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## **PLO2 Mechanisms of action of new natural antiinflammatory drugs**

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A wide range of mediators participate in the recruitment and activation of cells during inflammation, suggesting multiple therapeutic strategies for inflammatory conditions. Increased expression of cyclooxygenase-2 and high levels of prostaglandins can be detected in rheumatoid synovial tissues, where they mediate erosion of cartilage and bone, as well as angiogenesis. These effects would be prevented by drugs able to inhibit enzyme activity or expression. As cytokines play a critical role in this response, the control of their synthesis, release or effects are important targets for new antiinflammatory drugs. Thus, inhibition of kinases involved in intracellular signaling would lead to transcriptional and posttranscriptional regulation of cytokines, whereas inhibition of some proteolytic enzymes would prevent cytokine activation. Transcription factors play a crucial role in the expression of proinflammatory mediators. Inhibition of nuclear factor- $\kappa$ B-mediated transcription can suppress the production of a large number of proinflammatory proteins including cytokines, chemokines, receptors for these mediators, cell adhesion molecules, nitric oxide synthase, cyclooxygenase-2 and other inducible enzymes. Several mechanisms may account for this effect. We have studied new antiinflammatory agents such as cacospongionolide B and petrosaspongionolide M, which inhibit the nuclear factor- $\kappa$ B pathway through an interference with the phosphorylation and degradation of inhibitory proteins. Apart from direct antioxidant properties, some natural phenolic derivatives and synthetic analogs can induce antioxidant genes in mammalian cells. The resulting enzyme activity can contribute to the modulation of inflammatory responses. In addition, apoptotic death of inflammatory cells contribute to immunosuppressive and antiinflammatory drug effects in chronic conditions.



### **Prof. Dr. María José Alcaraz**

She is professor in Pharmacology at the Department of Pharmacology, University of Valencia, Spain. She got the Ph D. in 1981 at the University of Valencia with Extraordinary Award, followed by a postdoctoral training at the Department of Pharmacology, King's College of London (1983-1984). After the positions of assistant and lecturer, she got the professorship in 1991, when she was elected Head of the Department of Pharmacology, University of Valencia. In 1998 she worked as a visiting researcher at the Unité 348 INSERM, Paris. Her research has always been focused on inflammation and antiinflammatory agents, mainly natural products, with ca. 100 international publications in the field and a large number of funded projects. She has recently received the Dr. Esteve Foundation Award to the best scientific publication in Pharmacology. Referee of different international journals and expert for scientific projects evaluation in several countries and international organizations, such as the International Foundation for Science or the European Commission, she has played an active role in international cooperation, mainly with Latin America. At present, she coordinates an international project on antiinflammatory natural products within the CYTED program.