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# Review: Revolutionizing Drug Delivery And Cancer Therapeutics Through Niosome Innovation

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## Abstract

Niosomes are vesicular nanocarriers, biodegradable, relatively non-toxic, stable, and inexpensive, that provide an alternative for lipid-solid carriers, niosomes similar to liposomes, can tackle challenges associated with instability, rapid degradation, bioavailability, and insolubility of various drugs or natural compounds. Niosomes are highly efficient systems for the targeted delivery of anticancer, antioxidant, anti-inflammatory, antimicrobial, and antibacterial agents. This review aims to provide an overview of their composition, the most common formulation techniques, and recent applications as delivery systems in cancer therapy.

Cancer remains a major health concern worldwide, and the need for effective treatment options is crucial. Drug delivery systems, such as niosomes, have shown promise in improving cancer treatment outcomes by enhancing drug delivery efficiency. This review explores the role of niosomes in cancer treatment and how they can improve outcomes through efficient drug delivery. The method, results, Discussion, and conclusion will be discussed in detail

Recently, nanotechnology is involved in various feilds of science, of which medicine is one of the most obvious. Nanoparticles have revolutionized the field of disease treatment and diagnosis, offering novel therapeutic strategies with efficient mechanisms of action. Personalized medicine aims to minimize treatment side effects and provide targeted therapies. Therefore, targeted drug delivery is crucial, particularly for patients on combination therapies, as different drug structures often require distinct delivery systems to maintain efficacy. Niosomes, a type of polymeric nanoparticle, have shown promise in drug delivery due to their favorable characteristics. These include biocompatibility, high absorption, reduced drug dosage requirements, and the ability to target drug release. Moreover, Niosome vesicles can encapsulate both hydrophilic and lipophilic drugs, enhancing the versatility and effectiveness of treatment. Various factors, such as components, preparation methods, and optimization techniques, affect the size and formation of niosomal structures. In this review, we first examined the characteristics of niosome vesicles and then explained the in silico tools used for designing, predicting, and optimizing them. We also compared and

discussed anticancer drugs delivered by niosomes, highlighting their potential as a model for designing therapeutic strategies. This research aimed to explore all aspects of drug delivery engineering using niosomes, and we presented clinical examples of these nanocarriers in cancer treatment to illustrate their clinical benefits.

Keywords: Cancer, Niosomes, Structure, Drug delivery, Treatment outcomes, Nanocarrier, Formulation techniques; Cancer therapy; Delivery systems.

## Introduction

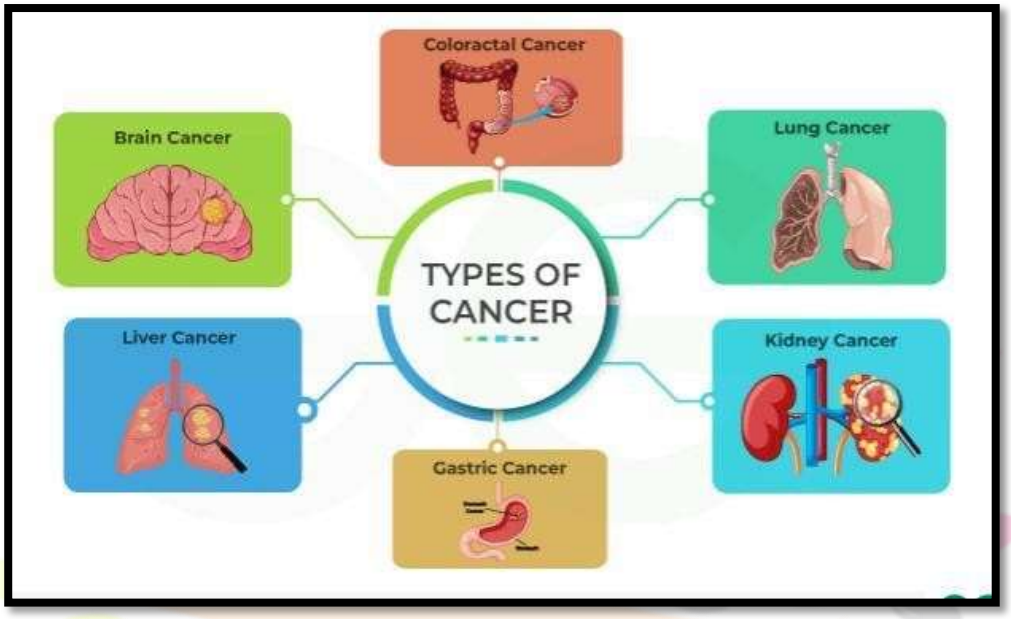
- **History**

The term 'cancer' is a Latin phrase which was previously known as 'karkinoma' in Greek. Cancer was identified thousands of years ago, even before the birth of Jesus Christ. The term 'karkinoma' was used by Hippocrates around 2300 years ago to describe various kinds ofcancer.[1,2]

Hippocrates, a renowned Greek physician from the Classical Greece era (ca. 460 – ca. 370 BC), is considered the "Father of Medicine."[2,3,4,5,6,7,8]. Hippocrates observed tumors with long, distended veins radiating in all directions, resembling the limbs of a crab or crayfish extending from its body. This resemblance led to the term 'karkinoma' to describe these tumors.[1,2,9].He based his observations on the cut surfaces of solid malignant tumors, such as breast tumors. He provided descriptions by making drawings of skin, nose, and breast tumors, which were outwardly visible, as it was against Greek tradition to dissect bodies for examination. Later, the Roman encyclopedist Aulus Cornelius Celsus (ca. 25 BC – ca. 50 AD) translated the Greek word 'karkinos' into 'cancer,' which means crab or crayfish in Latin. [10,11,12,13, 14]. Additionally, the Greek physician Claudius Galenus (also known as Galen; ca.130- ca. 200 AD) implemented the Hippocrates theory and proposed black bile and yellow bile caused incurable and curable cancer respectively; he began to use another term 'oncos' (means swelling in Greek) to describe any benign tumours, reserving Hippocrates' using of the term 'karkinos' for malignant tumours [14,15,16]. Galen also added –oma as suffix giving the name carcinoma (or karkinoma) to indicate cancerous lesions [16] and from his uses the modern word oncology was derived. However, the description of human cancer had been considerable much earlier by Egyptians. It was first described in the Edwin Smith Papyrus dated 3000 BC that illustrated a case of breast cancer. Moreover, several other types of tumors such as of skin, uterus, stomach, and rectum were recorded in other available documents as well as Ebers Papyrus dating from 1500 BC. In these old Egyptian documents cancer was represented as grave incurable disease and believed to be the curse of the gods[12, 14].From the time of Hippocrates to the post genomic era today, thousands of theories and scientific findings have paved the way to a far better scientific understanding of cancer today and modern approaches to this disease are based upon many of these theories as fundamental. Since there are many diseases that are developed due to uncontrolled division of cells in the body, cancer comprises a large group of diseases which are more than 100-200 diseases[1, 10, 17, 18, 19,20, 21, 22].While cancer may develop in any part of the body tissues or organs with each type having distinctive features, the basic

processes of developing into cancer are quite similar in all forms of the diseases[17, 23, 24]. When the abnormal body cells start to grow uncontrollably, they move beyond their usual borderlines of the tissue or organ and invade/spread into the adjoining areas and/or to other parts of the body organs. The latter process of spreading or invading to organs is calledmetastasis which is a major cause of death from cancer.

Fig.1Types of cancer




- **Current status**

According to the WHO, cancers cause the biggest health problems worldwide, affecting both men and women. Men have a higher burden (137.4 million DALYs) compared to women (107.1 million DALYs), with a total of 244.6 million DALYs. This is followed by heart disease (203.7 million DALYs) and stroke (137.9 million DALYs). The cancer burden is slightly higher in men than in women (9.6% vs. 8.6%), but this difference is not significant. Most of the disease burden is seen in people over 60 years old (124.2 million DALYs; 50.8%).

In children aged 14 years or younger, the most common cancers are leukemia (37%), brain and nervous system cancers (16%), and lymphomas (13%). In people aged 15-49 years, breast cancer (13%) is the most common, followed by liver cancer (12%) and lung cancer (9%). For those aged 50-59 years, lung cancer is the most frequent (18%), followed by liver (11%) and breast (9%) cancers. In people aged 60 years or older, the most common cancers are lung (21%), colorectal (9%), stomach (9%), and liver (9%).

In 2018, 18.08 million new cancer cases were diagnosed worldwide. The most common types were:

1.Lung cancer (including trachea and bronchus): 2.09 million cases2.Breast cancer: 2.09 million cases

3. Prostate cancer: 1.28 million cases

- Breakdown by Gender:
- Men:

1.Lung cancer: 1.37 million cases 2.Prostate cancer: 1.28 million cases 3.Stomach cancer: 0.68 million cases

4.Liver cancer (including intrahepatic bile ducts): 0.60 million cases

- Women:

1.Breast cancer: 2.09 million cases 2.Lung cancer: 0.72 million cases 3.Cervical cancer: 0.57 million cases

4.Colon cancer: 0.58 million cases5.Colorectal Cancer:

Overall: 1.80 million cases, making it the third most frequent cancer.Women: 0.79 million cases, second most frequent.

Men: 0.98 million cases, third most frequent.

In terms of prevalence, the Global Burden of Diseases, Injuries, and Risk Factors Study reported 100.48 million cancer cases in 2017, showing a 1.59-fold increase since 1990.[25]

Breast cancer has the highest age-standardized incidence rate at 46.3 per 100,000 people, followed by prostate cancer at 29.3, lung cancer at 22.5, colorectal cancer at 19.2, cervical cancer at 13.1, and stomach cancer at 11 per 100,000.

