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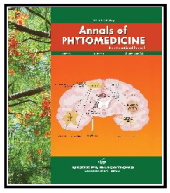

Review Article : Open Access

Niosomes : A promising novel drug delivery systems for phytoconstituents

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Abstract

Nanomedicine and nanodelivery systems employ nanoscale materials for diagnostics and targeted therapeutic delivery. Niosomes, as a substitute for conventional liposomes, are biodegradable, non-ionic surfactant vesicles that boast non-toxicity, longevity, and affordability. Their bilayer structure enhances drug bioavailability, and they can encapsulate lipophilic or hydrophilic molecules. Niosomes offer controlled release, targeted distribution, and can be administered through various routes. They hold potential for biotechnology products and novel vaccines. We collected relevant information on niosomes from electronic databases, textbooks, and libraries from January 2010 until now. This review explores the basics of niosomes, encompassing their benefits, drawbacks, their role in delivering phytoconstituent drugs, and potential future developments.

1. Introduction

Innovative drug delivery methods enhance the pharmacokinetics and pharmacodynamics of medicinal compounds, enhancing efficacy, safety, and bioavailability while minimizing toxicity and adverse reactions. They offer targeted drug delivery to reduce exposure to healthy tissues, controlled drug release to improve efficacy and reduce dosing frequency, and improved drug stability to prevent degradation. For instance, liposomes, niosomes, phytosomes, and nanoparticles can target specific tissues like cancer cells and release drugs at the desired site (Chandu *et al.*, 2012; Das, 2021; Srinivasan, 2022; Yasamineh *et al.*, 2022).

Liposomes and niosomes, as vesicular drug delivery mechanisms, vary in aspects such as composition, stability, drug release, size, shape, and cost. Phospholipids constitute liposomes, whereas nonionic surfactants and cholesterol form niosomes. Niosomes are more stable than liposomes due to cholesterol presence, and they release drugs slowly and in a more controlled manner. Liposomes are larger and more spherical, while niosomes' size and shape can vary based on surfactant used. Niosomes are less expensive to produce because of their use of relatively inexpensive surfactants (Ag Seleci *et al.*, 2016; Bhardwaj *et al.*, 2020).

Niosomes represent a vesicular drug delivery approach that has emerged as a potential substitute for liposomes. These systems consist of nonionic surfactants and cholesterol, which spontaneously organize into bilayer formations in water-based solutions. Niosomes provide multiple benefits compared to traditional drug delivery methods, including enhanced medication stability, extended drug release, and precise targeting of specific tissues.They have shown great potential in delivering a wide range of therapeutic agents, including phytoconstituents, peptides, proteins, and small molecules. Due to their versatility and potential for use in various biomedical applications, niosomes have emerged as an active area of research in drug delivery (Kaur and Kumar, 2018; Yeo *et al.*, 2017).

Niosomes hold potential as a drug delivery mechanism for anti-inflammatory drugs, anticancer drugs, and vaccines. They offer advantages like improved drug stability, targeted drug delivery, and sustained drug release. For anti-inflammatory drugs, niosomes can enhance efficacy and reduce toxicity. For anticancer drugs, niosomes can target specific cancer cells and improve bioavailability. Niosomal vaccines can improve stability, antigenicity, and targeted delivery to specific cells or tissues.

Niosomes can improve the delivery of phytoconstituents with therapeutic properties. Phytoniosomes, a commonly used term in scientific literature, are essentially niosomes that encapsulate herbal medicines. Niosomes are innovative drug delivery systems that work well for a range of medicines, including herbal ones. They're like cells and act as bioreactors to target and release natural medicines. Niosomal formulations of phytoconstituents can enhance their bioavailability, stability, and targeted delivery to specific tissues, resulting in improved therapeutic efficacy. Phytoconstituents are often poorly soluble in water and have low bioavailability when administered orally, but niosomes can increase solubility and protect them from degradation. Niosomes can also be designed to target specific cells or tissues using ligands or antibodies attached to the vesicle surface, reducing potential side effects associated with systemic distribution. Niosomes possess the capacity to enhance the therapeutic outcomes of natural drug products.

