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Gefitinib-Loaded Polymeric Nanoparticles for Non Small Cell Lung Cancer (NSCLC): Advantages, Targeted Delivery and Therapeutic Potential

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Abstract: Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer-related deaths worldwide and accounts for nearly 85% of all lung cancer cases. Gefitinib, an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, is widely used in the treatment of NSCLC, especially in patients with EGFR mutations. However, conventional gefitinib therapy faces several limitations such as poor water solubility, low bioavailability, non-specific drug distribution, systemic side effects, and development of drug resistance. To overcome these drawbacks, polymeric nanoparticles have emerged as a promising drug delivery system. Gefitinib-loaded polymeric nanoparticles improve drug solubility, enhance bioavailability, provide sustained and controlled drug release, and enable targeted delivery to tumor tissues through passive and active targeting mechanisms. Various biodegradable polymers such as PLGA, chitosan, PEG, and PCL are commonly used in nanoparticle formulation due to their biocompatibility and controlled release properties. Different preparation methods including emulsion solvent evaporation, ionic gelation, nanoprecipitation, and microfluidic techniques are employed to develop stable nanoparticles with high drug encapsulation efficiency. These nanoformulations demonstrate improved cellular uptake, enhanced anticancer activity, reduced systemic toxicity, and potential to overcome gefitinib resistance in NSCLC treatment. Therefore, gefitinib-loaded polymeric nanoparticles represent a promising and advanced therapeutic approach for improving the effectiveness and safety of NSCLC therapy.

Key Words: Non-Small Cell Lung Cancer (NSCLC),Gefitinib,Polymeric Nanoparticles ,EGFR Inhibitor,Targeted Drug Delivery, Nanotechnology in Cancer Therapy,Drug Resistance,Tumor targeting

INTRODUCTION

Non-small cell lung cancer (NSCLC) is the most prevalent form of lung cancer and remains a major cause of cancer-related morbidity and mortality worldwide. It accounts for approximately 85% of all diagnosed lung cancer cases and represents a significant public health challenge due to its high incidence and often

poor prognosis. Despite advances in diagnosis and treatment, NSCLC continues to contribute substantially to global cancer deaths. (1)

NSCLC is a heterogeneous group of epithelial lung malignancies that includes three major histological subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Among these, adenocarcinoma is the most frequently diagnosed subtype and is commonly observed in non-smokers and younger individuals. Squamous cell carcinoma is strongly associated with tobacco smoking and generally arises in the central airways of the lungs. Large cell carcinoma is less common but is characterized by aggressive growth and a greater tendency for rapid metastasis. Understanding the biological and pathological differences among these subtypes is essential for selecting appropriate therapeutic strategies. (2,3)

Gefitinib, marketed under the brand name Iressa, is an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor widely used in the treatment of NSCLC patients carrying activating EGFR mutations. By blocking EGFR-mediated signaling pathways, gefitinib suppresses tumor cell proliferation and survival. Although it has demonstrated significant clinical benefits, its therapeutic efficacy may be limited by poor aqueous solubility, suboptimal bioavailability, non-specific distribution, and the development of acquired drug resistance during prolonged treatment. (4)

To address these limitations, nanotechnology-based drug delivery systems have attracted considerable attention. Among them, polymeric nanoparticles have emerged as promising carriers due to their ability to improve drug solubility, enhance bioavailability, provide controlled drug release, and facilitate targeted delivery to tumor tissues. These nanoscale systems, typically prepared from biodegradable and biocompatible polymers, can protect the encapsulated drug from degradation while promoting greater accumulation at the tumor site. (5)

The integration of gefitinib with polymeric nanoparticle technology offers a novel approach for improving NSCLC therapy. Such nanoformulations may enhance therapeutic efficacy, reduce systemic toxicity, and overcome some of the challenges associated with conventional gefitinib treatment. Therefore, gefitinib-loaded polymeric nanoparticles represent a promising strategy for the development of more effective and targeted therapies against NSCLC.

OVERVIEW OF NON-SMALL CELL LUNG CANCER

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for nearly 85% of all diagnosed cases worldwide. It remains a major health concern because of its high prevalence and substantial contribution to cancer-related mortality. Despite advances in diagnostic and therapeutic approaches, NSCLC continues to pose significant challenges in clinical management due to its complex biology and variable response to treatment.

