Novel poloxamer-Xyloglucan nano micelle as an Intranasal delivery system

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Abstract— Lung's cancer is the highest universally spread of invasive cancer in men. While significant progress has been made in lung cancer, diagnostic and therapeutic effective prevention and treatment options remain scarce. Concerning xyloglucan-based chemotherapeutic therapies, the studies reported cell migration resistance, improved drug absorption, membrane interaction and permeability, immune stimulating behaviour, and extended in-vitro drug release. Targeted distribution is ensured by xyloglucan-based ligand conjugated carrier systems in conjunction with active moieties such as DNA, RNA, proteins, and therapeutic agents. The purpose of this context is to emphasize the efficient drug delivery to lung cancer cell lines using xyloglucan. This article discusses the various xyloglucan -based ligand conjugated carrier systems. From the studies reviewed it can be concluded that xyloglucan derivatives are promising materials for targeted and non-viral gene delivery in treatment of lungs cancer. lung cancer continues to present a huge challenge for health policies with over 22% cases reported annually in South Asia. This figure represents approximately 12% of all cancers, 65% of which are diagnosed in men.

Keyword: xyloglucan, Nanoparticles, Cellular uptake, endocytosis: lung cancer,targeted gene therapy.

Highlights:
• Targeted distribution ensured by xyloglucan - ligand conjugated carrier systems.
• Extended in-vitro drug release improves medication absorption.

1. INTRODUCTION

Lung cancer has steadily increased since the 1930s, owing primarily to changes in tobacco consumption patterns, and has become one of the world's most serious cancers. The current risk of lung cancer is defined by the population's cigarette usage 30 years ago. As a result, reducing the impact of lung cancer on the community requires a two-pronged approach. On the one hand, to limit future cancer incidence through cessation efforts, and on the other, to decrease fatality among those who already have a high cancer risk.The drug delivery paradigm is shifting, and scientists are gradually moving toward a new era of targeted drug administration that goes beyond traditional and non-targeted approaches. Traditional and non-targeted distribution present number of issues. Mechanisms. There's also a requirement to build nanocarriers that carry active moieties to the right places. While limiting off-target delivery, the target sites are reliably and preferentially delivered. The concept of to overcome the issues, an active targeted distribution system was implemented above. To improve projectile accuracy, survivability, and absorption by target cells, inserting high-affinity ligands on the surface of nanocarriers is known as active targeting. One of the most prevalent systemic therapies for breast cancer is chemotherapy. Traditional chemotherapy is still used despite substantial breakthroughsin diagnosis and treatment.A lung cancer deterrent the successful treatment of cancer. Drug resistance, in addition to metastases, aconcern is another risk that can result in a tumour recurrence and treatment failure.

As a result, drug resistance overcoming methods may provide sensible treatment solutions to improve chemotherapy effectiven ess and improve the clinical prognosis of cancer patients.

Nanoparticles are now being developed as a significant development in cancer therapy. Nanotherapeutics help to overcome so me of the disadvantages of chemotherapies, such as lack of selectivity, multidrug resistance, and low bioavailability, as well as rapid systemic clearance, low water solubility, and significant systemic toxicityFurthermore, because of their nanoscale size an d capacity to extravagate past the endothelium in tumours, nanoparticles can be ingested by a variety of cell types.

These are nano-sized colloidal units having a diameter of 10–500 nm that the drug can pass through.loaded, adsorbed, or conjugated are all terms used to describe how something is loaded, adsorbed, or conjugated Polyionic nanocomplexes made up of positively charged polycations and negatively charged polycatio ns are currently being investigated. The xyloglucan is one of them because of their unique feature. Nanoparticle have attracted lot of attention because they are biodegradable, biocompatible. Nanoparticle cellular uptake and membrane permeability xyloglucan mucoadhesive characteristics prolongs absorption time. [1,2]

