

## **Abstract**

Arthritis is main cause of disability in humankind in developed and developing countries. Among which rheumatoid arthritis and gouty arthritis are most prevalent ones. Immunosuppressants (Tacrolimus) and xanthine oxidase inhibitors (Febuxostat) are the choice of treatment for RA and gouty arthritis respectively. However, Tacrolimus and Febuxostat have several limitations of gastrointestinal related disturbances and low oral bioavailability due to first pass metabolism and low aqueous solubility. Thus, to improve bioavailability, transdermal drug delivery systems of Tacrolimus and Febuxostat were developed as their treatment options.

Tacrolimus is immunosuppressant which acts by inhibiting immune response of human body. First, a cubosomes of Tacrolimus/Febuxostat were developed and then, these developed cubosomes were loaded into the microneedle patch to achieve better permeation of drug through skin. The developed cubosomes of Tacrolimus/Febuxostat were characterized for various parameters like % entrapment efficiency, vesicle size, Polydispersity index, Transmission electron microscopy, in-vitro drug release, Small angle x-ray scattering, head-space gas chromatography, etc. After loading it in Microneedle patch it was also characterized for further evaluation parameters like in-vitro dissolution time, axial fracture force, Scanning electron microscopy, in-vitro drug release, pore closure kinetics, in-vitro drug release etc. All optimized formulations were evaluated for various ex-vivo characterization studies like in-vitro cell viability study, ex-vivo permeation study, ex-vivo fluorescence microscopy, histopathology study which indicates its safety with better permeation across the skin. Then, developed formulations were subjected to pharmacokinetic study which proves better bioavailability of drug from developed formulations compare to marketed formulations. Apart from this, developed formulations were also tested for pharmacodynamic study which indicated that the developed formulation were effective to disease induced rat model same as marketed formulation. According to the stability study of prepared formulations, it can be concluded that the prepared cubosomes of Tacrolimus/Febuxostat were stable at room temperature while Microneedle patch of Tacrolimus/Febuxostat required special type of packaging which prevent moisture absorption by Microneedle patch.