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Overview of drug delivery system by Nanocochleates

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Abstract

A unique drug delivery method called a nanocochleate involves trapping the target drug molecules inside a spiral-shaped solid-lipid bilayer that is part of a multilayered structure. Encapsulated molecules are protected from the hostile environs by the Nanocochleates structure. Additionally, because it has both kinds of drug molecules on its surface and in its structure, it has the ability to transport both hydrophilic and lipophilic drug molecules. There are numerous ways to make nanocochleates and a wide variety of active substances can be delivered using them for a variety of applications. Because nanocochleates have a lot fewer restrictions than other dosage forms and delivery systems, they are more extensively applicable and have greater potential as drug delivery systems.

Keywords: Nanocochleates, Phagocytosis, Liposomes, Phospholipids.

Introduction

The essence of nano cochleate drug delivery vehicles is the encapsulation of drugs in multilayer lipid crystalline matrices for potentially safe and effective drug delivery. Nanocochleates are cylindrical (cigar-like) microstructures composed of a series of lipid bilayers. Nanocochleate delivery vehicles are simply natural substances, generally stable phospholipid cationic precipitates composed of phosphatidylserine and calcium. They have a unique multi-layered structure composed of densely spirally coiled or stacked lipid bilayers with little or no internal water space.

This structure provides protection from degradation of the associated 'enucleating' molecule. This is a series of solid layers and components in which the entire nano cochleate is encapsulated inside the nano cochleate and remains intact even when the outer layer of the nano cochleate is exposed to harsh environmental conditions and enzymes. because it is configured. This is because nanocochleates contain both hydrophobic and hydrophilic surfaces suitable for encapsulating both hydrophobic and hydrophilic drugs.

1) For oral administration- Capsules, cachets, pills, tablets, lozenges, powders, granules, or a solution or a suspension an emulsion.

2) For topical or transdermal administration- Powders, sprays, ointment, pastes, creams, lotions, gels, solutions, patches, and inhalants.

3) For parenteral administration- Sterile isotonic aqueous or non-aqueous solutions, dispersions, suspensions or emulsions, or sterile powders which may be reconstituted into sterile injectable solutions or dispersions immediately prior to use.

Merits of nano-cochleate drug delivery system

1) Lipids in nanocochleates are more stable than liposomes because they are less susceptible to oxidation. The structure of liposomes is destroyed by freeze-drying, but the structure is retained after freeze-drying.

2) They show that biomolecules, especially those with hydrophobic moieties, are efficiently incorporated into cochleate lipid bilayers.

3) As the nanocochleates slowly unwind or dissociate, biomolecules can be slowly or timidly released in vivo.

4) They have a lipid bilayer matrix that acts as a carrier, composed of simple lipids found in animal and plant cell membranes, so the lipids are non-toxic, non-immunogenic, and non-inflammatory. 5) Easy and safe to make.

6) They improve the oral bioavailability of a wide range of compounds, including poorly water-soluble compounds and previously difficult-to-administer protein and peptide biopharmaceuticals. (eg ibuprofen for arthritis).

7) Reduces toxic gastric irritation and other side effects of encapsulated drugs.

8) They encapsulate or trap the drug in a crystalline matrix instead of chemically binding it. 9) They prevent the degradation of cochlear active substances and avoid exposure to adverse environmental conditions such as sunlight, oxygen, water, and temperature.

10) They can be prepared as defined formulations consisting of specific amounts and ratios of drugs or antigens.

Boundaries of nano-cochleate drug delivery

1) Requires specific storage conditions.

2) Manufacturing costs are very high.

3) Agglomeration may occur during storage.

Mechanism of nano cochleate drug delivery

1. After oral administration, nanocochleates are absorbed from the intestine.

2. The Nanocochleates traverse the digestive epithelium and deliver their cargo molecules into blood vessels.

3. Absorption of nanocochleates from the intestine by non-intravenous routes, they pass through relevant cells and enter the circulation.

4. After they reach circulation, they are delivered to target cells.

Work done on the nanocochleates drug delivery system

Laura Machín et.al. 2019

Bixa orellana L. (Bixaceae) and Dysphania ambrosioides (L.) Mosyakin & Clemants (Amaranthaceae) Essential Oils Formulated in Nanocochleates against Leishmania amazonensis.