2. COVID-19 AND LUNG CANCER

The coronavirus disease 2019 (COVID-19) pandemic has had a substantial impact on lung cancer patients in several ways. First, practically all data show that the complexity of the disease and mortality rates in patients with lung cancer after COVID-19 infection are comparatively higher.[2]

Lung cancer: -

Lung carcinoma is the most prevalent risk factor for mortality in the developed world, with over 40 000 fatalities every year in the Uk. While lung cancer in men is began to diminish in the West, lung cancer in women is continuing to grow and it has now exceeded breast cancer in several countries. In countries with relatively high smoking rates, mortality will continue to increase well into the next century. In the Uk, fewer than 5% of patients surviving for more than 5 years after being diagnosed. This series of reviews aims to show ways to improve these dismal survival time. [2][4]

Smoking remains the principal cause of lung cancer

Studies also displayed that women's risk is 100 times higher than in men. Lung cancer is a group of diseases in which uncontrolled cells in lymph nodes tissue alter and divide, typically leading to a lump or mass formation of grades, and tumour stages, invasive, or Situ appearance classes. However, a single Lung tumour can be a combination of numerous types of cells.[2] Control of lung cancer is a foremost clinical challenge due to its complexity, heterogeneity, and aggressiveness.

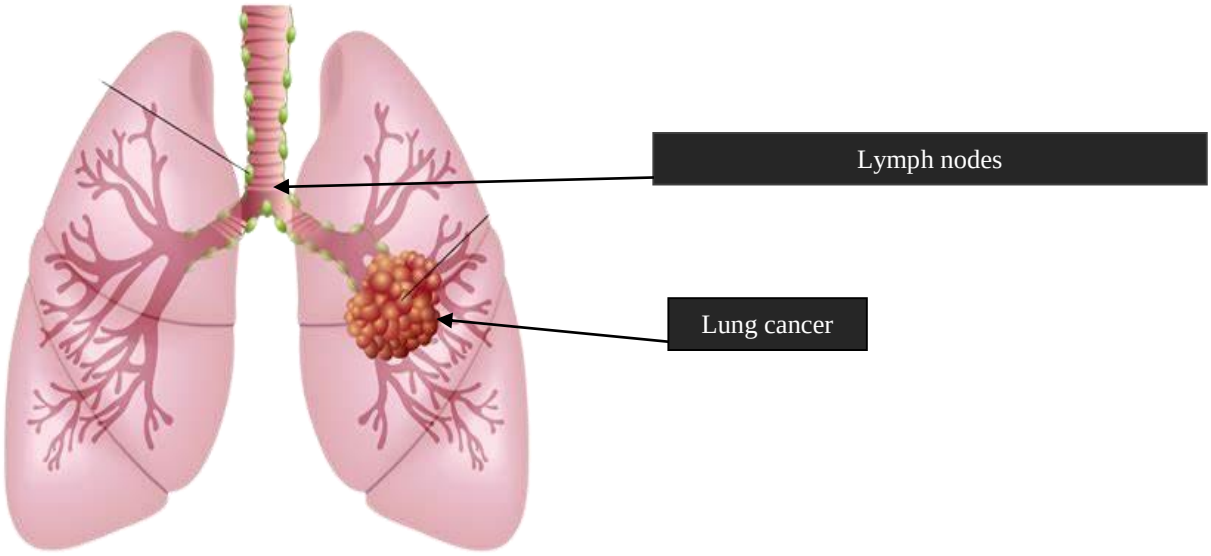


Figure 1 ***Lung cancer (Tumoral mass)***

3. XYLOGLUCAN

Xyloglucan is a hemicellulose polymer found in the main cell wall of higher plants and can be found in seeds such as tamarind, where it accounts for 50% of the storing energy material resources. Xyloglucan from tamarind seeds has a unique chemical composition A cellulose-like main chain of -(14)-linked d-glucosyl residues is routinely replaced at C-6 with -d-xylosyl and -d-galactosyl-(12) residues. —d-xylosylresidues.The xyloglucan's availability (in terms of amount and purity) facilitated the development of a wide range of commercial, industrial, and pharmaceutical applications . It is widely utilised in the food business in Japan and other Asian countries as thickeners, gelling agents, and stabilisers. Medication delivery via xyloglucan gels is common and xyloglucan-based nanoparticles were recently developed to encapsulate an anti-cancer drug. (10)

Distinct branches in the structure of xyloglucans may lead to variations in viscosity, solubility, and conformational flexibility of the main chain; hence, diverse branches may give the polysaccharide different properties.

