Hydrophobin-Coated Noisomes as Drug Carriers in Lung Cancer Cells - A Review

Srishti Namdeo [1], Chandrapratap Dhimar [1]

Abstract

Nanoparticles loaded with anti-cancer drugs are designed to selectively target Lung Cancer Cells (LCCs) by interacting with various receptors. Hydrophobin-coated niosomes, a type of carrier system, show lower cytotoxicity in vitro compared to existing anti-cancer drugs. The hydrophobin-coated formulation demonstrates higher cytotoxicity against cancer cells than control cells. Lung cancer can spread to distant organs, posing challenges such as multidrug resistance and recurrence. Traditional chemotherapies may face resistance due to genetic mutations. Convolutional Neural Network (CNN)-based automatic organ segmentation has been validated for radiation treatment planning in lung cancer patients. LCCs-CNN niosomes, similar to liposomes, offer enhanced cellular membrane permeability and high biocompatibility. This carrier system shields the drug molecule from breakdown and deactivation. Hydrophobin-coated niosomes outperform polyethylene glycol-coated ones in various aspects, including size distribution, entrapment efficiency, release profile, biocompatibility, and cancer prevention success.

Keywords: Lung cancer cells, Drugs, Patients, Convolutional Neural Network.

Significance | Targeted nanoparticle delivery to Lung Cancer Cells, using hydrophobin-coated niosomes, addressing multidrug resistance, and enhancing treatment efficacy.

*Correspondence: Srishti Namdeo, Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.
Email: ku.srishtinamdeo@kalingauniversity.ac.in

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1. Introduction

Lung cancer remains a significant global health challenge, often characterized by its aggressive nature and fast-dividing cells. This review provides the realm of innovative drug delivery as a potential solution for targeted treatment of lung cancer. Conventional drug delivery methods, such as oral consumption and intravascular injection, often result in minimal drug reaching the target tissue through blood circulation (Barani, M., 2020). Niosomes, characterized by controlled release and tailored distribution, emerge as a promising innovation for treating cancer, infectious diseases, and various challenges (Bashkeran, T., 2023). Particularly in cancer medication, niosomes offer improved drug stability, extended treatment duration, reduced severe side effects, and targeted delivery to cancer cells (Yasamineh, S., 2022). In the context of lung cancer, characterized by uncontrollable cell mutation and rapid growth, niosomes present a valuable solution. Fast-dividing lung cancer cells impede the generation of healthy tissues, leading to restricted airflow and breathing difficulties as cancer infiltrates the pleural space between the lungs and chest barrier (Caicun, Z. H. O. U., 2020; Fukuoka, M., 2023). Lung cancer's impact on major airways can induce shortness of breath and coughing up blood, while fluid accumulation behind the lungs exacerbates breathing difficulties (Bade, B. C., 2020). Utilizing niosomes addresses challenges in medication bioavailability, drug instability, and insolubility, contributing to cost-effective treatment (Mansoori-Kermani, A., 2022). Polysorbate-containing niosomes demonstrate efficacy in drug development and genetic material transfection due to their polyethylene glycol chains (Ge, X., Wei, M., 2019). Nanoparticles inhaled in lung cancer can prolong macrophage-mediated clearance and interact with pulmonary epithelial cells (Lu, X., 2014). Targeted drug

Author Affiliation:
[1] Department of Pharmacy, Kalinga University, Naya Raipur, Chhattisgarh, India.

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administration becomes critical in treating various illnesses, especially in patients receiving combination medications, to maintain therapeutic efficacy (Witika, B. A., 2022). Niosomes, with their surface modification, non-immunogenicity, and cost-effectiveness, emerge as superior drug delivery carriers for various therapeutic moieties (Kondapi, A. K., 2021). The multifaceted impact of lung cancer, involving infiltration into lymph nodes and spreading through blood circulation to the brain, adrenal glands, and bones, necessitates a comprehensive medical approach, combining surgery, chemotherapy, and radiation (Kobir, M. E., 2023; Gunter, N. V., 2023). These treatments aim to reduce pain and alleviate symptoms associated with advanced lung illnesses and cancer spread. Lung cancer's blockage of main airways induces shortness of breath, while fluid accumulation around the lungs further complicates breathing (Li, M. C., 2023; Hasan, G. M., 2023). The complexity of illnesses with toxicities and side effects underscores the need for suitable therapeutic moieties and drug communication systems (Aparajay, P., 2022). In summary, niosomes present a promising avenue for overcoming these challenges, offering an efficient, versatile, and economical solution for drug delivery in various medical scenarios.

