



# Inhalable Icariin-Loaded Micelles-in-microparticles Targeted IL-4 Signal Pathway for COPD Treatment

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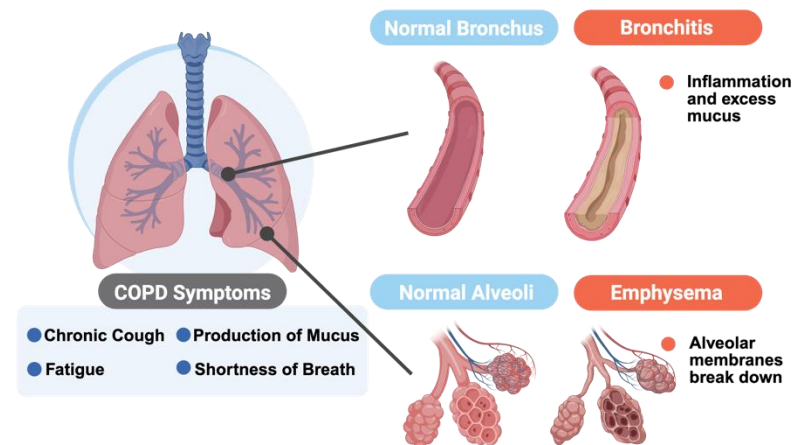
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# COPD

Chronic Obstructive Pulmonary Disease

- In 2021, COPD was **the third** leading cause of death globally
- Estimated **3.4 million deaths** and **79.9 million DALYs (Disability-Adjusted Life Years)** were attributable to COPD

(Wang et al., *Respiratory Research*, 2025)



## Key Challenges of COPD Treatment

- Mainly symptomatic and limited treatment effect
- Inflammation resistance
- Drug delivery challenges

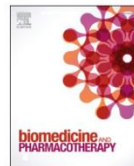
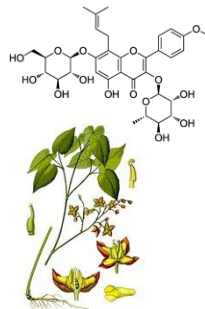
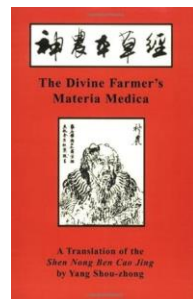
(Barnes, P. J. et al., *Nat. Rev. Dis. Primers*, 2015)

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## Inspiration from Traditional Chinese Medicine (TCM)

- Icariin (ICA)** is the main active compound in *Epimedium* (Horny Goat Weed).
- Epimedium* has been used for nearly **2,000 years** to treat cough and asthma.



Icariin attenuates bleomycin-induced pulmonary fibrosis by targeting Hippo/YAP pathway

Wenjing Du<sup>a</sup>, Zhao Tang<sup>a</sup>, Fangyong Yang<sup>a</sup>, Xijun Liu<sup>c</sup>, Jingcheng Dong<sup>a,b,\*</sup>

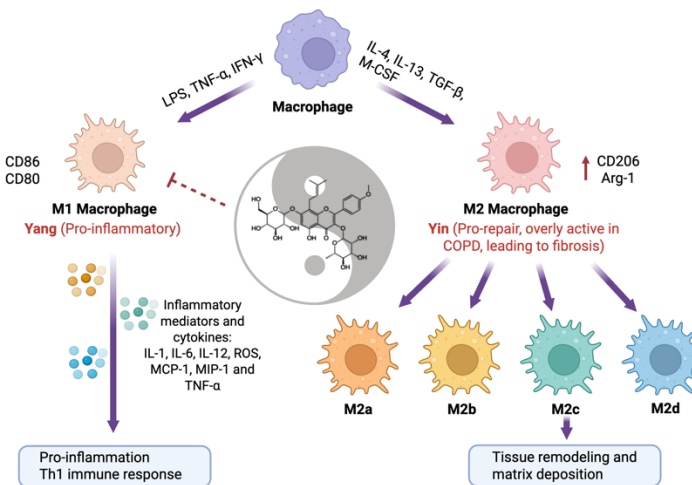
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*Epimedium*. From [https://en.wikipedia.org/wiki/Epimedium\\_alpinum](https://en.wikipedia.org/wiki/Epimedium_alpinum) (open web site, accessed on 2nd July 2025).