Tobacco smoking is recognized as the leading risk factor for NSCLC and is responsible for the majority of lung cancer cases. Cigarette smoke contains numerous carcinogenic compounds that can induce DNA damage and genetic alterations, ultimately leading to malignant transformation of lung cells. The likelihood of developing NSCLC increases with both the duration and intensity of smoking exposure. Furthermore, individuals exposed to secondhand smoke also have an elevated risk of developing lung cancer, highlighting the harmful effects of passive smoking. (8)

In addition to smoking, several environmental and occupational factors contribute to the development of NSCLC. Long-term exposure to hazardous substances such as asbestos, arsenic, chromium compounds, and diesel exhaust has been associated with an increased incidence of lung cancer. Radon gas, a naturally occurring radioactive element present in soil and building materials, is considered the second most important cause of lung cancer after smoking. Moreover, air pollution, particularly fine particulate matter (PM2.5), has been linked to a higher risk of lung malignancies, especially among individuals living in densely populated urban and industrial regions. (9,10)

TYPES OF NSCLC

A. Adenocarcinoma

Adenocarcinoma is the most frequently diagnosed subtype of NSCLC and accounts for approximately 35–40% of all lung cancer cases. It commonly develops in the peripheral regions of the lungs and is often observed in non-smokers, women, and younger patients. The tumor originates from glandular epithelial cells and may occasionally arise in areas of previous lung injury, scarring, or chronic inflammation.

A distinct variant of adenocarcinoma, previously known as bronchioloalveolar carcinoma, originates from type II pneumocytes and proliferates along the alveolar walls. Clinically, it may present as

a solitary pulmonary nodule, multifocal lesions, or a diffuse pneumonia-like pattern. Patients with advanced disease may experience the production of large amounts of watery sputum, which is considered a characteristic feature of this subtype.

B. Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) represents approximately 25–30% of all lung cancer cases and is strongly associated with tobacco smoking. Unlike adenocarcinoma, SCC typically arises in the central airways and major bronchi of the lungs. It frequently presents as a cavitary lesion and may obstruct the bronchial passages, resulting in respiratory symptoms.

Histologically, squamous cell carcinoma is characterized by the presence of keratin formation and intercellular bridges. Due to its tendency to shed malignant cells into the airways, SCC can often be detected through cytological examination of sputum samples. This subtype is also commonly associated with paraneoplastic syndromes, particularly hypercalcemia resulting from ectopic hormone production.

C. Large Cell Carcinoma

Large cell carcinoma is a relatively uncommon subtype of non-small cell lung cancer (NSCLC), accounting for approximately 10–15% of all lung cancer cases. It commonly presents as a large mass located in the peripheral regions of the lung and is often associated with rapid tumor growth and aggressive clinical behavior.

From a histopathological perspective, large cell carcinoma is characterized by poorly differentiated malignant cells with marked cellular atypia and areas of necrosis. Unlike squamous cell carcinoma, it lacks evidence of keratin formation, and unlike adenocarcinoma, it does not demonstrate glandular differentiation. Because of these features, large cell carcinoma has traditionally been considered a diagnosis of exclusion.

Advances in immunohistochemistry, molecular pathology, and electron microscopy have significantly improved the classification of lung tumors. As a result, many tumors that were previously categorized as large cell carcinoma are now more accurately identified as poorly differentiated adenocarcinomas or, less commonly, squamous cell carcinomas. Consequently, the number of cases classified as true large cell carcinoma has decreased over time.

Clinically, undifferentiated large cell carcinomas generally exhibit a prognosis comparable to that of adenocarcinoma. For this reason, they are frequently grouped with adenocarcinomas in clinical studies and therapeutic evaluations. (7)