The study identified leishmaniasis as a group of neglected tropical diseases caused by single-celled parasites of the genus Leishmania. The lack of an effective vaccine and the limitations of current treatment options make the search for effective treatments a real necessity. Certain plant essential oils (EO) show anti-leishmanial activity, especially from Bixa Orellana L. (EO-Bo) and Dysphania ambrosioides (L.) Mosyakin & Clemants (EO-Da). In this study, we estimated His EO-Bo and EO-Da (EO-Bo-NC and EO-Da-NC, respectively) formulated in nanocochleaetes against L. in vitro and in vivo. Amazonensis. EO-Bo-NC and EO-Da-NC did not enhance the in vitro inhibitory activity of EO, whereas EO-Bo-NC had a less cytotoxic effect. In animal models, both formulations (30 mg/kg/intralesional route/every 4 days/4 times) showed no mortality or body weight loss greater than 10%. In animal models (mice), EO-Bo-NC contributed to infection control compared with his EO-Bo treatment ($p < 0.05$), whereas mice treated with EO-Da-NC had larger lesions. ($p < 0, 05$). 0.05) is associated with patients treated with EO-Da. The increased in vivo activity observed for EO-Bo-NCs supports the ability of lipid-based nanoformulations such as nanocochleates to adequately deliver drugs for effective treatment of cutaneous leishmaniasis, particularly It suggests that it should be evaluated for its ability to deliver hydrophobic substances.

In conclusion, to understand the moderate effects after EO-Da-NC treatment, further studies need to be carried out, focusing on investigating interactions that may occur as a result of EO-Da encapsulation. be. Nevertheless, the present study showed that nanoencapsulation of oily active ingredients such as EO-Bo can contribute to better control of leishmaniasis. These optimistic findings may therefore represent a new starting point for the development of alternative treatments for CL.

K. MULRAJANI et.al., 2023

Nanocochleates and Drug-Phospholipid Complex: Novel Approaches for Phospholipid Based Oral Delivery of Anti-Cancer Agents.

In this study, we investigated that phospholipids were designed to address various challenges that limit the therapeutic potential of conventional drug delivery systems. Phospholipids are becoming more and more important as formulation additives. This review describes the basic properties and usefulness of phospholipids (i.e., nanocochleates and drug-phospholipid complexes) in oral delivery systems to solve problems related to the solubility and permeability of anticancer drugs. It is intended to summarize gender. The first section of the review provides insight into nano cochleaetes, cylindrical cigar-like structures capable of delivering both hydrophobic and hydrophilic drugs. The second area outlined the phospholipid complexes that form as a result of drug-phospholipid interactions. In summary, their review presents two of his techniques for enhancing the use of phospholipids in oral anticancer drug delivery, which overcome existing problems and contribute to the development of oral drug delivery systems. It can help open new paths and progress in

In recent decades, the number of cancer cases has increased, forcing researchers to discover new treatments to combat cancer. Among new therapeutics, nanosystems, especially phospholipid-based systems, are gaining popularity due to their unique advantages such as biocompatibility, small size, and high surface area. Phospholipid-based formulations have proven beneficial in improving the bioavailability of anticancer agents. Many anticancer drugs have low oral bioavailability. The promising results of these strategies offer the potential for further research to push the limits of such drug molecules. They also have the advantage of being inexpensive compared to other delivery systems, as these strategies are easy to formulate. These serve as platform technologies to enhance the clinical efficacy of potent but difficult-to-administer drugs. These strategies may be considered as alternatives to existing delivery systems with improved efficiency and bioavailability. However, given the increasing focus on oral drug delivery, these approaches may lead to a significant increase in commercial formulations in the near future.

Thanigaivel Shanmugam et.al., 2020

Aerosol Delivery of Paclitaxel-Containing Self-Assembled Nanocochleates for Treating Pulmonary Metastasis: An Approach Supporting Pulmonary Mechanics.