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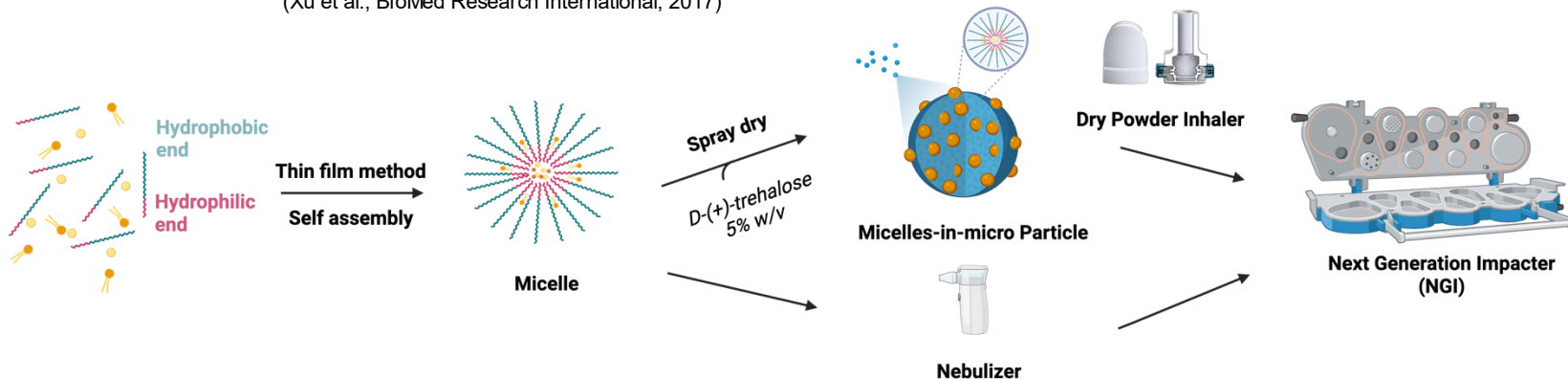
## Icariin for COPD:

- Inhibits macrophage M2 polarization (↓CD206)
- Regulates macrophage M1/M2 polarization (Yin-Yang balance)

## Challenges of ICA Delivery

- Poor water and lipid solubility
- Low oral bioavailability. Reported oral bioavailability is as low as 1.9% to 12.1% in animal models.

(Xu et al., BioMed Research International, 2017)

