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Transferosomes: A Versatile and Ultradeformable Approach for Targeted Delivery of Anticancer Drugs in the Treatment of Diverse Cancers

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Abstract

Nanoparticles, particularly transferosomes, have emerged as promising drug delivery systems in the field of cancer therapy. With their unique properties and high adaptability, transferosomes have shown great potential in improving the targeted delivery of chemotherapeutic drugs, including through transdermal applications. This article provides a comprehensive review of the advancements and applications of transferosomes in cancer therapy and gene delivery; by highlighting the advantages of nanoparticles in cancer treatment, such as their ability to passively target tumors through the enhanced permeation and retention effect. It then focuses on the composition, preparation methods, and advantages of transferosomes over conventional liposomes, including their high stability, high carrier capacity, and ability to deliver drugs to deeper skin layers. The article further explores the applications of transferosomes in cancer therapy. It presents studies that demonstrate the effectiveness of transfersomes in delivering chemotherapeutic drugs, such as doxorubicin hydrochloride, carvedilol, and various natural compounds, for enhanced cancer treatment. Furthermore, it also discusses the use of transfersomes as adjuvant treatments to reduce the risk of cancer recurrence. Overall, this comprehensive review provides valuable insights into the advancements and applications of transferosomes in cancer therapy and gene delivery. The findings emphasize the potential of transferosomes as effective drug carriers, offering improved treatment outcomes and reduced side effect in the fight against cancer

Keywords: Transferosomes; Targeted Therapy; Nanoparticles; Advancements; Cancer

Abbreviations: DOX: Doxorubicin Hydrochloride; DTX: Docetaxel; 5FU: 5-Fluorouracil; 4-OHT: 4-Hydroxytamoxifen; TDLN: Tumor-Draining Lymph Nodes; Anti-PD1: Programmed Cell Death Protein 1; DCs: Dendritic Cells; Th1: T Helper Type 1.

Introduction

Nanoparticles typically have dimensions smaller than a few hundred nanometers, comparable in size to important biological molecules such as enzymes, receptors, and antibodies. Being around one hundred to ten thousand times smaller than human cells, these nanoparticles have the potential to bring about groundbreaking advancements in cancer diagnosis and treatment. They can interact in ways never seen before with biomolecules present on the surface of cells as well as within them [1]. Emerging technologies such as liposomes and nanoparticles are being utilized on a nano-scale to deliver chemotherapeutic drugs effectively in cancer treatment. These advanced systems provide various

benefits, including enhanced pharmacokinetics, precise control over drug release, and reduced overall toxicity to the body [2]. The utilization of liposomes to transport drugs was found to have a restricted effect on the outermost layers of the skin. Consequently, transferosomes emerged as an innovative type of vesicles that possess the ability to regulate and adapt themselves [3]. Transferosomes can dynamically permeate the intact corneum layer via two intracellular lipid pathways that vary in their bilayer characteristics [4].

Nanoparticles as drug carriers offer significant technological benefits such as exceptional stability, large capacity for carrying drugs, the ability to incorporate both hydrophilic and hydrophobic substances, and the option of administering drugs through various routes, including orally and through inhalation [5]. Moreover, nanoparticles can be engineered to achieve controlled release of drugs, ensuring a sustained effect over time. These characteristics of nanoparticles have the potential to enhance drug bioavailability, reduce the frequency of dosing, and address the issue of non-adherence to prescribed therapy, which is a major hindrance [6]. Nanoparticles possess the benefit of selectively concentrating in cancerous tumors through accumulation and entrapment (passive targeting) [7]. This effect, known as enhanced permeation and retention, is a result of leaky blood vessels formed due to angiogenesis and limited lymphatic drainage. Consequently, nanoparticles are observed to have higher proportions within tumors in comparison to regular tissues [6]. Transferosomes, a lipid-based vesicle, are increasingly being recognized as an innovative means of delivering drugs and are becoming widely favored. They represent a highly promising drug delivery system with significant potential, exhibiting impressive efficacy in transporting medications to specific cells [8].