Cancer Risk Statistics:

Overall risk of developing cancer between ages 0-74 is 20.2% (22.2% in men and 18.1% in women).

Highest cancer risk in men:

Lung cancer: 3.80%

Prostate cancer: 3.73%

Colorectal cancer: 2.71% Highest cancer risk in women:

Breast cancer: 5.02%

Colorectal and lung cancers: both 1.77%Cervical cancer: 1.36%

Gender Ratio of Cancer Frequency:

The frequency ratio is higher in men than in women for all cancers except thyroid cancer, where the ratio is 0.30.

The highest men-to-women ratios are for:

Bladder cancer: 3.38

Liver and intrahepatic bile duct cancers: 2.44Esophageal cancer[51]

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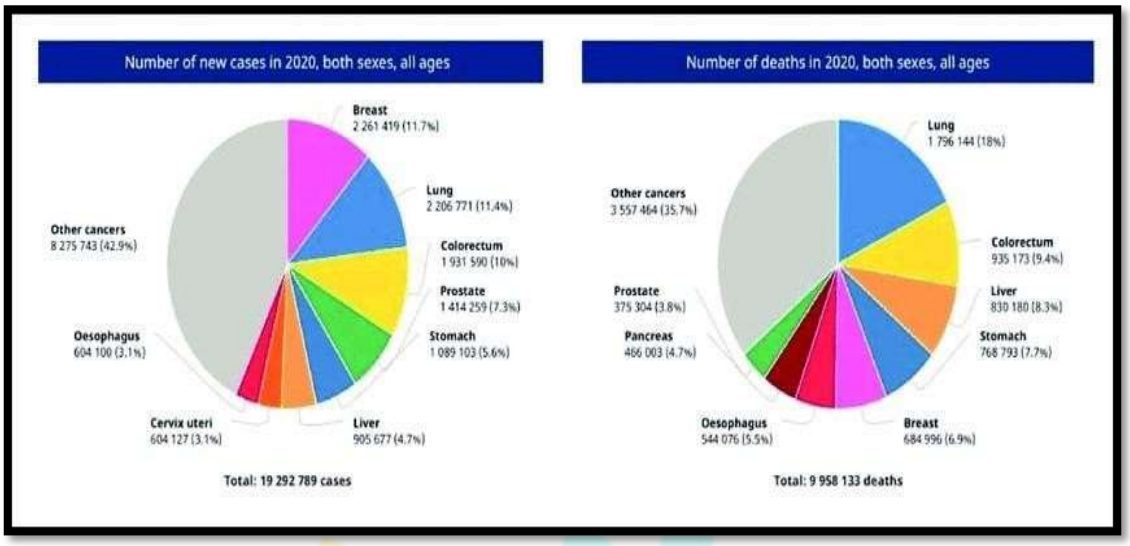
Fig.2.Current status of cancer

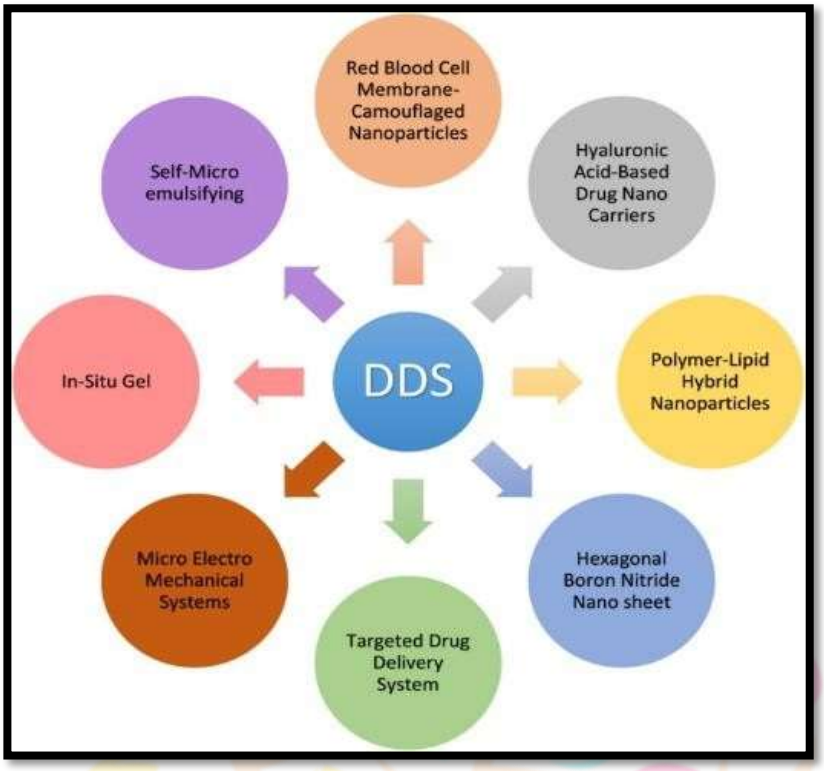



- **Revolutionizing Drug Delivery System**

Recent advancements in drug delivery systems (DDS) have led to the development of innovative nanoparticle-based carriers, significantly enhancing the effectiveness of chemotherapy and other treatments. These carriers, made from organic, inorganic, and hybrid nanoparticles, offer numerous advantages over traditional dosage forms. Key improvements in recent DDS include: particle size, increased permeability, increased solubility, efficacy, specific site targeting, stability, toxicity, and sustained delivery. They can significantly improvetherapeutic agent performance over conventional dosage forms[26,27]..

In the development of an optimal drug delivery system, recent drug delivery systems are recognized to be the newest developments and innovation in understanding of the pharmacokinetic and pharmacodynamic behavior of pharmaceuticals. Because these DDS are transporters, they can keep medication concentrations in the therapeutic range for a extended period while also delivering material to the site of action. The adoption of the delivery mechanism is directly linked to the commercial and therapeutic success of the innovation. This would entail involving patients early in the development process, recognizing any problems, and ensuring that they receive the most out of the device. Improving delivery systems that enhance efficacy by reducing toxicity. The various types of drug delivery systems are depictedin Fig.3.

Fig.3.Several types of recent drug delivery systems for different therapeutic purposes




## ➢ Drug Delivery On Cancer Treatment

Nanoparticles are currently studied for their use in detection of cancer at its earlier stage and in targeted anti-cancer drug delivery of the above mentioned drugs. Detecting cancer at its initial stage of carcinogenesis is a critical step in effective cancer treatment. Results of the numerous researches done in nanotechnology are inspiring the scientific community to discover new innovative non-Invasive tools at the nanoscale level for such purposes. Nanoscale cantilevers[28] and quantum dots [29, 30] are being studied as cancer detection tools at the cellular level. If the tumour has not been detected in its early stage, treatment methods should be devised to eradicate the fully developed cancer cells without harming the normal healthy cells of human body. Targeting of nanoparticles Can be divided into 'active' and 'passive' targeting[31]. Active targeting can be further subdivided into 'chemical/biological' and 'physical' targeting. Chemical/biological targeting involves modification of a nanoparticle surface by chemical/biological tumour-specific ligands. Physical targeting involves directing the nanoparticles to tumour cells under the influence of an external magnetic field. Passive targeting involves modifying the nanoparticle itself without the addition of any ligands or physical methods, thereby strengthening the circulation time. This enables accumulation of nanoparticles in tumours by an effect called 'enhanced permeability and retention effect' (EPR) effect. The EPR effect utilizes the property by which certain sizes of molecules, typically liposomes or macromolecular drugs, tend to accumulate more in tumour tissue than in normal tissues[32,33]. In order for the tumour cells to grow quickly, they must stimulate the production of blood vessels (angiogenesis). Tumour cell aggregates of size as small as 150-200 Um, start to become dependent on blood supply for nutritional and oxygen supply. These newly formed tumour vessels are usually abnormal in form and architecture. Furthermore, tumour tissues usually lack effective lymphatic drainage. All these factors lead to abnormal molecular and fluid transport dynamics especially for macromolecular drugs. The EPR-

effect is even more enhanced by many pathophysiological factors like more vascular endothelial growth factor (VEGF) production by the newly developing capillaries. The EPR effect also provides a great opportunity for more selective targeting of lipid or polymer-conjugated anticancer drugs [34, 35]. The various types of nanoparticles that are currently studied for their use as drug delivery systems are polymeric micelles, magnetic nanoparticles, colloidal gold nanoparticles and ceramic nanoparticles[36-37]. These nanoparticle-based drug delivery systems can be characterized for their localization in tumour cells by coating them with tumour-specific antibodies, peptides, sugars, hormones and anti-carcinogenic drugs, to mention a few. These nanoparticles have been effectively coupled with the above mentioned anti-carcinogenic chemotherapeutic agents and have been tested for their target-specificity. These nanoparticles are superior over the conventionally available drug delivery systems as the chemotherapeutic agents can be targeted to a specified area of the human body by adding nanoscale surface receptors. These receptors specifically recognize the target tissue and bind to it and release the drug molecules [38]. Thus healthy cells can be spared from cytotoxic effects of the drug. Drugs can also be protected from degradation by encapsulating them with nanoparticle coatings [39]. As nanoparticles are very small, they can penetrate through smaller capillaries and are easily taken up by cancer cells. This causes efficient drug accumulation at the target site. Use of biodegradable nanoparticles allows sustained drug release over a period of time [40]. Thus nanoparticles as drug delivery systems with enhanced target specificity can overcome the limitations of conventional cancer treatment techniques.