Although the XGs are water soluble, the individual macromolecules do not fully hydrate, resulting in aggregated species persisting even in very dilute solutions. The biopolymer has a good combination of hydrophobic and hydrophilic properties, and the cellulose-like backbone's high chain stiffness makes it easier to work with. (6)

Anticancer activity of xyloglucan

Certain polysaccharides are harmful to tumor cells because they activate the immune system and promote maturation, differentiation, and differentiation. Lymphocytes, macrophages, and natural killer cells proliferate Surprisingly, the impact of these biopolymers can be altered by a variety of factors. Chemical alterations Deglutamylation of xyloglucans increased its immunomodulatory action, according to a previous study. Increases the release of proinflammatory mediators such NO, TNF-, IL-1, and IL-6 when compared to the native biopolymer. DirectPolysaccharides, both native and chemically modified polysaccharides, have been shown to have cytotoxic effects on cancer cells. It is significant in this regard.

The complexation of polysaccharides with metals is important among chemical alterations, owing to the use of certain metals in medicinal therapy. Vanadium compounds, for example, have demonstrated important biological effects such as mimicking insulin, cytotoxicity on tumor cells as evidenced by inhibition of DNA and RNA synthesis. increased reactive oxygen species (ROS) formation of permeability transition pore, and cytochrome c release.

Mechanism of anti-cancer activity of xyloglucan

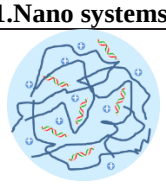
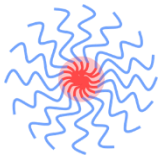
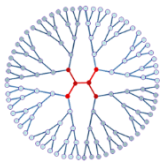
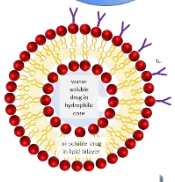
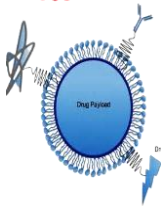
Xyloglucan anti-metastatic efficacy is due to its penetration-enhancing mechanism. It has been found that treating lung cancer cells with a high concentration of xyloglucan prevents them from migrating across a Matrigel-coated barrier. Xyloglucan has been found to open the tight junction between epithelial cells, increasing drug permeability and triggering tight junction rupture at the molecular levelbecause of mucoadhesive property meant that cell membrane contact was increased, which was important for boosting cell uptake and membrane permeability. Themucoadhesive Nessand permeability of chemotherapy drugs can affect drug absorption and chemotherapy efficacy because xyloglucan do not increase endotoxin absorption, their effect on tight junction is deemed harmless. Xyloglucan anticancer properties are link to its ability to promote biodistribution. The drug accumulation in the tumour cell has a strong drug entrapment capacity.it introduces cross-linked acetate functional groups, producing the desired matrix for effective encapsulation and prolonged release of different medicines. xyloglucan nanoparticles can also increase permeability and retention while reducing cytotoxicity increase medication physicochemical qualities and aid in the progression of apoptosis different carcinomas in-vivo results are reported where xyloglucan nanoparticles were used enhanced cumulation of oncolytic medicines and the production of an anticancer effect in tumour tissue.

4. MICELLES AND NANOPARTICLES

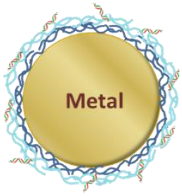
Particles with a size of 1e100 nm are commonly referred to as nanocarriers.

