



# pharmadvances

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Abstracts of

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DELLA SOCIETÀ ITALIANA  
DI FARMACOLOGIA –  
PROCEEDINGS**

**THE SCIENTIFIC  
VALUE AND  
APPROPRIATE USE  
OF DRUGS**



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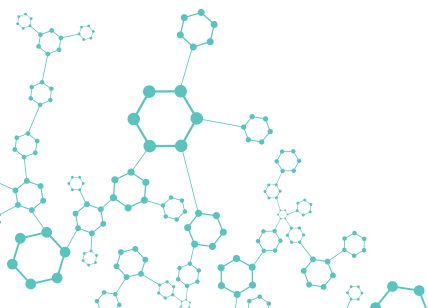
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astrocyte activation and other adverse effects as sedation, motor incoordination, anhedonia. Consistently, CL39 determine a significant, aversion-free antinociception in animal model

of acute and chronic pain; thus emerging as a promising candidate to be further investigated as innovative analgesic and anti-addiction therapeutic.

## KYNURENINE NEGATIVELY EXACERBATES THE THC EFFECTS ON TETRAD AND SENSORIMOTOR RESPONSES IN ADULT MICE

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**BACKGROUND:** The main psychoactive component of marijuana ( $\Delta$ -9-tetrahydrocannabinol, THC) and synthetic cannabinoids intake, is correlated with untoward physiological effects in vulnerable individuals (D'Souza et al., 2016). Thus, cannabinoids misuse could be considered as a relevant factor in precipitating and/or perpetuating psychosis in these subjects. It has been reported, in rats and monkey, that the reinforcing effects of THC can be reduced by increasing endogenous kynurenic acid (KYNA) levels (Justinova et al., 2013). KYNA, a neuroactive metabolite deriving from tryptophan degradation (Schwarcz et al., 2012). Several studies suggest a pathophysiologically relevant association between increased brain KYNA levels and cognitive dysfunctions

in individuals with schizophrenia (Wonodi and Schwarcz, 2010; Sathyasaikumar et al., 2011).

**METHODS:** Male ICR (CD-1®) mice (25-30 g body weight) were treated with THC (30 mg/kg; i.p.) and kynurenine (20 mg/kg, i.p.), alone or in combination. Following the drug administration, body temperature, acute mechanical and thermal analgesia, motor activity sensorimotor responses (to visual, acoustic and tactile stimulation) were evaluated. Furthermore, brain levels of KYNA were measured 1 and 4 hours after kynurenine injection.

**RESULTS:** Brain KYNA levels were significantly increased 1 hour, but not 4 hours, after kynurenine administration. The administration of kynurenine, amplified the THC-induced impairment of sensorimotor responses. In particular, kynurenine increased the THC-induced reduction in the visual placing response, acoustic response and tactile response (vibrissae, corneal and pinna reflexes). Furthermore, by using the "tetrad paradigm for screening cannabinoid-like effects" it has been observed that kynurenine significantly increased THC-induced motor activity reduction (as evaluated by the bar test, drag test and rotarod test) and hypothermia (core and surface body temperature), but not THC-induced analgesia.

**CONCLUSIONS:** Overall, the present data indicate that increased brain KYNA levels exacerbate "tetrad" and sensorimotor responses induced by the acute administration of THC. This confirms the existence of a cross-talk between the KP and endocannabinoid system which could be involved either in the psychotropic properties of THC or in the etiopathogenesis of schizophrenia.