Lung cancer, predominantly caused by tobacco use, faces additional risk factors like radon, asbestos, pollution, and infections. Addressing accurate detection, the model LCCs-CNN utilizes visual scans to identify potentially malignant lung nodules, employing an ensemble strategy for enhanced precision. Furthermore, niosomes exhibit versatility by carrying hemoglobin in oxygen-permeable cells of impoverished individuals, augmenting skin medication absorption for efficient nanoparticle delivery. This review describes the realm of innovative drug delivery as a potential solution for targeted treatment of lung cancer. The focus is on niosomes, exploring their versatility and effectiveness in addressing the challenges posed by rapidly proliferating cancer cells. The introduction of the LCCs-CNN ensemble technique for lung nodule detection adds a critical dimension to lung cancer diagnosis and therapy. Additionally, the review highlights the broader applications of niosomes, such as carrying hemoglobin for impoverished individuals and enhancing skin medication absorption.

2. Literature Review

In recent studies, researchers have explored innovative technologies to advance the early diagnosis and effective treatment of lung cancer. S. Sasikumar and colleagues (2020) introduced the Attention-based Recurrent Neural Network (ARNN) designed for early lung cancer diagnosis. This innovative ARNN incorporates an attention layer, autonomously extracting features and efficiently executing encoding and decoding operations on distinct sequences utilizing variable-length vectors. The evaluation process is swift, utilizing the ARNN promptly, yielding highly accurate results within a limited analytical timeframe. Significantly, the reduced time for diagnosis is critical in mitigating higher fatality rates associated with challenging detections.

Pankaj Nanglia and team (2021) outlined their current study, emphasizing the practical outcomes of applying the combined Feed-Forward Back Propagation Neural Network (FFBPNN) as a decision-making tool for lung cancer (Nanglia, P., 2021). They presented a three-step classification method, where the initial block preprocesses the dataset, the second extracts features, followed by optimization using a genetic algorithm, and the final block classifies using FFBPNN. Recognized as a kernel attribute-selected classifier, this hybrid classification approach exhibits a notably high overall accuracy.

Janee Alam and colleagues (2018) investigated a multi-class Support Vector Machine (SVM) classifier, proposing an efficient approach for lung cancer detection and prediction (Alam, J., 2018). Early recognition and prediction of lung cancer can substantially improve patient lifespan. An intelligent computer-aided diagnostic system proves invaluable for radiologists in identification, prediction, and diagnosis of lung cancer. Techniques such as image scaling, color space modification, and contrast enhancement contribute to enhanced image quality.

Maryam Moghtaderi and her team (2022) introduced the versatile applications of Nanotechnology (NT), notably in medicine (Moghtaderi, M., 2022). Their research focused on analyzing essential factors for drug delivery engineering using niosomes. The study emphasized clinical qualities by illustrating instances of using nanocarriers in cancer treatment. The findings underscore the significance of targeted drug delivery in various illnesses, especially for patients receiving combination medications, as diverse drug structures necessitate distinct mechanisms to ensure optimal efficacy.

Several challenges arise with the treatment of lung cancer cells using hydrophobin-coated niosomes as drug carriers in contemporary times (Barani, M., 2020). The development of multidrug resistance and relapse poses significant hurdles in the advancement of cancer drug therapies. Traditional chemotherapeutic treatments, while eliminating cancer cells and damaging their genetic information, often lead to drug resistance due to cellular variations. Overcoming these challenges is possible with the proposed method LCCs-CNN, offering a potential solution to address these drawbacks.

3. Lung Cancer Treatment through Nanoencapsulated Medicines and Innovative Detection Techniques

This review has explored the targeted drug delivery for lung cancer treatment using nanoencapsulated medicines. Specific receptors on lung cancer cells are targeted to deliver anti-cancer medications, resulting in cancer regression. The review also discusses the role of nanotechnology in cancer therapy, the challenges in drug delivery systems, and the potential of LCCs-CNN for early-stage lung cancer detection. We have discussed various aspects, including intelligent responsive drug delivery systems, the structure of niosomes, gene expression analysis, and the importance of optimizing LCCs-CNN risk assessment. Additionally, equations or algorithm models are presented to predict the complexities of lung cancer development.