The term “Transferosomes carrier” refers to an artificial vesicle created to mimic the properties of a cellular vesicle or a cell involved in exocytosis, with the purpose of facilitating controlled and potentially directed transportation of drugs [9]. This name originates from the Latin term ‘transferre’, which means ‘to transport over’, and the Greek term ‘soma’, which denotes ‘a physical form’ [10]. Transferosomes are structures made up of phospholipids, specifically phosphatidylcholine. These phospholipids naturally arrange themselves into a double-layered structure in a watery environment, forming a vesicle. To enhance the flexibility and permeability of the lipid bilayer, a softening ingredient is included, which can be a biocompatible surfactant and an amphiphilic drug Figure 1. This additional component, known as an edge activator, that alters the stability of lipid bilayer which is typically consist of single chain surfactant, as a result, fluidity and elasticity also increased [11]. The ability to encapsulate the active substance either within the core or within the lipid bilayer depends on its lipophilicity. Unlike liposomes, transfersomes have the advantage of effectively reaching deeper layers of the skin when applied topically [12]. This enables them to deliver higher concentrations of active substances, making them a successful carrier for transdermal drug applications [13]. The skin’s barrier function makes it difficult for nanoparticles to enter the tissue, yet the barrier is substantially weakened in cases of injury or swelling, such as in skin cancer. This may promote nanoparticle penetration [14]. These lipid molecules, known as transfersomes, possess biocompatibility and biodegradability since they are derived from phospholipids found naturally in liposomes. Their entrapment efficiency is remarkably high, reaching approximately 90% for lipophilic drugs [15]. They shield the enclosed drug from metabolic breakdown and serve as depots, gradually and slowly releasing their contents [16]. They can be utilized for delivering drugs systemically or topically. Consequently, transdermal flux of transfersomes elevates, lengthen the drug release, and furthermore elevates the targeted delivery of bioactive substances [17]. However, there are drawbacks associated with transfersomes. One major disadvantage is their chemical instability, as they are prone to oxidative degradation [18]. Another factor that hinders the acceptance of transfersomes as drug delivery systems is the requirement for high purity of natural phospholipids. Additionally, the cost of formulating transfersomes is relatively high [19] (Figure 1).

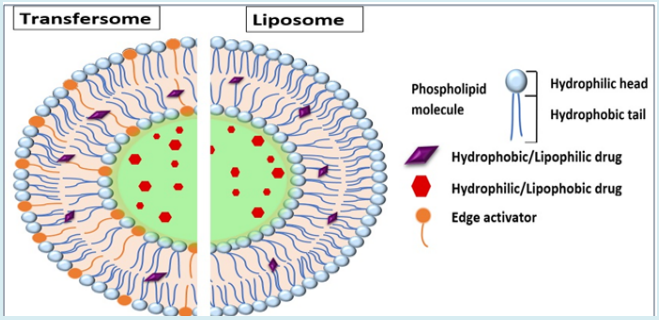

Figure 1: Structural comparison of Transfersomes and Liposomes.

Conventional Methods

The conventional rotary evaporation sonication technique which is also known as thin film hydration was used to create transfersomes [20]. Specifically, a round-bottom flask was used to hold a clean and dry mixture of phosphatidylcholine surfactant and a surfactant in varying ratios (ranging from 95% to 80% for phosphatidylcholine and 5% to 20% for the surfactant, by weight). This lipid mixture was dissolved in a solvent mixture of chloroform

