Title: Design and pharmacological evaluation of Ibuprofen amides derivatives as dual FAAH/COX inhibitors.

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Fatty acid amide hydrolase (FAAH) is a serine hydrolase enzyme responsible of the hydrolytic degradation of N-acylethanolamine endocannabinoids, such as the Arachidonoylethanolamide (anandamide, AEA), which it has been shown to alleviate pain and inflammation (1). In particular, the anti-nociceptive and anti-inflammatory effects of AEA could be enhanced by the simultaneous block of FAAH and COX enzymes (2). For this reason, several studies have been carried out in order to develop new FAAH/COX inhibitors (2). In 1997 it was reported that the NSAID ibuprofen inhibited FAAH, although with a modest potency (3), and successively the first dual inibhitor, the amide derivative of ibuprofen with a 2-amino-3-methylpyridine side chain (Ibu-AM5) was reported (4). -5). Benzylamides and piperazinoamides analogs of Ibuprofen have been also designed as less potent FAAH inhibitors than Ibu-AM5 (5). Here, I discuss the computational studies and the structure–activity relationships leading to the design, of novel Ibuprofen amide derivatives with a higher inhibition potency of FAAH and COX, which represent novel powerful anti-nociceptive agents.

References

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Biography

Dr. Federica Moraca graduated in Pharmacy in 2010 at the University "Magna Graecia" of Catanzaro (Italy), where she has also completed her Ph.D in Pharmaceutical Sciences in 2014 being mostly involved in the discovery of new

promising anticancer drugs. During her Ph.D, she spent one year in the prestigious laboratory of Prof. Michele Parrinello in Lugano, where she learnt about the computation of ligand/protein absolute binding free energy through Metadynamics. In 2018, she moved to University “Federico II” in Naples, where she is currently studying the drug design of novel profen analgesic derivatives as fatty acids amide hydrolase inhibitors.

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