INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Nanocochleates: A Novel Platform in Delivery Therapeutic Cargo

Kesharwani Anubhav*, Pandey Prince, Ram Vishal, Pratiksha Sonawane

Siddhi's Institute of Pharmacy, Nandgaon, Thane.

ARTICLE INFO

Published: 20 May 2025
Keywords:
Lipid, Liposome, Nanocochleates, Targeted Drug Delivery
DOI:
10.5281/zenodo.15471652

ABSTRACT

This review article explores the exciting potential of nanocochleates as a novel drug delivery platform. Lipid-based drug delivery (LDDs) systems attract increasing interest in the pharmaceutical industry due to their advantages in solubility and bioavailability of poorly water-soluble drugs. Nanocochleates are the lipid based multi-layered spiral structure that resemble a small shell-like structure which is achieved through the interaction of negatively charged lipid and positively charged calcium ions which causes lipid bilayer to roll into cochlear-like structure. Due to these structures nanocochleates can encapsulate drugs in their hydrophobic structure while keeping them in a stable protected form. The structure of nanocochleates is highly stable, making them protected from harsh environmental conditions such as pH and enzymatic degradation. The nanocochleates can deliver a wide range of therapeutic agents inc. small molecules peptides, proteins and nucleic acid. Due to their unique property nanocochleates are being explored in various medical applications inc. Cancer therapy, vaccine delivery, anti-inflammatory treatment and gene therapy. Nanocochleates represents a promising platform in the field of nanomedicine and drug delivery, providing innovative solutions for effective and targeted therapy. This comprehensive overview aims to provide a thorough understanding of the current landscape and future prospects of nanocochleates in the field of drug delivery.

INTRODUCTION

Nanocochleates are the innovative drug delivery system that are composed of lipid bilayer that forms a stable cylindrical cigar like structure formed by interaction of negatively charged liposomes with cationic salts, usually calcium-ions. Nanocochleates are nano-sized, cylindrical, multilamellar vesicles, resembling tiny, rolled-up scrolls. They are formed by the self-assembly of negatively charged phospholipids (like phosphatidylglycerol phosphatidylserine and /or phosphatidylcholine) with positively charged divalent cations (like calcium or magnesium). This assembly process, known as the "cochleate phase

***Corresponding Author:** Kesharwani Anubhav
Address: *Siddhi's Institute of Pharmacy, Nandgaon, Thane.*
Email ✉: kesherwanianubhav4@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

transition", results in the formation of a unique, stable structure with an internal lumen that can encapsulate various therapeutic agents, including small molecule drugs, proteins, and nucleic acids. Phospholipid based drug delivery may overcome the problem of low bioavailability but the application and development is limited because of the enzymatic and chemical degradation by intestinal pH. The lipid bilayer is susceptible to attack by harsh environmental conditions like enzyme degradation, temperature and pH. Hence to maximise the therapeutic potential of phospholipid by novel strategic formulation ie. the Nanocochleates. Cochleates were first discovered in 1975 by Dr. Dimitrious Papahadjoupoullos and since evolved significantly and later in 1999 nanocochleates were introduced to develop smaller and consistent structure. Nanocochleates are the innovative drug delivery system that are composed of lipid bilayer that forms a stable cylindrical cigar like structure formed by interaction of negatively charged liposomes with cationic salts,usually calcium ions.The fusion of bilayer produces transformation to form a large sheets that coil to form a cochleates having cigar like structures. Cochleates have a unique multilayered structure consisting of solid, lipid bilayer sheets rolled up in a spiral or in stacked sheets, with little or no internal aqueous space. have unique multilayered structure consisting of solid, lipid bilayer sheet rolled up in a spiral or in stacked sheets, with little or no internal aqueous space.Therapeutic agents that are encapsulated within the interior of the nanocochleate structure which remain intact, even though the outer layers of the nanocochleate may expose to harsh environmental conditions or enzymes. They can encapsulate various types of therapeutic agent, including hydrophilic, hydrophobic and amphiphilic molecules.

