

CALL FOR EXPRESSION OF INTEREST (EOI) FOR AUTOCLAVABLE NANOVESICULAR COMPOSITION AND PHARMACEUTICAL NANOELASTIC VESICULAR SYSTEMS

PATENT GRANTED: 341360; 274013; 320207

PRESENT STATUS: TRL 4

Purpose

An autoclavable nanovesicular (NV) composition and pharmaceutical nanoelastic vesicular systems for effective delivery of an active ingredient by different routes particularly, ocular and parenteral delivery.

Specifications

- Nanovesicular (NV) composition comprising a first aqueous phase and a second organic phase wherein said aqueous phase comprises water soluble polymers while said organic phase comprises suitable surfactants, and active ingredient is present in said aqueous phase or organic phase based on its solubility and entrapment tendency.
- The NV system is a **simple and optimized (DoE) vesicular system, which is novel both in terms of composition and its method of preparation.**
- NV system is different from conventional liposomal systems. Latter are phospholipid based which although a versatile component is prone to oxidation and hydrolysis. High cost of components (cholesterol and phospholipid), drug leakiness and batch-to-batch variation are some limitations of liposomes. Furthermore, the methods of preparation like thin film evaporation, reverse phase evaporation, ethanol/ ether injection and/ or use of homogenisation or ultrasound technology, are more suited to laboratory scale production and less amenable to scale up.
- Further, pharmaceutical nanoelastic vesicular systems comprising fluconazole or its pharmaceutically acceptable salts, solvates, enantiomers, polymorphs or mixtures thereof, processes for preparing the same and methods of use and treatment.
- The nanoelastic vesicular systems are prepared using non-ionic surfactants such as but not limited to span 40, span 60 and span 80 and edge activators such as but not limited to sodium taurocholate, sodium cholate, sodium deoxycholate, tween 80 and the like in ratios 85:15 or 80:20 or 75:25 or 70:30 or 50:50.

Highlights of the systems are:

- GRAS, low cost and stable components
- Simple and easy to scale up method of preparation
- Prolonged release upto 144 h (6 days)
- Autoclavable
- Three tier safety established: in vitro cytotoxicity (corneal and conjunctival cell lines), ex-vivo and in vivo toxicity in rabbits, as per OECD guidelines
- Nanovesicular (NV) composition: stable under refrigerated conditions for 6 months and at 37° C for 3 months – extended stability studies remain to be conducted
- Pharmaceutical nanoelastic vesicular systems: stable under refrigerated conditions for 2 and extended stability studies remain to be conducted.

Applications

- Has been explored to incorporate water soluble and insoluble actives viz. Bimatoprost, acetazolamide and capsaicin.
- A secondary vehicle like hydrogelling polymer or in situ gelling system can be incorporated directly into the NV aqueous dispersion to achieve implant like characters. Bimatoprost loaded (BMT) -NV-GEL (optimised by DoE) showed sustained release for > 240 h (10 days). BMT is an antiglaucoma medication.
- Single topical drop of BMT-NV-GEL reduced IOP for 7 days in glaucomatous rats – can be marketed as once a week drops
- Long acting single dose applications will reduce repeat exposure to BAK
- Vesicles can also be concentrated by centrifugation at ~ 2000 rpm and then incorporated into any other vehicle.
- NVs can withstand repeated freeze-thaw cycles and autoclaving
- Amenability to autoclaving making them a highly promising carrier system for parenteral drugs including anticancer and antimicrobial agents
- High permeation and capacity to reach viable skin layers & internal eye tissue.
- Suited to be developed as long-acting (once a week formulation) eye drops or implant (once in three months sub-conjunctival injection).
- Can be used for topical applications viz. dermal, nail, cosmetic, dental, oral cavity and vaginal delivery of hydrophilic and hydrophobic carriers.
- Can be used to improve permeation and controlled release for orally delivered actives for systemic application.
- Pharmaceutical nanoelastic vesicular systems: the system may be used for ocular or dermal application.

