



**EFFECTS OF ACYLETHANOLAMIDES, ALONE OR IN COMBINATION, ON INFLAMMATORY AND METABOLIC ALTERATIONS RELATED TO OBESITY**

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Over the past three decades, the prevalence of obesity has rapidly increased worldwide. During obesity, a state of chronic inflammation occurs as well as the development of multiple co-morbidities increasing cardiovascular risk and mortality. Visceral adiposity and metabolic dysregulation lead to kidney or heart damage and fibrosis. Given the physiological interdependence of the two organs, this detrimental condition is called cardiorenal syndrome and can ultimately result in renal and/or cardiac failure.

N-acylethanolamines (NAEs) are non-canonical endocannabinoids, namely ethanolamides of long-chain fatty acids belonging to the large family of endogenous lipids which can exert their multiple pharmacological effects by binding different and specific receptors. Among these, oleylethanolamide (OEA), palmitoylethanolamide (PEA), stearoylethanolamide (SEA) and linoleylethanolamide (LEA) play key functional activities including the improvement of lipid metabolism, besides the well-known analgesic and/or anti-inflammatory effects.

This project aims to evaluate the beneficial effects of these NAEs, alone or in combination, in restoring glucose and lipid homeostasis compromised by obesity and limiting the development of obese phenotype and related complications, including cardio-renal syndrome.

To this purpose, mouse models of both genetic and nutritional obesity may be used, examining the modulation of mechanisms underlying the tissue specific-inflammatory process, and mitochondrial bioenergetics and function. Immortalized cell lines (hepatocytes, cardiomyocytes, and kidney cells) or different types of organoids will be used for assessing direct tissue effects and molecular mechanisms underlying the activity of NAEs, alone or in combination.

**References**

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