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2. Methodology

The content of this review is derived from a variety of up-to-date sources, including peer-reviewed journal articles, bibliographic databases, and official websites. Information was gathered using platforms such as PubMed, Taylor and Francis, Wiley interscience, Springer Link, Science Direct, SCIELO, DOAJ, Science Alert, Research Gate, Semantic Scholar, and Google Scholar. A range of keywords was employed to locate relevant articles for this review. This review focused on both *in vivo* and *in vitro* research published in English from January 2010 until the present. Out of 67 initially evaluated publications, 52 were ultimately incorporated into the study. The review solely encompasses primary literature and omits duplicate articles, irrelevant content, and languages other than English. The literature analysis is confined to peer-reviewed publications pertaining to Niosomes and Phytoniosomes.

3. Advantages of niosomes

i. Niosomes excel over liposomes due to their enhanced chemical stability, and extended longevity.

ii. Niosomes are easy to make and change because their hydrophilic heads have a functional group on them.

iii. The lack of charge in niosomes renders them less toxic and more compatible.

vi. Niosomes are biodegradable by biological systems, meaning they can be broken down and metabolized without causing harm to the body. Additionally, they do not initiate immunogenic reactions, making them an attractive option for drug delivery and medical applications.

v. Niosomes have the versatility to encapsulate drugs of varying solubilities, including both hydrophilic and hydrophobic compounds. This makes them a promising option for drug delivery, as they can accommodate a wide range of therapeutic agents with different properties.

vi. Niosomes can boost the bioavailability of active pharmaceutical compounds through two methods: by augmenting their physical stability and by elevating their biological stability. By providing a protective barrier around the drug, niosomes can shield it from degradation, thus increasing its physical stability. Additionally, the biological stability of the drug can be improved by facilitating its absorption and uptake by cells, ultimately leading to increased bioavailability.

vii. Niosomes provide a versatile drug delivery option as they can be administered through several routes, including oral, parenteral, transdermal, ocular, and pulmonary. Additionally, when administered as an aqueous suspension, niosomes enhance patient adherence to treatment.

viii. Changes or modifying in parameters, such as additives, ratios, or combinations, can alter the shape, size, and entrapment of drugs within niosomes. As such, niosomes offer the potential to deliver medications in a targeted, regulated, and prolonged fashion (Bhardwaj *et al.*, 2020; Kaur and Kumar, 2018).

4. Disadvantages of niosomes

While the niosomal delivery system offers numerous advantages, it is not without its potential drawbacks. Stability can be a concern when using niosomes in the form of an aqueous suspension, as the drug may be susceptible to hydrolysis, which could compromise its effectiveness. Moreover, drug leakage from the entrapment site or the development of niosome aggregates may pose a risk and potentially compromise the intended drug delivery system. These challenges must be considered when developing and utilizing niosomal delivery systems and should be addressed through careful formulation and testing processes.

5. Niosomal drug delivery for phytoconstituents

Herbal medicine has been utilizing natural plant products for centuries, based on traditional knowledge and practices, to address various health concerns. However, natural compounds are presently undergoing screening to determine their potential in treating significant ailments such as cancer, diabetes, cardiovascular, inflammatory, and microbial infections. This is due to their distinct benefits, including lower toxicity, fewer side effects, lower cost, and greater therapeutic potential. Nonetheless, using natural compounds as medicine is challenging due to concerns about biocompatibility and toxicity. Drug delivery employing larger materials poses significant hurdles, including *in vivo* instability, limited bioavailability, poor solubility and absorption, target-specific delivery issues, weak therapeutic efficacy, and potential adverse drug effects. Thus, employing new drug delivery systems that specifically target particular body regions could help resolve these critical concerns. Nanotechnology plays a vital role in advanced medicine and drug formulations, allowing for targeted drug delivery to precise regions with controlled release and delivery, resulting in remarkable success.