This study found that paclitaxel (PTX) is a potent anticancer drug and is clinically used as an infusion to treat lung metastasis of various cancers. Systemic injection of PTX is expected to treat pulmonary metastases of various cancers, but their combination causes many serious complications in the body. In this study, we demonstrate a non-invasive route to deliver her PTX into deep lung tissue via an inhalable phospholipid-based nano cochleate platform and explore its potential in treating lung metastasis from melanoma cancer. Proven. Nanocochleates have been previously investigated for the oral delivery of anticancer agents. Their application to aerosol-based administration has hitherto not been described in the literature. Their results show that PTX-carrying aerosol nanocochleates (PTX-CPT) have exceptional pulmonary surfactant activity characterized by high surface activity and when combined with comparable commercial taxol formulations, are effective in vitro. demonstrated to promote terminal airway patency in the Percentage of Cremophor EL. They used in vitro twin impinger analysis to investigate that PTX-CPT is likely deposited in stage II (alveolar regions of the lung), demonstrating the ability of CPT to reach deep alveolar regions. Did. Furthermore, when exposed to a human lung adenocarcinoma cell line (A549), PTX-CPT exhibits striking cytotoxicity mediated by increased cellular uptake through energy-dependent endocytosis. Aerosol-based administration of PTX-CPT in a mouse model of pulmonary metastatic melanoma (B16F10) resulted in a significant ($p<0.05$) inhibition of tumor growth when compared to intravenous taxol doses. Inhibition of tumor growth in aerosol-based PTX-CPT-treated animals was significantly ($p <0.05$) demonstrated by a decrease. Taken together, their results suggest that the newly developed CPT system can safely administer PTX in the form of an aerosol, which can be used as a vehicle for drug delivery and as a pulmonary surfactant in the treatment of pulmonary metastases. It serves a dual purpose as an agent. Their results indicated that aerosol-based PTX delivery using a nano cochleate platform is a potential non-invasive approach to treat lung metastasis from melanoma cancer in mice. PTX-based chemotherapy is already suitable for treating primary lung cancer. His aerosol delivery of PTX using novel nanostructures may offer a complementary therapeutic approach for lung metastases. Moreover, our study clearly demonstrated pulmonary surfactant-mimicking activity, as cochleate-based nanocarriers themselves help reduce respiratory complications and treatment side effects. Therefore, aerosol routes may provide a broad basis for such types of cancer chemotherapy, potentially leading to changes in the entire therapeutic paradigm. Importantly, inhalation-based therapy can achieve better clinical acceptance and higher patient compliance as a non-invasive procedure. It can also be performed under

supervision with minimal training and expertise, reducing frequent visits to tertiary care centers and reducing healthcare costs.

Sidney Gomes Azevedo et.al.,2022

Pulsatile Controlled Release and Stability Evaluation of Polymeric Particles Containing Piper nigrum Essential Oil and Preservatives.

A conscious effort is made to use environmentally friendly particles to encapsulate essential oils. Polymer particles based on gelatin and poly-ε-caprolactone (PCL) media were prepared to encapsulate Piper nigrum essential oil. Gas Chromatography (Flame Ionization Detection (GC/FID) and Mass Spectrometry (GC/MS)), Atomic Force Microscopy (AFM), Nanoparticle Tracking Analysis (NTA), Confocal Laser Scanning Microscopy (CLSM), Attenuated Total Reflectance - Fourier full transform infrared spectroscopy (ATR-FTIR) and ultraviolet-visible spectroscopy (UV-VIS) were used to characterize the colloidal system. The essential oil was mainly composed of β-caryophyllene (~35%). The stability of the encapsulated system was measured. It is evaluated by encapsulation efficiency (EE%), conductivity, turbidity, pH, and sensory properties (color and odor) after adding various preservatives. Phenoxyethanol/isothiazon-3-one (PNE system) mixtures independently showed improved stability for approximately 120 and 210 days in constant handling and storage testing. The developed polymer systems exhibited similarly controlled release at acidic, neutral, or basic pH, and release curves indicated a pulsatile release mechanism due to the complexation of the essential oil in the PCL matrix. Their results indicate that the developed system has a bias as an alternative stable product and control agent due to the remarkable bioactivity of the encapsulated essential oils.

This study successfully developed a controlled release system on polymer-carriers for encapsulating P. nigram essential oil. Formulation stability was ensured by the addition of preservatives and the original design of media, PCL, and gelatin. A pulsatile release mechanism was achieved by compounding a certain amount of essential oil within the PCL matrix. The active ingredients of medicinal plants are usually widely used by people. In the encapsulated form, such bioactive molecules are greatly amplified and appear directly in the release process, despite their released concentration. In terms of practical feasibility as a product, we calculated that his PNE system “and perhaps the PTI” is suitable for the future. It was a more stable system. Application as a repellent to combat human disease vectors (such as Aedes aegypti and Anopheles mosquito larvae and mosquitoes) by evaluating several parameters such as EE%, pH, electrical conductivity, turbidity, and sensory properties can now be proposed. for therapeutic purposes. Several reports have addressed the effectiveness of P. nigram essential oil in controlling a wide range of agricultural pests. As an alternative means of control, the system is less reusable due to its pulsatile release mechanism. As pharmaceuticals, encapsulated essential oils, when used internally or externally (at safe concentrations), offer great benefits in the treatment of various ailments and most importantly in patient empowerment and rehabilitation. Ensuring safe use requires further development of technical and scientific knowledge to ensure the mode of use and mechanism of action. Scientific research wants to contribute to this development, and that is certainly the purpose of this research.