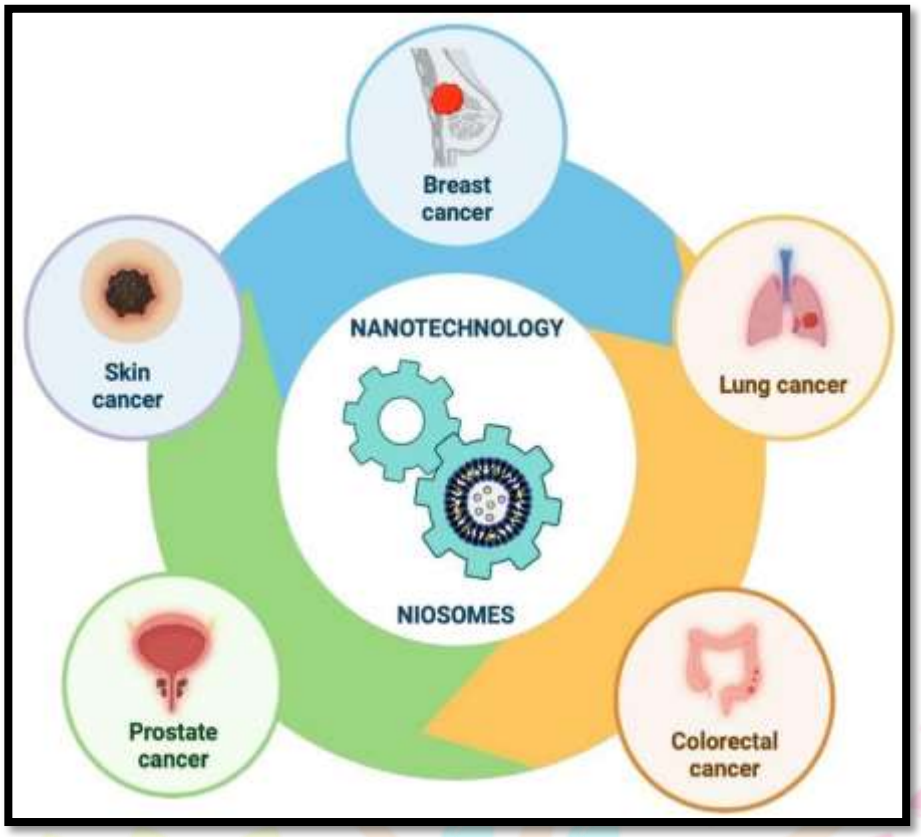
- **Recent Progress in Niosomes as Delivery Systems in Cancer Therapy**

Surgery, chemotherapy, radiotherapy, immunotherapy, gene therapy, magnetic hyperthermia, and others are available in the current clinical treatments for malignant tumor, which is one of the deadliest diseases in the world [41–43]. Surgery is crucial in many Cancer therapies, but achieving safe, timely, and efficient cancer surgery is a challenging task. Other therapeutic clinical treatments rely on molecules with anticancer activities, but they are usually limited by multiple issues such as poor solubility and bio distribution, adverse reactions, reduced therapeutic efficacy, or even treatment failure.

Advanced techniques, strategies, and materials to fight cancer have been the subject Of tremendous research efforts during the last decades [44,45,46]. Nanotechnologies have become broadly investigated for cancer treatment, in line with advances in biotechnology, to enhance safety, accuracy, and effectiveness by utilizing the unique properties of designed nanomaterials[46,47]. Until now, targeted cancer therapy has been engineered using a different of organic (e.g., polymeric micelles, liposomes, niosomes, dendrimers) and inorganic nanoparticles (e.g., gold nanoparticles, silver nanoparticles, iron-oxide nanoparticles), some of them being currently studied or approved in preclinical or clinical trials [46–50].

Our review focused on recent relevant studies aimed at enhancing the targeted delivery Of different chemotherapeutic molecules (drugs or natural compounds) using nanotechnology, specifically on niosomes nanoparticles, exploring their use in the most common types of cancers found worldwide (Fig.4.).

Fig.4.Recent progress in niosomes in the most common types of cancers found worldwide




- **Recent Progress in the Development of Niosomal Formulations for Drug/NaturalMolecules Delivery in Different Types of Cancer**

Table 1. Various niosome formulations functionalized with specific agents/ligands in different types of cancer: composition, formulation method, type of drug or Natural molecule encapsulated, and the main results obtained.

| Type of Cancer | Formulation Method | Drug/Natural Molecules | Composition | Niosomal Formulation Results | Referenc |
|---|---|---|---|---|---|
| Breast Cancer | Thin-film hydration | Tamoxifen | Spans (20, 40, 60, 80), cholesterol | Inhibitory effects on cancerous lines: MDA-MB-231, SKBR3 cells;Less IC50 values; Significant down regulation of cyclin D, cyclin E, VEGFR-1, MMP-2, MMP-9 genes and up regulation of caspase-3, caspase-9 genes; Increase caspase activity and apoptosis induction in | 52 |

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| | | | | cancerous cells. | |
| | | Docetaxel | Span 40, PF108 | AD = 244.9 nm; EE (%) = 97.43 ± 1.2%; PDI = 0.75; ZP = −10 mV;Niosomal formulation improved the Docetaxel stability; Sustainable release duringan in vitro drug releasestudy; MCF-7 cells significantly affected; | 53 |

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| | | Metformin,Celecoxib | Span 60, cholesterol/<br><br>Span 60, cholesterol,<br><br>Tween 80 | Metformin-loaded niosomes: AD = 110.6 ± 0.6nm; EE (%) = 68.94 ±1.28%; RD (%) = 89.2%; PDI = 0.139 ± 0.017; ZP = −44.42 ± 1.990 mV; Celecoxib-loaded niosomes: AD = 96.7 ± 0.7nm; EE (%) = 94.44 ±2.09%; RD (%) = 77.80%; PDI = 0.278 ± 0.003;ZP = −53.89 ± 5.680 mV; Metformin-loaded niosomes (62.44% viability)outperformed free Metformin (80.37% viability), showing significantly lower cell viability; free Celecoxib exhibited a viability of 3.18%,while Celecoxib-loaded niosomes showed 1.59% viability;In MDA-MB-231 cells, both Metformin-loaded niosomes and Celecoxib-loaded niosomes showed lower IC10 and IC20 values than their respective free drugs, non-lethal doses; | 54 |

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| | | | | Penetration rate of Metformin-loaded niosomes (85.26%) surpassing free Metformin(61.50%), and the penetration rate of Celecoxib-loaded niosomes (71.08%) compared to free Celecoxib (31.29%). | |
| | | Gemcitabine | Cholesterol, Span 60, Tween 60 | AD = 205 nm; EE (%) = 89.9 ± 1.27%; PDI = 0.19 ± 0.03; RD (%) = 49.7 ± 1.3% after 48 h, while about RD (%) = 87% free Gemcitabine after 4 h; Anticancer activity is superior to free Gemcitabine in treating SH-SY5Y and MCF7 cells during the same incubation period (14.0 and 19.7 ng/mL, respectively); | 55 |

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| | | Ascorbic acid,<br><br>Geranium oil | Cholesterol, Span 60,<br><br>Tween 60 | AD = 219.4 ± 44.5 nm; EE (%) = 98.3 ± 4.2% (ascorbic acid), 98.7 ± 3.1% (geranium oil); PDI = 0.23 ± 0.20; ZP = −11.1 ± 1.39; IC50 (µg/mL) = 7.69 ± 8;Significantly higher increase apoptotic effect on MCF-7 cells;<br>Antioxidative activity. | 56 |
| | | Curcumin | Span 80, diacetyl<br><br>phosphate, Cholesterol,<br><br>Calcium alginate | AD = 167.1 nm; EE (%) = 94.949%; RD (%) = 61.7 ± 1.23%;<br><br>Greater biocompatibility in cytotoxicity tests than particles without free Curcumin;<br>Enhanced chemotherapy effect due to the alginate. | 57 |
| | | Cisplatin, Epirubicin | Spans, cholesterol,PEG | AD = 192.5 ± 8.9 nm; EE (%) = 91.24 ± 1.32 (Cisplatin),71.93 ± 1.11% (Epirubicin);<br>RD (%) = 36.78% (Cisplatin), 56.30% (Epirubicin);PDI = 0.142 ± 0.012;Improved stability for two months and continued release in<br>physiological pH; | 58 |

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| | | | | Antitumor activity toward SKBR3 and 4T1 cancercells; Exhibit lower cytotoxicity toward healthy cells; Significant inhibition of cancer cells' migration and division than with free drugs. | |
| | | Curcumin,Folic acid | Spans, diacetyl phosphate, cholesterol | AD = 187.13 ± 7.55 nm; EE (%) = 98.2517 ± 0.7851%;PDI = 0.160 ± 0.033; ZP = −8.1 mV;Exhibit higher cellular uptake efficiency in vitro; Induce high apoptosis ratein breast cancer cells (MCF7 and 4T1). | 59 |
| | | Letrozole, Cyclophosphamide, Folic Acid | Span 60, cholesterol | AD = 213.9 ± 3.2 nm; EE (%) = 94.10 ± 1.85%(Cyclophosphamide), 98.50 ± 1.88% (Letrozole); PDI = 0.143 ± 0.007; IC50 values (µg/mL) for MDA-MB-231 = 31.13 ± 1.35 (48 h) and 23.18 ± 1.07 (72 h);IC50 values (µg/mL) for SKBR3 cell = 24.92 ± 1.35 (48 h) and 20.94 ± 1.07 (72 h);Treatment led to a significantly higher increase | 60 |