Nanocochleates are made up of purified soy based phospholipid that may be phosphatidylserine (PS), phosphatidylglycerol (PG), phosphatidylinositol (PI), dioleoyl phosphatidylserine (DOPS), dioleoyl phosphatidic acid (DOPC), and/or mixture of one or more of these phospholipid. A multivalent cation, which can be Ca+2, or Zn+2 or Mg+2 and a drug which may be anticancer agent, immunosuppressant, NSAIDs, herbal product, antiviral agents, antimicrobial agent, nucleic acid, proteins , etc. Thus providing a potential carrier for a wide range of therapeutic agents. A study comparing purified soy PS (PSPS) to non-purified soy PS (NPSPS) concluded that PS should be present in an amount of at least 75% of the total lipid in order to allow the formation of cochleates. The other 25% phospholipids present can be selected either from the anionic group such as PA, PI, PG or phosphatidylcholine (PC).The preparation of nanocochleates typically involves a simple, aqueous-based process. A lipid solution containing the desired phospholipids and a divalent cation solution are mixed under controlled conditions. The mixture is then subjected to gentle agitation or sonication to facilitate the self-assembly of the cochleate structure. The resulting nanocochleates can be further characterised using techniques like dynamic light scattering (DLS) and transmission electron microscopy (TEM). The precise formulation of nanocochleates can be adjusted by varying the lipid composition, cation concentration, and processing conditions to achieve specific properties and functionalities. This versatility in formulation allows for tailoring nanocochleates for specific drug delivery applications.

Composition:

Nanocochleates are composed primarily of phospholipids and divalent cations. The phospholipids, typically anionic in nature, arrange

themselves into bilayers, forming the core of the nanocochleate structure. The divalent cations, such as calcium or magnesium ions, interact with the negatively charged phospholipids, stabilising the structure and facilitating the formation of the helical shape. The precise composition and ratio of phospholipids and cations can be manipulated to adjust the properties of nanocochleates, such as their size, stability, and drug loading capacity.

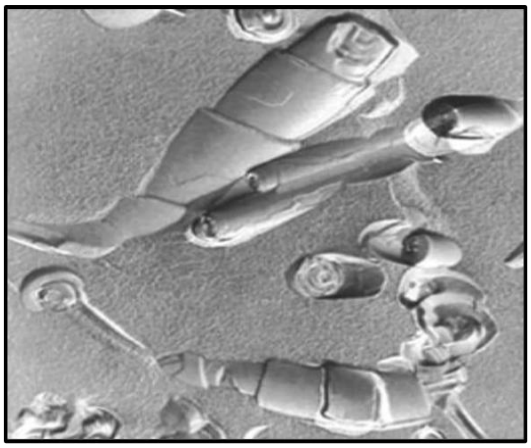
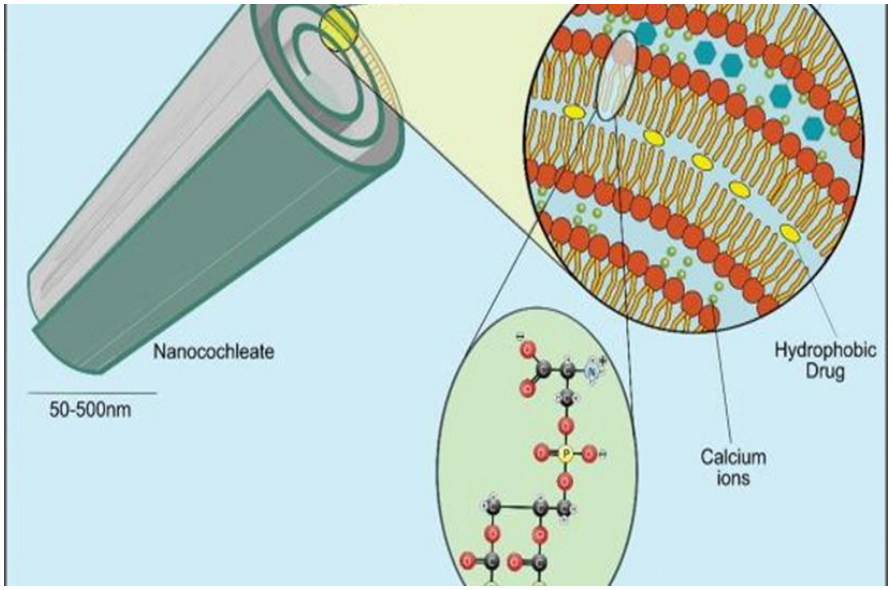