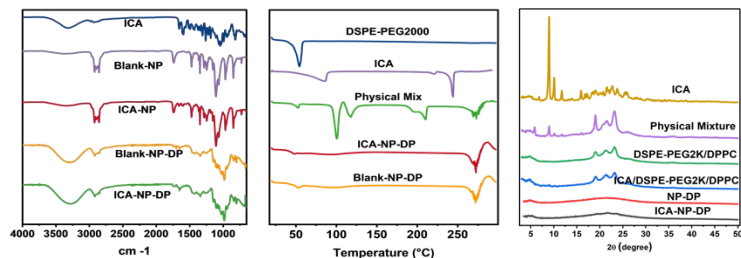


## Hypothesis

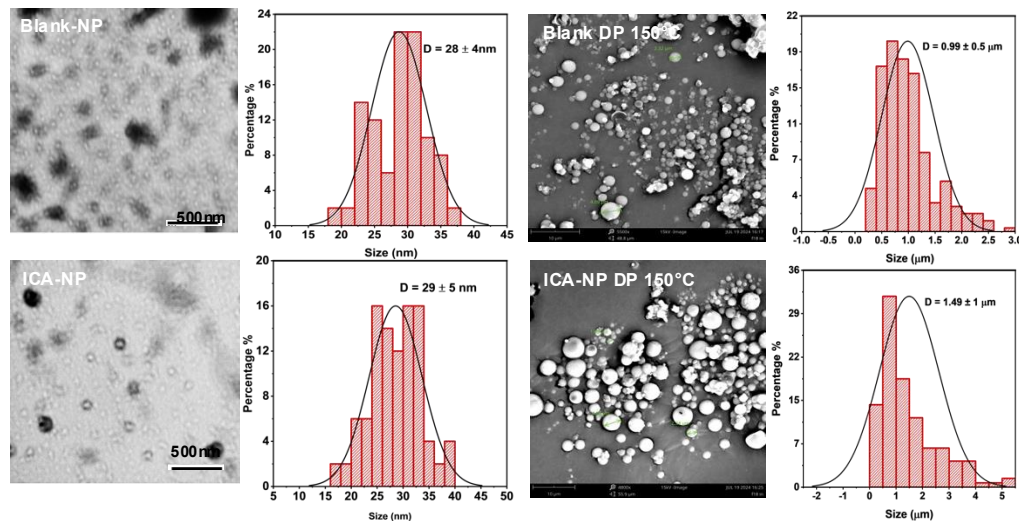
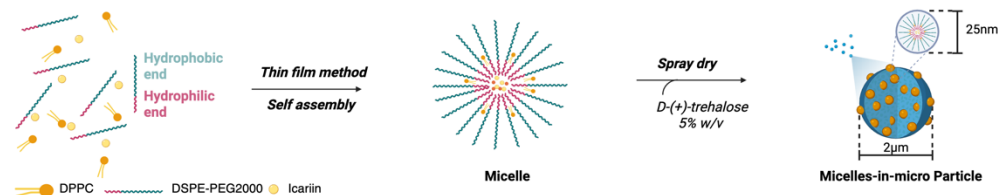
- Micelles can increase ICA water solubility, be effectively delivered to the lungs, and inhibit macrophage M2 polarization.

- Optimized formulation, ICA/DSPE-PEG2000/DPPC, 15:70:30 (w/w) achieved **95% EE** and **12.4% DL**
- Increased Icarin water solubility around **70-fold**
- Formed uniform micelles (**~29 nm**) and spray-dried microstructures (**~1.5  $\mu\text{m}$** )

| Formulations                         | EE %             | DL %             |
|--------------------------------------|------------------|------------------|
| ICA/DSPE-PEG2000 15:100 (w/w)        | 40.37 $\pm$ 2.11 | 6.80 $\pm$ 0.13  |
| ICA/DSPE-PEG2000/DPPC 15:80:20 (w/w) | 84.96 $\pm$ 4.32 | 7.83 $\pm$ 1.22  |
| ICA/DSPE-PEG2000/DPPC 15:70:30 (w/w) | 95.17 $\pm$ 2.02 | 12.40 $\pm$ 0.36 |

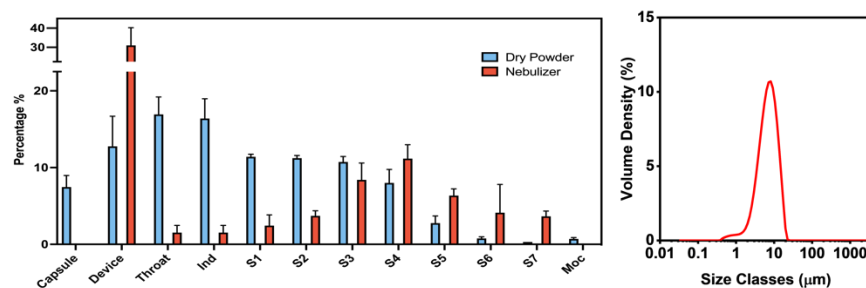


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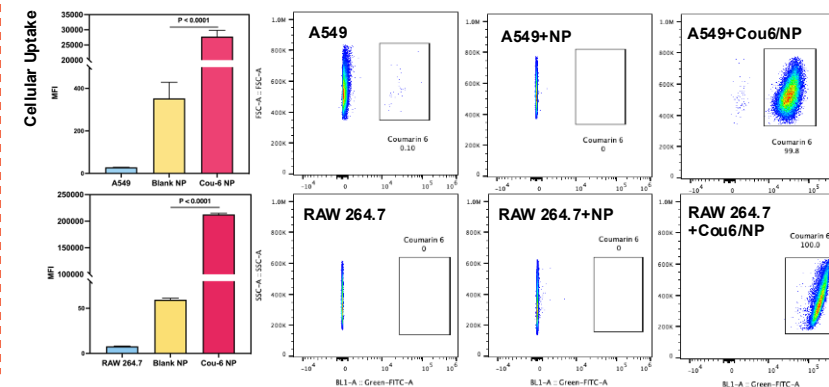
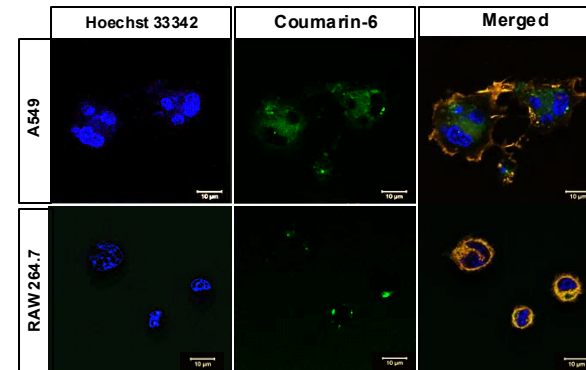
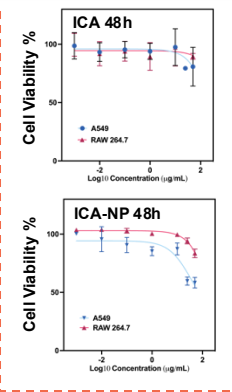