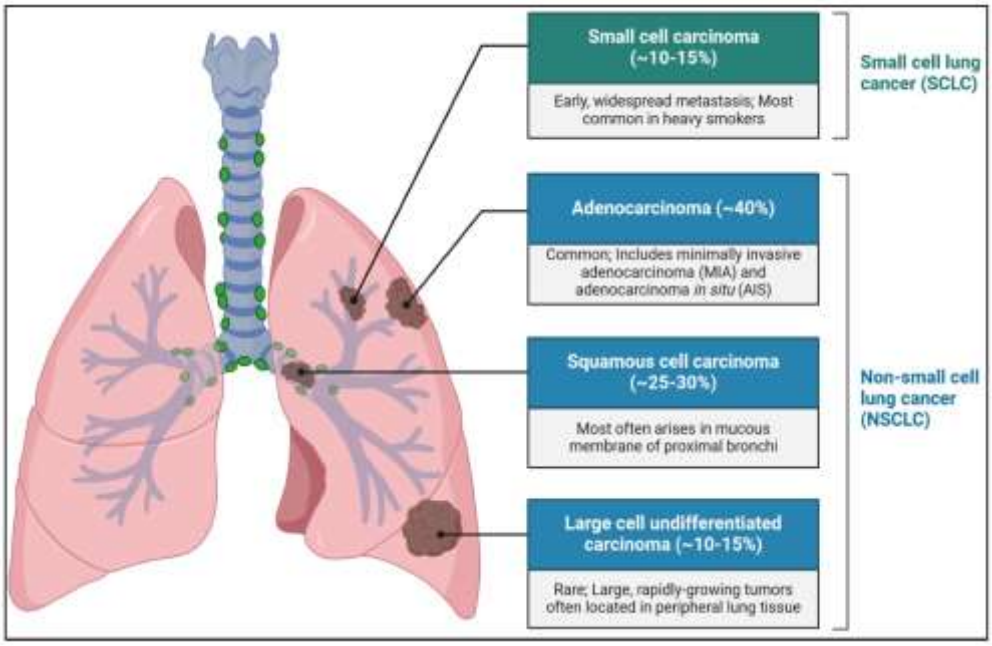


Fig 1: Overview of NSCLC types of cancers that develop from the lung's epithelial cells, with three main subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. [11]

GEFITINIB

Gefitinib, sold under the brand name Iressa, is a medication used for lung cancer.

Gefitinib is an EGFR inhibitor, which interrupts signaling through the epidermal growth factor receptor (EGFR) in target cells. Therefore, it is only effective in cancers with mutated and overactive EGFR, but resistances to gefitinib can arise through other mutations. It is marketed by AstraZeneca and Teva.

Gefitinib is an anilinoquinazoline derivative.[3][4] .Its chemical structure is characterized by quinazoline core, which is substituted with a (3-chloro-4-fluorophenyl)amino group at position 4,a 3-(morpholin-4-yl)propoxy group at position 6, and a methoxy group at position 7.

DRUG PROFILE [12]

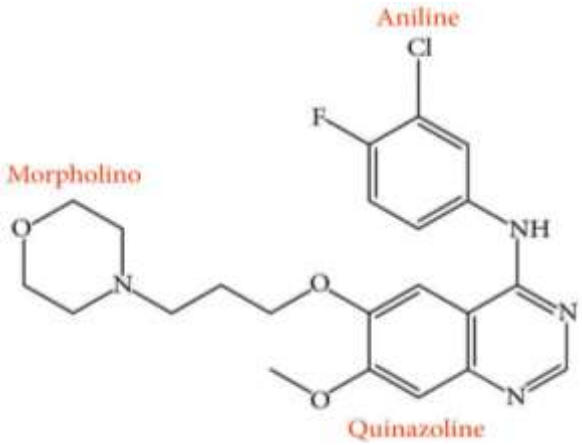
IUPAC Name: N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholin-4-ylpropoxy) quinazolin-4-amine

Chemical Formula: $C_{22}H_{24}ClFN_4O_3$

Molecular Weight: 446.90 g/mol

CAS Number: 184475-35-2

Chemical structure;

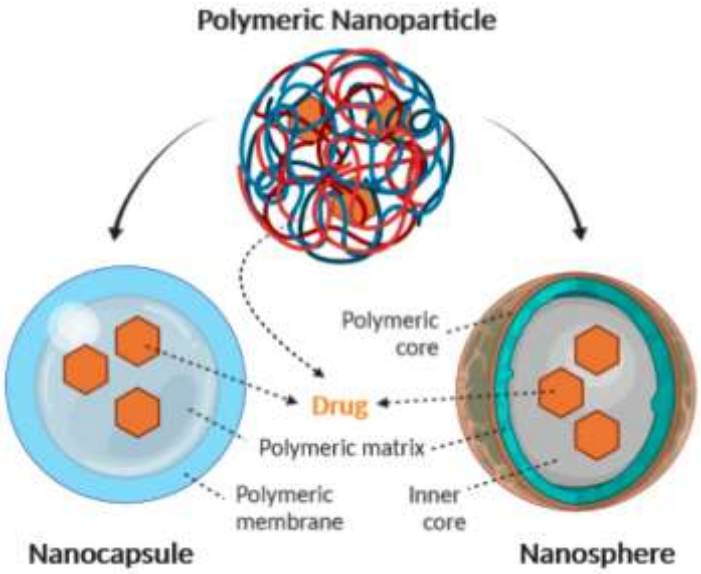


https://pubchem.ncbi.nlm.nih.gov/compound/Gefitinib

POLYMERIC NANOPARTICLE

Polymeric nanoparticles are tiny colloidal particles ranging from 1–1000 nm made from natural or synthetic polymers. They are widely used in drug delivery systems because they improve drug stability, bioavailability, controlled release, and targeted delivery to diseased tissues like tumors.

