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Review

Management of Glaucoma: Effective Drug Delivery via Niosomes

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Abstract:
Glaucoma is a term used for a group of diseases; associated with optic nerve damage which leads to loss of retinal ganglionic cells. Niosomes which are nano-sized, non-ionic surfactant vesicles, offer a superior drug delivery system for glaucoma by overcoming traditional eye drop limitations like rapid drainage and poor penetration, leading to sustained drug release, prolonged ocular residence, better patient compliance, and reduced side effects by encapsulating drugs like latanoprost or brimonidine within their bilayers, enhancing drug availability at the target site to effectively lower intraocular pressure (IOP) and prevent blindness.
Keywords: Niosomes, Glaucoma, novel drug delivery.

Introduction:

Glaucoma is one of the leading causes of irreversible blindness worldwide. According to the World Health Organization (WHO), millions of people are affected by glaucoma, and the prevalence is expected to increase due to aging populations. The disease primarily affects the optic nerve and is commonly associated with increased intraocular pressure resulting from impaired drainage of aqueous humor.

Topical eye drops are the most commonly used dosage forms for glaucoma treatment. However, these formulations suffer from poor ocular bioavailability (less than 5%) due to physiological barriers such as blinking, tear turnover, nasolacrimal drainage, and corneal epithelium. Frequent dosing is required, which leads to poor patient compliance and increased risk of side effects. To address these challenges, advanced drug delivery systems like niosomes have gained attention. Niosomes are vesicular systems composed of non-ionic surfactants and cholesterol, capable of encapsulating both hydrophilic and lipophilic drugs. Incorporation of niosomes into a gel base further enhances ocular residence time and provides controlled drug release, making niosomal gel a promising approach for glaucoma management.

Glaucoma: Types and Classification

Glaucoma is classified into several types based on anatomical and pathological differences:

1. Primary Open-Angle Glaucoma (POAG)

This is the most common form of glaucoma. It occurs due to gradual blockage of the trabecular meshwork, leading to slow elevation of intraocular pressure. It is usually asymptomatic in early stages and progresses silently.

2. Angle-Closure Glaucoma

This type occurs when the drainage angle between the iris and cornea becomes blocked, resulting in a sudden rise in intraocular pressure. It is a medical emergency and may present with severe eye pain, blurred vision, headache, and nausea.

3. Normal-Tension Glaucoma

In this condition, optic nerve damage occurs even when intraocular pressure remains within normal range. Reduced blood flow to the optic nerve is considered a major contributing factor.

4. Secondary Glaucoma

Secondary glaucoma develops as a result of other conditions such as eye injury, inflammation, diabetes, cataract surgery, or prolonged steroid use.

5. Congenital Glaucoma

This rare form is present at birth and results from abnormal development of the eye's drainage system.

Table 1: Risk Factors Implicated in Disease [(4)]

Development: Risk factors	Attributes

Elevated Intraocular pressure7,13,20	Greater than 25 mm Hg
Cup-to-disk ratio15,20	Greater than 0.3
Age6-8	Over 40, higher incidence of those over 70
Familial history of glaucoma7,13,16	Genetic predisposition
Heritage6-8,16-18	African; Asians; Hispanic
Ocular diseases7,13	Eye trauma, thinning in central cornea, myopia or hyperopia
Metabolic diseases7,13	Those suffering from diabetes, migraines, high blood pressure, poor circulation

Table 2: Route of drug administration

Routes of drug administration	Examples of drugs
Intravenous Route	Doxorubicin, methotrexate, tretinoin, Vincristine
Peroral route	DNA vaccines, proteins, peptides, insulin
Ocular route	Timolo maleate, cyclopentolate
Nasal route	Sumatriptan, influenza viral vaccine
Inhalation	All transretinoic acid
Transdermal Route	Fluriprofen, piroxicam, ketorolac
Vaginal	Insulin
Topical	Clobetasol propionate, Rofecoxib, Minoxidil, Propyl thiouracil

Causes and Risk Factors of Glaucoma

The primary cause of glaucoma is increased intraocular pressure due to imbalance between production and drainage of aqueous humor. Other contributing factors include:

- Genetic predisposition
- Advancing age
- Diabetes mellitus
- Hypertension
- Long-term corticosteroid therapy
- Eye trauma or inflammation
- Thin cornea
- Poor blood supply to optic nerve

Current Treatment Approaches for Glaucoma

The main objective of glaucoma treatment is to reduce intraocular pressure and prevent further optic nerve damage.