Curcumin, a phytochemical found in the rhizome of *Curcuma longa* L. has been utilized in a diverse array of biological applications, ranging from antibiotics to cancer therapy (Naikodi *et al.*, 2021; Sumathi, *et al.,* 2021). Curcumin has many pharmacological benefits, from antibiotics to treatments for cancer but its poor solubility and stability have led to low bioavailability. Various nanostructures have been developed to address these limitations (Srinivasan and Sivakrishnan, 2022). A novel niosome system, comprising nonionic surfactants was developed to facilitate curcumin delivery. Loaded with curcumin, niosomes serve as an effective drug delivery mechanism for treating ovarian cancer. Niosomes provide stable safeguarding and high entrapment efficiency (92.3 ± 0.4%) for curcumin. Curcumin niosomes exhibited improved cellular uptake, cytotoxic activity, cell cycle arrest, and apoptotic rate against ovarian cancer A2780 cells (Xu *et al.*, 2016). The free and niosomal formulation of curcumin and paclitaxel demonstrated diminished toxicity on healthy human MCF-10A cells in contrast to MCF-7 cells. Conjoining paclitaxel and curcumin therapy with a cationic PEGylated noisome delivery system could potentially represent an effective approach for treating breast cancer (Alemi *et al.*, 2018). Another study demonstrated that niosomes incorporating curcumin and hyaluronan exhibited significantly higher levels of antioxidant activity and a two-fold increase in anti-inflammatory activity compared to curcumin suspensions with the same potency (Sadeghi Ghadi and Ebrahimnejad, 2019). Another study, in comparison to conventional niosomes, hyaluronan-based niosomes displayed reduced size and greater values of zeta potential and entrapment. The hyaluronan niosomes loaded with quercetin demonstrated superior anti-inflammatory and antioxidant potential when compared to traditional niosomes (Ghadi *et al.*, 2019). Curcusomes were produced using thin film hydration technique to improve the delivery of curcumin to

the skin. This approach facilitated drug delivery to the intended location, resulting in enhanced efficacy of curcumin as an anti-nociceptive and anti-inflammatory agent (Akbari *et al.*, 2020). Tween : curcumin niosomes are prepared using curcumin as a stabilizer and Tween as a non-ionic surfactant. The curcumin has the ability to form vesicles at a molar ratio of 7:1 with T80 and can carry other small molecules along with curcumin using Tween-curcumin niosomes. This is the important implications for the development of multidrug therapy and transdermal administration of curcumin, as well as the improvement of its therapeutic efficacy through controlled release (Sahu *et al.*, 2020). Animal-borne diseases such as brucellosis are widespread, particularly in developing countries. The combination of doxycycline and curcumin is frequently recommended for treating brucellosis to prevent relapse and protracted drug administration. A potential therapy for brucellosis involves utilizing chitosan-sodium alginate nanoparticles loaded with doxycycline and niosome hydrogels loaded with curcumin. This treatment yielded a reduction in brucella counts in the spleen and blood of guinea pigs artificially infected with the disease (Abo El-Ela *et al.*, 2020). The curcumin-loaded niosomal formulations, composed of nonionic surfactants and cholesterol, displayed greater encapsulation efficacy of curcumin compared to the suspension form. Additionally, the niosomal emulgel formulation demonstrated increased deposition of curcumin in the skin and improved anti-inflammatory activity (Shehata *et al.*, 2021). Niosomes incorporating curcumin and a calcium alginate shell serve as an effective drug delivery mechanism for transporting hydrophobic medications to specific cancer cells with minimal adverse effects (Akbarzadeh *et al.*, 2021). The combination of curcumin and silver/copper nanoparticles loaded niosomes exhibits synergistic activity against the growth and biofilm formation of *S. aureus* and *P. aeruginosa*, surpassing the effects of curcumin, AgNPs, or CuNPs used alone (Targhi *et al.*, 2021). *In vitro* testing showed that when curcumin and methotrexate were delivered together using niosomes, they were more toxic to the HCT-116 cell line than when they were administered alone. This approach of using nanocarriers for the co-delivery of curcumin and methotrexate proved effective in targeting cancer cells *in vitro* (Mousazadeh *et al.*, 2022). The curcumin-loaded niosomes were synthesized and decorated with folic acid and polyethylene glycol to reduce the risk of breast cancer. Gene expression analysis showed that Bax and p53 levels were significantly higher with the polyethylene glycol-Folic acid-decorated niosomes compared to the free drug and undecorated niosomes. Additionally, Bcl2 levels were lower with the polyethylene glycol-Folic acid-decorated niosomes than with the free drug and undecorated niosomes. In cell uptake experiments, polyethylene glycol-Folic acid-modified niosomes demonstrated the highest rate of endocytosis in both MCF-7 and 4T1 cells. The nano-formulations were developed and exhibited efficient uptake by breast cancer cells while preserving their drug-release attributes (Honarvari *et al.*, 2022). Curcumin-loaded niosomes were administered both orally and intramuscularly to rats to prevent the development of oral cancer. Curcumin-loaded niosomes inhibited cancer cell growth and necrosis more effectively than free curcumin. It was demonstrated that the niosome strategy was effective in preventing oral cancer in rats. Niosomes loaded with curcumin were found to prevent severe dysplasia and suppress cancer cell proliferation (Fazli *et al.*, 2022). The use of PEGylated and RIPL peptide-conjugated nanostructured lipid carriers to co-administer docetaxel and curcumin demonstrated enhanced cytotoxic and apoptotic effects, as well as improved *in vivo* antitumor efficacy in both drug-sensitive and drug-resistant cell lines (Kim *et al.*, 2022).

