

## Effects of palmitoylethanolamide and luteolin in an animal model of anxiety/depression

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The antidepressant effect of a compound formed by co-ultramicroemulsified palmitoylethanolamide (PEA) and luteolin (PEA+luteolin) was investigated in a mouse model of anxiety/depressive-like behavior. 129Sv/Ev mice were subjected to 6 weeks of corticosterone administration, and then behavior, neurogenesis, neuroplasticity, neurotrophic and apoptotic proteins expression were evaluated. The effect of PEA+luteolin compound treatment (1mg/kg, i.p.), on depression-like behaviour was assessed using different paradigms such as open field, novelty suppressed feeding, forced swim test and elevated plus maze. In particular in the open field, novelty suppressed feeding and elevated plus maze the time spent in the open arm was employed as an indicator of anxiety; forced swim test was used to evaluate the antidepressant capacity of PEA+luteolin on immobility time as an indicator of depression. Adult hippocampal neurogenesis and neuroplasticity were evaluated by immunohistochemical techniques; brain-derived neurotrophic factor and apoptotic protein (Bax and Bcl2) expression were studied by immunostaining and Western blot analysis. For the first time we demonstrated that PEA+luteolin compound exerts a significant antidepressant effect a low dose and may be considered as a novel therapeutic strategy in depression.