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| | | | | in Caspase-3, Caspase-9 levels, and a more significant decrease in cyclin-D, Cyclin-E, MMP- 2, and MMP-9 expression levels; Increase total apoptosis in treated cancer cell lines. | |
| | | Farnesol,Gingerol | Tween 60, Span 60, cholesterol | AD = 224 ± 14.60 nm; EE (%) = 67.29 ± 1.46% (Gingerol), 92.63 ± 2.57% (Farnesol);PDI = 0.171; Controlled drug release atpH = 7.4;Excellent improved biocompatibilityin comparison to free Farnesol and Gingerol; Show significant cytotoxicity toward MCF7, and SKBR3 breast cancer cells; Synergistic inhibitory effect of combined drugs improved chemotherapy; Induce apoptosis in both MCF7 and SKBR3 cell lines. | 61 |

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| | | Doxorubicin | Span 60, cholesterol, gelatine, alginate | AD = 226.4 ± 7.95 nm; EE (%) = 73.69 ± 1.68%; PDI = 0.189 ± 0.011; ZP = −13.74 ± 1.49 mV; Excellent biocompatibility with non-tumorigenic breast cells (MCF-10A); High cytotoxicity against breast cancer cells (MCF-7). | 62 |
| | | Cisplatin, Doxorubicin | Span 60, cholesterol | AD = 313.0 ± 9.22 nm; EE (%) = 80.65 ± 1.80% (Doxorubicin), 65.54 ± 1.25% (Cisplatin); PDI = 0.261 ± 0.01; ZP = −30.65 ± 0.64 mV; Higher synergetic inhibitory effect of combined drugs; The caspase activity assay indicated that the cancer cells treated had significantly higher Caspase 3/7 activities compared to uncoated niosomes and free drugs; Higher effective apoptosis induction rate, and cell cycle arrest in cancer cells; | 63 |

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| | | Epirubicin,<br><br>Hyaluronic acid | Span 60, cholesterol | AD = 225.9 nm; EE (%) = 82.1%;PDI = 0.160;CD44-mediated internationalization into breast cancer cells; Improve Epirubicin impacton breast cancer cells, including an increase in cytotoxicity and apoptosis,as well as inhibition of metastasis. | 64 |
| | | Morusin | Span 60, cholesterol | AD = 479 nm; EE (%) = 97 ± 1.25%;PDI = 0.29; ZP = −19.8 mV;Inhibit the survival of MDA-MB-453;Cause considerable toxicityin the cells treated, leading to a decrease in the numberof alive cells and an increase in dead cells. | 65 |
| | | Melittin | Span 60, Tween 60,<br><br>cholesterol | Affects gene expression by down regulating the expression of Bcl2, MMP2, MMP9 genes while upregulating the expressionof Bax, Caspase3, Caspase9;Enhanced the apoptosis rate and inhibited cell migration. | 66 |

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| | | Paclitaxel | Tween 60, Span 60, ergosterol, cholesterol hemi succinate | AD = 240 nm; EE (%) =77.0 ± 2.3%;<br>Show high efficacy against human cancers derived from cervix and breast tumors. | 67 |
| | | Paclitaxel | Span 60, cholesterol | AD = 192.73 ± 5.50 nm;<br>EE (%) = 94.71 ± 1.56%;<br>Significant cytotoxicity on breast cancer cell lines including MCF-7, T-47D, SkBr3,MDA-MB-231 in a time- and dose-dependent manner. | 68 |
| | | Curcumin | Tween 60, Tween 80, cholesterol | AD = 110 ± 0.45 nm; EE(%) = 78.34%; RD (24 h, 37 ◦C) = 19 ± 0.67%; PDI = 0.21 ± 0.16; ZP = −24 ± 0.34 mV;<br>The presence of both positive charge and niosome promote cellularuptake via changing the penetration mechanism to endocytosis;<br>Reduce the expression ofNF-κB and improve the p53 better than their free states. | 69 |

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| | | 2,5-Diketopiperazine | Span 60, Tween 60, cholesterol; Tween 40, Span 40, cholesterol | AD = 149.43 ± 3.2 nm; EE (%) = 70.22 ± 0.13%; PDI = 0.171 ± 0.025;Inhibit proliferation and invasion of MCF-7, MDA- MB-231, AU-565 malignant cells in vitro;Breast cancer cells' proliferation is directly influenced by the presence of niosome-encapsulated BHPPD. | 70 |
| | | Carnosine,Melittin | Span 60, cholesterol | AD = 58 ± 0.50 nm (Carnosine), 163 ± 1.3 nm (Melittin);PDI = 0.16441 ± 0.04 (Carnosine), 0.0424 ± 0.1 (Melittin);ZP = −20 ± 0.3 mV (Carnosine), −86.6 ± 0.9 mV (Melittin); Melittin-loaded niosomes showed significantly greater anticancer activity on breast cancer cells compared to Carnosine- loaded niosomes; Carnosine-loaded niosomes inhibit the cells at the G2/M phase transition in MCF-7 cells and S phase atMDA-MB- 231 cells; Melittin-loaded niosomes inhibit both cells at the G0/1 phase transition and occur inhibition of cells atS phase. | 71 |

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| | | Ascorbic acid, Curcumin | Tween 60, Span 60, cholesterol | AD = 224.30 ± 6.52 nm; EE (%) = 74.75 ± 1.35% (Ascorbic acid), 93.19 ± 1.88%(Curcumin); PDI = 0.084 ± 0.012; ZP = −23.7 ± 1.03 mV;Exhibit a higher apoptotic rate and enhance anticancer effects against breast cancer MCF-7 cells | 72 |
| | | Doxorubicin, Curcumin | Tween 60, Span 60, cholesterol, PEG | AD = 273.1 ± 3.2 nm; PDI = 0.39 ± 0.08;EE (%) =62.90 ± 1.1% (Doxorubicin), 96.50 ± 3.7% (Curcumin); ZP = −43.2 ± 1.0 mV; IC50 value (µg/mL) on the MCF-7 cell line = 20.7 ± 2.3;Show a more controllable release mannerand enhance cytotoxicity on cancer cells after PEGylation. | 73 |
| | | Trastuzumab, Mcl-1 Nioplex | Span 20, cholesterol-basedcationic lipids | Exhibit cell-growth inhibition in both HER2-positive and HER2- negative breast cancer cells; Decrease cell survival and promote apoptosis compared to single treatment in HER2-overexpression breast cancer cells | 74 |

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| Lung cancer | Thin-film hydration | Nintedanib | Span 60, cholesterol, 1,2-dioleoyl-3-trimethylammonium-propane(DOTAP) | AD = 246.2 ± 2.3 nm; EE (%) = 73.1 ± 2.7%; PDI = 0.19 ± 0.08;<br>ZP = −20.5 ± 1.9 mV;<br>IC50 values in different human non-small-cell lung cancer cell lines: 1.5 ± 0.8 (A549),<br>1.8 ± 0.3 (H2122), 2.1 ± 0.8 (H1299), 1.1 ± 0.4 (H358), 1.3 ± 0.5 (H460);<br><br>Incorporation of cationically charged lipidincreased drug<br><br>encapsulation in niosomes along with optimum vesicle size and size distribution;<br><br>Possess appropriate aerosolization propertiesfor efficient pulmonary delivery;<br><br>Significant inhibitory action on the metastatic property of NSCLC cells. | 75 |
| | | Artemisin,Metformin | Span 60, cholesterol | AD = 256 nm; EE (%) =95%; PDI = 0.202;<br><br>Increase Bax levels in a dose-dependent manner;<br><br>Anticancer effect against A549 cancer cells. | 76 |

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| | | Metformin,Silibinin | Span 60, cholesterol, PEG | AD = 162.5 ± 1.8 nm; EE(%) = 95%; PDI = 0.424;<br><br>ZP = −17.7 ± 7 mV;<br>Induce apoptosis and cell cycle arrest in the A549 lung cancer cell line; Significant reduction in expression of hTERT andBCL-2 genes. | 77 |
| | | Sunitinib | Span 60, cholesterol | Triggered apoptosis in in vitro experiments of lung cancer cell lines (A549); Caused downregulation or upregulation of genes associated with apoptosis; | 78 |
| Colorectal cancer | Various techniques formulation (thin-film hydration, reverse- phase evaporation, sonication, ethanol injection) | 5-fluorouracil | Span 60, Tween 60, cholesterol | 5-Flurouracil-loaded niosomes displayed a slight decrease in cell viability (reduced cell index) compared to the pure drug. | 79 |

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| | Thin-film hydration | Oxaliplatin,Paclitaxel | Span 60, Tween 80, TPGS | AD = 285.8 ± 23.5 nm (Oxaliplatin), 258.6 ± 13.3nm (Paclitaxel); EE (%) = 91.03 ± 2.80% (Oxaliplatin), 93.31 ± 3.31% (Paclitaxel); PDI = 0.295 ± 0.07 (Oxaliplatin), 0.287 ± 0.09 (Paclitaxel); ZP = −33.25 ± 1.41 mV (Oxaliplatin), −32.99 ± 1.08 mV (Paclitaxel); Using vesicular niosomes to administer both drugs altered their release rate in comparison to their free counterparts, as they demonstrated extended drug release; Oxaliplatin and Paclitaxel's cytotoxicity and apoptosis efficacy were significantly improved by encapsulation into niosome particles compared to the free drugs. | 80 |
| | | Curcumin, Saccharomyces Cerevisiae | Span 60, cholesterol, PEG | AD = 201 ± 9.94 nm; EE(%) = 88%; PDI = 0.193; ZP = − 17.14 ± 4.8 mV; Show favorable results compared to free curcuminin gene expression, cytotoxicity, apoptosis induction, cell cycle arrest, and invasionrate reduction tests. | 81 |