Nanoencapsulated medicines precisely target lung cancer cells expressing specific receptors, inducing cancer regression. In cancer therapy, nanotechnology optimizes drug delivery, enhancing pharmacokinetics and minimizing systemic toxicity. Pembrolizumab, in combination with conventional treatment, significantly improves overall survival in advanced squamous non-small cell lung cancer patients. (Saeidi, Z., 2023)

Figure 1 highlights the pivotal role of the tumor microenvironment in developing responsive drug delivery systems. These systems, inert in normal tissues, adapt to trigger local drug release in the tumor's environment, enhancing therapeutic effects. However, this approach is incompatible with medications targeting organelles. The chosen signal module employs an endogenous biological cascade reaction, amplifying signals to assemble drug-carrying particles efficiently. The environmental protection effect of active targeting with nanoparticles and ligands underpins conventional targeting techniques. To elevate success in tumor-targeted treatment, a shift from modified particles to receptors is crucial, emphasizing "receptor signal" reinforcement at the tumor site. Evidence supports manufactured receptors stimulating particle endocytosis, though further improvement is needed, considering intracellular fate. Chemotherapy-induced autophagy increase, linked to treatment resistance, highlights the need for refining targeting strategies to combat cancer cell division, metastasis, and resistance. Telomerase activity in cancer cells challenges previous beliefs, emphasizing the need for innovative approaches to address atypical enzyme expression and activity.

Figure 2 illustrates niosomes, bilayer non-ionic vesicles resembling liposomes but lacking a lipid bilayer. Unlike liposomes, niosomes are both chemically stable and cost-effective. With a structure defined by a hydrophilic head and a hydrophobic tail, niosomes can capture a diverse range of medicines. Lipophilic drugs are housed in the hydrophobic region, while hydrophilic ones are placed in the aqueous core. Composed mainly of a hydration medium, lipids, and non-ionic surfactants, niosomes' success hinges on individual components. Understanding their fundamental structure enhances knowledge of niosome mechanisms and encapsulated pharmaceuticals. Uniflagellar niosomes feature bilayer structures, while multilamellar ones contain bilayer vesicles within layers. Despite a tendency to agglomerate, niosomes remain effective at encapsulating hydrophilic medicines at a lower concentration, leveraging their substantial water content.

Figure 3 highlights the potential of gene expression analysis in the respiratory epithelium to aid in evaluating LCCs-CNN risk for early-stage detection, an ongoing area of investigation. Evidence suggests shared molecular features between tumor-adjacent cells and usual neighbors. Vital to LCCs-CNN success is the accurate treatment of indeterminate lung nodules. Exploring genetic indicators and integrating plasma protein indicators with clinical risk factors for indeterminate nodules has proven effective. Diagnostic and treatment monitoring in early-stage lung cancer heavily relies on medical imaging techniques, necessitating a nuanced approach for optimal detection. Further research into LCCs-CNN-associated gene expression in non-tumor respiratory epithelium is crucial for enhanced risk assessment and cancer pathophysiology understanding.

$$\boldsymbol{Y = (\alpha * \beta) + (O|W) * \omega \pm \sqrt[2]{(W)\frac{O-1}{U+2}}} \qquad (1)$$

Where Y is a lung cancer that develops during regular lung cells change, and $\sqrt[2]{(W)\frac{O-1}{U+2}}$ mutate, in a manner that disrupts their usual growth and W death cycle, $\alpha * \beta$ is mathematical resulting in uncontrolled cell division and O the production of ω an excessive number of cells. The quickly proliferating cells perform various lung cell activities and grow into healthy lung tissue.

$$\boldsymbol{V = \log p \int N \sin K \times \max_{Q} (Y)} \qquad (2)$$

Where V cancer cells, N is a, unlike normal cells, proliferate uncontrolled and K cluster together to form a tumor, $\max_{Q}$ killing healthy lung tissue along their path. Symptoms Y normally disappear until cancer cells have moved to $\log p$ various body regions and $\sin$ are interfering with the healthy functioning of other organs. If lung cancer is discovered at an early stage, and the tumor is minuscule and has spread, cancer is more likely to be effectively treated. Lung cancer screening is indicated for certain people who smoke or used to smoke but with neither indication and symptoms of the disease.

$$\boldsymbol{I = (d + H) * (\omega - \beta) \div \sum \max_{j} L \pm \sqrt{\sqrt{j - L} \times \frac{\sqrt{H^2 - 1}}{d_{n-1}}}} \qquad (3)$$

