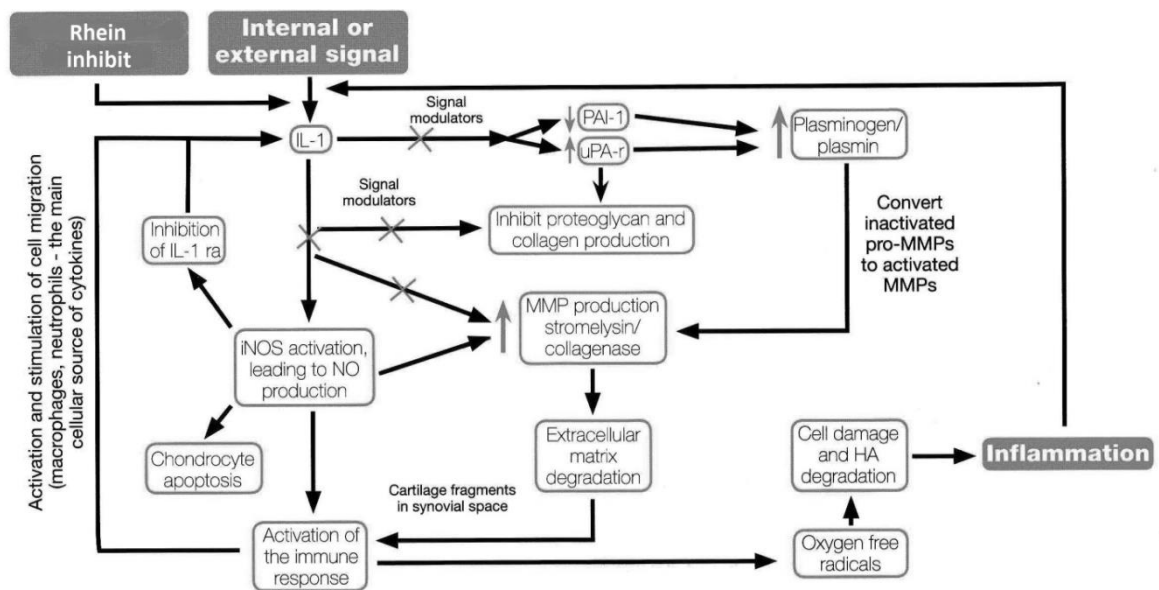


the nucleus and expression of NF- $\kappa$ B-dependent genes. Rhein also reduces the production of ICE protein in chondrocytes, leading to a reduction in IL-1 activation.

### *Anti catabolic effects*

Through inhibition of IL-1 production and activity, diacerein leads to a reduction in IL-1-induced events such as MMP production by chondrocytes and subsequent cartilage degradation. Furthermore, diacerein down-regulates IL-1-mediated inhibition of TIMP production in chondrocytes leading to further inhibition of MMP activity. Diacerein also reduces the uPA receptor level on chondrocytes and associated plasmin activity, which may reduce the activation of MMPs and other proteases and prevent cartilage matrix degradation. In addition, the synthesis and expression of iNOS is significantly inhibited, reducing the production of the free radical NO. As a result, diacerein also prevents NO mediated chondrocyte apoptosis and MMP activation, which may reduce the extent of cartilage damage.



**Figure 9:** Anti-catabolic effect of rhein (Novartis osteocerein brochure, n.d.)