Paclitaxel, used in cancer chemotherapy, originates from the bark of the Pacific yew, *Taxus brevifolia* Nutt. Its cytotoxic effect is achieved by stabilizing microtubules, leading to mitotic arrest and cellular apoptosis. The Carbopol 974P-coated niosomes had a greater accumulation of paclitaxel in the intestine and liver, indicating the potential for effective treatment of localized carcinomas. Niosomes, both uncoated and coated with Carbopol 974P, enhanced the relative bioavailability of paclitaxel by 3.8 and 1.4 fold, respectively, indicating their potential to improve the oral bioavailability of this medication (Sezgin-Bayindir *et al.*, 2013). Paclitaxel-loaded Span 40 niosomes were orally administered, the AUC value of paclitaxel was increased by 4.44 fold compared to Taxol and by 8.09 fold compared to previous results. The spleen was found to filter niosomes from the blood, resulting in prolonged detection of paclitaxel in plasma. Compared to Taxol, niosomes produced significantly lower levels of paclitaxel in the liver, kidneys, and heart. Paclitaxel-loaded Span 40 niosomes could be directed towards tumours with minimal effect on healthy organs (Bayindir *et al.*, 2015). The pH-sensitive niosomes formulated with ergosterol demonstrated the ability to deliver paclitaxel, exhibiting a nanometric size, spherical shape, 77% entrapment efficiency, and pH-triggered release. Compared to free paclitaxel, niosomal paclitaxel showed lower IC_{50} value and induced evident morphological changes in cancer cell lines with fewer toxic effects in rats (Barani *et al.*, 2021). Niosomes were produced utilizing a response surface D-optimal factorial design and incorporating both hydrophilic and hydrophobic anticancer medications, including Oxaliplatin and Paclitaxel. The optimized formulation demonstrated superior entrapment efficacy, drug release, *in vitro* cytotoxicity, and apoptotic efficacy in contrast to free drugs when tested against HT-29 colon cancer cells (El Far *et al.*, 2022).

Quercetin, also called 3, 3', 4', 5, 7-pentahydroxy-flavone, is a polyphenolic bioflavonoid that can be found abundantly in the plant kingdom. Niosomes containing quercetin were found to improved solubility and photostability, the niosomes demonstrated enhanced transdermal penetration and skin retention (Lu *et al.*, 2019). Integrating hyaluronic acid in to the polymer-based niosomes for quercetin delivery addresses its low water solubility, inadequate absorption, and extensive first-pass metabolism. The quercetin-loaded niosomes exhibited a spherical shape, measuring 231.07 ± 8.39 nm in size and possessing a zeta potential of – 34.00 ± 0.95 mV. With an entrapment efficiency of 94.67 ± 1.62%, the release of quercetin followed to the Higuchi model. In addition, these niosomes displayed remarkable antioxidant potency and superior anti-inflammatory effects compared to the simple suspension of quercetin when orally administered to rats (Sadeghi Ghadi *et al.*, 2021). The niosomes containing quercetin were prepared using a 1:1 molar ratio of glucose laurate and cholesterol, demonstrating remarkable drug encapsulation efficiency and prolonged drug release. Compared to free quercetin, these niosomes displayed superior hepatoprotective effects in rats, as evidenced by serum biomarker enzymes and histopathological examination (Elmowafy *et al.*, 2020). Surfactant-based vesicles of doxorubicin and quercetin were prepared using Tween-60 and siRNA was loaded utilizing 1, 2-dioleoyl-3-trimethylammonium-propane as a cationic lipid. The cationic PEGylated niosomes have the potential to enhance anticancer activity. The drug release was controlled and small interfering RNA (siRNA) was successfully loaded into the niosomes. The encapsulated drugs exhibited increased toxicity against cancer cells and displayed a

