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# Formulation And Evaluation of A Polyherbal Nanoparticle-Loaded in Situ Ophthalmic Gel Containing Camellia Sinensis and Ocimum Sanctum

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***Abstract-*** ***The present investigation focuses on the development of a novel ocular drug delivery system incorporating herbal extracts of Camellia sinensis and Ocimum sanctum. The study was designed to overcome the limitations associated with conventional ophthalmic preparations such as poor bioavailability and rapid precorneal elimination. Hydroalcoholic extracts of both plants were prepared and characterized for phytochemical constituents. Polymeric nanoparticles were formulated using chitosan and sodium tripolyphosphate through ionic gelation technique. The prepared nanoparticles were further incorporated into a pH-responsive in situ gel system using Carbopol 934 and HPMC K4M. The nanoparticles exhibited nanoscale size distribution with a positive surface charge and satisfactory drug entrapment efficiency. Drug release studies demonstrated a sustained release profile over 12 hours. The in situ gel formulations were evaluated for clarity, pH, viscosity, gelation behavior, drug content, sterility, and ocular irritation. Among the five formulations, F3 showed optimum characteristics, including suitable viscosity, strong gelation, high drug content, and controlled drug release without causing irritation. The developed system successfully combined nanoparticle technology with in situ gelation, resulting in enhanced ocular residence time and improved drug release behavior. This approach offers a promising strategy for delivering polyherbal therapeutics in ocular disorders.***

***Keywords: In-situ Gel, Nanoparticles, Camellia sinensis and Ocimum sanctum***

## I. INTRODUCTION

Delivering drugs to the eye remains a significant challenge due to its complex protective mechanisms. Rapid tear turnover, blinking, and nasolacrimal drainage reduce the residence time of conventional eye drops, often leading to less than 5% drug absorption . As a result, frequent dosing becomes necessary, which may reduce patient compliance and therapeutic effectiveness.

To address these issues, advanced drug delivery systems have been explored. Among them, polymeric nanoparticles have gained attention because of their ability to improve drug stability, enhance penetration, and provide sustained release. Their small size allows interaction with ocular tissues, while surface properties can be modified for better retention.

Simultaneously, in situ gel systems offer another advantage by transforming from liquid to gel upon contact with tear fluid. This transition increases precorneal residence time and reduces drug loss. Combining nanoparticles with in situ gel creates a dual-delivery approach that enhances both retention and controlled release.

Herbal drugs such as *Camellia sinensis* and *Ocimum sanctum* possess strong antioxidant, anti-inflammatory, and antimicrobial activities. However, their therapeutic use is limited by instability and poor permeability. Incorporating these extracts into nanoparticle-loaded in situ gels can significantly improve their efficacy [1-4].

## II. MATERIALS AND METHODS

### 2.1 Organoleptic Evaluation of Plant Materials

#### 2.1.1 Camellia sinensis

Dried leaves were examined for color, odor, taste, and texture. The sample showed green to brownish-green color, mild characteristic odor, slightly bitter and astringent taste, and brittle texture after drying, confirming good quality [5-6].

2.1.2 Ocimum sanctum
Leaves were evaluated similarly and exhibited greenish-brown color, strong aromatic odor, slightly bitter and pungent taste, and brittle texture, indicating suitability for further processing [7].

2.2 Collection and Processing of Plant Materials
2.2.1 Collection
Fresh leaves of both plants were collected from local sources in Lucknow and authenticated based on morphological characteristics [8].

2.2.2 Processing
Leaves were washed, shade-dried, powdered, and stored in airtight containers under controlled conditions to preserve phytoconstituents [9].

2.2.3 Procurement of Materials
All excipients and chemicals were obtained from standard suppliers and stored under appropriate conditions to maintain quality and stability [10].

2.3 Extraction of Drugs
2.3.1 Camellia sinensis Extraction
Hydroalcoholic maceration was carried out using ethanol–water mixture. The extract was filtered, concentrated, and dried to obtain a semi-solid mass [11].

2.3.2 Ocimum sanctum Extraction
Extraction was performed similarly using hydroalcoholic solvent, followed by filtration and concentration to obtain a stable extract [12].

2.3.3 Yield Determination
Extract yield was calculated as percentage of dried extract relative to initial plant material weight [13].

2.4 Solubility Study
Extracts (0.1 g) were tested in different solvents (water, methanol, ethanol, hexane, chloroform), and solubility was determined visually after mixing and standing [14].

2.5 pH Determination
Diluted extract solutions were analyzed using a calibrated digital pH meter at room temperature [15-16].

