# Drug discovery from naturally isolated compounds

**Salman Khan***

Pharmacological Sciences Research Lab, Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan
Email: skhan@qau.edu.pk Phone: 051-90644056

## Abstract

Inflammation is a dynamic process with pro-inflammatory mediators and cytokines. A number of drugs have been developed to treat inflammation including agents that reduce the activity of specific mediators and cytokines. In the current study, we are set up to define the molecular targets of naturally occurring natural compounds actions. We investigated that capillarisin produce a marked inhibition of NF-κB and MAP-kinase regulating mediators in various pharmacological models. Capillarisin, chromone derivative from *A. capillaris* exhibits potent anti-inflammatory activity. The capillarisin dose-dependently inhibited the pro-inflammatory mediators in LPS-stimulated RAW 264.7 macrophage and primary macrophages isolated from BALB/c mouse. Molecular analysis using quantitative real time polymerase chain reaction (qRT-PCR) revealed that several pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were reduced by capillarisin, and this reduction correlated with the down-regulation of the NF-κB signaling pathway. Capillarisin suppressed the LPS-induced phosphorylation and degradation of IκBα. Moreover, the MAP-kinase study demonstrated that capillarisin inhibited the p-p38 and p-JNK expressions. To further study the mechanisms underlying its anti-inflammatory activity, an electrophoretic mobility shift assay (EMSA) using a $^{32}$P-labeled NF-κB and AP-1 probes were conducted. LPS-induced NF-κB DNA binding was drastically abolished by capillarisin. Furthermore, we also focused on the anti-nociceptive and neruoprotective activities of capillarisin in in vitro and in vivo models. Based on anti-inflammatory properties of capillarisin, various signaling pathways were brought under investigations which demonstrate potent activities in these pharmacological models. Hence, the present data suggest that capillarisn are major anti-inflammatory agent and may be a potential therapeutic candidate for the treatment of inflammatory disorders.

**Keywords**: Anti-inflammatory, capillarisin, anti-nociceptive, neuroprotecitve, signaling pathways