Polymeric nanoparticles (NPs) have attracted considerable interest over recent years due to their properties resulting from their small size. [13,14,15] Advantages of polymeric NPs as drug carriers include their potential use for controlled release, the ability to protect drug and other molecules with biological activity against the environment, improve their bioavailability and therapeutic index[16]. The term “nanoparticle” comprises both nanocapsules and nanospheres, which differ with respect to their morphology[17]. Nanocapsules are composed of an oily core in which the drug is usually dissolved, surrounded by a polymeric shell which controls the release profile of the drug from the core. Nanospheres are based on a continuous polymeric network in which the drug can be retained inside or adsorbed onto their surface. These two types of polymeric NPs recognized as a reservoir system (nanocapsule), and matrix system (nanosphere). [18,19,20]



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PROBLEMS OF CONVENTIONAL GEFITINIB

Poor Water Solubility:

Gefitinib is poorly soluble in water, especially at higher gastric pH, which reduces dissolution and therapeutic activity.

Low Bioavailability:

Gefitinib belongs to BCS Class II drugs and has low oral bioavailability due to poor solubility and absorption limitations.

Systemic Side Effects;

- Skin rash
- Diarrhea
- Nausea
- Vomiting
- Hepatotoxicity
- Interstitial lung disease [21]

Non-Specific Drug Distribution

Traditional oral dosage forms distribute the drug throughout the body rather than specifically to tumor tissues, causing off-target effects.[22]

Drug Resistance

Long-term gefitinib therapy may lead to acquired resistance in cancer cells, reducing therapeutic effectiveness.[23]

Poor Tumor Targeting

Only a limited amount of free drug reaches lung tumor tissue effectively. Nanocarriers are therefore investigated to improve targeted accumulation [24]

NANOTECHNOLOGY:

Over the past 30 years, nanotechnology has played a crucial role in advancing global health. This progress has paved the way for promising developments in nanomedicine, along with the emergence of new terms like "nanobiotechnology," which combines nanotechnology and molecular biology.

Nanobiotechnology is a branch of nanoscience that centers on creating functional nanoscale materials using both chemical and physical methods.

The nanoscale refers to sizes typically between 1 and 100 nanometers. Achieving precise control over matter at this extremely small scale has opened new possibilities in medicine, particularly in developing nanoscale drug delivery systems.

These advanced systems allow pharmaceutical agents to be administered more efficiently and with greater targeting accuracy, improving therapeutic effectiveness and minimizing side effects. A major advancement brought by nanotechnology in the field of pharmacy is the ability to design and create nanoparticles specifically for drug delivery purposes. This innovation has greatly enhanced the pharmacokinetic properties of many drugs—such as their absorption, distribution, metabolism, and elimination—resulting in improved therapeutic effectiveness.

Additionally, the use of nanoparticles helps to minimize adverse side effects and lowers the frequency of required doses, making treatments more convenient for patients. In cancer therapy, nanotechnology has become an especially valuable approach, enabling highly precise and targeted treatment strategies that align with the principles of precision medicine, thereby improving patient outcomes.

Nanotechnology has introduced groundbreaking advancements in regenerative medicine by supplying novel tools and materials engineered at the nanoscale. These innovations offer significant promise in areas such as tissue engineering, organ transplantation, and the repair or regeneration of damaged or deteriorated tissues. By integrating nanotechnology with regenerative medicine, researchers are developing more effective strategies to stimulate tissue growth, improve compatibility of transplanted materials, and enhance the overall healing process. This powerful combination has the potential to transform medical treatments dramatically, providing new solutions to critical challenges such as the shortage of donor organs and the management of chronic tissue diseases, ultimately improving patient outcomes and quality of life. [25,26,27]

Gefitinib loaded polymeric nanoparticles

Gefitinib-loaded polymeric nanoparticles are advanced drug delivery systems developed for the treatment of Non-Small Cell Lung Cancer (NSCLC).

They improve the solubility and bioavailability of gefitinib, which is poorly water soluble and has limited oral absorption.

These nanoparticles enhance targeted delivery of the drug to tumor tissues through the Enhanced Permeability and Retention (EPR) effect, reducing damage to healthy cells.

They also provide sustained and controlled drug release, helping to maintain therapeutic drug levels for a longer duration.

In addition, gefitinib polymeric nanoparticles show potential in reducing side effects and overcoming drug resistance associated with conventional gefitinib therapy.[28]

POLYMERS USED IN GEFITINIB POLYMERIC NANOPARTICLES

1. PLGA (Poly Lactic-co-Glycolic Acid)

PLGA is the most commonly used biodegradable polymer for gefitinib nanoparticles because of:

- Biocompatibility
- Controlled release
- Biodegradability
- FDA approval
- It improves sustained release and anticancer activity.

2. Chitosan

Chitosan is a natural polymer used either alone or as coating material over PLGA nanoparticles.

Advantages:

- Mucoadhesive property
- Enhanced cellular uptake

- Improved permeability
- Better tumor targeting.[29]

3. PEG (Polyethylene Glycol)

PEG is used for PEGylation to:

- Increase circulation time
- Reduce immune clearance
- Improve nanoparticle stability
- PEG-containing systems improve bioavailability and targeting efficiency [30]

4. PCL (Polycaprolactone)

PCL is a biodegradable polymer used for prolonged and controlled release formulations.