| | | | | | |
|---|---|---|---|---|---|
| | | Silibinin | Span 60, Tween 80, cholesterol | AD = 70 nm; PDI = 0.52;ZP = −19.0 mV; Cytotoxic effects on HT-29 colon cancer cells in a dose- and time- dependent manner;Show accelerated release rate in acidic pH in cancer cells compared to the neutral condition. | 82 |
| Prostate cancer | Thin-film hydration followed by bath sonication | Lycopene | Tween 60/Span 60, cholesterol | AD = 136.00 ± 8.83 nm; PDI = 0.460 ± 0.02; ZP = −36.0 ± 3.45 mV; Significantly reduce cell viability for PC-3 and LNCaP cells; Increase antiproliferativeand apoptotic effects on PSMA + LNCaP cell; Increase cellular uptake. | 83 |
| Skin cancer | Microfluidic mixing | Hippadine | Span 60, cholesterol | AD = 138.40 ± 1.40 nm; EE (%) = 35.98 ± 0.99%; PDI = 0.15 ± 0.01; ZP = −32.80 ± 2.50 mV; Significantly improve the characteristics of hippadineby increasing its cytotoxic properties; Improve molecule solubility and enhance druguptake by the cells at a higher rate. | 84 |

| | | | | | |
|---|---|---|---|---|---|
| | Solvent injection Method | Gammaoryzanol | Span 60, dicetyl phosphate, Carbopol 940 | AD = 196.6 ± 0.9 nm; EE (%) = 78.31%; PDI = 0.268 ± 0.02;ZP = − 41.6 mV; pH niosomal gel = 7.3 ± 0.1; Reduce the frequency of drug administration | 85 |
| | Thin-film Hydration | Amygdalin | Cholesterol, Tween 60,DDP, Carbopol934 | Show significant antitumor activity compared with oral Tamoxifen; Enhance permeation into deep skin layers. | 86 |
| | | Ozonated olive oil | Cholesterol, Span 60,Tween 60 | AD = 125.34 ± 13.29 nm; EE (%) = 87.30 ± 4.95%;PDI = 0.24 ± 0.04; ZP = −11.34 ± 4.71 mV; Ensure sustained release behavior and improve skin permeation; Exert anticancer activity on A375cells. | 87 |

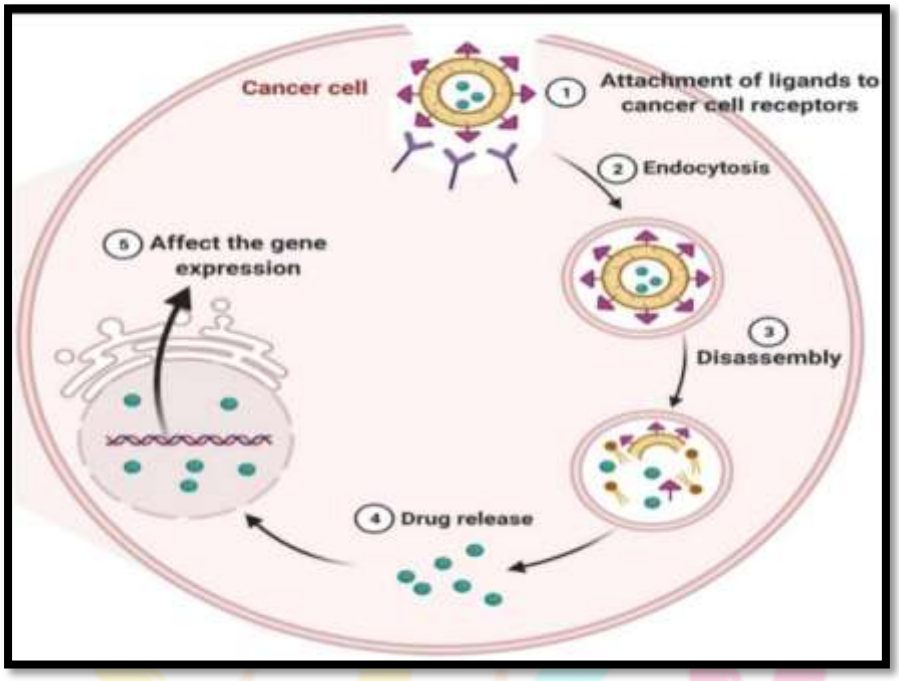
AD = average diameter; EE (%) = encapsulation efficacy; RD (%) = released drug; ZP = zetapotential; PDI = polydispersity index.

- **Anticancer properties**

Cancer is the major cause of death and poor quality of Life worldwide. Several strategies have been developed to decrease mortality, reduce chronic pain, and improve quality of life, but the adequacy of these cancer treatments is flawed. One of the most important steps to ensure optimal treatment of cancer is the early detection of cancer cells and the administration of extremely specific drugs to reduce toxicity. Due

to the ubiquitous toxicity and inefficacy of conventional cancer diagnosis and therapy, other strategies, including nanotechnology, are being used to improve diagnosis and reduce the severity of the disease. For many years, nanotechnology-based immunotherapeutic agents have been used to treat many types of cancer by keeping healthy cells at the target by reducing cancer cell invasion[88]. The drug's poor solubility results in low bioavailability and quick degradation, complicating its clinical application. To overcome this, S. Agarwal Et al. enhanced the solubility of the drug in the aqueous phase using a niosomic system containing a neon surfactant SPAN 60 and cholesterol. Highly cytocompatible niosomes, averaging 479 nm in size, were easily synthesized, exhibiting a smooth and uniform spherical morphology. Unlike free morocin, nanomorocin is readily dispersed in an aqueous environment. A very high entrapment efficacy (97%) controlled and sustained release of moracin was observed, resulting in improved therapeutic efficacy in 4 different cancer cell lines. The results suggest that the morose niosome system is a promising strategy to increase antitumor activity against several cancer types and may be an important tool for future targeted chemotherapy strategies [89]. Another study was reported by Kong et al. in which operated niosomes were used as a transdermal drug delivery system for cancer Therapy. These researchers have developed a new drug Nanoparticle based on hyaluronic acid and niosomes that facilitates drug delivery through the skin and has potential for cancer targeting. Their results demonstrated that The combination of hyaluronic acid significantly increased The endocytosis of nanocarriers in cancer cells. Hyaluronic Acid niosomes can be considered as effective and safe carrier's for penetration through the skin and also an effective and promising tool for treating tumors by dermal administration [90]. In another investigations by Bayindir et al. The physiological and biological physiological properties Of niosomes which was loaded with the nucleophilic Ru(III)-complex HoThyRu as an anticancer agent and the Nucleolin-targeting AS1411 aptamer allowing to recognition of cancer cells selectively. Using various biophysical Techniques, the morphology, average size, zeta potential, electrophoretic mobility, and stability were analyzed. The results showed that antiproliferative activity of HeLa Cells enlarged significantly. In all the tested cell lines, AS1411 proved to efficiently enhance the bioactivity of The Ru (III)-containing niosomes[91,92,93].Applications of niosomal formulations in cancer diseases is shown in Fig.5.

Fig.5.Applications of niosomal formulations in cancer diseases




**NIOSOME**

❖ DEFINITION:

A Niosome is defined as a nonionic surfactant based liposome. Niosomes are formed mostly by with or without incorporation of cholesterol as an excipient and their lipids as an excipient. Niosomes are biodegradable and biocompatible immunogenic vesicles.

❖ ADVANTAGES AND DISADVANTAGES:

1.**Advantages:**

1. Drug molecules of broad range of solubilities can be accommodated in the niosomes provided by the Infrastructure consisting of hydrophilic, lipophilic and amphiphilic moieties.
2. They can release the drug in sustained or controlled manner.
3. They can act as a depot formulation, thus permitting the drug release in a controlled manner.
4. They have stable structure even in emulsion form.
5. Surfactants are biodegradable, biocompatible, non-toxic and non-immunogenic.6.They are economical for large scale production.
7. They can protect a drug from enzyme metabolism.
8. Therapeutic performance of the drug molecules can be improved by tardy clearance from circulation.
9. They can protect a active moiety from biological circulation.[94,95] 10.The characteristics features like size, shape, nature can be changed.11.Enhances the stability of the entrapped drug.
12. Improves the penetration of drug into the skin.
13. They are osmotically active therefore has longer storing period.14.Better patient compliance.[96]
15. Handling as well as storage of surfactants do not require any special conditions.

16. They can increase the oral bioavailability of drugs.
17. They can be assemble to reach the site of action by oral, parenteral, and also topical routes.
18. They can entrap both hydrophilic as well as hydrophobic drugs.
19. They are chemically stable compare to liposomes.
20. No tissue irritation and damage was caused by penetration enchancers.[97]

2. **Disadvantages:**

1. Aggregation
2. Leaking of Entrapped Drug3.Physical instability
4. Time consuming[98]
5. In rare cases, non-ionic surfactant interacts with other components of the system rendering the formulation homogenous or from precipitates.
6. Fusion[99]

❖ TYPES OF NIOSOME: [100]

| | | |
|---|---|---|
| Multi lamellar vesicles(MLV) 1-5 micron | Large unilamellar vesicles(LUV) 100-250nm | Small unilamellar vesicles(SUV) 20-100nm |

