

11<sup>th</sup> World Congress on

# Pharmaceutical Sciences and Innovations in Pharma Industry

February 27-28, 2017 Amsterdam, Netherlands

## Intravaginal delivery of polyphenon 60 and curcumin nanoemulsion gel

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Polyphenon 60 (P60) and curcumin (CUR) were loaded in a single nano emulsion system and their combined antibacterial action was studied against uropathogenic *Escherichia coli*. To enhance bioavailability at target organs and to inhibit enzymatic degradation in gastric intestinal tract, vaginal route of administration was explored. P60+CUR nanoemulsion (NE) was formulated by ultra-sonication and optimized using Box-Behnken design. Optimized NE showed Z-average of 211.2 nm, polydispersity index 0.343 and zeta potential -32.7 mV. Optimized P60+CUR NE was characterized for stability and transmission electron microscopy (TEM) and it was observed that NE was stable at 4°C for 30 days and monodispersed in nature with particle size in the range of 195-205 nm. P60+CUR NE was further formulated to gel and characterized by viscosity parameters and in-vitro permeation studies. In vitro drug release studies in simulated vaginal media showed maximum release (84±0.21%) of curcumin within 5 h and (91±0.16%) of P60 within 8 h. Both the drugs maintained sustainable release up to 12 h. To investigate the transport via intravaginal route, gamma scintigraphy and biodistribution study of P60+CUR NBG was performed on Sprague-Dawley rats using 99m technetium pertechnetate for radiolabeling to P60 molecule. Following intravaginal administration, P60+CUR NBG dispersed in kidney and urinary bladder with (3.07±0.15) and (3.35±0.45) percentage per gram after 3 h, respectively and remained active for 12 h. Scintigraphy images and biodistribution findings suggested that the P60+CUR NBG given by intravaginal route led to effective distribution of actives in urinary tract to eradicate urinary tract infection.

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