Min Liu et.al., 2017

Chitosan functionalized nanocochleates for enhanced oral absorption of cyclosporine A.

In this study, we study nanocochleates functionalized with chitosan. Its residues pose a significant challenge in overcoming the low permeability of cyclosporin A and enhancing its oral absorption. In this study, we found a positively charged chitosan that can induce the rotation of anionic lipids into nanocochleates with an average size of 114.2 ± 0.8 nm without the need for calcium ions. These functional chitosan-derived nano coils enhanced the gastrointestinal absorption of cyclosporine A and increased oral bioavailability by up to 3-fold. Fluorescent labeling studies confirmed that absorption occurs primarily in the duodenum and jejunum. Transport studies showed that uptake of chitosan-induced nanocochleae by Caco-2 cells occurred through clathrin- and caveolae-mediated endocytosis, but not through macropinocytosis. In addition, three cellular tight junction proteins, ZO-1, F-actin, and claudin-4, were predominantly downregulated and chitobiose-induced nanocochleicles remodeled and opened tight junctions in intestinal epithelial cells, suggesting that it can enhance drug absorption. In conclusion, these novel bifunctional chitosan-induced nanocochleates tend to facilitate the oral administration of cyclosporine A.

In summary, they successfully developed a new nano cochleate formulation with added chitobiose. Chitobiose-induced nanocochleates cross the intestinal barrier and exhibit several solid-state properties that enhance oral absorption of CsA.

C. Bothiraja, et.al.,2018

Development of novel biofunctionalized chitosan decorated nanocochleates as a cancer-targeted drug delivery platform.

In this study, we found that a new group of biofunctionalized chitosans loaded with nano-cochlear-mediated drug delivery systems was developed. In this system, nanocochleates are uniquely combined with anticancer agents to provide controlled drug release, targeted delivery, and enhanced bioavailability with reduced toxicity. This system loaded nanocochleates (DOX-NC) with doxorubicin (DOX) via calcium ion swelling of negatively charged dimyristoyl phosphatidylcholine (DMPC) phospholipids and cholesterol-containing vesicles. It was then further developed by encapsulating DOX-NC with folic acid. Acid-conjugated chitosan (FA-CHIDOX-NC). The release of DOX showed a strong pH dependence, suggesting a hydrogen-bonding interaction between the nanocochleates and DOX. Formulated FA-CHI-DOX-NC showed higher anticancer activity in vitro in MCF-7 human breast cancer cells overexpressing folic acid. The targeting effect of FA-CHI-DOX-NC was also demonstrated. The drug concentration required to inhibit cell proliferation (GI50) by 50% over time was 9.1 mg/mL for DOX and 31.68% inhibition for DOX-NC (6.2 mg/mL). Next, the GI50 for FA-CHI-DOX-NC was 4.4 mg/mL. H. An increase of 51.64 was observed compared to the DOX solution. Furthermore, the bioavailability of DOX from FA-CHIDOX-NC was increased four-fold compared to the DOX solution, resulting in longer circulation times, slower plasma clearance, and no evidence of histotoxicity. The proposed strategy is beneficial in terms of targeted drug delivery and has a high potential to address current drug delivery challenges. The new conditioned medium thus extends new formulations combining the individual properties of biodegradable materials, chitosan and nanocochlea to biomedical applications. They developed and demonstrated novel nanocochleate-based drug carriers that exhibited properties such as controlled release, targeted delivery, and improved bioavailability with reduced systemic toxicity. Drug release was pH dependent and the vehicle system was found to have higher drug release at pH 5.3 than at pH 7.4. This is probably due to the reduced interactions between DOX and drug carriers. This pH-sensitive behavior makes this system a promising candidate for controlled and targeted drug delivery. The drug release of FA-CHI-DOX-NC was found to be more promising compared with DOX-NC. This is likely due to the presence of polymeric CHI chains that are susceptible to degradation and subsequent diffusion of the drug to the target site, and hydrogen bonding interactions between DOX and the nanocochlea. In addition, CHI decomposes rapidly in acidic media, leading to the breaking of hydrogen bonds. Furthermore, FACHI-DOX-NC showed a positive targeting effect on human breast MCF-7 cells overexpressing folic acid, resulting in a 4-fold increase in bioavailability in the peritoneal cavity compared with DOX solution and in the heart. Reduces toxicity. This also enables dose reduction. Reduce costs and improve patient compliance. The distribution of FA-CHI-DOX-NCs in vivo is thought to be due to overexpression of folate receptors on cancer cells, making this novel approach useful for the development of nanopharmaceuticals, including cancer therapeutics. influence. It can have an obvious impact. Evaluation of histotoxicity of DOX and FA-CHI-DOX-NC (folate-chitosan-loaded DOX-loaded nanocochleae) in mice. Prior to histopathological examination of tissue sections of heart, liver, kidney and spleen, mice were sacrificed and stained with H and E stains. 40x magnification. Artificial Cells, Nanomedicine, and Biotechnology the S459 Nanocarrier System offers practical applications in biomedical applications.