Table 1 The Various Constituents of a Cochleate

Cations	Lipids	Drug
Zn^{2+}, Ca^{2+}, Mg^{2+}, Ba^{2+}	Phosphatidylserine	Protein
	Phosphatidic acid	Peptide
	Phosphatidylinositol	Polynucleotide
	Phosphatidylglycerol	Antiviral agent
	Phosphatidylcholine	Anaesthetic agent
	Phosphatidylethanolamine	Anticancer agent
	Phosphatidylglycerol	Immunosuppressant
	Dioleoyl phosphatidic acid	Anti-inflammatory agent
	Distearoyl phosphatidyl serine	Tranquilizer
	Dipalmitoyl phosphatidylglycerol	Nutritional supplement
		Vitamins or vasodilator

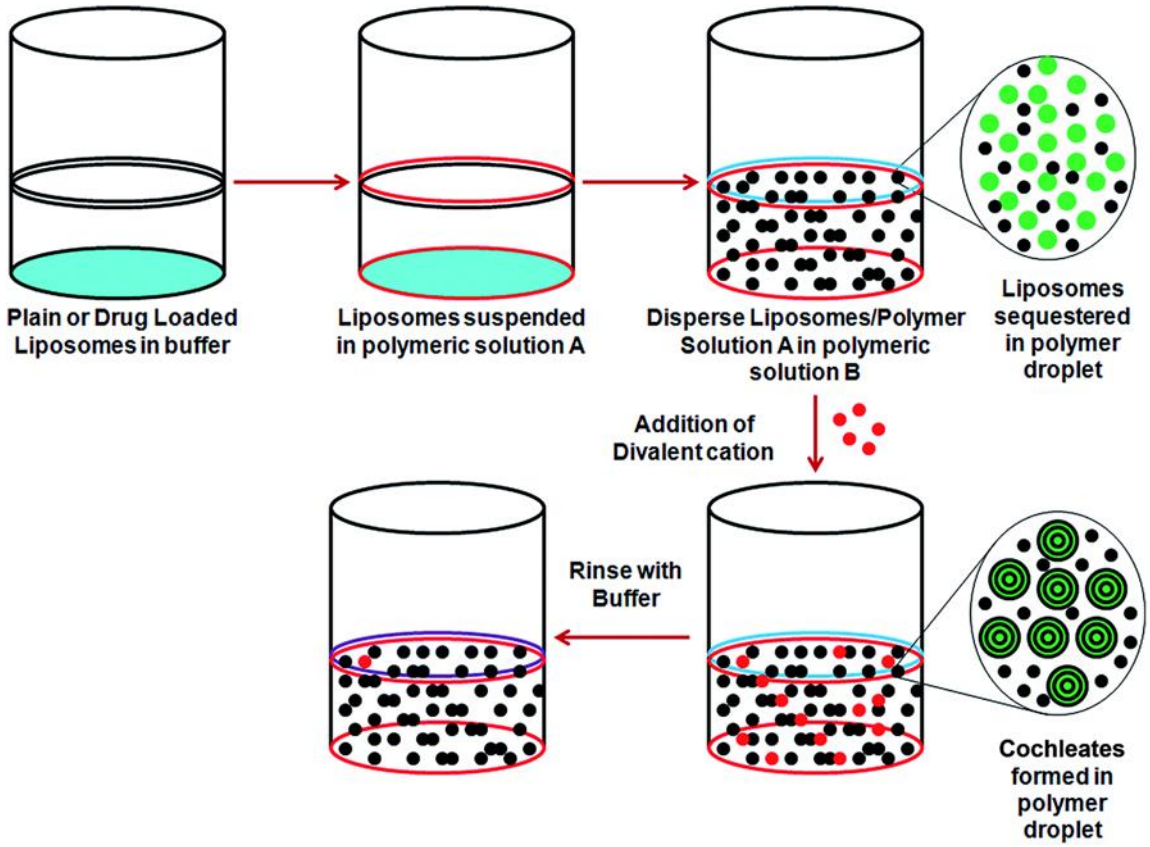


H. Kaya-Celiker and K. Mallikarjunan, Food Eng. Rev., 2012, 2, 114 CrossRef.

Preparation Of Cochleates

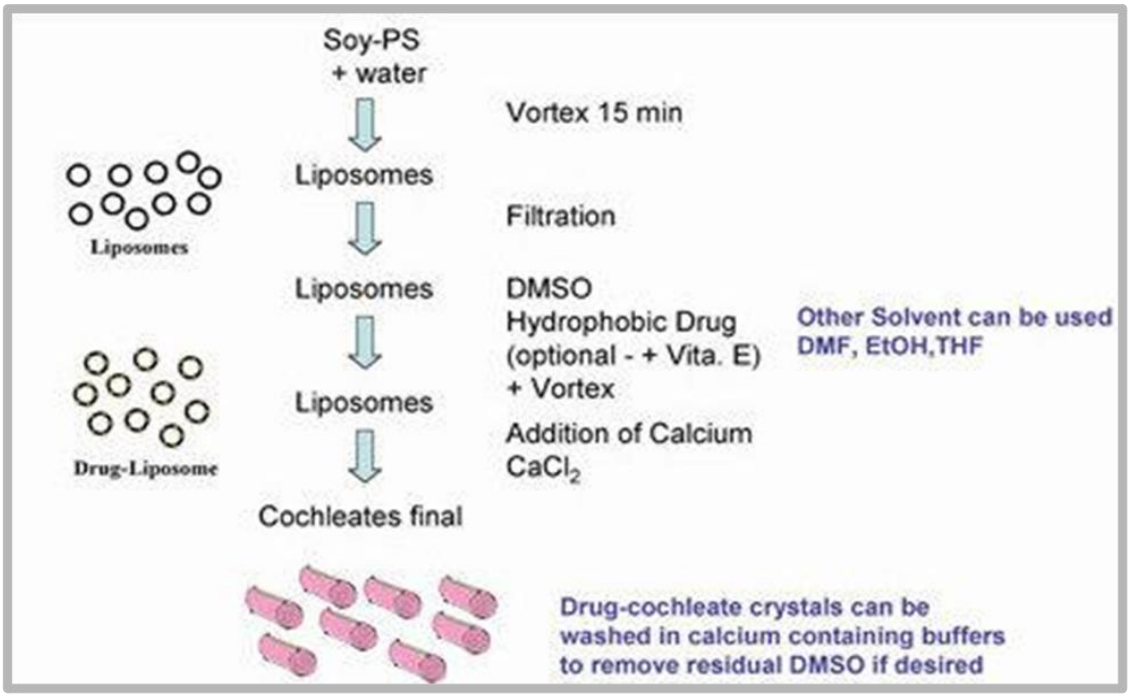
- Hydrogel Method.
- Trapping method.
- Liposome before cochleates dialysis method.
- Direct calcium dialysis method.
- Binary aqueous- aqueous emulsion system.
- Hydrogel Method

In this method initially the small unilamellar drug loaded liposomes were prepared, which were added to polymer A (phosphatidylserine, dextran/ polyethylene glycol, etc.). This dispersion phase was then added to another polymer B (polyvinylpyrrolidone/ Polyvinyl alcohol/ Ficoll/ polyvinyl methyl ether, etc.) There is formation of aqueous two phase system ,due to the immiscibility of polymer A and polymer B There after, an cation salt solution was added to the polymer two-phase system and lead to formation of cross linking of polymer, such that the cation diffuses into the second polymer ,and then particles composed of liposome /polymer.



