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CURCUMIN LOADED NIOSOMES AS TARGETED DELIVERY FOR THE TREATMENT OF BREAST CANCER

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ABSTRACT :

Breast cancer is one of the most common malignancies among women globally. In order to address the shortcomings of traditional diagnostic and therapeutic methods, nanotherapeutics are constantly in development. Nanotechnology-derived nanocarriers have numerous benefits including, low cytotoxicity, enhanced stability, increased half-life and improved entrapment efficiency. Curcumin is a bioactive molecule isolated from turmeric, has been thoroughly researched for its anti-cancer and chemopreventive activities. But its therapeutic use in breast cancer is restricted due to poor bioavailability and fast metabolism. To combat these issues, curcumin-loaded niosomes provide an effective drug delivery system. Niosomes are vesicular structures based on non-ionic surfactants, can entrap hydrophobic drugs such as curcumin by enhancing their solubility, stability and therapeutic activity. This formulation increases the controlled and sustained release of curcumin, also facilitating targeted delivery to breast cancer cells. In addition to this, this method is also found to have the capability to reduce side effects of traditional chemotherapies. Curcumin-loaded niosomes have proven to be an effective way of improving curcumin delivery to breast cancer cells.

KEYWORDS: Breast cancer, Niosomes, Curcumin, Targeted delivery, Controlled release.

INTRODUCTION:

Breast cancer is the leading cancer in females, which originates from the unrestrained growth of epithelial lining cells of breast ducts or lobules.
It is also second most frequent causes of cancer mortality globally. Breast cancer is determined by a mix of genetic, environmental and lifestyle determinants. Breast cancer is extremely heterogeneous disease, which results from the complex interaction between genetic risk factors and environmental factors. This dynamic interaction initiates a cascade of genetic and epigenetic changes in breast cells, eventually leading to the development of breast cancer. In spite of improvements in early diagnosis and treatment, such as surgery, chemotherapy and radiation therapy, problems like drug resistance, side effects and recurrence still limit the efficacy of existing treatment modalities. This has prompted intense research into new therapeutic approaches to enhance the efficacy and selectivity of treatments. New alternative treatment for breast cancer is most critical to alleviate patient suffering and mortality rates. Curcumin is a bioactive compound extracted from turmeric (curcuma longa).
It has various pharmacological activities. Curcumin, as a complex anticancer agent, utilizes various mechanisms to suppress cancer including modulation of signal transduction pathways, inhibition of cell growth, induction of apoptosis and generation of reactive oxygen species. In spite of its therapeutic potential, poor water solubility and bioavailability of curcumin suppress its therapeutic potential. To counter these issues, the progress of targeted drug delivery on the basis of nanoparticles is highly crucial. During the past decade, niosomes were recognized as a hopeful drug delivery, primarily for the drug with low stability, swift degradation and brief half-life. Niosomes have displayed outstanding advantages in cancer therapy as a targeted and effective drug delivery system.

BENEFITS OF CURCUMIN LOADED NIOSOMES FOR BREAST CANCER TREATMENT:

- **Enhanced bioavailability:**

Curcumin due to its poor solubility and absorption, it has limited bioavailability when administered orally. Niosomes encapsulate curcumin improving its solubility, stability and adsorption and allowing for better therapeutic efficacy.

- **Targeted delivery to tumors:**

Niosomes can be engineered to target specific cancer cells, such as breast cancer cells, through surface modifications. This targeted delivery minimizes the systemic exposure of curcumin, reducing side effects and improving therapeutic outcomes.

- **Reduced toxicity:**

By delivering curcumin directly to cancer cells, niosomes help to reduces the toxicity associated with conventional chemotherapies, which affect both cancerous and healthy tissues.

- **Controlled and sustained release:**

The niosomal formulation provides controlled and sustained release of curcumin over time. This ensures prolonged drug action at the tumor site, potentially reducing the frequency of administration and improving patient compliance.

- **Improved stability:**

Curcumin is prone to degradation due to its chemical instability under physiological conditions. Niosomes protect curcumin from degradation, ensuring that the active compound remains effective during treatment.

NIOSOMES IN CANCER TREATMENT:

Niosomes are bilayer structured molecule and these are vesicular systems composed of non-ionic surfactants and cholesterol. The combination of this enables the formation of a stable and flexible vesicle bilayer, allowing niosomes to effectively encapsulates and delivers the therapeutic agents. Niosomes are in the size ranges from 10-1000nm.

Niosomes are composed of amphiphilic molecules, which enable them to encapsulate both hydrophilic and hydrophobic therapeutic agents. These amphiphilic molecules self-assemble into a bilayer structure, forming the membrane of the vesicles. Since, niosomes have lower toxicity and enhancing penetration they are treating tumour cells at the targeted site without any side effects.