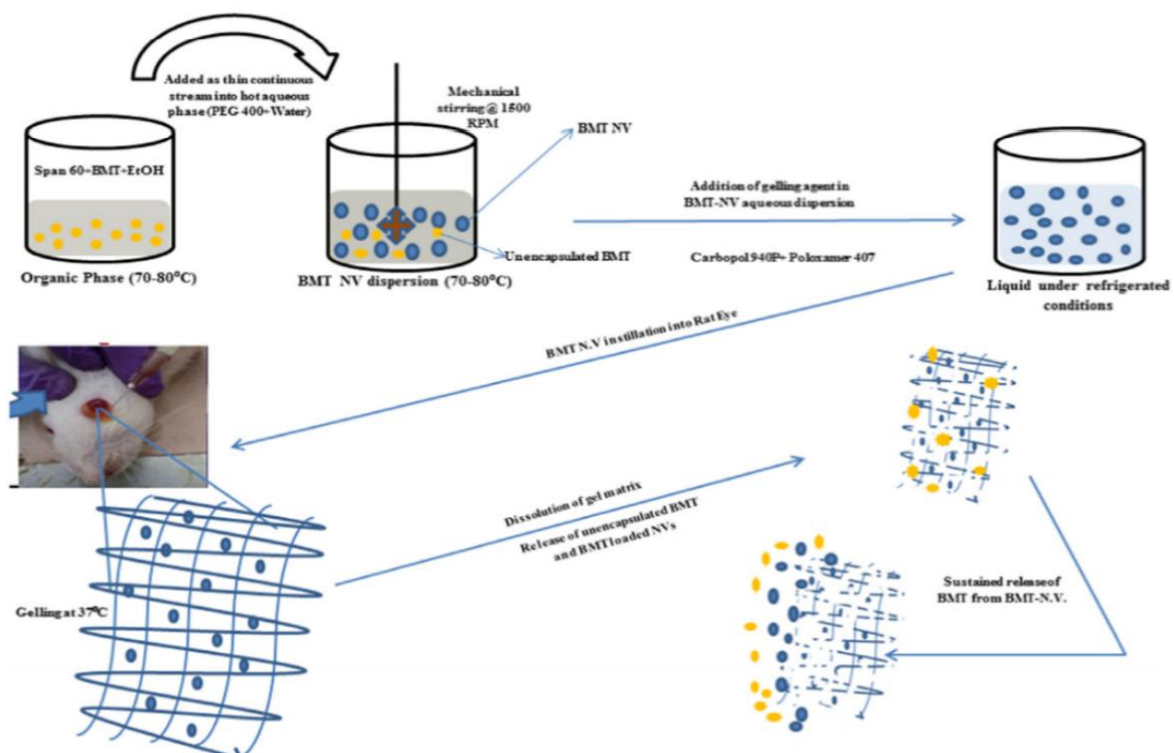
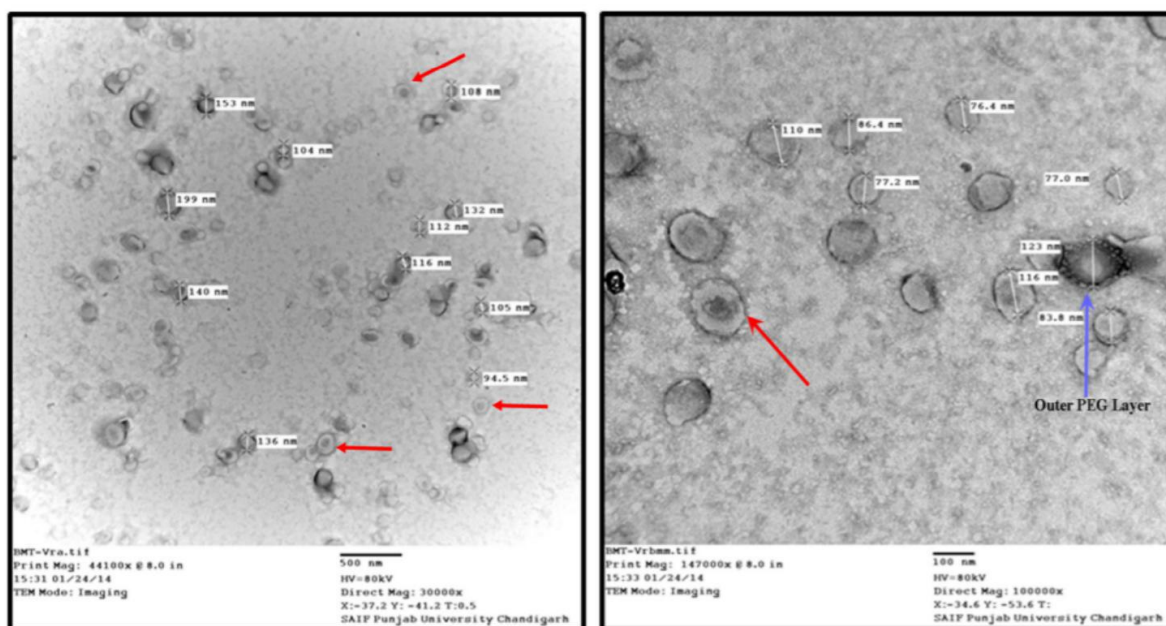