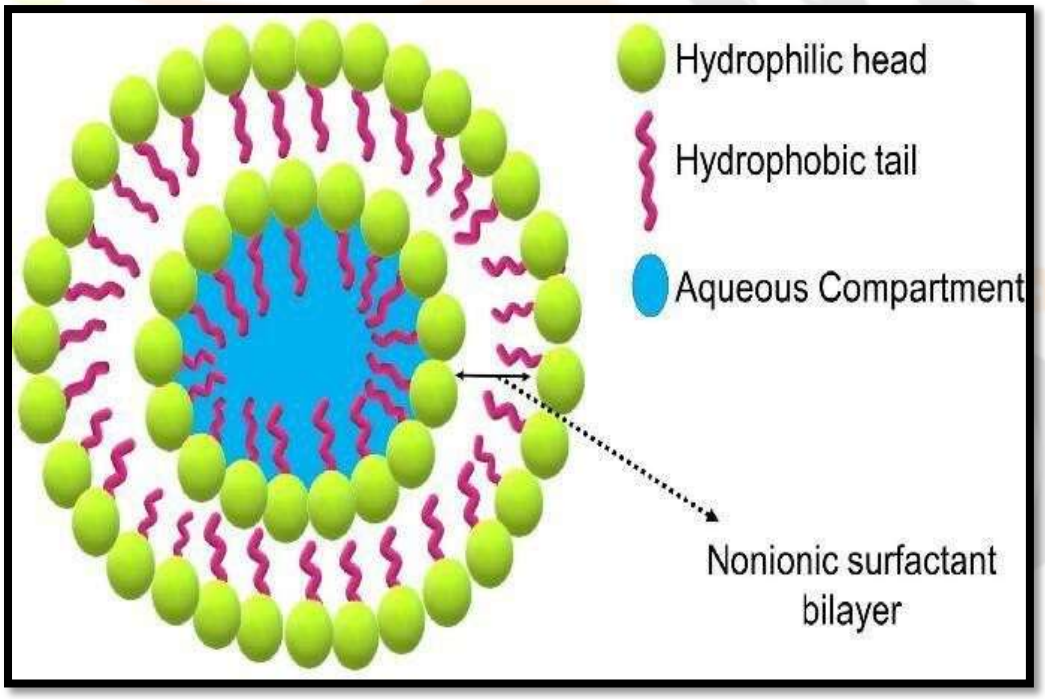


➢ TYPES OF SPECIALIZED NIOSOME:

Fig.6.Types of specialized niosome


❖ STRUCTURE OF NIOSOME

Fig.7.Structure of niosome




A typical niosome vesicle would consist of a vesicle forming amphiphile i.e. a non-ionic surfactant such as Span-60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as the dicetyl phosphate, which also helps in stabilizingthe vesicle.[101,102]

❖ COMPOSITION OF NIOSOME :

In the preparation of niosomes, 2 Components is used:

1. Cholesterol

2. Non-ionic surfactants

A Cholesterol have steroid like structure that provides stability and proper shape, and configuration to the niosome form.

B.For the Manufacturing of niosomes, non-ionic surfactants are Commonly used.

Examples: a. Tween 40, Tween 20, Tween 60, Tween 80

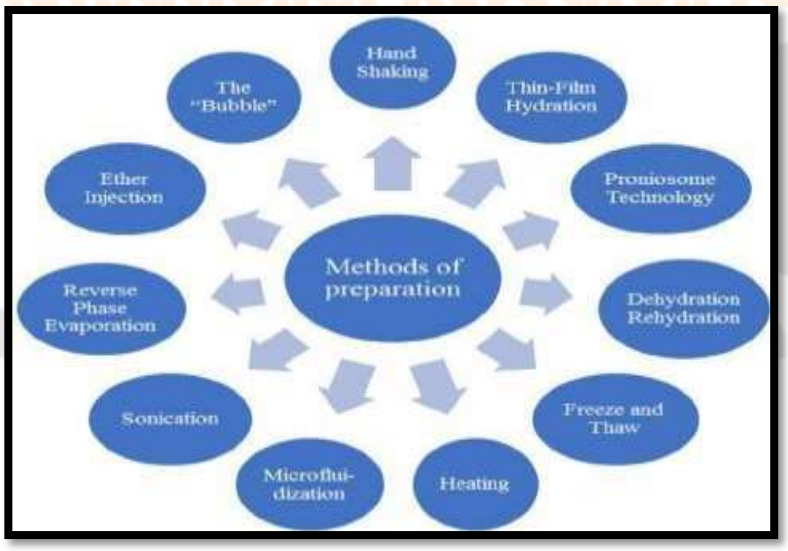
b. Span 80, Span 60, Span 40, Span 20, and Span 85

c. Brij 76, Brij 30, Brij 35, Brij 52, Brij 58, Brij 72[103]

❖ METHODS OF PREPARATION:

a) Ether injection method
b) Hand shaking method/thin film hydration method
c) Micro fluidization
d) Multiple membrane extrusion method
e) Reverse phase evaporation technique
f) Sonication
g) Transmembrane PH gradient drug uptake
h) The bubble method
i) Formation from pro-niosomes

Fig.5..Methods Of Preparation Of Niosome Formulation




➢ General method of preparation: [104]

Cholesterol + Non-ionic surfactant

↓

Dissolve in organic solvent

↓

Solution in organic solvent

↓

Drying

↓

Formation of thin film

↓

Dispersion (Hydration)

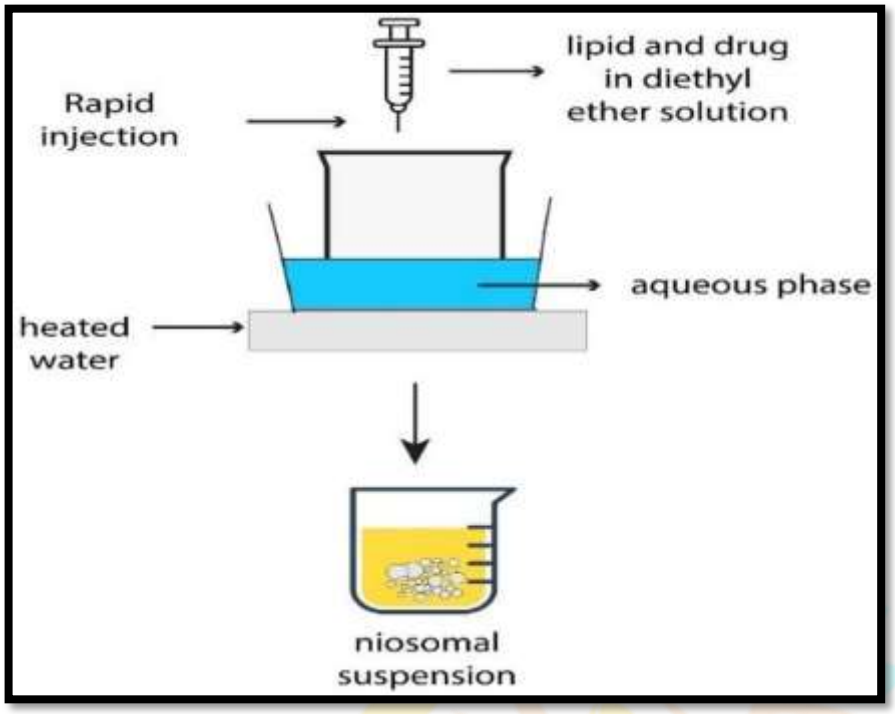
↓

Formation of niosomal Suspension

A. Ether injection method

This method provides preparation of niosomes by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. A surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Vaporization of ether leads to formation of single layered vesicles. Depending on the conditions used the diameter of the vesicle range from 50 to 1000 nm.

Fig.6.Ether Injection Method




✓ Preparation steps

Surfactant is dissolved in diethyl ether

↓

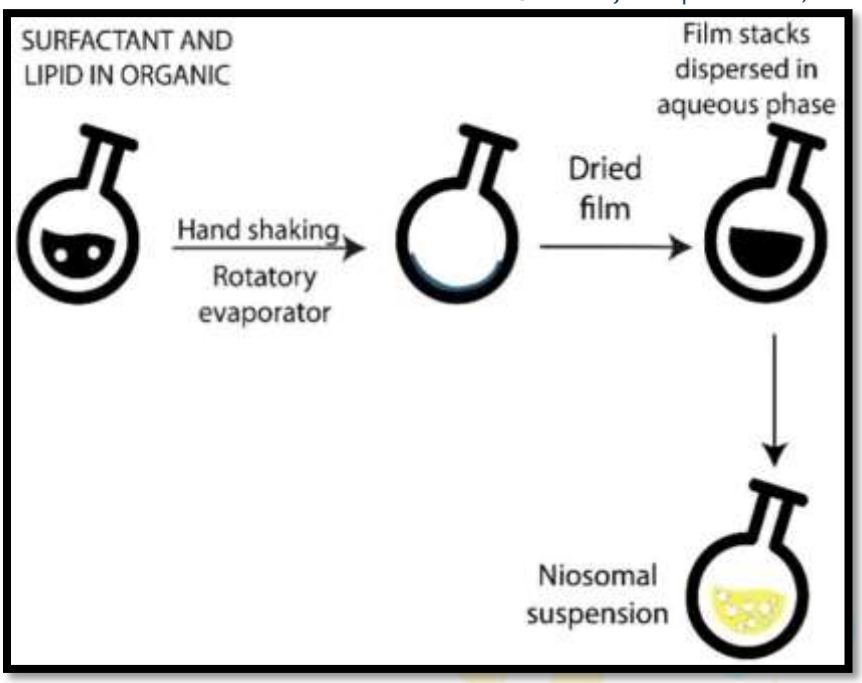
Then injected in warm water maintained at 60oC by a 14 gauze needle Ether is vaporized to form single layered niosomes[105]

↓

B. Hand shaking method (thin film hydration technique):

A mixture of vesicles forming ingredients like surfactant and cholesterol are dissolved in a volatile organic solvent (diethyl either, chloroform or methanol) in a round bottom flask. The organic solvent is removed at room temperature (20°C) by operating rotary evaporator leaving a thin layer of solid mixture deposited on the wall of the flask. A dried surfactant film can be rehydrated with aqueous phase at 0-60°C with gentle agitation. This process forms typical multilamellar niosomes.

Fig.7.Hand shaking method




✓ Preparation steps Surfactant + cholesterol + solvent

↓

Remove organic solvent at Room temperature

↓

Thin layer formed on the Walls of flask

↓

Film can be rehydrated to formation of multilamellar Niosomes.

