

# A chemical-biological study of bioactive compounds from propolis provides new details on the molecular basis of the anti-inflammatory effects of this multifunctional food

ShT-03.3-3

M.L. Bellone<sup>I</sup>, M. De Leo<sup>II</sup>, A. Braca<sup>II</sup>, N. De Tommasi<sup>I</sup>, **F. Dal Piaz**<sup>III</sup>

<sup>I</sup>Dipartimento di Farmacia, Università degli studi di Salerno, Via Giovanni Paolo II, Fisciano (SA), Italy, <sup>II</sup>Dipartimento di Farmacia, Università di Pisa, Pisa, Italy,

<sup>III</sup>Dipartimento di Medicina, Università di Salerno, Via S. Allende, Baronissi (SA), Italy

Propolis is a very complex mixture of polyphenols, terpenoids, lipids and sugars, whose multiple beneficial effects on humans are widely reported. One of the major biological activities for which propolis is credited is anti-inflammatory, and its use for preventive or therapeutic treatments of rheumatoid arthritis (RA) has been suggested. As part of research on the functional characterization of propolis produced in the internal areas of the Italian region of Campania, we undertook a study aimed at shedding light on the biochemical mechanisms underlying their anti-inflammatory activity. As a first step, we subjected an ethanolic extract of propolis to chromatographic separation. We assayed the resulting fractions to evaluate their ability to reduce interleukin-6 secretion from human synoviocytes in which inflammation was induced, selected as an in vitro model of RA. The most active fraction was essentially composed by pinobanksin and phenethyl caffeate (CAPE). Therefore, we investigated the biological activity of these two compounds. Firstly, we analyzed their effect on the expression of inflammatory proteins in 2D cell model, thus revealing that pinobanksin and CAPE treatment induced down-regulation of COX-2, STAT-3 and phosphorylated-STAT-3. Conversely, CAPE seemed to affect marginally the levels of COX-2. Therefore, we used Drug Affinity Responsive Target Assay, a chemical-proteomic approach, to identify the putative target(s) of this compound in synoviocytes. Among the protein emerged as potential targets of CAPE, we focused on transportin-2 and AP2 adaptor complex. Indeed, they are involved in nuclear-cytosolic shuttling of proteins, which plays a pivotal role in the inflammation processes. Finally, a 3D-synoviocytes culture was used to confirm the results in an innovative model of inflammation.