Advantages:

- Slow degradation
- Sustained release
- Good drug entrapment efficiency.[31]

5. Poloxamer 407 (P407)

Poloxamer 407 is used along with PLGA and chitosan to improve:

- Stability
- Drug solubility
- Cellular uptake [32]

TARGETED DRUG DELIVERY MECHANISM

1. Passive Targeting (EPR Effect) [33]

Administration of Gefitinib Polymeric Nanoparticles
↓
Circulation in Bloodstream
↓
Avoidance of Immune System Clearance
↓
Tumor Blood Vessels Become Leaky
↓
Nanoparticles Penetrate Tumor Tissue
↓
Poor Lymphatic Drainage Causes Retention
↓
Accumulation of Nanoparticles in NSCLC Tumor
↓
Enhanced Drug Concentration at Tumor Site

2. Active Targeting (Ligand–Receptor Binding) [34]

Surface Functionalization of Nanoparticles
with Ligands / Antibodies / Peptides
↓
Administration into Bloodstream
↓
Nanoparticles Reach NSCLC Tumor Site
↓
Ligands Bind to Overexpressed EGFR Receptors
on Cancer Cells

↓
Receptor–Ligand Interaction
↓
Receptor-Mediated Endocytosis
↓
Internalization of Nanoparticles into Cancer Cells
↓
Targeted Delivery of Gefitinib

3. pH-Sensitive Drug Release [35]

Nanoparticles Enter Cancer Cell
↓
Formation of Endosome
↓
Transfer to Lysosome
↓
Acidic pH Environment Encountered
↓
Polymeric Matrix Swelling / Degradation
↓
Breakdown of Nanoparticle Structure
↓
Controlled Release of Gefitinib
↓
High Drug Concentration Inside Tumor Cell

4) Therapeutic action of gefitinib [36]

Release of Gefitinib from Nanoparticles
↓
Binding to EGFR Tyrosine Kinase Domain
↓
Inhibition of EGFR Phosphorylation
↓
Blockage of Downstream Signaling Pathways
↓
Inhibition of Cancer Cell Proliferation
↓
Induction of Apoptosis
↓
Reduction in NSCLC Tumor Growth

CHARACTERIZATION OF GEFITINIB LOADED POLYMERIC NANOPARTICLES:

1. Physicochemical Characteristics:

a) Particle Size: Ranges from 50nm to 250nm allowing the nanoparticles to passively accumulate at the tumor site via the Enhanced Permeation and Retention (EPR) effect.

b) Polydispersity Index (PDI): Typically optimized below 0.400 indicating a uniform and monodisperse size distribution.

c) Zeta Potential: Values range between -20 mV and+30mVdepending on the polymer coating used (e.g., negative for pure PLGA, and positive if surface-coated with chitosan to enhance cellular mucoadhesion).

d) Encapsulation Efficiency (EE): Consistently high across formulations, often falling between 70%and 90%. [37]

2. Materials & Formulation Techniques

a) Polymers: Common biodegradable and biocompatible polymers include PLGA (Poly(lactic-co-glycolic acid)), PCL (Polycaprolactone), chitosan, and dextran-based polymersomes.

b) Fabrication: Methods usually involve nanoprecipitation, ionic gelation, or microfluidic techniques, frequently utilizing Quality by Design (QbD) principles to optimize drug-loading content.[38]

3. Therapeutic Performance & In Vitro Findings

a) Sustained Drug Release: In vitro studies commonly show a biphasic or sustained drug release pattern (often following Higuchi or Korsmeyer-Peppas models), allowing prolonged therapeutic action and lower dosing.

b) Cellular Uptake & Cytotoxicity: Studies on NSCLC cell lines (such as A549) demonstrate that polymeric nanoparticles significantly improve cellular uptake and reduce the IC50 of the drug compared to free gefitinib. [39]