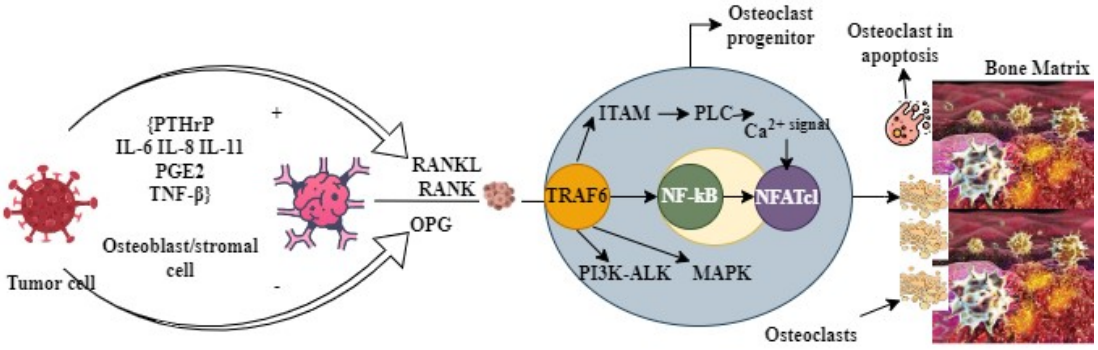

Figure 1. Immunohistochemical activity in Bone Metastases

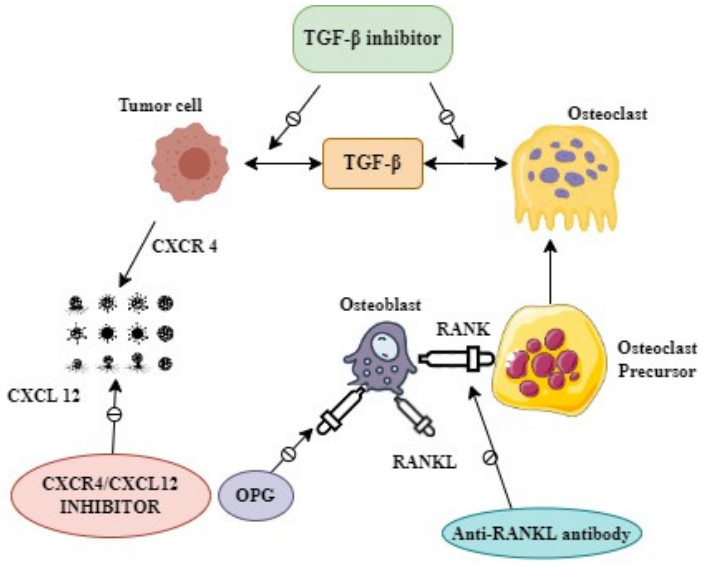

Figure 2. Clinically Inhibiting Bone Metastasis Pathways

Table 1 Estimation of deaths in lung cancer cell

Number of years	ARNN	FFBPNN	SVM	LCCs-CNN
2011	35.2	40.2	57.7	75.3
2012	23.9	38.9	25.3	70.3
2013	49.6	65.3	45.3	74.2
2014	29.5	42.2	32.7	77.3
2015	40.5	52.2	55.4	85.6
2016	43.3	59.2	53.2	72.5
2017	18.2	32.3	48.6	81.3
2018	38.2	46.3	59.6	50.7
2019	26.2	53.3	39.3	44.2
2020	41.9	52.2	55.4	85.6