2.6 Qualitative Phytochemical Screening
Standard tests were performed to detect alkaloids, flavonoids, tannins, saponins, phenolics, steroids, & glycosides based on color change and precipitation reactions.

2.7 Formulation of In Situ Gel
2.7.1 Preparation of Nanoparticles
Nanoparticles were prepared using ionic gelation of chitosan with TPP in the presence of plant extracts.

2.7.2 Formulation of Gel
Five formulations (F1–F5) were prepared using Carbopol 934 and HPMC with nanoparticle dispersion.

Table 1: Composition of formulation

| Ingredient | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|
| Carbopol 934 (% w/v) | 0.2 | 0.3 | 0.4 | 0.5 | 0.6 |
| HPMC K4M (% w/v) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Nanoparticle dispersion | 10 mL | 10 mL | 10 mL | 10 mL | 10 mL |
| Sodium Chloride (% w/v) | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 |
| Benzalkonium Chloride (% w/v) | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| Distilled Water | q.s. to 100 mL | q.s. | q.s. | q.s. | q.s. |

2.7.3 Preparation Method
Polymers were hydrated and mixed with nanoparticles, followed by addition of sodium chloride and preservative. Final volume was adjusted and pH maintained.

2.7.4 Sterilization and Storage
Formulations were sterilized and stored in sterile containers under controlled conditions.

2.7.5 Mechanism of Gel Formation
Gelation occurred due to pH-triggered ionization of Carbopol in tear fluid, forming a viscous gel for sustained drug release [17].

2.8 Evaluation of Formulations
2.8.1 Evaluation of Nanoparticles
Particle Size Analysis: Particle size was measured using dynamic light scattering after suitable dilution. The average size and distribution were recorded to assess uniformity and suitability for ocular delivery.

Zeta Potential Measurement: Zeta potential was determined to evaluate surface charge and stability. Higher values indicated good dispersion and reduced aggregation.

Entrapment Efficiency: Nanoparticle dispersion was centrifuged, and free drug in the supernatant was analyzed spectrophotometrically. The difference from total drug gave the percentage of drug entrapped.

Drug Content: A known volume of nanoparticle dispersion was dissolved, filtered, and analyzed using UV spectroscopy to determine the actual drug present.
In Vitro Drug Release Study: Drug release was studied using a dialysis membrane in phosphate buffer (pH 7.4) at 37°C. Samples were withdrawn at intervals and analyzed to determine cumulative drug release. [18]

2.8.2 Evaluation of In Situ Gel
Appearance: Formulations were visually examined against a black and white background to check clarity, color, and absence of particulate matter.

pH Determination: The pH was measured using a calibrated digital pH meter to ensure compatibility with ocular conditions.

Viscosity Measurement: Viscosity was determined using a Brookfield viscometer to assess flow behavior and suitability for instillation.

Gelation Capacity: Gelation was evaluated by adding the formulation to simulated tear fluid (pH 7.4) and observing the time and strength of gel formation.

Drug Content: A known volume of formulation was diluted and analyzed spectrophotometrically to determine uniform drug distribution.

In Vitro Drug Release Study: Drug release was studied using a Franz diffusion cell, and samples were analyzed at regular intervals to determine cumulative release.

Sterility Test: Formulations were incubated in suitable culture media to check for microbial growth.

Ocular Irritation Test: The formulation was evaluated for irritation by observing redness, swelling, or discomfort after administration. [19]

## III. RESULTS AND DISCUSSION

3.1 Results of Extraction and Physicochemical Evaluation of Extracts
The hydroalcoholic extraction method produced satisfactory yields for both plant materials, with *Camellia sinensis* showing higher extractive value compared to *Ocimum sanctum*.

Both extracts appeared as semi-solid masses and exhibited good solubility in polar solvents, indicating the presence of polar phytoconstituents such as phenolics and flavonoids.

The pH values were found to be near neutral, suggesting suitability for further formulation development.

Table 2: Results of Extraction and Physicochemical Evaluation of Extracts

| S. No. | Parameter | Camellia sinensis | Ocimum sanctum |
|---|---|---|---|
| 1 | Extraction Method | Hydroalcoholic maceration | Hydroalcoholic maceration |
| 2 | Initial Drug (g) | 100 g | 100 g |
| 3 | Solvent Used (mL) | 500 mL (Ethanol:Water 70:30) | 500 mL (Ethanol:Water 70:30) |

| | | | |
|---|---|---|---|
| 4 | Final Extract (g) | 22.4 g | 17.6 g |
| 5 | % Yield | 22.4% | 17.6% |
| 6 | Color | Greenish brown | Dark green |
| 7 | State | Semi-solid | Semi-solid |
| 8 | Solubility | Soluble in water, methanol, ethanol; insoluble in hexane, chloroform | Soluble in water, methanol, ethanol; insoluble in hexane, chloroform |
| 9 | pH | 6.2 ± 0.03 | 6.5 ± 0.04 |

3.2 Evaluation of Polyherbal Nanoparticles

The evaluation of polyherbal nanoparticles demonstrated satisfactory physicochemical properties suitable for ocular drug delivery. The particle size analysis confirmed that the majority of particles were in the nanometer range, indicating successful formation of nanoparticles with acceptable uniformity, although slight aggregation was observed.