Trapping Method

In trapping method , phosphatidylserine liposome was formed by vortexing , and adding solution of calcium chloride ($Cacl^2$) drop by drop and then by addition of water to phospholipid powder or by adding water to phospholipid film and The resulting cochleates were washed with calcium buffer to remove residual solutes.



- **Liposome Before Cochleates Dialysis Method**

In this method mixture of lipid and detergent are used as the starting material and the removal of detergent is done by double dialysis. The mixture is dialysed initially by buffer and followed by calcium chloride solution which leads to formation of cochleates. This method is suitable for encapsulation of hydrophobic material or drug containing hydrophobic region such as membrane proteins.

- **Direct Calcium Dialysis Method**

This method does not involve the intermediate liposome formation and the cochleates are going to be in size. The mixture of lipid and detergent is directly dialysed against calcium chloride solution. In this method needle shaped large dimensional structures are formed due to the competition between the removal of detergent from the detergent/lipid/drug micelles and the condensation bi-layer by calcium. Mixture of phosphatidylserine and cholesterol (9:1 wt ratio) in extraction buffer & non-ionic detergent is mixed with a preselected concentration of polynucleotide and the solution is vortex for 5min. The clear, colourless solution which resulted is dialysed at room temperature against three changes of buffer. The final dialysis routinely used is 6mM Ca2+. The ratio of dialysed to buffer for each change is minimum of 1:100. The resulting white calcium-phospholipids precipitates have been termed direct calcium cochleates.

Advantages of Nanocochleate-Based Delivery

Enhanced Drug Efficacy: Nanocochleates can significantly enhance drug efficacy by delivering drugs directly to the target site, minimising systemic exposure and reducing off-target effects. The targeted delivery of therapeutic agents can result in higher drug concentrations at the intended site of action, maximising therapeutic impact and minimising side effects.

Enhanced Drug Efficacy: Nanocochleates can significantly enhance drug efficacy by delivering drugs directly to the target site, minimising systemic exposure and reducing off-target effects. The targeted delivery of therapeutic agents can result in higher drug concentrations at the intended site of action, maximising therapeutic impact and minimising side effects.

Improved Drug Stability: The multilamellar structure of nanocochleates provides a protective environment for encapsulated drugs, shielding them from degradation and prolonging their stability. This enhanced stability translates to longer circulation times and improved bioavailability of the drug, ensuring sustained therapeutic effects.

Controlled Drug Release: Nanocochleates can be designed for controlled release of drugs, delivering the therapeutic agent at a specific rate and time. This controlled release mechanism allows for sustained therapeutic effects and reduces the frequency of drug administration. The release rate can be adjusted by manipulating the phospholipid composition, cation concentration, and external stimuli, such as pH or temperature.

Reduced Toxicity: Nanocochleates can minimise the toxicity of drugs by reducing their systemic exposure and targeting delivery to the desired cells or tissues. This targeted delivery strategy minimises off-target effects, reducing the risk of adverse reactions and enhancing patient safety.

