Involvement of serotonergic system in the antidepressant-like effect of a novel curcumin derivative CUD003 in mice

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Curcumin, a natural polyphenol compound which is contained in turmeric (Curcuma longa), has been reported to exert antidepressant-like effect in various animal models of depression. In this study, we investigated the antidepressant-like effect of a novel synthetic derivate of curcumin CUD003 and the possible mechanism of its action in mice using behavioral tests. Treatment with CUD003 (3 mg/kg, p.o.) decreased the immobility time in the forced swim test (FST) without affecting locomotor activity in the open field test. CUD003 was more effective than curcumin in the FST. The antidepressant-like effect of CUD003 was abolished by the pretreatment with p-chlorophenylalanine (a tryptophan hydroxylase inhibitor), WAY-100635 (a selective 5-HT_{1A} antagonist), ketanserin (a 5-$HT_{2A/C}$ antagonist), or ondansetron (a selective 5-HT_3 antagonist). Moreover, social defeat stress-induced depressive behaviors as evidenced by an increased immobility time in the FST, and a decreased grooming time in the sucrose splash test were attenuated by the treatment of CUD003. These results suggest that CUD003 has more potent antidepressant-like effect than curcumin, which may be mediated by the serotonergic signaling through 5-HT_{1A}, 5-$HT_{2A/2C}$ and 5-HT_3 receptors.