and methanol, with a ratio of 3 parts chloroform to 1 part methanol, and heated to a temperature above the lipid transition point. With the help of rotary evaporator, a thin film formulated as the outcome. To eliminate the excess of traces, left it overnight under the vacuum. Using 10% ethanol solution, the lipid film hydrated in phosphate buffer saline (PBS) at pH 6.5. The hydration process involved rotating the film at a speed of 60 rpm for 1 hour at room temperature. To achieve the desired concentration (1% w/v) of the drug in the preparation, it was added to the hydrated film. The resulting vesicles were allowed to swell for 2 hours at room temperature to form larger multilamellar vesicles. The thick suspension obtained from this process was then agitated for 1 minute to break it down. Subsequently, the suspension was sonicated for 35 minutes at a temperature of 4°C to achieve the desired size of the vesicles. Finally, the vesicles were forced through a sandwich-like structure composed of polycarbonate membranes with pore sizes of 200 and 450 nm, resulting in their extrusion [21].

Reverse phase evaporation method is alternative conventional method. To initiate this method, first of all take the round bottom flask and mix the phospholipids and edge activator into it, in which they get dissolve in a blend of organic solvents like diethyl ether and chloroform. Then the lipophilic drug is added at this stage. Next, the solvent is eliminated through evaporation utilizing a rotary evaporator, leading to the creation of lipid films. These films are subsequently dissolved once more, but now dissolved in an organic phase predominantly consisting of either isopropyl ether or diethyl ether. Afterward, this phase is mixed with an aqueous phase, resulting in the formation of a two-phase system. It is at this point that the hydrophilic drug can be included. The water in oil emulsion achieved when it is exposed in the bath sonicator where sonication helps to achieve this emulsion. Through rotary evaporation, the organic solvent is slowly removed which leads to the formation of dense gel [22]. Ultimately, this gel undergoes a transformation into a suspension of vesicles.

Ethanol Injection Method is another approach [23]. To generate the organic phase, the phospholipid, edge activator, and lipophilic drug are mixed in ethanol using magnetic stirring for a predetermined period, until a clear solution is achieved. On the other hand, phosphate buffer is mixed in a substance which is water soluble to generate the aqueous phase. It is during this stage that the hydrophilic drug can be added. Preferred temperature range of 45-50°C used to heat the both solutions. Following that, phospholipids which is in ethanolic solutions is gradually added to the aqueous solution while stirring constantly for a specific duration. To eliminate ethanol, the resulting dispersion is transferred to a vacuum evaporator and subsequently subjected to sonication to reduce particle size [11].

Transferosomes in Cancer Therapy

Transfersomes, which are vesicles composed of phospholipids, serve as effective carriers for transdermal drug delivery. They significantly improve the effectiveness of anticancer drugs, exhibiting high efficiency in their therapeutic actions [24]. Transfersomes are clusters formed by themselves, featuring a highly adaptable outer layer that consistently transports the medication into or across the skin [25]. By traversing the intracellular lipids that tightly seal the outermost layer of the skin, transfersomes effectively address the challenge of penetrating the skin [26]. Cancer is an extremely destructive illness that poses a significant threat to human well-being. To counteract this disease, numerous treatment approaches involving combinations of therapies have been devised. Numerous diseases and irregularities, such as genetic mutations, protein misfolding, and cellular dysfunction, arise from abnormal biological processes at the molecular level. Cancer, in particular, is a devastating condition resulting from uncontrolled cell proliferation, initiated by a cascade of genetic mutations that spread throughout the body. Employing combination therapy proves to be an effective approach for enhancing effectiveness and minimizing the adverse effects associated with the use of individual treatments [27].