Nanoparticles and Lung cancer

Table 1.Nano systems applied in gene therapy for lung cancers

Cationic polymer complexes		Oligonucleotides form complexes with cationic polymers such as PEI and modified polymers. Complexes are rapidly and easily prepared.
Polymeric micelles		The micelles are formed by the self-assembly of block copolymers via electrostatic interactions. The inherent and modifiable properties of micelles are suitable for gene delivery.
Dendrimers		3D macromolecules consist of a central core from which the highly branched polymer chains grow in symmetric structures. Dendrimers have unique physiochemical proper- ties from highly symmetric architecture. The properties of dendrimers can be controlled by varying the number of generations.
Solid polymeric nanoparticles		Nanoparticles are formed by biodegradable polymers in different forms such as hollow or porous structures. Solid polymeric particles show high stability and controllable release of loaded drugs.
Liposomes		The most commonly used nanoparticles in gene delivery for lung cancer research. The lipid bilayers of liposomes provide high biocompatibility and express efficient cellular uptake.
Solid lipid nanoparticles		Solid lipid nanoparticles (SLNs) is consisted of solid lipid core matrix that are enclosed and stabilized by a lipid monolayer on surface. Solid lipid particles have the same high durability as polymeric nanoparticles, as well as the same str ong affinity for the cellular membrane as liposome s.

Metal-based nanoparticle systems



Multifunctional metal-based nanoparticle systems can be used in therapeutic and diagnostic applications. Metal- based nanoparticles are usually coated or conjugated with polymers and lipids (also encapsulated in micelles or liposomes) for gene delivery purpose.