C. Micro fluidization Method

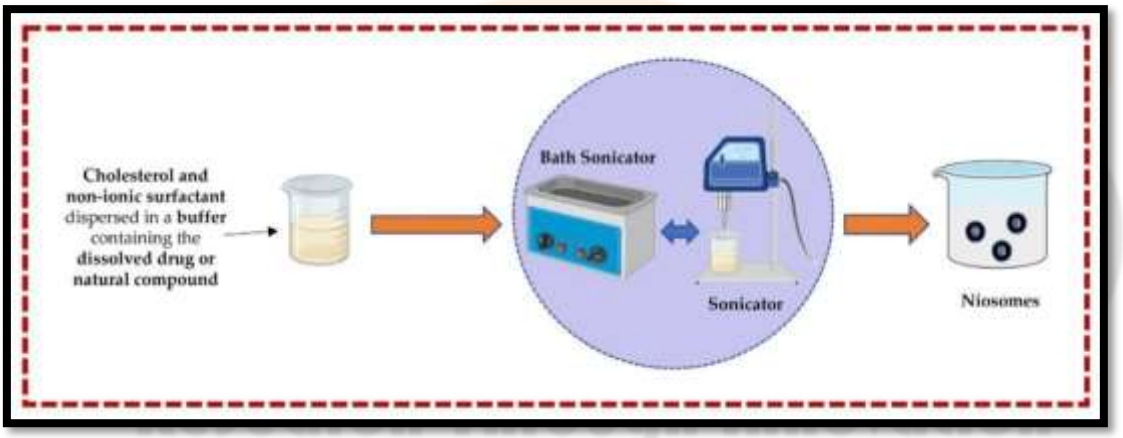



Fig.8.Micro fluidization method

Micro fluidization is a modern technique used to prepare unilamellar vesicles of defined size distribution. This method is based upon submerged jet principle in which two fluidized streams interact at ultra high velocities, in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains inside the area of niosomes formation. The result is a greater uniformity, smaller size and better reproducibility of niosomesformed.[106]

✓ Preparation steps

2 ultra high speed jets inside interaction chamber

↓

Impingement of the thin layer of Liquid in micro channels

↓

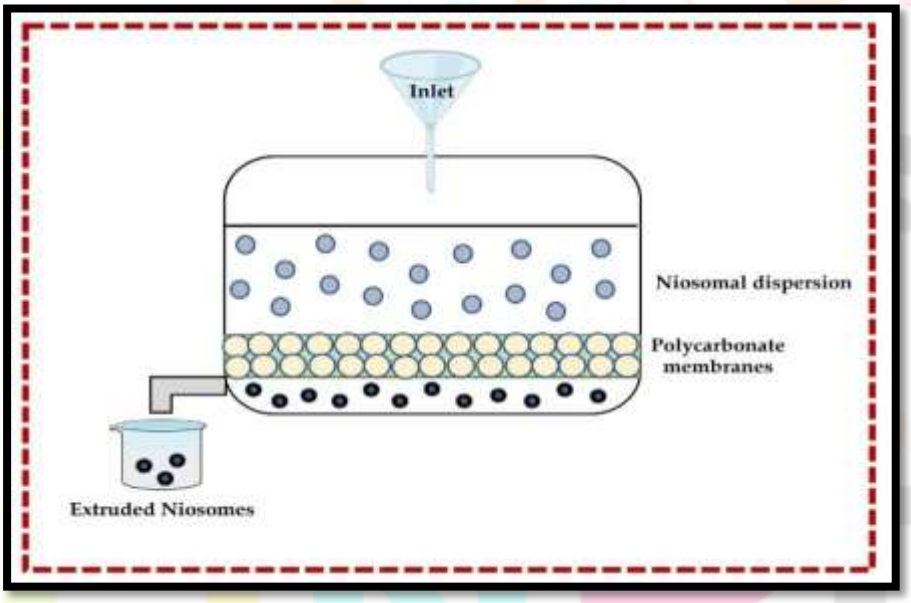
Formation of the uniform Niosomes

D. Multiple membrane extrusion method

Mixture of surfactant, cholesterol and dicetyl phosphate in chloroform is made into thin filmby a evaporation. The film is hydrated with the aqueous drug.

Raja Naresh et al. have reported the preparation of Diclofenac Sodium niosomes using theTween 85 by this method.

Fig.9.Multiple membrane excursion method




✓ Preparation steps

Cholesterol + surfactant dissolved in ether + chloroform

↓

Sonicated at 5o c and again sonicated after adding PBS

↓

Drug in aqueous phase is added to above mixture

↓

Viscous niosomes suspension is diluted with PBS

↓

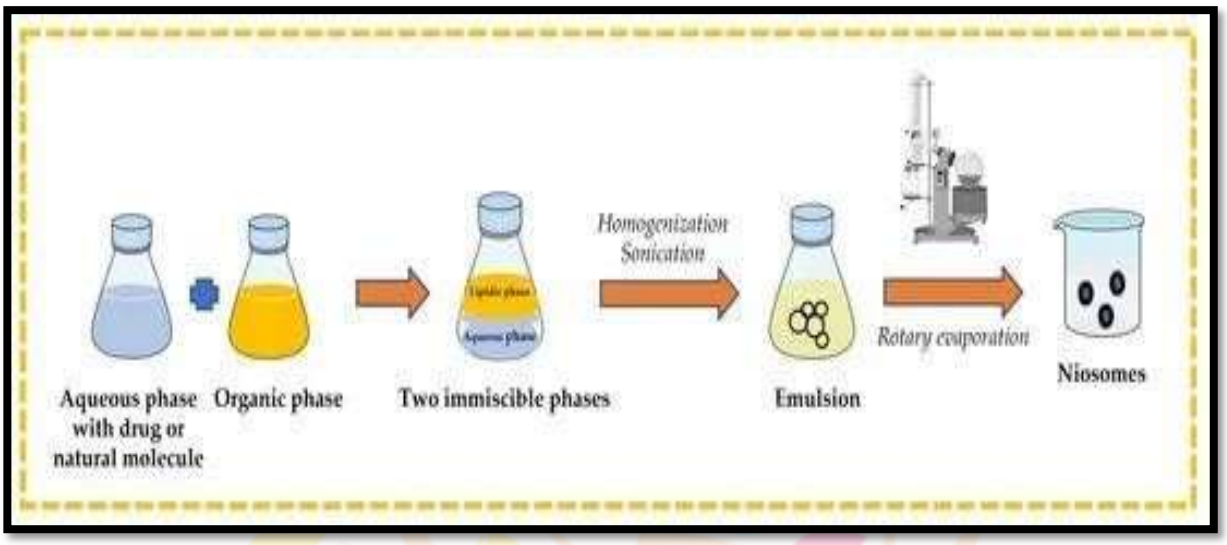
Organic phase is removed at 40oC at low pressure

↓

Heated on a water bath for 60oC for 10 mints to yield niosomes.

E. Reverse phase evaporation technique:

Fig.10.Reverse phase evaporation technique




The reverse-phase evaporation technique uses a mixture containing surfactant and cholesterol in a 1:1 ratio, in addition to ether and chloroform. A aqueous phase containing the target drug is added to the mixture followed by sonication at 4–5°C. Sonication is continued after adding small amount of phosphate-buffered saline to the mixture. The organic solvent is removed at 40°C under a low pressure, and remaining suspension is diluted with phosphate- buffered saline. After heating the mixture at 60°C for 10 min, the final product of niosomes areobtained(107)

F. Sonication Method

A typical method of production of vesicles is by sonication of solution as described by Cable. In this method an part of drug solution in buffer is added to the surfactant/cholesterol mixture in a 10-ml glass vial. A mixture is probe sonicated at 60°C for 3 minutes using a sonicator witha titanium probe to yield niosomes.

✓ Preparation steps

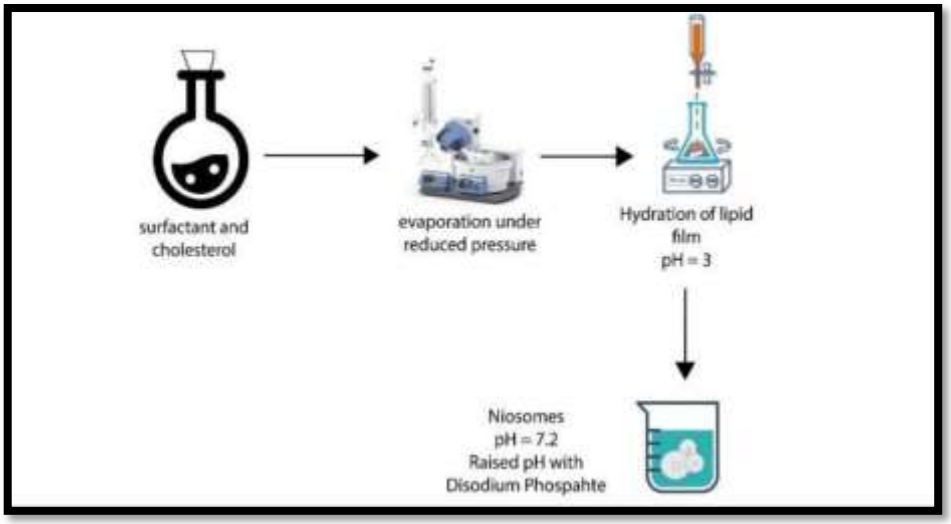
Drug in buffer + surfactant/cholesterol in 10 ml

↓

Above mixture is sonicated for 3 mints at 60oCusing titanium probe yieldingniosomes.