- Doxorubicin hydrochloride (DOX), a type of chemotherapy drug, belongs to the subclass of anthracycline antibiotics. Despite being hydrophilic and commonly used for treating various cancers, its utilization is limited due to the significant risks of adverse effects, such as cardiac toxicity and photosensitivity. While the combination of photodynamic therapy (PDT) and chemotherapy has shown promise in cancer treatment, concerns exist regarding the stability of light, side effects, and extensive metabolism in the liver. To address these challenges, a carrier system called transfersome, which belongs to the liposome class, is created using an edge activator (EA) as a surfactant to ensure a robust bilayer structure with flexible properties. The flexibility of transfersomes offers advantages in passive targeting strategies for cancer treatment. In this particular study, a combination pharmaceutical formulation containing DOX and P18Na is loaded into transfersomes with the aim of achieving effective cancer treatment through the use of chemotherapy and PDT [28]. Doxorubicin-loaded transfersomes were able to adequately permeate deep skin tissue, resulting in increased lymphatic absorption. Most notably, hyaluronic acid increased tumor cell absorption of drug-loaded nanocarriers [29].

- The increasing prevalence of skin cancer around the world necessitates the development of multiple treatment approaches. Chemotherapy, immunotherapy,

excision through surgery, radiation, and cryotherapy are all widely recognized treatments for skin cancer [30].

A research investigation has demonstrated the potential of transfersomes loaded with carvedilol in the prevention of skin cancer. The mechanism employed to protect against cancer aim to counteract and hinder UV induced oxidative stress, inflammation, oncogenic signaling pathways and DNA damage. The transfersomes were prepared using the thin-film hydration method, employing different ratios and utilizing Tween-80 and sodium cholate as surfactants. To ensure deeper penetration into the skin layers, the nanovesicles were maintained at a size of 300 nm or smaller. Consequently, the formulation with the smallest particle size was selected for further analysis. Furthermore, a mouse epidermal cell line was utilized to assess cytotoxicity and investigate the internalization of transfersomes within the cells. The results of the study confirmed the internalization of transfersomes into the cells, with concentrations exceeding 10 μM potentially leading to cytotoxic effects. Crucially, the research showcased that applying F18 transfersomes topically resulted in protective benefits against DNA damage, inflammation, and apoptosis caused by UV exposure [31]. In this film method, the thin film was dried in a desiccator overnight before being hydrated with a solution of phosphate-buffered saline at the transitional temperature of 51°C [32].

Besides carvedilol, some other natural drugs like sulforaphane aslo have antiproliferative action towards melanoma and other skin cancers in vitro. Inevitably, due to its low percutaneous penetration as indicated by its physico-chemical properties, this natural molecule cannot be administered freely to the skin [33]. Transferosomes are the best option to administer these agents. Curcumin, trans-resveratrol, kaempferol, and apigenin are also natural lipid soluble compounds with potent anti-inflammatory and antiproliferative characteristics [34].