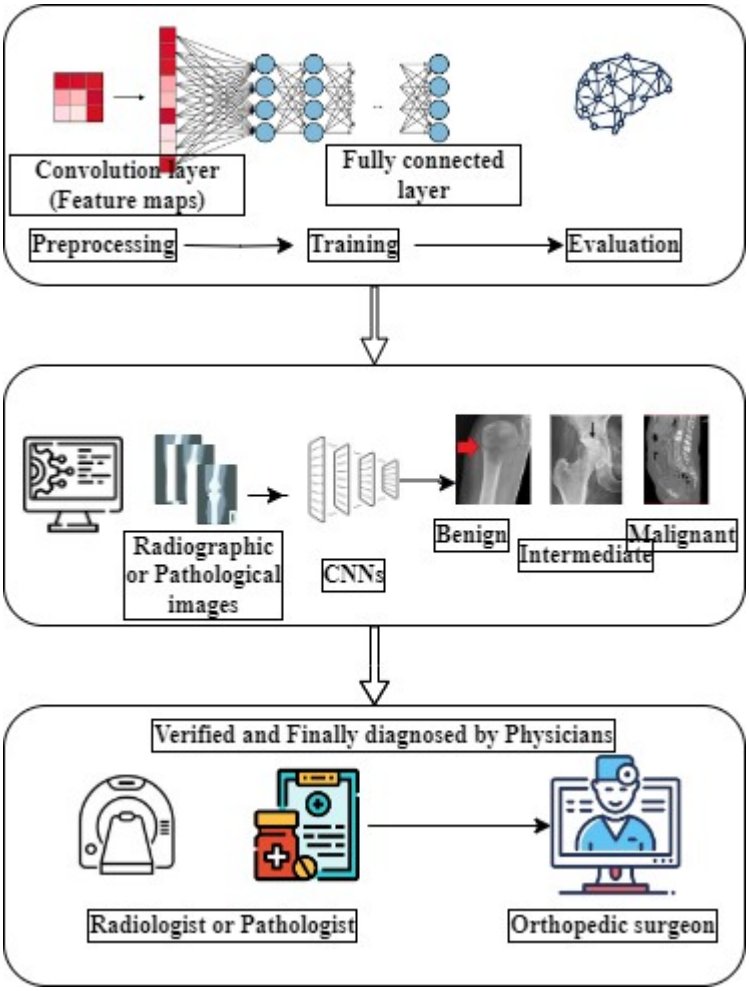

Figure 3. Deep learning based Bone Metastases retrospective diagnosis

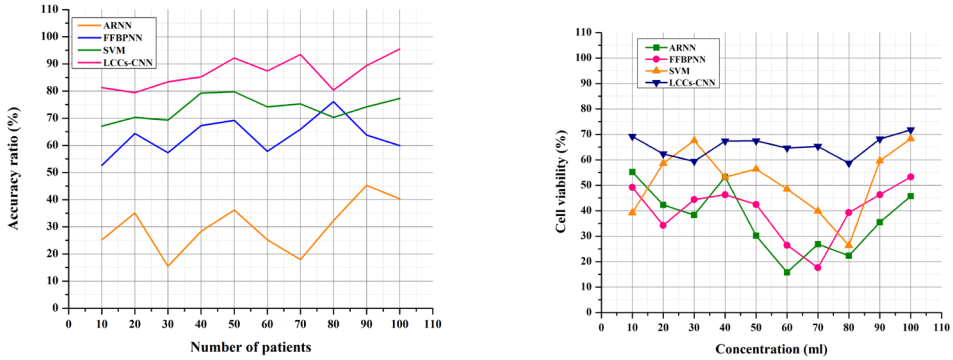

Figure 4. Accuracy of lung cancer cells on CNN (left), and Testing of cell viability in lung cancer (right)

Table 2. Validation sets of niosomes formulation

Methods	Cholesterol	Glycerol Solution	Actual value	Predicted value	RSE (%)
ARNN	0.95	62.62	196.55	193.65	1.50
FFBPNN	1.15	64.42	230.20	207.02	1.13
SVM	1.05	61.47	211.10	168.09	1.97
LCCs-CNN	1.10	62.52	194.60	228.10	1.26

In equation (3) I to be healthy, H the lungs must maintain ω several critical populations of cells alveolar epithelial cells, $\max_{i} L$ that create the small sacs where gas exchange occurs, and $\sqrt{j-L}$ bronchiolar epithelial cells, referred to the airway cells, $\frac{\sqrt{H^2-1}}{d_{n-1}}$ that are lined with smooth muscle. That need to be validated further with doing cascade impactor research, d that indicated their advantages to correspond with the deposited medication into the lungs the inhalation.

4. Advancements in Cancer Treatment Strategies and Early Detection Techniques

Exploring cancer treatments involves conventional therapies enhancing standard techniques. Notably, combining pembrolizumab with chemotherapy significantly improves overall survival in advanced lung cancer. Early lung cancer detection focuses on sputum and blood testing, analyzing genetic markers. Diverse carriers, including nanotubes and nanoparticles, target drug delivery. The dataset highlights cancer's global impact, leading cause of mortality, and prevalent types. Deep learning and cell line research advance translational discoveries. Cell viability tests and drug carriers' efficiency, exemplified in Tables 1 and 2, contribute to therapeutic progress in cancer treatment.