G. Trans membranes PH gradient (inside acidic)

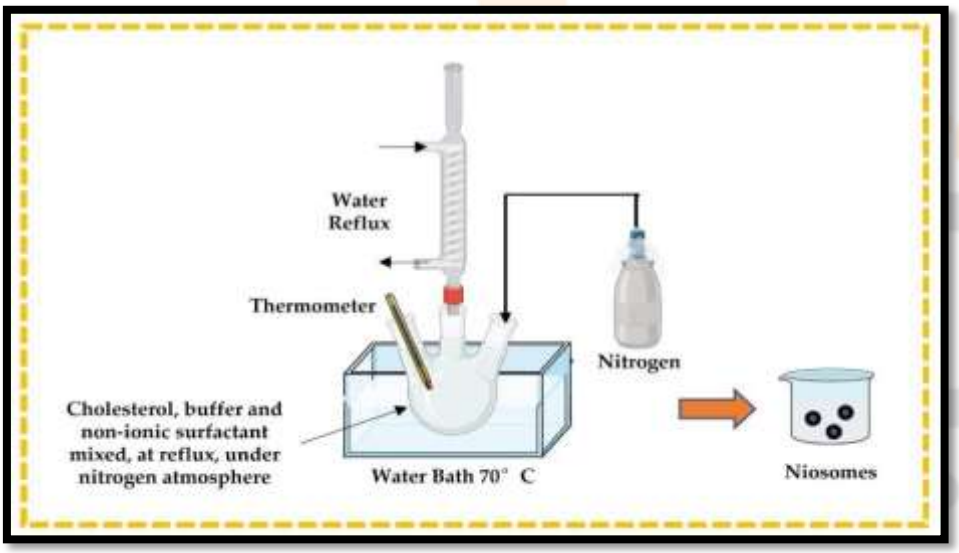
Fig.11.Trans membrane PH gradient




Drug Uptake Process: or Remote Loading Technique Surfactant and cholesterol are dissolved in chloroform. A solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. The firm is hydrated with 300mM citric acid (PH 4.00 by vertex mixing. An multilamellar vesicles are frozen and shared 3 times and later sonicated. To this niosomal suspension. Aqueous solution containing 10 mg ml of drug is added and vortex. The PH of the sample is then raised to 7.0-7.2 with the 1M disodium phosphate. This mixture isafter heated at 60°c for 10 minutes so give niosomes.[108]

H. The bubble method

Fig.12. The bubble method




Niosomes could be produce without the use of organic solvents using the "bubble" method. A "bubbling unit" consists of a round-bottom flask with 3 necks positioned in a water bath; a water-cooled reflux condenser and thermometer are positioned in the first and second necks, respectively, while nitrogen is supplied through the third neck. Surfactant and cholesterol that are mixed at 70°C in buffer are homogenized and "bubbled" at 70°C using the"bubbling unit"[109]

I. Formation of niosomes from pro-niosomes:-

Water or saline at 80ºc is added in a screw capped vial and proniosomal powder is filled in it. Then it is

mixed by vortexing followed by agitation for 2min. it results in the formation of niosomal suspension.[110]

The niosomes are formed by addition of aqueous phase at T >Tm and brief agitation. T= temperature Tm=mean phase transition temperature.

## ❖ Separation of Unentrapped Drug

The removal of unentrapped solute from the vesicles can be accomplished by differenttechniques, which include:

1. Dialysis

An aqueous niosomal dispersion is dialyzed in dialysis tubing against phosphate buffer ornormal saline or glucose solution.[111]

2. Gel filtration

The unentrapped drug is removed by the gel filtration of niosomal dispersion through aSephadex G-50 column and elution with phosphate-buffered saline or normal saline.[112,113]

3. Centrifugation

The niosomal suspension is centrifuged and supernatant is separated. The pellet is cleansedand then resuspended to obtain a niosomal suspension free from unentrapped drug.[114]

## ❖ Evaluation of Niosomes [115,116]

1. Measurement of the angle of repose

The angle of repose of dry niosome powder was measured by a funnel method. The niosome powder was poured into a funnel which was fixed at a position so that the 13 mm outlet orifice of the funnel is 5 cm above a level black surface. The powder flows down from funnel to form a cone on the surface, and the angle of repose was then calculated by measuring the height of the cone and the diameter of its base. Scanning electronmicroscopy (SEM)

Particle size of niosomes is a very important characteristic. The surface morphology (roundness, smoothness, and formation of aggregates) and the size distribution of niosomes were studied by SEM. Niosomes were sprinkled on the double sided tape that was affixed on aluminum stubs. The aluminum stub was placed in the vacuum chamber of a SEM (XL 30 ESEM with EDAX, Philips, Netherlands). The samples were observed for a morphological characterization using a gaseous secondary electron detector (working pressure: 0.8 ton and acceleration voltage: 30.00 KV) XL 30, (Philips,Netherlands)

2. Optical microscopy

The niosomes were mounted on glass slides and viewed under a microscopewith a magnification of ×1200 for morphological observation after suitable dilution.

The photomicrograph of the preparation was also obtained from the microscope using a digitalSLR camera.

3. Measurement of vesicle size

The vesicle dispersions were diluted about 100 times in the similar medium used for their preparation. Vesicle size was measured on particle size analyzer (Laser Diffraction Particle Size Analyzer, Sympatec, Germany). The apparatus consists of a laser beam of 632.8 nm focused with a minimum power of 5 mW using a Fourier Lens (R85) to point at the center of multielement detector and a small volume sample holding cell (Su cell). A sample was stirred using a stirrer before determining the vesicle size. Hu and Rhodes[20-22] in 1999 reported that the average particle size of niosomes derived niosomes is approximately 6 Um while that of conventional niosomes is about 14 Um.

4. Entrapment efficiency

Entrapment efficiency of the niosomal dispersion can be done by separating the unentrapped drug by dialysis centrifugation or gel filtration as described above, and the drug remained entrapped in niosomes is determined by complete vesicle disruption using 50% propanol or 0.1% Triton ×100 and analyzing the resultant solution by appropriate assay method for the drug. Where

Percentage entrapment=total drug-diffused drug/total drug

5. Osmotic shock

The change in vesicle size can be determined by osmotic studies. Niosome formulations are incubated with hypotonic, isotonic, and hypertonic solutions for 3 h. Then, the changes in the size of vesicles in the formulation are viewed under optical microscopy.

6. Stability studies

To determine the stability of niosomes, the optimized batch was stored in airtight sealed vials at various temperatures. Surface characteristics and percentage drug retained in niosomes and niosomes derived from proniosomes were selected as parameters for evaluation of the stability, since instability of the formulation would reflect in drug leakage and decrease in the percentage drug retained. The niosomes were sample at regular intervals of time (0, 1, 2, and 3 months), observed for color change and surface characteristics, tested for the percentage drug retained after being hydrated to form niosomes, and analyzed by suitable analytical methods (UV spectroscopy, HPLC methods, etc.,)

7. Zeta potential analysis

The zeta Potential analysis is done for determining the colloidal properties of the prepared formulations. The suitably diluted niosomes derived from pronoisome dispersion can be determined using zeta potential analyzer based on electrophoretic light scattering and laser Doppler velocimetry method (Zeta plus™, Brookhaven Instrument Corporation, New York, USA). The temperature was set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of measurements were obtained directly from measurement

- **Future Perspective**

Nanotechnology has provided a new perspective in medical field to overcome several barriers associated with traditional cancer treatments. In recent years, niosomes, a noble lipid- based nanoparticle, have attracted increasing attention because they can deliver drugs or natural compounds with high safety, easy production, storage, and minimal negative effects. Niosomes are expected to have a significant impact on new cancer therapies in the future as ideal candidates due to their ability to act as drug carriers and tumor-targeting molecules.

Cancer therapy can benefit from the use of various niosomal formulations that contains a wide range of drugs and natural compounds, which will ensure their continued popularity for the next decade. Numerous studies has been demonstrated that niosomes-based therapeutic approaches have significantly facilitated cancer therapy compared to conventional treatment methods. Sustainable concepts are being growingly considered worldwide, and niosomes technology could have a prosperous future in cancer therapy through the combination of sustainability and nanotechnology.

Niosomes represent a promising drug delivery molecule. There is a lot of scope to encapsulate toxic anti-cancer drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory drugs, anti-viral drugs, etc. in niosomes along with use them as promising drug carriers to achieve better bioavailability and targeting properties aa well as for reducing the toxicity and side-effects of the drugs. The ionic drug carriers are relatively toxic and unsuitable whereas niosomal carriers are safer. Handling and Storage of niosomes require no special conditions.

## Conclusion

In conclusion, the use of niosomes in cancer treatment shows great promise in improving treatment outcomes through efficient drug delivery. Niosomes can enhance the efficacy of anticancer drugs, reduce their toxicity, and improve patient outcomes. Further research is needed to optimize niosome formulations, improve drug loading efficiency, and enhance targeting capabilities. Overall, niosomes represent a valuable drug delivery system in the fight against cancer and have the potential to Revolutionize cancer treatment in the future .

Niosomes are a relatively current drug delivery system whose structure consists of two layers of non-ionic surfactants. By changing the experiment conditions and the ratio of surfactant and cholesterol used, various drugs can be loaded in niosomes. additionally, because of their amphipathic nature, hydrophobic and hydrophilic drugs can be loaded into the niosomes. Niosomes also increase drug stability, slow drug release, and reduce drug toxicity. As compared to other drug delivery systems, niosomes do not require specifc conditions for preparation and storage. Due to recent developments in computational optimization as well as new theoretical advances, in future, in silico tools can play a signifcant role in the feld of drug delivery. In summary, it seems that with more studies, we can expect good market for niosomes in pharmaceutical biotechnology and also cancer researches which is a promising way to treatment of cancer in future.

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