Beatriz Tamargo et.al., 2017

In Vitro and In Vivo Evaluation of Essential Oil from Artemisia absinthium L. Formulated in Nanocochleates against Cutaneous Leishmaniasis.

This study provides an in vitro and in vivo evaluation of mugwort essential oil formulated in nanocochlea against cutaneous leishmaniasis. They found that leishmaniasis is a zoonotic disease caused by a protozoan parasite of the genus Leishmania. There are currently no effective vaccines available, and available treatments are far from ideal. In particular, improved new therapeutic strategies to combat infections caused by Leishmania amazonensis would be desirable. Various herbal products, such as Artemisia absinthium L. (EO-Aa) and Asteraceae essential oil (EO), have shown antiishmanian activity. In the present study, her EO-Aa formulated in nanocochleates (EO-Aa-NC) was tested in vitro against intracellular amastigotes of L. amazonensis and uninfected macrophages of BALB/c mice. bottom. In addition, EO-Aa-NC was evaluated in vivo against experimental cutaneous leishmaniasis, calculating body weight, lesion progression, and parasite burden. result:

EO-Aa-NC showed IC50 values of 21.5±2.5 μg/ml and 27.7±5.6 μg/ml against intracellular L. amazonensis amastigotes and uninfected peritoneal macrophages, respectively. In animal models, EO-Aa-NC (30 mg/kg/intralesional route/4 times every 4 days) does not cause more than 10% mortality or weight loss. At the same time, EO-Aa-NC inhibited infection by approximately 50% in the mouse model, which was statistically superior to reference drug administration ($p<0>0.05$). Aggregation of EO-Aa resulted in a stable, well-tolerated, and potent anti-Tylmania formulation with increased activity compared to the administration of free EO-Aa, facilitating systemic administration of EO. This new formulation shows promising potential for future research targeting new therapeutic strategies for leishmaniasis. In this study, EO-Aa has collected over 15 years ago and maintained under standard conditions with the aim of preserving specific physicochemical and biological properties of the oil. Therefore, the samples just shown above were used in this formulation. However, in

tropical countries where leishmaniasis is endemic, high temperatures and severe economic problems can make it very difficult to maintain standard storage conditions, as blackouts and low temperatures cannot be accommodated. is higher. Therefore, it is highly desirable to find new alternatives for arming products and maintaining their physical stability and activity. Therefore, in this study, we enucleate EO from A. Absinthium provides a stable, well-tolerated, and potent anti-leishmanial formulation that facilitates systemic administration of EO. This study demonstrates the in vivo activity of nano cochleate formulations when administered intralesional and may potentially be studied as an adjunctive treatment option for leishmaniasis and as a delivery system for EO, and free cochleate the activity of this formulation is increased compared to the administration of the formulation. Form EO.

Diploma:

Nanocochleates show great potential for oral and systemic delivery of a wide range of molecules with important therapeutic activity, including drugs, genes, and vaccine antigens. Encocration helps improve formulation quality by extending shelf life, increasing stability, increasing bioavailability, reducing dosage and toxicity, and ultimately increasing final product potency. In the future, this technology could be used as an alternative method for delivering biological or therapeutic entities. The rapid increase in patent filings and publications on nanocochleates indicates a growing industry and academic interest in the field of drug delivery. Although much research has been done to develop nano cochleate dosage forms, it is surprising that this area of nanotechnology has been under-researched. Further research is needed to make more nano-cochleate dosage forms available for oral use.

knowledge:

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Conflict of interest:

The authors have no conflict of interest.

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