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# Apatinib-loaded polymeric micelles for ophthalmic delivery to the posterior segment

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## PURPOSE

Apatinib, a VEGFR-2 inhibitor, is effective against abnormal angiogenesis in AMD and diabetic retinopathy. However, intravitreal injections (IVI) of anti-VEGF agents involve risks and reduce patient compliance. To address this, we developed Apatinib-loaded polymeric micelle (PM) eye drops as a non-invasive strategy for posterior eye delivery.

## METHOD(S)

- **Formulation:** Apatinib-loaded polymeric micelles (PMs) were prepared using direct dissolution and thin-film hydration techniques.
- **Physicochemical Characterization:**
  - ✓ Particle size and polydispersity index (PDI): Measured by dynamic light scattering (DLS)
  - ✓ Zeta potential: Determined using a zeta potential analyzer
  - ✓ Encapsulation efficiency: Analyzed by high-performance liquid chromatography (HPLC)
- **Cellular Uptake:** Uptake in ARPE-19 cells was visualized using confocal laser scanning microscopy (CLSM).
- **In Vivo Evaluation:** Conducted in a mouse choroidal neovascularization (CNV) model
  - ✓ SHRM area quantification: Performed via optical coherence tomography (OCT)
  - ✓ CNV area quantification: Assessed by fluorescence fundus imaging with Isolectin B4 staining

**Table 1.** Formulation of the Apatinib-loaded polymeric micelles.

| Component | Formulation No. | | | | | |
|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 |
| Apatinib | 18.9 | 18.9 | 18.9 | 6.3 | 6.3 | 6.3 |
| Soluplus® | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| DPPE-PEG, 2k | - | 1.3 | - | - | 1.3 | - |
| DPPE-PEG-CPP | - | - | 0.7 | - | - | 0.7 |
| Preparation method | A | A | A | B | B | B |

A: Direct dissolution method
B: Thin film hydration method

## RESULT(S)

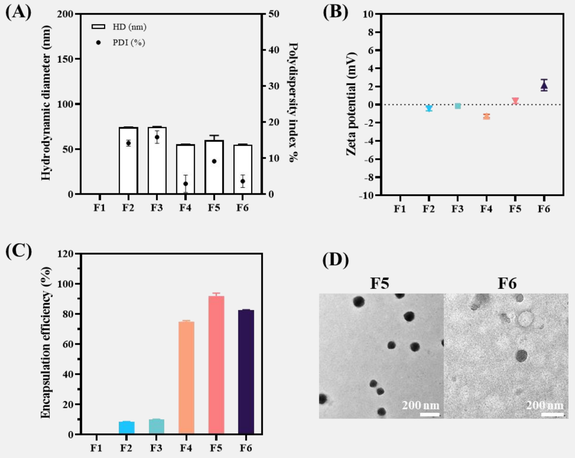


**Figure 1.** Physicochemical characterization of Apatinib loaded polymeric micelle. (A) Hydrodynamic diameter and PDI, (B) Zeta potential, (C) Encapsulation efficiency and (D) TEM image. Each value represents the mean ± standard deviation (n=3).

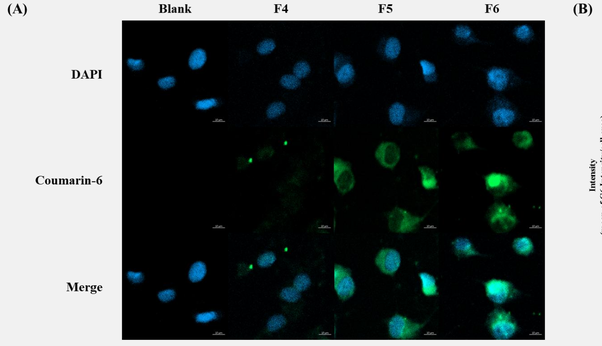


**Figure 2.** ARPE-19 cell uptake of coumarin-6-loaded polymeric micelles. (A) CLSM images showing micelle uptake in ARPE-19 cells, and (B) average fluorescence intensity of coumarin-6 per cell area (mean ± standard deviation, n = 20).

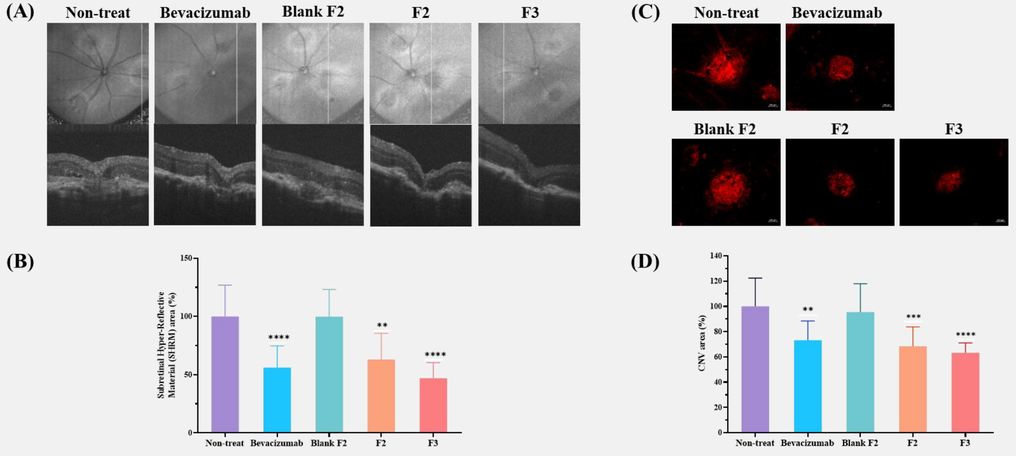


**Figure 3.** (A) OCT images of retinas treated with AP-PM and (B) percentage of SHRM area. (C) Isolectin B4-stained images of laser-induced CNV in flat-mounted choroids treated with AP-PM and (D) percentage of CNV area based on red fluorescence intensity.

- **Uniform particle size under 200 nm**
- **High encapsulation efficiency up to 90%**
- **Enhanced cellular uptake with DPPE-PEG modification**
- **In vivo efficacy:**
  - ✓ **SHRM area reduced by 53%**
  - ✓ **CNV area reduced by 46%**
- **Comparable therapeutic effect to intravitreal Bevacizumab injection**

## CONCLUSION(S)

The Apatinib-loaded PM formulation offers a promising alternative to IVI therapy, providing high encapsulation efficiency while presenting a less invasive and more effective treatment option for ocular diseases.

## FUNDING

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