthy organs. The organization of the lipid bilayer inside Niosomes enables the effective encapsulation of anticancer medications possessing both hydrophilic and hydrophobic characteristics, hence enhancing the drugs' durability and solubility. Surface modifications provide the inherent capability to augment specific interactions with breast cancer cells, hence enhancing the effectiveness of drug administration to the desired site. Furthermore, the prolonged release characteristics shown by Niosomes have the potential to augment the length of therapeutic advantages, hence improving the entire therapeutic strategy. The investigation and progression of niosomal formulations for the management of breast cancer underscore a promising avenue in the pursuit of improved and targeted cancer treatments [26].

The niosomal formulation is a unique medication delivery method that offers several advantages. These characteristics include the capacity to enclose both hydrophilic and hydrophobic pharmaceuticals, a notable level of entrapment efficacy, improved stability, and less toxicity in comparison to liposomes. An additional advantage of this specific formulation lies in its potential to augment bioavailability when compared to conventional dose forms. Furthermore, the selection of Niosomes for the formulation of the extract-loaded patch was based on their notable flexibility, which facilitates efficient skin penetration. The primary objective of this focused delivery method is to selectively carry the extract to malignant cells [27].

Niosomes are formed by the phenomenon of self-assembly, wherein nonionic surfactants and cholesterol come together in an aqueous medium. Lipid bilayers has the capacity to encapsulate medicinal compounds, hence providing protection against degradation and improving their bioavailability. Niosomes has the potential to be manipulated with specific characteristics that enable the targeted delivery of pharmaceutical agents to breast cancer cells. Ligands with targeting capabilities, such as antibodies or peptides, have the potential for integration into the surface of niosomes. Ligands have the capacity to selectively recognize and bind to certain receptors that are overexpressed on the outer membrane of breast cancer cells, hence enhancing the targeted delivery of drugs. The use of targeted drug delivery to cancer cells demonstrates a significant reduction in the potential damage inflicted upon healthy tissues, hence restricting the occurrence of undesirable outcomes [28].

Improved drug stability enables the effective control of drug release, so ensuring a sustained therapeutic effect. Niosomes has the capacity to exhibit prolonged circulation within the bloodstream, so enabling a longer and sustained release of the therapeutic substance exclusively at the site of the tumor. This specific characteristic enhances the therapeutic effectiveness and reduces the frequency of pharmacological dosing. The tuning of niosomes, with regards to their size and surface charge, is crucial in order to attain effective drug delivery. Ensuring the preservation of stability in the niosomal formulation throughout storage and transit is of utmost significance. Contemporary scientific investigations are focused on the refinement of niosomal formulations with the aim of maximizing their effectiveness in the management of breast cancer. A multitude of studies have been undertaken to explore the combined use of Niosomes with various anticancer drugs, as well as the incorporation of imaging agents to enhance diagnostic purposes. Therefore, the use of niosomal formulations as a precise delivery system in the treatment of breast cancer has promise for improving the therapeutic effectiveness of anticancer drugs while minimizing undesirable side effects. Academic researchers continue to study and enhance these formulations with the aim of enhancing their effectiveness in clinical settings [29].

2. CONCLUSION

In summary, this research highlights the promise of niosomal formulations as a precise and focused method of delivering therapeutic agents in the field of breast cancer treatment. Niosomes has distinct characteristics that render them very promising for the advancement of cancer therapies. These traits include their capacity to support prolonged drug release and permit precise intracellular delivery, making them ideal candidates in this field. The urgent issue of breast cancer, especially in the Indian setting, requires the development of novel therapeutic strategies that emphasize effectiveness while avoiding negative consequences. Niosomes, due to their versatile nature and capacity for modification, provide a possible pathway to attain this equilibrium. The continuous endeavors of scholarly researchers to examine and improve these formulations underscore their dedication to augmenting their efficacy in clinical contexts. The ongoing development of cancer medication has led to the investigation of niosomal formulations as a promising approach for delivering breast cancer treatments with more precision and targeting, hence enhancing efficacy and prioritizing patient needs.