synergistic effect when co-delivered with siRNA, doxorubicin, and quercetin across various cancer cell lines (Hemati *et al.*, 2019). Molecular hybridization has been used to develop a captopril-quercetin prodrug that has been encapsulated in a niosomal formulation for improved drug delivery. In addition to exhibiting suitable properties, the formulation also demonstrated sustained drug release. ACE and ROS inhibition enhanced blood pressure-lowering effects *in vitro* and *in vivo*. The hybrid formulation's potential in treating oxidative stress and cardiovascular complications is due to its synergistic effects (Sayyad *et al.*, 2021).

Antioxidants such as ferulic acid, oryzanol, and phytic acid, which are bioactive components of rice bran, find use in skincare products. However, their effectiveness decreases when they are exposed to air or light. Niosomes enhance the stability of these compounds and promote skin hydration. As compared to placebo formulations, gel and cream formulations containing rice bran extracts encapsulated within niosomes demonstrated enhanced antioxidant activity and lipid peroxidation inhibition. Moreover, three distinct methodologies (Corneometer, Vapometer, and Confocal Raman Microspectroscopy) corroborated that these gel or cream preparations augmented skin hydration by 20%, 3%, and 30%, respectively (Manosroi *et al.*, 2011). In another study, based on closed patch tests with a mexameter and visual inspection, gel and cream formulations with semi-purified rice bran extracts encapsulated in niosomes did not cause erythema or edema on shaved rabbit skin within 72 hours. As well, these formulations resulted in increased hydration, skin lightening, thickness, roughness, and elasticity in 30 human participants over a 28 days treatment period (Manosroi *et al.*, 2012). Non-ionic surfactant vesicles serve as appropriate colloidal carriers with flexible physicochemical attributes for ammonium glycyrrhizinate delivery. These vesicles displayed no toxicity or skin irritation and possessed suitable stability for *in vivo* use. Moreover, they augmented ammonium glycyrrhizinate anti-inflammatory properties in mice by reducing oedema and nociceptive behaviour. The niosome-delivered ammonium glycyrrhizinate also exhibited enhanced anti-inflammatory performance in treating chemically induced skin erythema (Marianecci *et al.*, 2012). *Ginkgo biloba* extract niosomes were prepared using the film dispersion-homogenization method, with the optimal system having a 141 nm particle size. Spray drying demonstrated higher drug entrapment efficiency than freeze drying. Stability remained unchanged after three months. *In vitro* release showed prolonged flavonoid glycoside release for 48 hours, while *in vivo* distribution revealed higher content in organs and blood compared to oral *Ginkgo biloba* L. extract tablets (Jin *et al.*, 2013). Marigold (*Calendula officinalis* L.) is rich in lutein, zeaxanthin, carotenoids, flavonoids, and triterpenoids, with lutein and zeaxanthin being particularly abundant. These two carotenoids have antioxidant properties that protect cells from oxidative damage. Anthocyanins-loaded niosomes are prepared using the thin-film hydration method and incorporated into a mucoadhesive gel formulation. *In vitro* cell line studies demonstrate a significant increase in the bioactivity of *C. officinalis* methanolic extract upon loading into the phytoniosome (Tween 60 niosomes) formulation (Un *et al.*, 2015). The combination of Span 60 or Maisine 35-1 as surfactants and dodecanol as a stabilizer in niosomes containing resveratrol exhibited high entrapment efficiency and good stability. Incorporating resveratrol encapsulated niosomes did not alter the textural properties of regular yogurt, implying their suitability as dairy additives (Pando *et al.