# Development of a Topical Proniosome Gel Formulation of Berberine For CHIKV-Induced Arthritis

Ayça Altay Benetti1, Ma Thinzar Thwin1, Ahmad Suhaimi2, Ryan Sia Tze Liang1, Lisa Fong-Poh Ng2, Fok-Moon Lum2, Camillo Benetti1

1 Department of Pharmacy and Pharmaceutical Sciences, National University of Singapore, Singapore;  
2 A\*STAR Infectious Diseases Labs (A\*STAR ID Labs), Agency for Science, Technology and Research (A\*STAR), Singapore.

Background and aims. Chikungunya virus (CHIKV) infection is associated with prolonged arthritis and inflammatory joint symptoms. Berberine, a plant alkaloid with antioxidant and anti-inflammatory properties, shows potential for alleviating viral arthritis but suffers from poor oral bioavailability. To address this, we developed a proniosome gel formulation for topical delivery of berberine and evaluated its physicochemical properties, biological efficacy, and safety.  
  
Methods. A series of proniosome gels were prepared with varying concentrations of berberine (0.5–3%) and excipients (hyaluronic acid, ascorbic acid, resveratrol, and menthol). The gels were assessed for rheological behavior, skin permeation using ex vivo porcine skin in Franz diffusion cells, and long-term physical stability. Antioxidant and cytotoxic profiles were evaluated in HaCaT cells. Anti-inflammatory activity was tested in LPS-stimulated RAW264.7 macrophages. Pharmacokinetic and efficacy profiles were evaluated in a CHIKV-infected mouse model.  
  
Results. Gels with berberine demonstrated enhanced structural integrity, skin permeability, and antioxidant capacity. HA incorporation improved gel stability and viscoelastic properties. RT-qPCR analysis showed reduced expression of TNF-α, IL-6, and IL-1β in treated cells. In vivo, the formulation reduced joint swelling without altering viral RNA loads and extended plasma half-life to 16 h. No signs of liver or kidney toxicity were observed.  
  
Conclusion/Discussion. This proniosome-based topical formulation offers a promising strategy to deliver berberine locally to joints for the treatment of CHIKV-associated arthritis. Its demonstrated anti-inflammatory, antioxidant, and stability profiles warrant further development for musculoskeletal applications.