REFERENCES

[1] Sabarwal, A., Kumar, K., & Singh, R. P. (2018). Hazardous effects of chemical pesticides on human health–Cancer and other associated disorders. *Environmental toxicology and pharmacology*, *63*, 103-114.

[2] Milosevic, M., Jankovic, D., Milenkovic, A., & Stojanov, D. (2018). Early diagnosis and detection of breast cancer. *Technology and Health Care*, *26*(4), 729-759.

[3] Mirza, Z., & Karim, S. (2021, February). Nanoparticles-based drug delivery and gene therapy for breast cancer: Recent advancements and future challenges. In *Seminars in cancer biology* (Vol. 69, pp. 226-237). Academic Press.

[4] Azer, K., Kaddi, C. D., Barrett, J. S., Bai, J. P., McQuade, S. T., Merrill, N. J., ... & Baliga, N. S. (2021). History and future perspectives on the discipline of quantitative systems pharmacology modeling and its applications. *Frontiers in physiology*, *12*, 637999.

[5] Luo, Y., Tang, W., Xiang, S., Feng, J., & Zu, X. (2022). Non-coding RNAs in breast cancer: Implications for programmed cell death. *Cancer Letters*, 215929.

[6] Nathanson, S. D., Detmar, M., Padera, T. P., Yates, L. R., Welch, D. R., Beadnell, T. C., & Cheung, K. (2022). Mechanisms of breast cancer metastasis. *Clinical & experimental metastasis*, *39*(1), 117-137.

[7] Sharma, R. (2019). Breast cancer incidence, mortality and mortality-to-incidence ratio (MIR) are associated with human development, 1990–2016: evidence from Global Burden of Disease Study 2016. *Breast Cancer*, *26*, 428-445.

[8] Kashyap, D., Pal, D., Sharma, R., Garg, V. K., Goel, N., Koundal, D., & Belay, A. (2022). Global increase in breast cancer incidence: risk factors and preventive measures. *BioMed research international*, *2022*.

[9] Bhushan, A., Gonsalves, A., & Menon, J. U. (2021). Current state of breast cancer diagnosis, treatment, and theranostics. *Pharmaceutics*, *13*(5), 723.

[10] Kimmick, G. G., Li, X., Fleming, S. T., Sabatino, S. A., Wilson, J. F., Lipscomb, J., & Wu, X. C. (2018). Risk of cancer death by comorbidity severity and use of adjuvant chemotherapy among women with locoregional breast cancer. *Journal of geriatric oncology*, *9*(3), 214-220.

[11] Cieśla, S., Wichtowski, M., Poźniak-Balicka, R., & Murawa, D. (2021). The surgical anatomy of the mammary gland. Vascularisation, innervation, lymphatic drainage, the structure of the axillary fossa (part 2.). *Nowotwory. Journal of Oncology*, *71*(1), 62-69.

[12] Banerjee, S., Tian, T., Wei, Z., Shih, N., Feldman, M. D., Peck, K. N.,& Robertson, E. S. (2018). Distinct microbial signatures associated with different breast cancer types. *Frontiers in microbiology*, *9*, 951.

[13] Do Nascimento, R. G., & Otoni, K. M. (2020). Histological and molecular classification of breast cancer: what do we know? *Mastology*, *30*, 1-8.

[14] Poirier, É., Desbiens, C., Poirier, B., Boudreau, D., Jacob, S., Lemieux, J., ... & Provencher, L. (2018). Characteristics and long-term survival of patients diagnosed with pure tubular carcinoma of the breast. *Journal of Surgical Oncology*, *117*(6), 1137-1143.

[15] Zangouri, V., Akrami, M., Tahmasebi, S., Talei, A., & Hesarooeih, A. G. (2018). Medullary breast carcinoma and invasive ductal carcinoma: a review study. *Iranian Journal of Medical Sciences*, *43*(4), 365.