METHOD OF PREPARATION

1. Emulsion Solvent Evaporation Method [40]

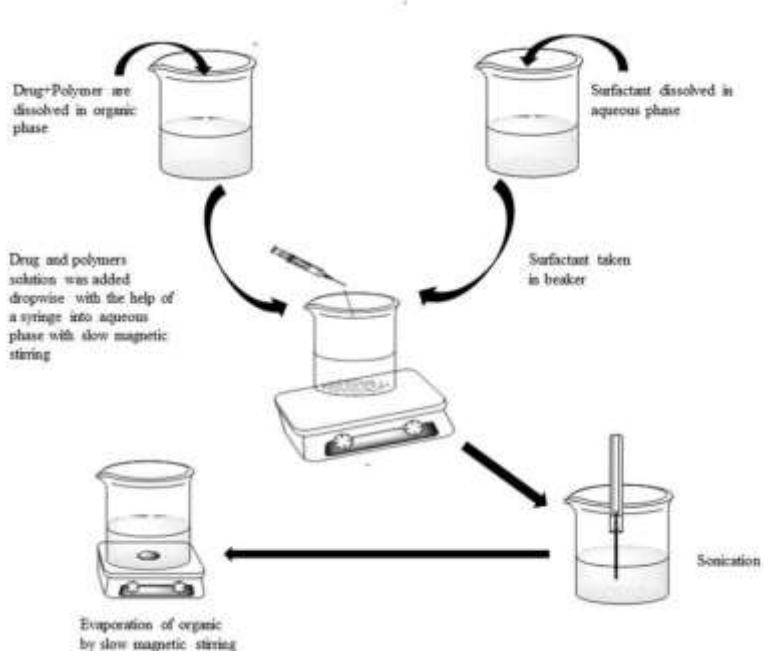
This is the most widely used method for preparing gefitinib-loaded PLGA nanoparticles.

Principle

The drug and polymer are dissolved in an organic solvent and emulsified into an aqueous phase containing stabilizer. Evaporation of solvent forms nanoparticles.

Procedure

- Gefitinib and PLGA are dissolved in dichloromethane or acetone.
- Polyvinyl alcohol (PVA) aqueous solution is prepared separately.
- Organic phase is added slowly into aqueous phase under homogenization or sonication.
- Oil-in-water emulsion is formed.
- Organic solvent is evaporated under continuous stirring.
- Nanoparticles are collected by centrifugation and dried



https://www.researchgate.net/figure/Schematic-representation-of-the-emulsion-solvent-evaporation-method_fig1_327663281

2. Ionic Gelation Method [41]

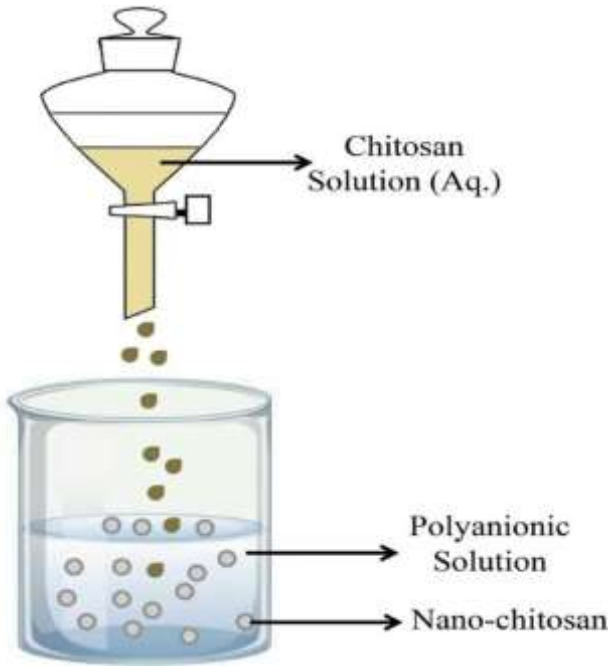
This method is commonly used for chitosan-based gefitinib nanoparticles.

Principle

Nanoparticles are formed by electrostatic interaction between positively charged chitosan and negatively charged cross-linking agents such as sodium tripolyphosphate (TPP).

Procedure

- Chitosan is dissolved in dilute acetic acid.
- Gefitinib is dispersed in chitosan solution.
- TPP solution is added dropwise under magnetic stirring.
- Ionic cross-linking forms nanoparticles spontaneously.
- Nanoparticles are separated and purified.



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3. Nanoprecipitation Method [42]

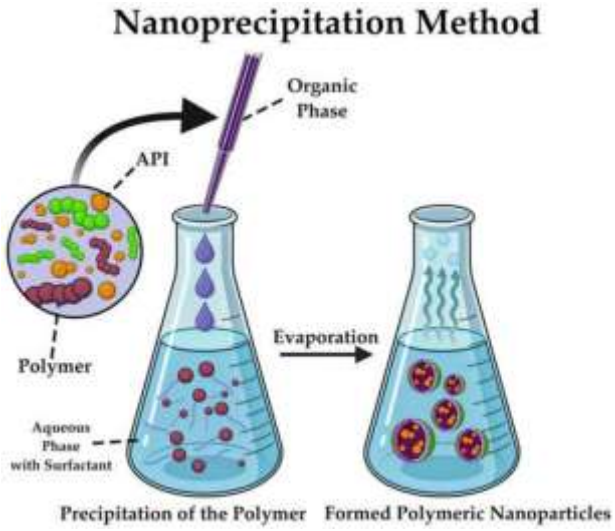
Nanoprecipitation is a simple and efficient method for poorly soluble anticancer drugs like gefitinib.

