

## PROTECTIVE EFFECT OF HYPERICUM PERFORATUM IN ZYMOSAN-INDUCED MULTIPLE ORGAN DYSFUNCTION SYNDROME

<sup>1</sup>Angelina De Sarro, <sup>1,2</sup>Emanuela Mazzon, <sup>1,2</sup>Rosanna Di Paola, <sup>1</sup>Carmelo Muià, <sup>1,2</sup>Tiziana Genovese, <sup>2</sup>Placido Bramanti, <sup>3</sup>Emanuela Esposito, <sup>4</sup>Marta Menegazzi, <sup>3</sup>Rosaria Meli, <sup>4</sup>Hisanori Suzuki, and <sup>1,2</sup>Salvatore Cuzzocrea

<sup>1</sup>Department of Clinical and Experimental Medicine and Pharmacology, School of Medicine, University of Messina, Italy; <sup>2</sup>IRCCS Centro Neurolesi "Bonino-Pulejo", Messina, Italy; <sup>3</sup>Dipartimento di Farmacologia Sperimentale, Università di Napoli "Federico II", Napoli, Italy; <sup>4</sup>Department of Neuroscience and Vision, University of Verona, Verona, Italy

*Hypericum perforatum* is a medicinal plant species containing many polyphenolic compounds, namely flavonoids and phenolic acids. Since polyphenolic compounds have high antioxidant potential, we have investigated the effects of *Hypericum perforatum extract* on the development of multiple organ dysfunction syndrome caused by zymosan (500 mg/kg, administered i.p. as a suspension in saline) in mice. Organ failure and systemic inflammation in rats was assessed 18 hours after administration of zymosan and/or *H. perforatum extract* and monitored for 12 days (for loss of body weight and mortality). Treatment of mice with *H. perforatum extract* (30 mg/kg i.p., 1 and 6 hours after zymosan) attenuated the peritoneal exudation and the migration of polymorphonuclear cells (PMNs) caused by zymosan, pulmonary, intestinal and pancreatic injury and renal dysfunction as well as the increase in myeloperoxidase (MPO) in the lung and intestine. Immunohistochemical analysis for inducible nitric oxide synthase (iNOS), nitrotyrosine and poly (ADP-ribose) (PAR) revealed positive staining in lung and intestine tissues obtained from zymosan-injected mice. The degree of staining for nitrotyrosine, iNOS and PAR were markedly reduced in tissue sections obtained from zymosan-treated mice, which received *H. perforatum extract*. In conclusion, this study provides evidence, for the first time, that *H. perforatum extract* attenuates the degree of zymosan-induced multiple organ dysfunction syndrome in mice.