Conventional cancer treatments aim to improve, complement, or replace standard cancer treatment techniques. Nonetheless, ongoing scientific efforts seek to substantiate the safety and efficacy of these therapies. Notably, patients with advanced squamous non-small cell lung cancer experience significantly prolonged median overall survival when treated with pembrolizumab alongside standard chemotherapy initially. Detection of lung cancer involves a focus on sputum and blood testing, where analyzing blood specimens for tumor cells and genetic markers aids in the initial diagnosis. Various carriers, including nanotubes and nanoparticles, offer potential for drug targeting in cancer treatment.

Cancer encompasses a diverse range of diseases originating in the uncontrolled development of abnormal cells within various organs and tissues. It stands as the leading global cause of mortality, claiming an estimated 9.6 million lives, with 100 patients affected in 2018 alone. Predominant cancer types in males include lung, prostate, colorectal, stomach, and liver cancer, while breast, colorectal, lung, cervical, and thyroid cancer are prevalent among females.

To detect lung cancer in its early stages, the research utilized a deep learning CNN model trained through an ensemble learning strategy, achieving a remarkable 95% accuracy—a feat unmatched by other ensemble learning algorithms (Figure 4, left). This breakthrough has significantly advanced translational research and biological discoveries, primarily driven by the utilization of lung cancer cell lines. These cell lines were systematically established and characterized, stemming from both tiny cell and non-small cell lung carcinomas.

Figure 4(right) illustrates that cell viability tests serve as an indirect measure of the remaining viable cells following a therapeutic application. Swarm formation experiments shed light on the therapeutic potential to straightforwardly inhibit cancer development. The cell viability rate, representing the percentage of healthy living cells in a given population, becomes pivotal in assessing the effectiveness of substances in killing test cells during exposure to specific conditions, as exemplified in drug screening.

Table 1 highlights the significance of deaths and lung cancer ligands on the surface of a drug-carrying molecule, facilitating their endocytosis, internalization, and subsequent expulsion from the endosome and the carrier. Notably, graphene's extraordinary physical characteristics enable the blending of therapeutic medications and genes with co-delivered graphene, effectively addressing the challenge of multi-drug resistance. Among the widely utilized drug carriers are liposomes, polymeric micelles, microspheres, and nanoparticles. The percentage of suspected parcels containing narcotics is utilized to estimate the overall number of drugs in the shipment. Polyamidation nanoparticles play a crucial role in transporting anti-malarial medication to specific locations. Additionally, the combination of doxorubicin with polymers has demonstrated improvements in drug solubility, blood half-life, toxicity, and targeting.

Table 2 underscores the importance of the fitted model by suggesting that patients randomize a small number of niosomes formulations. By comparing the measured and anticipated particle size of each randomized formulation, the percentage of residual standard error (RSE) is calculated. The results reveal that the model aptly suited the system, with RSE values below 2.00%, indicating minimal deviation in the particle size of the niosomes from the anticipated values.

The exploration of cancer treatments involves a continuous effort to establish the safety and efficacy of conventional and innovative medical therapies. Notably, patients with advanced squamous non-small cell lung cancer exhibited significantly improved median overall survival when treated with pembrolizumab in combination with standard chemotherapy. The focus on sputum and blood testing for the detection of lung cancer, including the analysis of genetic markers, contributes to early diagnosis.

5. Conclusion

In conclusion, the development of niosomes as carriers for chemical medications stands as a significant stride in the battle against various illnesses, ranging from cancer and diabetes to inflammatory conditions. Leveraging their unique properties, niosomes offer an effective means to enhance the bioavailability of

medications, presenting a valuable solution for improved drug delivery. Their composition, including surfactants and cholesterol, shares similarities with liposomes, underlining their excellent biocompatibility and membrane penetration capabilities. This membrane-like structure acts as a protective barrier, safeguarding drug molecules from immunological and pharmacological degradation facilitated by the LCCs-CNN carrier system. Radiation therapy emerges as a potential relief for symptoms in individuals facing advanced lung cancer or metastasis, complementing a diverse range of treatment options for non-small cell lung cancer, including surgery, chemotherapy, targeted therapy, and more. While advancements in therapy and ongoing research show promise, challenges persist in ensuring widespread access to screening, early diagnosis, and comprehensive care for lung cancer patients, highlighting the need for enhanced psycho-social support, resources, and fundamental infrastructure.

Author Contributions

S.N. and C.D. conceptualized, wrote, and reviewed the article.

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Competing financial interests

The authors have no conflict of interest.

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