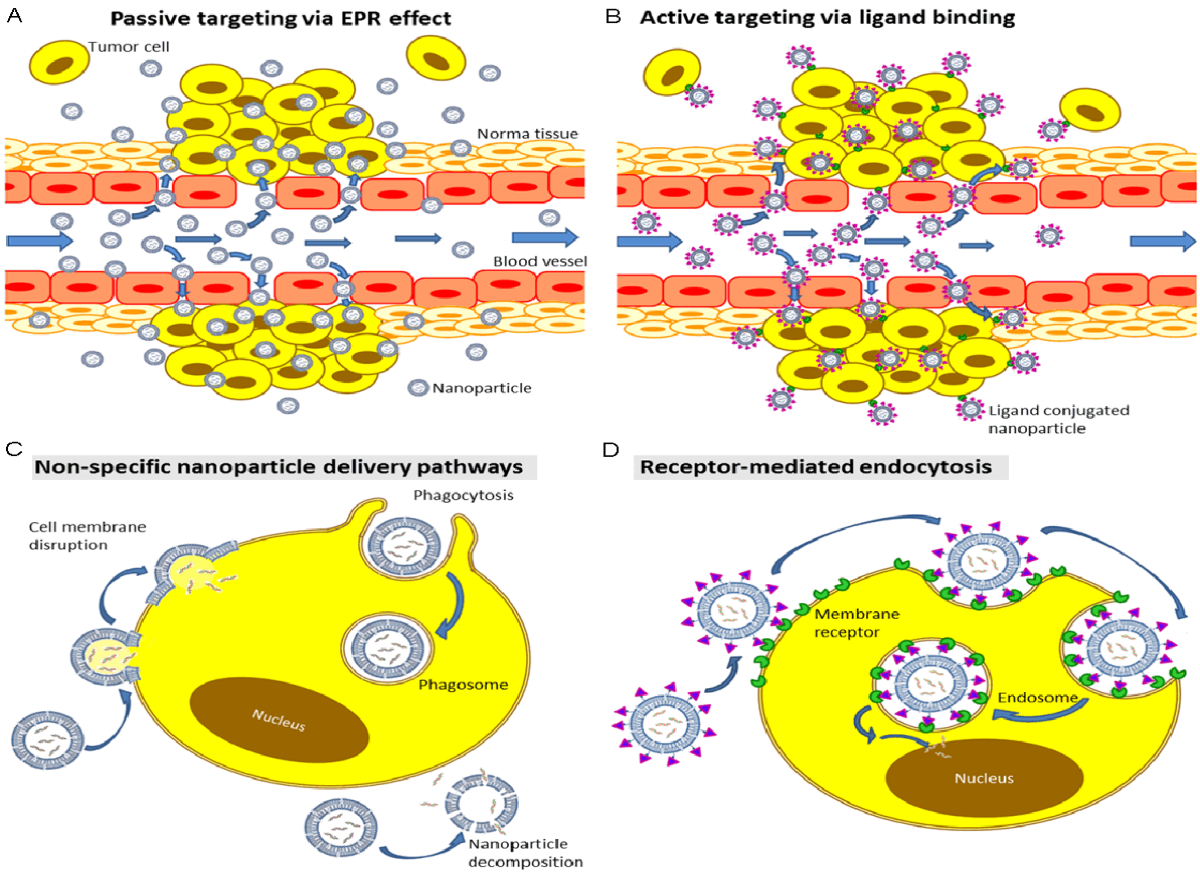


Figure 1. Mechanisms for nanoparticle targeting [6]

A. Nanoparticles use the EPR effect to perform nonspecific passive targeting in solid tumours by diffusing and aggregating throug h leaky vessels.
B. Nanoparticles that have been modified with targeting agents are used to actively target tumour cells that express certain recepto rs.
Nanoparticles are designed to target metastatic cancer cells specifically.
C. Nanoparticle fate in non-
specific gene delivery: phagocytosis, disintegration of nanoparticles outside of cells, and infusion of lipid or surfactant-based nanoparticles into cell membrane bilayers for drug release for lipid or surfactant-based nanoparticles.
D. Nanoparticles that have been modified with targeting ligands bind to the membrane receptor and cause endocytosis.
A higher percentage of gene molecules may end up in the nucleus.[6]

Micelles made up of polymers

Over the last few decades, polymers, one of the most versatile families of materials, have transformed our daily lives. Their increased promise in the realm of polymer and pharmaceutical sciences stems from their capacity to establish either spatial or temporal control of medication administration. To date, a variety of polymer-based nanocarriers have been used to treat posterior ocular disorders, including nanoparticles (NPs), liposomes, solid-lipid nanoparticles (SLNs), and dendrimers However, to overcome ocular barriers, the majority of these formulations are supplied by intracameral, intravitreal, and periocular injections, with multiple injections being necessary, which may cause side effects[35]. Polymeric micelles have recently emerged as a promising nanocarrier for overcoming these restrictions and delivering medicinal drugs.
Hydrophobic medicines, pDNA, siRNA, proteins, peptides, and photosensitizers are among the therapeutic substances delivered by poly (amino acid) copolymers.polymeric nanoparticlesand micelles are examined in further depth in this work. Nano capsules and nanospheres are two types of nanoparticles. Nanospheres are vesicles in which the drug core is surrounded by a polymeric film, whereasnano capsules are matrix particles in which the drug uniformly dispersed or dissolved in the polymer matrix. Micelles are made up of amphiphilic copolymers that self assembles into nanosized aggregates when the micellar concentration reaches a certain

level. The chitosan shell is then degraded by lysozymes,which is normally found inside cell lysosomes, that causing the micelles to break [8] [7]

Pluronic F127-xyloglucan nanoparticles

Naruphontjirakul and colleagues used 1-ethyl-3-(3-dimethylaminopropyl carbodiimide (EDC), N-hydroxy succinimide (NHS) as mediated cross-linking agents, and an anti-HER2 monoclonal antibody to encapsulate xyloglucan grafted with Pluronic F127 as a copolymer. In a nutshell, Pluronic and sodium dodecyl sulphate (SDS) formed micelles through self-assembly. Once within the target cells, nanoparticles can be taken up by the endocytosis process. The Xyloglucan shell is then degraded by lysozyme, which is normally found inside cell lysosomes, causing the micelles to break.[16][6]