Principle

Rapid diffusion of solvent into aqueous medium causes polymer precipitation and nanoparticle formation.

Procedure

- Gefitinib and polymer are dissolved in acetone or ethanol.
- Organic phase is injected into aqueous stabilizer solution under stirring.
- Solvent diffuses rapidly into water.
- Nanoparticles form immediately.
- Solvent is evaporated and nanoparticles are collected.



https://www.researchgate.net/figure/Schematic-representation-of-the-nanoprecipitation-method_fig1_351628845

4. Homogenization–Ultrasonication Method [43]

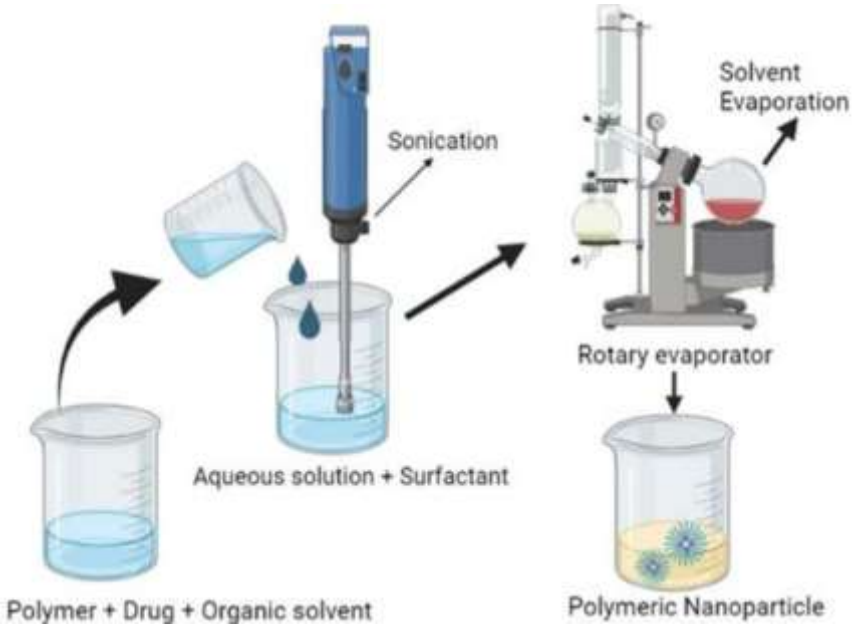
This technique is used to reduce nanoparticle size and improve stability.

Principle

High-speed homogenization followed by ultrasonication decreases droplet size and forms stable nanoparticles.

Procedure

- Drug and polymer are dissolved in organic solvent.
- Solution is homogenized at high speed.
- Probe ultrasonication further reduces particle size.
- Solvent evaporation produces nanoparticles.
- Nanoparticles are purified and dried.



https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/ultrasonication

5. Microfluidic Aerosol-Assisted Synthesis [44]

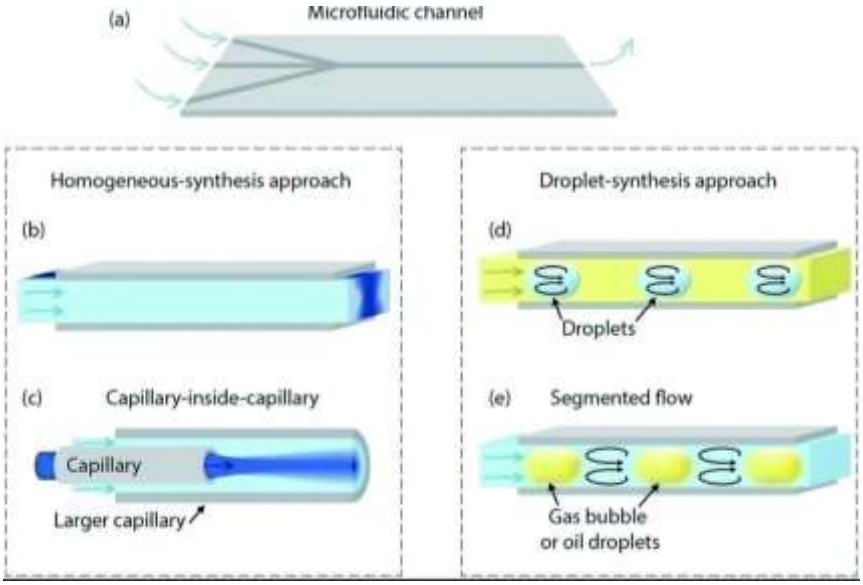
This is an advanced nanoformulation method for producing highly uniform gefitinib nanoparticles.