*, 2015). Lycopene, a nutraceutical present in various natural sources, is utilized to treat cancer and diabetes; nevertheless, its efficacy is limited due to its susceptibility to light, heat, and oxidants. To overcome this, a novel approach, the adsorption hydration method using glass wool, was developed for lycopene encapsulation to improve its bioavailability and maintain its activity. *In vitro* and *in vivo* studies demonstrated that the formulation inhibited cancer cell proliferation, specifically MCF-7 and HeLa cell lines, through the apoptotic pathway (Sharma *et al.*, 2016). In another study, a lycopene niosome formulation was made using Span 60 as the wall system and cholesterol as a membrane stabilizer, resulting in a stable and efficient entrapment of lycopene. The lycopene was securely embedded in the bilayer of the surfactant and cholesterol through a hydrogen bond, providing protection against oxidative stress and light. The formulation remained stable for three months and exhibited sustained lycopene release, with the highest concentration being released after 72 hours. This formulation displayed significant antidiabetic activity in rats, lowering blood glucose levels and improving biochemical parameters (Sharma *et al.*, 2017). Plant-based products may be used to treat diabetes rather than synthetic drugs, and embelin from *Embelia ribes* Burm.f. may be effective. The embelin-loaded oral niosome formulation showed significant hypoglycemic effects in STZ-induced diabetic rats. Embelin-loaded niosomes acted faster than repaglinide, possibly due to improved intestinal absorption. Embelin exerts its protective effect against STZ-induced diabetes through various mechanisms, including antioxidant activity and pancreatic rejuvenation (Alam *et al.*, 2018). Morusin is a prenylated flavonoid that may be effective against cancer. Its limited use in clinics is due to its poor solubility. To improve solubility, a niosome system was developed using Span 60 and cholesterol. The resulting niosomes were highly cytocompatible, with a uniform size and smooth spherical morphology. Morusin was entrapped with high efficiency (97%) and released in a controlled and sustained manner, with improved efficacy against multiple cancer cell lines (Agarwal *et al.*, 2018). The biological application of myrtle extract (*Myrtus communis* L.) is limited due to its low solubility and permeability. Various niosomal formulations were prepared using non-ionic surfactants and cholesterol with different molar ratios, and the best formulation was found to be F5 (Span 60: Tween 60: cholesterol - 3:3:4 molar ratio). It had a size range of 5.3 ± 15.9 nm and an EE% of 45.4 ± 93.4%. The F5 formulation exhibited optimal *in vitro* release and EE%, lower cell toxicity, and higher antibacterial activity than myrtle extract (Raeiszadeh *et al.*, 2018). Using nonionic surfactants, cholesterol, and varying *Centella asiatica* (L.) Urban extract and hyaluronic acid concentrations, niosomes were created. Optimal niosomes had 155 nm particle size, -15 mV zeta-potential, 71-77% encapsulation efficiency, and 3-7% drug loading capacity. Adding hyaluronic acid increased particle size and zeta potential but didn't affect encapsulation efficiency. Diffusion controlled *C. asiatica* extract release, with asiaticoside from *C. asiatica* extract-Nio-hyaluronic acid penetrating skin better. The developed Nio-hyaluronic acid system showed great stability and promises enhanced asiaticoside delivery, possibly applying to other hydrophilic natural compounds (Wichayapreechar *et al.*, 2020). Phytoniosomes loaded with aqueous extracts of *Psidium guajava* L. and *Justicia adhatoda* L. (AGN) leaves have demonstrated promising antiviral activity against the dengue virus-2 strain (DEN-2). Utilizing an ultrasonication method for extract preparation, PEGylated niosomes displayed a smaller particle size compared to their non-PEGylated counterparts. The AGN4