- **Dry powder inhaler** outperformed nebulizer with **higher FPF (43%)** and **smaller MMAD (3.79  $\mu\text{m}$ )**
- ICA-NP showed **low cytotoxicity** for ICA-NP at higher doses
- **Cellular uptake** of Coumarin-6 NPs was **high**, especially in **RAW264.7**



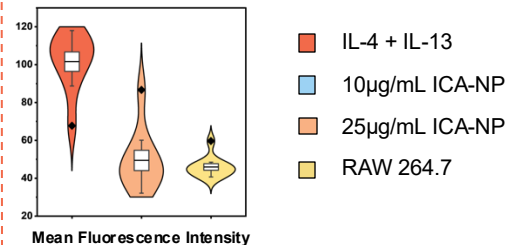
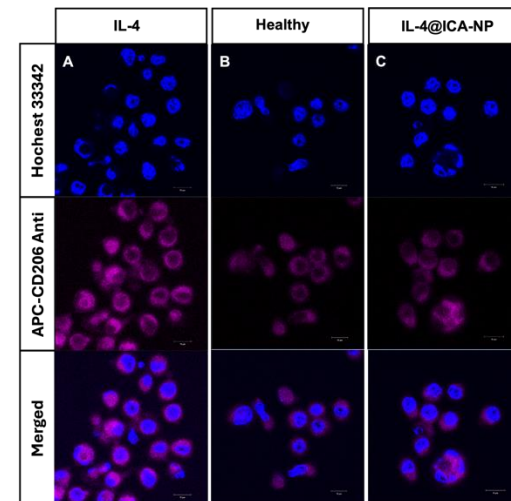
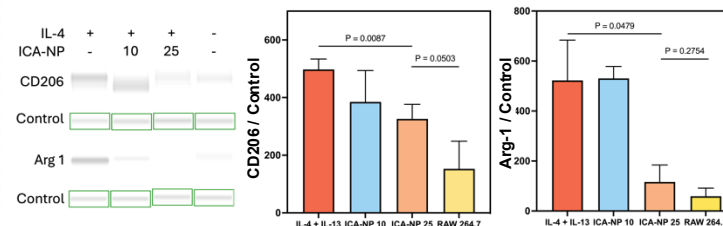
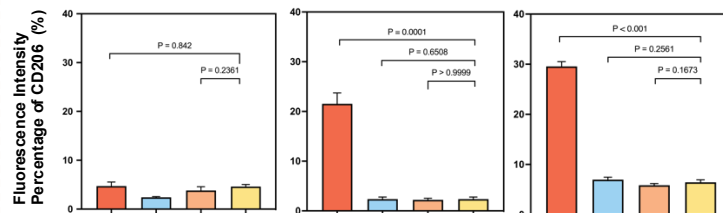
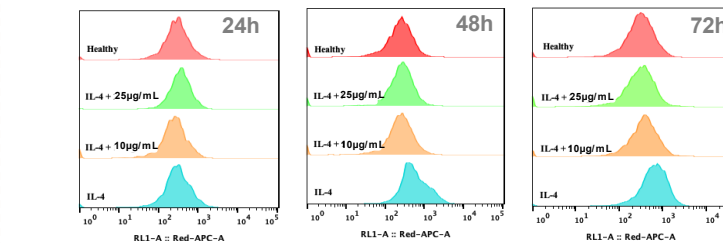
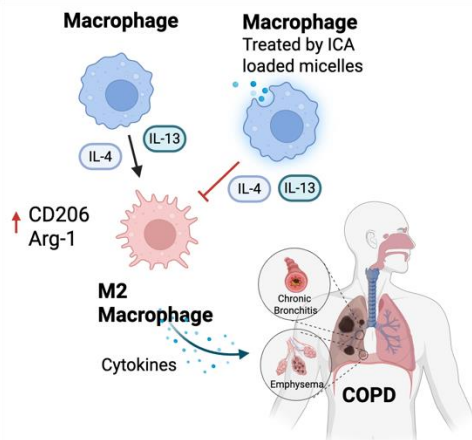
| Formulation                                                 | MB (%)     | EF (%)     | FPF (%)    | MMAD ( $\mu\text{m}$ ) | GSD ( $\mu\text{m}$ ) |
|-------------------------------------------------------------|------------|------------|------------|------------------------|-----------------------|
| ICA/DSPE-PEG2000/DPPC<br>15:70:30 <b>Nebulizer</b>          | 91 $\pm$ 4 | 68 $\pm$ 3 | 64 $\pm$ 4 | 4.52 $\pm$ 0.1         | 1.53 $\pm$ 0.02       |
| ICA/DSPE-PEG2000/DPPC<br>15:70:30 <b>Dry Powder Inhaler</b> | 94 $\pm$ 1 | 93 $\pm$ 2 | 43 $\pm$ 4 | 3.79 $\pm$ 0.1         | 2.24 $\pm$ 0.1        |