Principle

Microfluidic channels provide controlled mixing of polymer and drug solutions, resulting in precise nanoparticle formation.

Procedure

- Chitosan and gefitinib solutions are introduced into microfluidic channels.
- Aerosol-assisted mixing occurs within the chip.
- Nanoparticles form through controlled precipitation and cross-linking.
- Nanoparticles are collected and stabilized.



https://www.nature.com/articles/s41578-019-0126-z

Application in NSCLC

1. Overcoming Poor Solubility [45]

Gefitinib is a BCS Class II drug. By encapsulating it into hydrophilic or amphiphilic polymer matrices, researchers drastically increase its dissolution rate and aqueous stability.

2. Enhanced Bioavailability [46]

Nanocarriers protect the drug from rapid degradation in the stomach and avoid initial harsh first-pass metabolism. This allows for a much higher percentage of the administered dose to reach the bloodstream and tumor sites.

3. Tumor Targeting [47]

Polymeric nanoparticles allow for passive and active targeting. Passive targeting exploits the Enhanced Permeation and Retention (EPR) effect to accumulate heavily within the leaky, poorly formed blood vessels of tumors. Active targeting often involves functionalizing the nanoparticle surface with ligands, like specific antibodies or peptides, to seek out overexpressed EGFR receptors directly on NSCLC cells.

4. Sustained and pH-Sensitive Release [48]

Nanoscale formulations can be engineered to release the drug steadily over extended periods. Furthermore, many polymers (such as those integrating starch) demonstrate pH-responsive behavior, releasing the payload preferentially in the acidic microenvironment characteristic of tumor.

5. Toxicity Reduction [49]

By localizing the anticancer effects precisely at the tumor site, high systemic concentrations are avoided. This translates to fewer severe adverse drug reactions (like diarrhea, stomatitis, and liver enzyme elevations) normally associated with high-dose traditional pills.

Advantage of gefitinib polymeric nanoparticles

1. Enhanced Solubility and Bioavailability [50]

Gefitinib is highly hydrophobic, making it difficult for the body to absorb (only about 44% oral absorption). Nano-encapsulation vastly increases the surface area and dispersibility of the drug, allowing for better absorption and higher bioavailability.Passive.

2. Tumor Targeting (EPR Effect) [51]

Due to their microscopic size (typically 10 - 200nm), polymeric nanoparticles can slip through the leaky, irregular blood vessels surrounding tumor tissues and evade immune clearance. This Enhanced Permeability and Retention (EPR) effect allows the particles to accumulate directly inside the cancer cells.

3. Reduced Side Effects [52]

Because the drug is efficiently localized at the tumor site, less of it spreads to healthy organs. This helps mitigate debilitating adverse effects commonly associated with free Gefitinib, such as severe diarrhea, liver enzyme elevation (hepatotoxicity), and skin rashes.

4. Sustained and Controlled Release [53]

Polymeric nanoparticles act as a drug depot. They prevent a sudden "burst" of the drug into the bloodstream, releasing it slowly over an extended period. This minimizes the need for high or frequent dosing regimens.

Future Prospects of Gefitinib Polymeric Nanoparticles for NSCLC;

1. Better Targeting of Cancer Cells [54]

In the future, gefitinib polymeric nanoparticles may help deliver the drug directly to lung cancer cells. This can increase the drug effect on tumors and reduce damage to normal cells.

2. Overcoming Drug Resistance [55]

Many NSCLC patients develop resistance to gefitinib after long-term treatment. Polymeric nanoparticles may carry gefitinib together with genes or other drugs to overcome this resistance and improve treatment response.

3. Improved Drug Absorption [56]

Gefitinib has poor water solubility and limited absorption. Polymeric nanoparticles can improve its solubility and bioavailability, helping more drug reach the bloodstream and tumor site.

4. Reduced Side Effects [57]

Because nanoparticles can target cancer tissues specifically, future formulations may reduce common side effects of gefitinib such as skin irritation and diarrhea.

5. Combination Therapy [58]

Future nanoparticle systems may deliver gefitinib along with chemotherapy drugs or immunotherapy agents in a single carrier. This may improve treatment effectiveness in advanced NSCLC.

6. Clinical Development [59]

Although many studies are still in the laboratory stage, future clinical trials and large-scale production may help gefitinib polymeric nanoparticles become available for routine NSCLC treatment.

CONCLUSION

Gefitinib-loaded polymeric nanoparticles are a promising approach for NSCLC treatment.They improve the solubility and bioavailability of gefitinib effectively.These nanoparticles provide targeted and sustained drug delivery to tumor cells.They also reduce side effects and improve therapeutic efficiency. Thus, polymeric nanoparticles may become an advanced strategy for future lung cancer therapy.

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