- Lung cancer is an extremely serious form of cancer known for having the highest mortality rate among all cancer types. Various natural compounds, including theaflavins, quercetin, arctigenin, EGCG, curcumin, and cinnamaldehyde, possess notable anti-inflammatory and anti-cancer properties and can effectively suppress certain signal transduction pathways. However, all of these compounds, namely theaflavins, cinnamaldehyde, quercetin, arctigenin, curcumin, and EGCG, are highly unstable and degrade rapidly under pH 7.4 conditions. Consequently, conventional delivery methods are inadequate for transporting these compounds effectively [35,36]. As in China, herbal medicine is commonly used in conjunction with chemotherapy to treat lung cancer. ELE [β-elemene (1-methyl-1-vinyl-2, 4-diisopropenyl-cyclohexane)] is an antitumor agent extracted from the Chinese medicinal plant, Radix Curcumae. ELE has limited anticancer activity and is mostly used as an adjuvant medication to improve chemoradiotherapy efficacy, minimize toxicity, and reversal of drug resistance [37,38]. These herbal products and above mentioned plant flavonoids are delivered via transferosomes for treating lung cancer. Transfersomes, a type of nanoparticles, represent an innovative and advanced drug delivery system that exhibits remarkable stability compared to conventional nanoparticle systems, transfersomes demonstrate superior efficacy and drug entrapment capabilities. These nanoparticles are loaded with natural products and then incorporated into pMDI (pressurized metered-dose inhaler) canisters, such as fluorocarbon polymerization (FCP) plasma-coated canisters, which offer improved propellant characteristics. With the aid of spacers, the loaded nanoparticles can be efficiently delivered, providing an economically viable and effective treatment for lung cancer while minimizing side effects. Moreover, this approach ensures a reduced likelihood of cancer recurrence [39].
- Gene therapy, employing DNA recombination technology and gene cloning techniques, represents one of the most revolutionary milestones in modern medicine. This biomedical treatment approach revolves around modifying human genetic material, thereby providing a means to directly repair or replace disease-causing genes at the molecular level, thus restoring the function of faulty proteins. Currently, gene therapy drugs primarily consist of plasmid DNA, small interfering RNA, microRNA (miRNA), short hairpin RNA (shRNA), and antisense oligonucleotide (ASO). However, a significant challenge in gene therapy lies in effectively delivering these therapeutic agents to their intended targets. Nevertheless, the field has made significant progress through the utilization of novel viral and non-viral vectors, facilitated by advancements in materials science and nanotechnology. These vectors serve as vehicles for delivering gene therapy drugs, helping to overcome the aforementioned obstacles [40]. The human growth hormone (HGH) controls metabolism, aids in tissue repair and rejuvenation throughout life, and promotes growth in kids and adolescents. Igf1 is a transcriptional target of GH (growth hormone) signaling in liver and other tissues [41]. Transferosomes have been investigated as a viable option for delivering therapeutic gene sequences into cells. These structures offer several advantages, including stability and low toxicity, making them well-suited for gene therapy applications. Moreover, the manufacturing process for transfersomes is relatively straightforward, which enhances their potential as a novel vector in gene therapy. Notably, transfersomes possess key benefits such as the ability to effectively transport large molecules into cells, exhibit

low toxicity, and can be optimized based on the specific characteristics of the delivery system. Research findings indicate that transfersomes can enhance the efficiency of gene delivery when compared to other currently available systems [42].

Adjuvant treatment is often employed following primary therapies, such as surgery, to decrease the risk of cancer recurrence. Even if the surgery successfully removes all visible signs of the disease, tiny remnants of cancer cells may still exist, undetectable by current methods [43].

- A docetaxel loaded folate modified transfersomes formulation was developed by combining the permeation ability of d-a-tocopheryl polyethylene glycol 1000 succinate and the specific targeting of Folic acid in an ultradeformable vesicle for treating Glioblastoma. The synthesis of folic acid modified-a-tocopheryl polyethylene glycol 1000 succinate (TPGS-FA) was successful, resulting in transfersomes with a narrow particle size distribution, high encapsulation efficiency, and drug loading. In vitro assays showed that docetaxel loaded folate modified transfersomes exhibited greater cytotoxicity compared to the commercial docetaxel (DTX) formulation. TF-DTX-FA(docetaxel loaded folate modified transfersomes) also demonstrated enhanced cellular internalization in U-87 MG(Uppsala 87 Malignant Glioma)cells cultured in a 2D monolayer and higher uptake and permeability in 3D spheroids, likely due to the combined effect of TPGS(d-a-tocopheryl polyethylene glycol 1000 succinate) and FA(folic acid) on the transfersomes' surfaces [44].

- Transfersomes were prepared using the thin-film hydration method and characterized for particle size, polydispersity index, and zeta potential. The average particle size of 5FU (5-fluorouracil) and Etodolac (1:1)-loaded transfersomes was 91±6.4 nm, characterized by a polydispersity index of 0.28±0.03 and a zeta potential of (−) 46.9±9.5 mV. The encapsulation efficiency reached 36.9±3.8% for 5FU (5-fluorouracil) and 79.8±6.4% for Et (1:1). In FaDu (Fetal Derived Urogenital Sinus Mesenchymal Stem Cells) cells, the drug-loaded transfersomes exhibited a synergistic effect with a combination index of 0.36. The uptake of drug-loaded transfersomes by FaDu (Fetal Derived Urogenital Sinus Mesenchymal Stem Cells) cells was significantly higher ($p<0.05$) compared to free drugs [45] (Figure 2).

