Celastrol, a pentacyclic triterpene, attenuates fMLP-induced elastase release in human peripheral blood neutrophils

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Celastrol, a pentacyclic triterpene which originally identified from traditional Chinese Medicine (Thunder God Vine), has been used to treat the inflammatory diseases almost 3 decades ago. Several randomized clinical trials of Thunder God Vine have demonstrated the beneficial effects on the symptoms of inflammatory diseases, but its mechanism is not well understood. Neutrophils represent 50 to 60% of the total circulating leukocytes. Once an inflammatory response is initiated, neutrophils are the first cells to be recruited to sites of infection or injury. When neutrophils are activated, elastase rapidly released from the granules to degrade foreign organic molecules during phagocytosis by neutrophils. Accumulation of elastase can cause abnormal degradation of healthy tissues, resulting in the development of inflammatory diseases such as rheumatoid arthritis, pulmonary emphysema, and cystic fibrosis and also delayed wound healing. Therefore, the aim of the present study is to investigate the effect of celastrol on elastase release in human peripheral blood neutrophils.

Neutrophils were isolated from venous blood by dextran sedimentation and discontinuous percoll gradient centrifugation. The elastase release was assayed by spectrophotometric measurement (A405 nm) of released p-nitrophenol upon hydrolysis of Boc-ala-ONp. The effect of celastrol on neutrophil elastase release was expressed as the percentage of the inhibition of the response produced by a submaximal effective concentration of fMLP (final concentration of 100 nM).

The results showed that celastrol at the concentration of 0.1-100 μM inhibited fMLP-induced neutrophil elastase release in a dose-dependent manner. This result suggested the inhibitory effect of celastrol on fMLP-induced elastase release in human peripheral blood neutrophils.