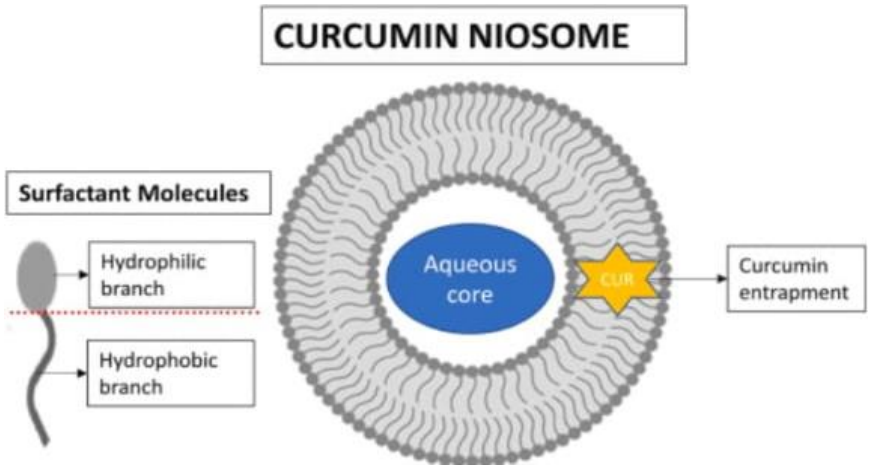
Recent research has demonstrated that niosomes can enhance the delivery of anticancer agents and offering several benefits such as targeted delivery, improved efficacy, reduced toxicity and mitigated side effects.

CURCUMIN-MECHANISM OF ACTION ON BREAST CANCER:

Curcumin produces anti-tumour activity, especially in breast cancer therapy. It produces its anti-cancer action through interference with a variety of signal transduction pathways responsible for breast cancer initiation and growth. Curcumin blocks certain processes such as, Wnt/β-catenin signaling inhibition, which is responsible for stem cell differentiation, tissue repair and cell proliferation. Blockade of P13K/Akt pathway, inhibiting angiogenesis, cell growth and proliferation.
Inhibition of EGFR signaling, responsible for cell growth and tumour growth.

CURCUMIN LOADED NIOSOME:

Niosomes are non-ionic, surface-active compounds with a bilayered compound contains a hydrophilic head, hydrophobic tail and aqueous core in the center of the vesicle. Niosomes can effectively encapsulate curcumin within their lipid bilayers, leveraging the hydrophobic nature of curcumin. This encapsulation strategy enhances curcumin's solubility, stability and bioavailability.



Curcumin noisome exhibits a bilayer structure, this dual region structure enables curcumin niosomes to enhance its solubility and bioavailability, improves drug entrapment efficiency and provide sustained release of curcumin. This structure of curcumin niosomes offers a versatile platform for delivering curcumin and other anticancer agents.

MECHANISM OF ACTION OF CURCUMIN-LOADED NIOSOMES:

- **Improved Bioavailability and Stability:**

Curcumin, a hydrophobic compound, has low bioavailability and is easily degraded in the body. Encapsulating curcumin in niosomes helps protect the drug from metabolic degradation and improves its solubility. This ensures that a higher concentration of curcumin reaches the bloodstream and target tissues, increasing its therapeutic efficacy.

- **Enhanced Cellular Uptake:**

Niosomes are designed to be small enough (typically 100–300 nm) to be efficiently taken up by cells via endocytosis. Once curcumin is encapsulated in niosomes, these vesicles facilitate the internalization of curcumin into cancer cells. The enhanced uptake of curcumin into breast cancer cells increases its intracellular concentration, allowing it to exert its anticancer effects more effectively.

- **Induction of Apoptosis (Programmed Cell Death):**

Once inside the cancer cells, curcumin activates various molecular pathways involved in apoptosis. It can induce the activation of caspases, a family of enzymes that play a central role in programmed cell death. Curcumin also modulates the expression of pro-apoptotic proteins (like Bax) and anti-apoptotic proteins (like Bcl-2), promoting cancer cell death.

- **Inhibition of Tumor Growth and Angiogenesis:**

Curcumin has been shown to inhibit the signaling pathways associated with tumor growth and angiogenesis (the formation of new blood vessels that feed the tumor). It inhibits key signaling molecules such as VEGF (vascular endothelial growth factor) and matrix metalloproteinases (MMPs), which are essential for tumor cell proliferation, invasion, and metastasis.

- **Anti-Inflammatory and Antioxidant Effects:**

Curcumin is a potent anti-inflammatory and antioxidant agent. In breast cancer cells, curcumin
suppresses the activation of inflammatory cytokines and transcription factors like NF-kB (nuclear factor kappa B), which are often upregulated in cancer and promote tumorigenesis. Additionally, curcumin scavenges reactive oxygen species (ROS), preventing oxidative damage to cancer cells and tissues.

CHALLENGES AND FUTURE DIRECTIONS:

Formulation and optimization: The optimization of niosomal formulations to maximize curcumin loading and ensure uniform size distribution remains a challenge. Further research is needed to fine-tune the surfactant composition and other factors influencing the formulation's stability and drug release.
Long term safety: Long-term safety studies are necessary to assess the chronic use of curcumin-loaded niosomes, particularly in terms of potential liver or kidney toxicity due to the accumulation of curcumin or surfactants.

CONCLUSION:

Curcumin has many properties like anti-fungal, anti-bacterial, anti-inflammatory and anti-tumour, whereas niosomes offers several advantages like enhanced bioavailability and reduced toxicity.
Curcumin loaded noisomes overcomes the problem in administering curcumin and improve the effective delivery.
Therefore, curcumin encapsulated niosomes are most promising nanomaterial for the treatment of anticancer.

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