Fig1. Diagrammatic representation of BMT nanovesicular system fabrication, gelling on instillation into rat eye and drug release



(a)

(b)

Fig2. TEM micrographs of active loaded NVs at (a) 30000X, (b) 100,000X magnification. Red arrows indicate bilamellar NVs. (For interpretation of the references to colour in this figure legend, the reader is referred to web version of this article.)

Transfer of Technology

The Inventors of technology are planning for 'Transfer of Technology' (ToT) for commercialization and are in process to shortlist the manufacturers in different region of country for commercial use of composition and system within the country as well as globally, as per the following broad terms and conditions:

- The Transfer of Technology will be through a mutually acceptable Agreement document, to be signed by the inventors (i.e. Licensor) and a representative of the company (Licensee) authorized to sign on behalf of the company. Once the Agreement is signed, the inventors will share the relevant information regarding synthesis, characterization etc.
- The Inventors of the technology (Licensor) will grant to the Licensee a limited, non-exclusive, non-transferable, non-sub licensable, revocable license to the Technology, for the purpose of commercialization of the technology as quickly as possible.
- The Licensee is expected to commercialize composition in the market within 1 year of execution of the Agreement (i.e. Transfer of Technology) at a reasonable price. The technology and its components should be as per standard grade, and be compliant with the relevant national standards.
- Failure of adherence to this timeline, and documentation of monthly milestones will be a sufficient reason for unilateral cancellation of the Agreement by the Licensors.
- The Licensee is expected to make an offer (i.e. bid) of a one-time payment of **License fee** to the Licensor, not less than **10 Lakhs** for Nanovesicular (NV) composition and not less than **5 Lakhs** for Pharmaceutical nanoelastic vesicular systems.
- **Royalty @ of 5% of net sale price** is to be paid to the Licensors by the Licensee, after every 6 months, during tenure of the Agreement.
- Licensor will make efforts to support the Licensee during the process towards commercialization by helping licensee in scaling of formulation and product at pilot plant level through emails and in-person visits.

Additional information

Reputed companies, interested in bidding for the Transfer of Technology may seek additional details through any of the following means:

1. Email correspondence with the Inventors (email Id:agawri@pu.ac.in) citing in the Subject line: Transfer of Technology
2. Personal meeting with the Inventors at a mutually convenient date/time confirmed via email.

Invitation to Bid

Reputed companies should submit the following information in response to this invitation:

1. A brief description of the company and products/services of company.
2. Audited balance sheet of three immediate past preceding years', including profit and loss account and annual report.
3. Reference list of similar engineering supplies of fabrication and services during past 2-3 years
4. A notarized affidavit conforming that the company has not been banned or blacklisted at any time for supplies to government agencies
5. Bid/offer of License Fee and Royalty (minimum expectation already mentioned above).
6. Clear vision and roadmap towards commercialization, with timelines.
7. Scope of shortening the above-mentioned timelines.
8. Anticipated price of the product in the market

Interested companies are requested to apply with all the required documents through email with subject "Bid for ToT" to pu_tec@pu.ac.in latest by 30th September, 2022.



For further information please contact

Sr. Manager

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