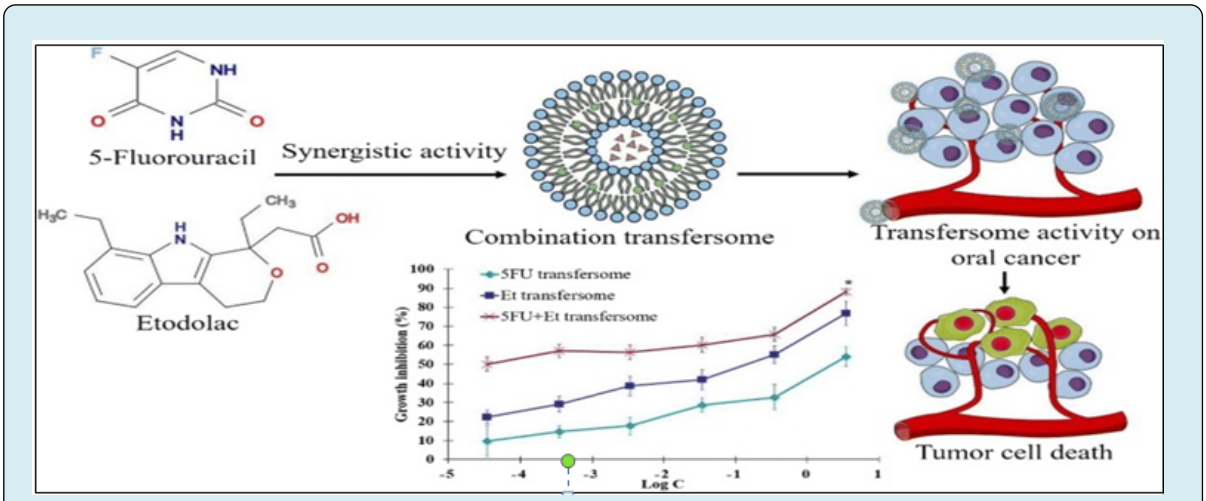

Figure 2: Activity of 5FU (5-fluorouracil) and Etodolac (1:1)-loaded transfersomes [45].

- The skin irritancy study indicated that neither pure emu oil nor transfersome formulations, with or without emu oil, induced skin irritancy. The 4-OHT (4-hydroxytamoxifen) transfersome formulations, with or without emu oil, demonstrated comparable tumor size reduction to oral Tamoxifen. Topical administration resulted in lower plasma levels of 4-OHT (4-hydroxytamoxifen), indicating reduced systemic circulation and potential avoidance of drug-induced toxicity in susceptible tissues. Animals treated topically with 4-OHT showed a higher degree of tumor necrosis, suggesting the potential superiority of these formulations over oral Tamoxifen [46].

- A novel approach was developed, involving the construction of nanovaccine complexed microneedles based on transfersomes, to enhance the effectiveness of anti-PD1 (Programmed Cell Death Protein 1) immunotherapy for skin tumor treatment through transdermal immunization. The transfersomes were modified with a targeting moiety called αCD40 (Cluster

of differentiation 40), and they were loaded with antigens and adjuvant poly I: C (polyinosinic-polycytidylic acid). Additionally, transdermal administration facilitated the accumulation of the transfersomes in tumor-draining lymph nodes (tdLN), promoting cellular uptake, triggering DCs (dendritic cells) maturation, and enhancing Th1 (T helper type 1) immune responses [47] (Table 1).