Application Of Nanocochleates

- Nanocochleates have been used to deliver proteins, peptides and DNA For vaccine and gene therapy application

- Nanocochleates have been used to deliver the anticancer PACLITAXEL drug for treatment of cancer
- Nanocochleates showed potential to deliver A mphotericinB,a potential antifungal agent, ora lly and parentally having a good safety profile with reduced cost
  of treatment. The prepared cochleates of amp hotericin B showed improved stability and eff icacy at low doses. They showed improved pa tient compliance.
- Nanocochleates have the advantage of reducing toxicity and improving bactericidal activity.
- Nanocochleates can encapsulate and protect the therapeutic cargo and hence improving patient compliance

REFERENCES

1. Sangita Fulchand Pawar, Sunil S. Bothara, Paresh R. Mahaparale and Vikram L. Musale. Nanocochleate – An Important Drug Delivery System Offering Unique Features. World Journal of Pharmaceutical Research SJIF Impact Factor 8.084 Volume 9, Issue 9, 621-637. Review Article ISSN 2277– 7105. DOI: 10.20959/wjpr20209-18413. 2020.
2. Meena Tilawat, Smita Bonde. Nanocochleates: A potential drug delivery system. Journal of Molecular Liquids 334 (2021) 116115.
3. Suchita B. Khairnar and R.B. Saudagar. Nanococleates: An Overview. International Journal of Pharmaceutical and Clinical Research. Review Article. ISSN 2395-3411.
4. Rohit Rajendra Bhosale, Prasanna Prasad Ghodake, Abhyangshree Nandkumar Mane, Amruta Avinash Ghadge. Nanocochleates: A novel carrier for drug transfer. Journal of Scientific and Innovative Research 2013; 2 (5): 964-969.
5. Dharmesh Gol, Viral Shah. Nanocochleates: A Novel Approach For Drug Delivery. World Journal of Pharmaceutical research Volume 3, Issue 2, 1920-1944. ISSN 2277 – 7105.Feb 2014. www.ijcrt.org © 2024 IJCRT | Volume 12, Issue 1 January 2024 | ISSN: 2320-2882 IJCRT2401206 International Journal of Creative Research Thoughts (IJCRT) www.ijcrt.org a659
6. V. Yadav, B. Parab and S. Shidhaye . Nanocochleate: A Novel Approach For Delivery Of Biological Molecules. Yadav et al., IJPSR, 2021; Vol. 12(7): 3581-3592. E-ISSN: 0975-8232; P-ISSN: 2320-5148 International Journal of Pharmaceutical Sciences and Research 3581 IJPSR (2021), Volume 12, Issue
7. Raut Pooja Mahendra. World Journal of Pharmaceutical and Life Sciences WJPLS. ISSN 2454-2229. 2022, Vol. 8, Issue 9, 43-49.
8. Suraj R. Wasankar, Kshitij V. Makeshwar, Abhishek D. Deshmukh, Rahul M. Burghate. Nanocochleate: A Review. Research J. Pharma. Dosage Forms and Tech. 2012; 4(3): 153-159.
9. Snehal & Manjusha (2021). "Nanocochleate: A Review" World Journal of Pharmaceutical Sciences, 9(11), pp. 87–94. This review discusses the multilayered structure of nanocochleates and their applications in drug delivery.
10. Ramasamy et al. (2009). "Nanocochleate – A New Drug Delivery System" FABAD Journal of Pharmaceutical Sciences, 34, pp. 91–101.
11. Panwar et al. (2011). "Nanocochleate: As Drug Delivery Vehicle" International Journal of Pharmacy and Biological Sciences, 1(1), pp. 31–38.
12. Priyanka & Batra (2023). "Overview of Drug Delivery System by Nanocochleates"International Journal of

Emerging Technologies and Innovative Research, 10(10), pp. f668–f675.

13. Godge et al. (2024). "An Overview of Nanocochleates for Improving Oral Absorption Using a Phospholipid-Based Drug Delivery System" Biomedical Engineering and Biosciences Advances, pp. 1–6.

HOW TO CITE: Kesharwani Anubhav*, Pandey Prince, Ram Vishal, Pratiksha Sonawane, Nanocochleates: A Novel Platform in Delivery Therapeutic Cargo, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 3350-3357. https://doi.org/10.5281/zenodo.15471652