\*MB (%): Mass balance, EF(%): Emitted fraction, FPF(%): Fine particle fraction, MMAD: Mass median aerodynamic diameter, GSD: Geometric standard deviation



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- ICA loaded Micelle reverses IL-4/IL-13-induced M2 macrophage polarization.
- 25  $\mu\text{g/mL}$ , 72h treatment restores marker expression toward a healthy phenotype.



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## | Takeaway

- Micellar encapsulation improved ICA solubility from **0.02 mg/mL to 1.4 mg/mL**
- Micelles aerosol showed optimal aerodynamic properties (MMAD 4.5  $\mu\text{m}$ , FPF 64%, EF 68%) for **deep lung deposition**
- **73% reduction** in CD206 expression, indicating M2 macrophage polarization inhibition.

## | Impacts

- Offers a **targeted pulmonary delivery** strategy for phytochemicals, overcoming their solubility limitations
- Represents a **novel inhalable anti-inflammatory therapy** for COPD
- Lays the foundation for future *in vivo* studies and preclinical development in chronic lung diseases



## Acknowledgment

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Prof. Ijeoma Florence Uchegbu

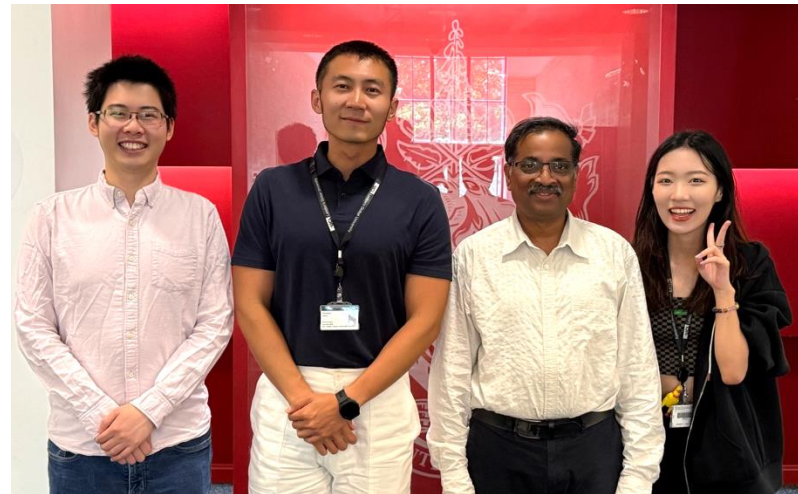
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# Thanks for your attention

I welcome collaboration and postdoctoral opportunities in the fields of:

- Emerging delivery systems
- Pulmonary drug & gene delivery
- Macrophage-targeted therapy
- AI in pharmaceutical formulation

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