Sr. No.	Therapeutic Agent	Method of Preparation of Transfersomes	Inference
1	Doxorubicin hydrochloride(DOX)	Sonication Method	P18Na- and DOX were successfully delivered to cancer cell through pH responsive Transferosomes resulting in less drug escape in body and sufficient therapeutic efficacy
2	Carvedilol	Film Hydration Method	Drug penetration and deposition through skin was effectively enhanced. It also showed photoprotective effects against UV-induced DNA damage, inflammation, and apoptosis
3	Docetaxel (DTX)	Thin-film hydration method followed by extrusion technique	Docetaxel loaded folate modified transfersomes exhibited greater cytotoxicity, cellular internalization, higher uptake and permeability compared to the commercial docetaxel (DTX) formulation
4	5FU (5-fluorouracil) and Etodolac (1:1)	Thin-film hydration method	Drug-loaded transfersomes considerably outperformed free drugs in terms of cell uptake (p 0.05)
5	4-OHT (4-hydroxytamoxifen)	thin-film hydration technique	Comparable tumor size reduction was seen between oral Tamoxifen and 4-OHT (4-hydroxytamoxifen) transfersome formulations. Topical route for these transfersomes was proved to be more effective in term of necrosis and protection from systemic toxicity
7	anti-PD1 (Programmed Cell Death Protein 1) immunotherapy	Lipid film method	The functionalized transfersome based nanovaccine facilitated the accumulation of the transfersomes in tumor-draining lymph nodes (tdLN), promoting cellular uptake, triggering DCs (dendritic cells) maturation, and enhancing Th1 (T helper type 1) immune responses. Nanovaccin complexed microneedle and PD1 combined transdermal therapy promoted infiltration of CD8+ T and CD4+ T in tdLN and tumor tissues

Table 1: Literature review on applications of transferosomes in various types of cancers.

General Testing Procedures

Size and Zeta Potential

Dynamic light scattering was used to measure the average size and polydispersity index (PDI) of ultra-deformable vesicles using Zetasizer Nano-S equipment from Malvern Instruments in Malvern, UK. A population is homogeneous and monodisperse when the PDI is less than 0.2. Zeta potential was measured using Zetasizer Nano-Z equipment and Laser-Doppler anemometry. Transfer some preparations were diluted with filtered water to a final concentration of 10 microliters for both measurements. Dynamic Light Scattering was used to measure the vesicle size, size distribution, and zeta potential. Malvern Zetasizer's method (DLS), which use a computerized assessment system.

Drug Content

According to the analytical method used for the pharmacopoeial drug, it may be possible to figure out the drug content using one of the instrumental analytical approaches, such as enhanced high performance liquid chromatography (HPLC) using a UV detector, auto sample, pump, and a computerized testing program [4].

Visualization of Vesicles by Transmission Electron Microscopy

An electron microscope H-8100 from Hitachi Ltd. was used to see transfersomes. Prior to use, 1 mL of water that had been distilled was used to dilute each sample (10 L). After that, a drop of the diluted material was allowed to

dry on a tiny copper-coated grid (formvar/carbon, 200 mesh Cu grid support sheets for transmission electron microscopy). A further drop of a 1% PTA aqueous solution was incorporated for negative staining after the surface had dried fully. The extra solution was removed using filter paper after 45 seconds. The specimen was then examined under a microscope using various magnifications and an increasing voltage of 75 kV.

SPC Quantification

SPC content was evaluated using an enzymatic and colorimetric technique at 505 nm and 37°C (Phospholipids kit; Spinreact, Sant Esteve de Bas, Spain).

Pressure-Driven Transport

Pressure-driven transport was used to determine how fast the vesicles were moving. In a nutshell, vesicles with a final lipid concentration of 1% were pushed to pass through polycarbonate membranes with 30 nm pore sizes etched with tracks under 0.6 MPa nitrogen stream pressure for at least 5 minutes. The Sartorius LA620P scale was used to collect the suspension in a container. Wedge program for Windows (TAL Technologies Inc., Philadelphia, PA, USA) was used to gather the data.