The zeta potential value was found to be positive and sufficiently high, suggesting good stability of the nanoparticle dispersion due to electrostatic repulsion. This also supports better interaction with the ocular surface.

Entrapment efficiency was observed to be high, indicating effective incorporation of the herbal extracts within the polymeric matrix. The drug content analysis showed values close to the theoretical amount, confirming uniform distribution of the drug in the formulation.

The in vitro drug release study revealed an initial release followed by a sustained release pattern over 12 hours. This behavior indicates controlled drug release from the nanoparticles, which is advantageous for prolonging therapeutic action and reducing dosing frequency.

Overall, the results confirm that the prepared nanoparticles possess suitable characteristics for incorporation into in situ ophthalmic gel systems.

Table 3: Evaluation of Polyherbal Nanoparticles

| S. No. | Parameter | Method | Result |
|---|---|---|---|
| 1 | Particle Size Analysis | Dynamic light scattering after dilution | Major particle size in nanorange (8–12 nm) with minor aggregation observed |
| 2 | Zeta Potential Measurement | Zeta potential analyzer | +32.1 mV indicating stable and positively charged nanoparticles |
| 3 | Entrapment Efficiency | Centrifugation followed by UV analysis of supernatant | 76.8% drug entrapped within nanoparticles |
| 4 | Drug Content | UV spectrophotometric analysis after dissolution | 96.2% drug content indicating uniform distribution |
| 5 | In Vitro Drug Release Study | Dialysis membrane in PBS (pH 7.4) at 37°C | 85.6% cumulative drug release over 12 hours (sustained release) |

3.3 Evaluation of In-situ Gel

The evaluation of nanoparticle-loaded in situ ophthalmic gel formulations (F1–F5) demonstrated that all batches were within acceptable limits for ocular application. The pH values were suitable for ocular use, while viscosity increased with polymer concentration, influencing gel formation and drug

release. Gelation capacity improved progressively from F1 to F5, confirming effective pH-triggered sol-to-gel transition. Drug content was uniform across all formulations, with F3 showing the highest value, indicating better drug distribution. In vitro drug release studies revealed that lower viscosity formulations released drug rapidly, whereas higher viscosity batches showed slower release; F3 exhibited an optimal sustained release profile. All formulations were sterile, ensuring safety, and no irritation was observed except mild discomfort in F5 due to higher viscosity. Overall, formulation F3 provided the best balance among all parameters, making it the optimized formulation for ocular drug delivery.

Table 4: Evaluation of In-situ Gel

| S. No. | Parameter | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|---|
| 1 | pH (Mean ± SD) | 5.80 ± 0.04 | 5.92 ± 0.05 | 6.10 ± 0.03 | 6.28 ± 0.04 | 6.41 ± 0.05 |
| 2 | Viscosity (cP) | 145 | 182 | 225 | 268 | 310 |
| 3 | Gelation Capacity | + | ++ | +++ | +++ | +++ |
| 4 | Drug Content (%) | 94.5 | 95.8 | 97.2 | 96.8 | 95.9 |
| 5 | % Drug Release (12 hr) | 92.4 | 89.6 | 86.2 | 83.5 | 80.1 |
| 6 | Sterility | Pass | Pass | Pass | Pass | Pass |
| 7 | Ocular Irritation | No irritation | No irritation | No irritation | No irritation | Mild discomfort |

## IV. CONCLUSION

The study successfully developed a polyherbal nanoparticle-loaded in situ ophthalmic gel using *Camellia sinensis* and *Ocimum sanctum*. The formulation addressed key challenges of ocular drug delivery by enhancing retention and providing sustained release.

The optimized formulation (F3) demonstrated the best performance in terms of physicochemical properties and drug release. The integration of nanotechnology with in situ gel systems proved effective in improving the therapeutic potential of herbal extracts.

This approach can be considered a promising alternative for the treatment of ocular conditions, offering improved efficacy and patient compliance.

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