[16] Sun, P., Zhong, Z., Lu, Q., Li, M., Chao, X., Chen, D.,& He, J. (2020). Mucinous carcinoma with micropapillary features is morphologically, clinically and genetically distinct from pure mucinous carcinoma of breast. *Modern Pathology*, *33*(10), 1945-1960.

[17] Kulka, J., Madaras, L., Floris, G., & Lax, S. F. (2022). Papillary lesions of the breast. *Virchows Archiv*, 1-20.

[18] Demir, S., Sezgin, G., Sari, A. A., Kucukzeybek, B. B., Yigit, S., Etit, D., & Kucukzeybek, Y. (2021). Clinicopathological analysis of invasive cribriform carcinoma of the breast, with review of the literature. *Annals of Diagnostic Pathology*, *54*, 151794.

[19] Ogata, H., Mitsuzuka, Y., Honma, N., Yoshida, M., Sumazaki, M., Saito, F., & Kaneko, H. (2018). Sonographic visualization of nipple blood flow can help differentiate Paget disease from benign eczematous nipple lesions. *PLoS One*, *13*(5), e0197156.

[20] Rayzah, M. (2020). Phyllodes tumors of the breast: a literature review. *Cureus*, *12*(9).

[21] Gucalp, A., Traina, T. A., Eisner, J. R., Parker, J. S., Selitsky, S. R., Park, B. H., ... & Cardoso, F. (2019). Male breast cancer: a disease distinct from female breast cancer. *Breast cancer research and treatment*, *173*, 37-48.

[22] Bertucci, F., Ng, C. K., Patsouris, A., Droin, N., Piscuoglio, S., Carbuccia, N., & André, F. (2019). Genomic characterization of metastatic breast cancers. *Nature*, *569*(7757), 560-564.

[23] Kaur, D., & Kumar, S. (2018). Niosomes: present scenario and future aspects. *Journal of drug delivery and therapeutics*, *8*(5), 35-43.

[24] Umbarkar, M. G. (2021). Niosome as a Novel Pharmaceutical Drug Delivery: A Brief Review Highlighting Formulation, Types, Composition and Application. *Indian Journal of Pharmaceutical Education & Research*, *55*.

[25] Ahmadi, S., Seraj, M., Chiani, M., Hosseini, S., Bazzazan, S., Akbarzadeh, I., & Mostafavi, E. (2022). In vitro development of controlled-release nanoNiosomesfor improved delivery and anticancer activity of letrozole for breast cancer treatment. *International Journal of Nanomedicine*, 6233-6255.

[26] Ananthalakshmi, A. (2022). *Formulation and Evaluation of Alpinia Galanga Extract Loaded Niosomal Patch for the Treatment of Breast Cancer* (Doctoral dissertation, College of Pharmacy, Madras Medical College, Chennai).

[27] Kyriakoudi, A., Spanidi, E., Mourtzinos, I., & Gardikis, K. (2021). Innovative delivery systems loaded with plant bioactive ingredients: Formulation approaches and applications. *Plants*, *10*(6), 1238.

[28] Raj, S., Khurana, S., Choudhari, R., Kesari, K. K., Kamal, M. A., Garg, N., & Kumar, D. (2021, February). Specific targeting cancer cells with nanoparticles and drug delivery in cancer therapy. In *Seminars in cancer biology* (Vol. 69, pp. 166-177). Academic Press.

[29] Raj, S., Khurana, S., Choudhari, R., Kesari, K. K., Kamal, M. A., Garg, N., & Kumar, D. (2021, February). Specific targeting cancer cells with nanoparticles and drug delivery in cancer therapy. In *Seminars in cancer biology* (Vol. 69, pp. 166-177). Academic Press.

[30] Sharma, A., & Malairaman, U. (2020). *Development of Targeted Drug Delivery System for Breast Cancer* (Doctoral dissertation, Jaypee University of Information Technology, Solan, HP).