Viscosity Measurement

The viscosity of UDV compositions was measured with a Brookfield® Electronic Viscometer (Model DV-II) at 5 rpm (23°C2°C) and a spindle number of 21. After thirty seconds, the readings were obtained [48].

Transfersomes Elasticity

The greater SC (sodium cholate) amount in the composition of transfersomes, according to the results regarding their elasticity, corresponds to a more elastic vesicular structure. This is due to the fact that SC softens the vesicle's membrane and greatly increases the bilayer's flexibility. As a result, transfersomes can quickly alter their form by responding locally to environmental stress. At the exact time, the SC concentration is important for the creation of transferosomes since these agents, at sublytic concentrations, give vesicle membranes adaptability while, at larger concentrations, they destroy vesicles.

Moreover, when compared to the same concentrations of SC, the non-ionic surfactants refused to make the vesicles flexible. Span transferosomes were not chosen for further research because they were highly viscous and considerably (P 0.05) less flexible than tween-transferosomes [49].

Determination of the Entrapment Efficiency of Transferosomes

Following the transfersome preparation process, 1 mL of the transfersomal dispersion created by hydration of the obtained thin film was sonicated for 5 minutes in 10 mL ethanol. The amount of felodipine in the final solution (F total) was estimated by spectroscopy via determining its UV absorbance at 362 nm. Furthermore, a suitable amount of the similar transfersomal dispersion was ultra-centrifuged for 1 hour at 22,000 rpm and 4°C utilizing a cooling centrifuge. Following this, 10 mL of ethanol and 1 milliliter of the isolated vesicles were combined, and the vesicles were allowed to dissolve using a sonicator for 5 minutes. The amount of felodipine in the created solution (F entrapped) was calculated as before. Considering the subsequent formula, entrapment efficiency was determined as a percentage (% EE) [50].

Surface Morphology

The recommended method was utilized to assess the structural integrity of the vesicles using light microscopy. They employed a light microscope. The preparation of the nano-transfersomes was adequately diluted with 10 mL of phosphate buffered saline (pH 7.4) before being gently shaken for 5 minutes to conduct light microscopy. A drop of the diluted formulation was put to an unprotected microscopic slide. With a light microscope (Leica DM11) adjusted to 1000, the formation of vesicles was visually seen, and a microphotograph was made.

SEM (Quanta 400, FEI, and Czech Republic) at a voltage of acceleration of 20 kV was used to study the surface shape of PR-transfersome vesicles. With 3 ml of Milli-Q water, 100 l of specimen was diluted, dropped on a cover sheet, and dried. Next, the sample was stained using a combination of Gram's iodine solution and 2-3 drops of the crystal violet solution [51].

PH Measurement

pH was calculated using digital pH meters. The physical qualities of solutions are represented by pH, which is an important metric. The evolution of the pH meter can be understood as moving from an intrusive to a non-invasive technology. The pH of the various micro transfersome gel formulations was instantly evaluated in samples at room temperature utilizing an electronic pH meter [52].

Conflict of Interest

The authors state that the study was carried out without any affiliations with commercial or financial entities that could be seen as a potential conflict of interest.

Conclusion

Transfersomes, advanced drug delivery systems composed of phospholipid bilayers, hold immense promise in the field of medicine, particularly in the treatment of cancer. These vesicles possess unique deformable properties that enable them to bypass biological barriers and reach deep within target tissues, including cancerous cells. By encapsulating anticancer drugs, transfersomes enhance their bioavailability and absorption, while providing sustained release capabilities for prolonged therapeutic effects. Moreover, transfersomes can be functionalized with ligands or antibodies that specifically recognize cancer cells, allowing for targeted drug delivery and minimizing systemic toxicity. Their ability to penetrate the skin also makes them suitable for transdermal drug delivery of anticancer agents. Overall, transfersomes offer a versatile and effective approach to enhancing the efficacy of cancer therapies, improving patient outcomes, and paving the way for personalized medicine in oncology.

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