formulation exhibited a significant 40% reduction in plaque-forming units, indicating its potential to combat the dengue virus. Upon lyophilization of AGN4 for capsule production, the capsules maintained acceptable weight variation and disintegration time, preserving their stability for up to 60 days (Wilson *et al.*, 2021). A topical emulgel containing colchicine and jojoba oil was developed, with a particle size of 220.7 nm, 65.3% entrapment efficiency, and three-month stability. The emulgel showed potential anti-inflammatory effects, indicating that combining niosomes and jojoba oil-based emulgel may be useful for delivering anti-inflammatory drugs like colchicines (Elsewedy *et al.*, 2021). Antibiotic resistance in malaria is a major issue in India. Researchers explored five home remedies for antimalarial and MRSA activity, developing a phytoniosome herbal formulation using cinnamon bark and black pepper seeds for antimalarial activity and thulasi leaves and black pepper seeds for MRSA activity. Flavonoids in cinnamon bark and black pepper seeds may contribute to antimalarial properties, while phenolic acid and flavonoids in thulasi leaves and black pepper seeds could be responsible for MRSA activity. The phytoniosomes exhibited antimalarial potency against *Plasmodium falciparum* 3D7 and low cytotoxicity, yielding a therapeutic index above 32 µg/ml (Tamilselvi *et al.*, 2021). The *Aconitum heterophyllum* Wall. ex Royle ethyl acetate root extract and its phytoniosome-loaded counterpart demonstrated concentration-dependent antioxidant and anti-proliferative effects against MCF-7 human breast cancer cells, possibly due to enhanced bioavailability of phytoniosomes. The phytoniosome-loaded extract exhibited lower IC_{50} values against MCF-7 human breast cancer cells, signifying greater effectiveness. *In silico* docking revealed several phytoligands capable of inhibiting tumour-associated proteins BRCA1, BRCA2, and HER-2, displaying amino acid interactions similar to those of the drug Doxorubicin (Saravanan *et al.*, 2022). The crude extract and novel phytoniosome formulation of *Tradescantia pallida* (Rose) D.R.Hunt leaves extract (50 mg/kg) effectively reduced blood glucose levels and improved body weight and blood biochemical parameters in alloxan-induced diabetic mice. Phytoniosomes treated groups showed better antidiabetic potential and pancreatic cell regeneration in histopathology analysis. Hyphenated chromatographic analysis confirmed the antidiabetic potential of the extract by inhibiting α-amylase and α-glucosidase. Molecular docking studies revealed specific compounds, such as 2, 4-Di-tert-butylphenol, stigmasterol, spathulenol, linoleic acid, and 2-Piperidinone, N-[bromo-n-buty], contribute to the antidiabetic effect of the extract by inhibiting α-amylase and α-glucosidase (Imtiaz *et al.*, 2023). To combat the emergence of drug-resistant tuberculosis (TB), non-antibiotic agents such as propolis have been explored. A niosome-based drug delivery system was developed using ethanolic extract of propolis (EEP) and Ag85A aptamer surface modification to specifically target *Mycobacterium tuberculosis* (Mtb). The Apt-PEGNio/EEP was found to specifically inhibit *Mycobacterium* expressing Ag85 membrane-bound protein *in vitro*, and no toxicity was observed in alveolar macrophages (Sangboonruang *et al.*, 2023).

6. Future prospective of niosomes

The future prospects of niosomes are based on their potential to revolutionize drug delivery systems as a result of their versatility and effectiveness. Further development of niosomes can lead to improved therapeutic efficacy and a reduction in side effects by precisely targeting specific tissues or organs. In addition to improving the stability of drugs, encapsulating them within niosomes can also ensure a longer shelf life and maintain the potency of the drugs. In complex diseases, such as cancer and chronic illnesses, niosomes may be able to deliver multiple drugs simultaneously, enhancing the effectiveness of treatment. Since niosomes are adaptable, they can facilitate the development of personalized treatments that are tailored to the needs of each individual patient. By optimizing niosomes for various administration routes, including oral, topical, ocular, and pulmonary, they can be used in a variety of drug delivery applications. It is possible that niosomes can be used to deliver gene therapies, vaccines, or any other novel treatment that requires precise targeting and controlled release. Research on the non-toxic and immune-neutral properties of niosomes could lead to the development of safer drug delivery systems with minimal side effects. Although niosomes show considerable promise, more research and clinical trials are needed to fully understand their capabilities and translate these advancements into practical applications.

7. Conclusion

Niosomes represent an effective drug delivery option, offering distinct advantages over liposomes, such as increased chemical stability, greater purity, and reduced expense. They possess the ability to encapsulate an extensive variety of hydrophilic and hydrophobic medications, and provide unique features including biodegradability and non-immunogenicity.Their non-toxic nature provides flexibility in administration routes and enhances drug absorption while reducing systemic toxicity. Even with challenges such as aggregation and leakage, niosomes hold promise as a superior drug delivery method for phytoconstituents compared to traditional drug delivery systems, potentially driving substantial advancements in the pharmaceutical sector.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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