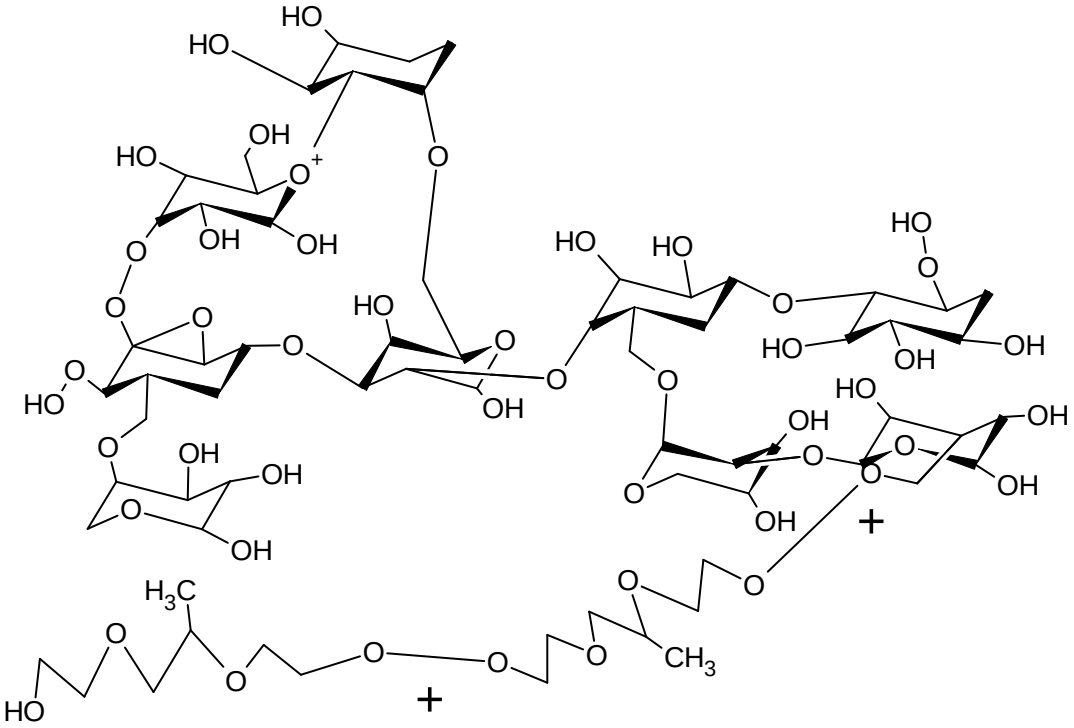


Figure:xyloglucan complex with poloxamer 407 and Pluronic p -68

CONCLUSIONS

The search for perfect lung cancer preventive solutions has long been a priority for scientists. In recent years, a large variety of xyloglucan have been created as drug delivery vehicles. The enormous benefits have been hailed as the most important elements of xyloglucan, and they are the cause for its widespread use in chemotherapy. In the drug delivery domain, chemical modification of xyloglucan or grafting xyloglucan with other ligands has shown promise. The materials that arise have improved drug loading capacity, sustained-release activity, and other unique features such as stimuli sensitivity, high mechanical strength, biocompatibility, and biodegradability. Several researchers believe that chemically modified xyloglucan is a viable controlled drug delivery strategy because it possesses sensitive swelling behaviour thesewith successful active targeting, you may expect more volume and a longer lifespan. A better understanding of the processes of these novel carriers would allow for more optimization and thus more intriguing potential for improved xyloglucan derivative administration to tumour tissues with adequate advances in medication delivery, gene transfer will be possible in the near future.

In lung tumours, xyloglucan will be thoroughly investigated for gene transfer, tissue engineering, medication delivery, and medicinal applications in lung cancer

CONFLICT OF INTEREST

There seems to be no conflict of interest for the author.

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