1. Pharmacological Therapy

- **Beta-blockers** (e.g., Timolol)
- **Prostaglandin analogs** (e.g., Latanoprost)
- **Carbonic anhydrase inhibitors**
- **Alpha-agonists**

2. Non-Pharmacological Therapy

- Laser trabeculoplasty
- Surgical procedures (trabeculectomy)

Challenges with Conventional Glaucoma Treatment

- **Short Residence Time:** Eye drops are quickly washed away by tears and nasolacrimal drainage, reducing drug contact with the eye.
- **Poor Penetration:** Ocular barriers limit drug entry to the affected tissues, decreasing efficacy.
- **Frequent Dosing:** Short action requires frequent administration, impacting patient adherence.
- **Side Effects:** High doses needed can increase adverse reactions.

These limitations highlight the need for an advanced drug delivery system such as niosomal gel.

Niosomes as Ocular Drug Delivery Systems

Niosomes are microscopic lamellar structures formed by self-assembly of nonionic surfactants in an aqueous medium. Cholesterol is added to enhance membrane stability.

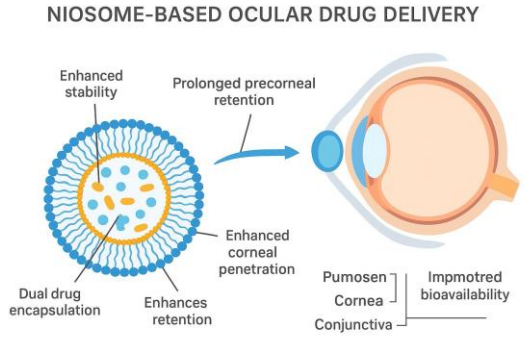

Figure 1: Niosome-Based Ocular Drug Delivery: Mechanism of Action and Therapeutic Advantages

Advantages of Niosomes

- Biocompatible and non-toxic
- Ability to encapsulate hydrophilic and lipophilic drugs
- Enhanced drug stability
- Controlled and sustained drug release

For ocular delivery, niosomes improve corneal penetration and prolong residence time.

Common Preparation Methods of Niosomes

1. **Thin Film Hydration (with or without Solvents)**:
   - Mix non-ionic surfactants (e.g., Span 60) and cholesterol in an organic solvent (like ether/chloroform mixture).
   - Add the glaucoma drug (e.g., Brimonidine) to this lipid solution.
   - Evaporate the solvent using a rotary evaporator to form a thin film on the flask walls.
   - Hydrate the film with an aqueous buffer (PBS pH 7.4) while heating (e.g., 60°C) and shaking, then sonicate (probe or bath) to form niosomes.
2. **Ether Injection:**
   - Dissolve surfactants, cholesterol, and the drug in diethyl ether.
   - Slowly inject this solution into a warm (60-65°C), agitated aqueous buffer (PBS).
   - Ether vaporizes, forming niosomes, which are then separated (e.g., by ultracentrifugation).
3. **Sonication (Solvent-Free/Green Method):**
   - Combine drug, surfactant (e.g., Span 60), and cholesterol in an aqueous buffer (PBS).
   - Use a probe sonicator to sonicate the mixture at controlled temperatures (e.g., 60°C) for a few minutes, directly forming niosomes.

3. Optimization Parameters

- Surfactant to cholesterol ratio
- Hydration time and temperature
- Drug concentration
- Gel viscosity and pH

Future Advancements in Glaucoma Therapy

- In-vivo and clinical evaluation of niosomal gels
- Targeted niosomes using ligands
- Stimuli-responsive vesicular systems
- Combination therapy in single formulation
- Integration with nanotechnology and ocular inserts

These advancements may significantly improve glaucoma management and patient outcomes.

Conclusion

Niosomes are non-ionic surfactant vesicle system, novel and efficient approach to drug delivery. Niosomes with the ophthalmic drug delivery proved significant advancement in present day. A wide range of drugs can be encapsulated into the niosomes, with the help of non-ionic surfactant and the cholesterol. Niosomes provides sustained release of the encapsulated drug, possess enhanced stability and reduce the toxic effects.

Niosomal gels overcome limitations of conventional eye drops by enhancing bioavailability, prolonging drug release, and improving patient compliance. With further clinical validation, this system may represent a promising future approach in glaucoma therapy.

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