

# Ultramicronized palmitoylethanolamide (PEA-um®) in the treatment of idiopathic pulmonary fibrosis

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The aim of this study was to examine the effects of an ultramicronized preparation of palmitoylethanolamide (**PEA-um®**), an endogenous fatty acid signalling amide belonging to the N-acylethanolamine family, in mice subjected to idiopathic pulmonary fibrosis. Idiopathic pulmonary fibrosis was induced in male mice by a single intratracheal administration of saline with bleomycin sulphate (1 mg/kg body weight) in a volume of 100 µL. **PEA-um®** was injected intraperitoneally at 1, 3 or 10 mg/kg 1 h after bleomycin instillation and daily thereafter. Animals were sacrificed after 7 and 21 days by pentobarbitone overdose. One cohort of mice was sacrificed after seven days of bleomycin administration, followed by bronchoalveolar lavage and determination of myeloperoxidase activity, lung edema and histopathology features. In the 21-day cohort, mortality was assessed daily, and surviving mice were sacrificed followed by the above analyses together with immunohistochemical localization of CD8, tumor necrosis factor- $\hat{\pm}$ , CD4, interleukin-1 $\beta$ , transforming growth factor- $\beta$ , inducible nitric oxide synthase and basic fibroblast growth factor. Compared to bleomycin-treated mice, animals that received also **PEA-um®** (3 or 10 mg/kg) had significantly decreased weight loss, mortality, inflammation (edema and leukocyte lung infiltration), lung damage at the histological level, and lung fibrosis (soluble collagen accumulation) at 7 and 21 days. **PEA-um®** (1 mg/kg) did not significantly inhibit the inflammation response and lung fibrosis. This study demonstrates that that **PEA-um®** (3 and 10 mg/kg) reduces the extent of lung inflammation in a mouse model of idiopathic pulmonary fibrosis.