

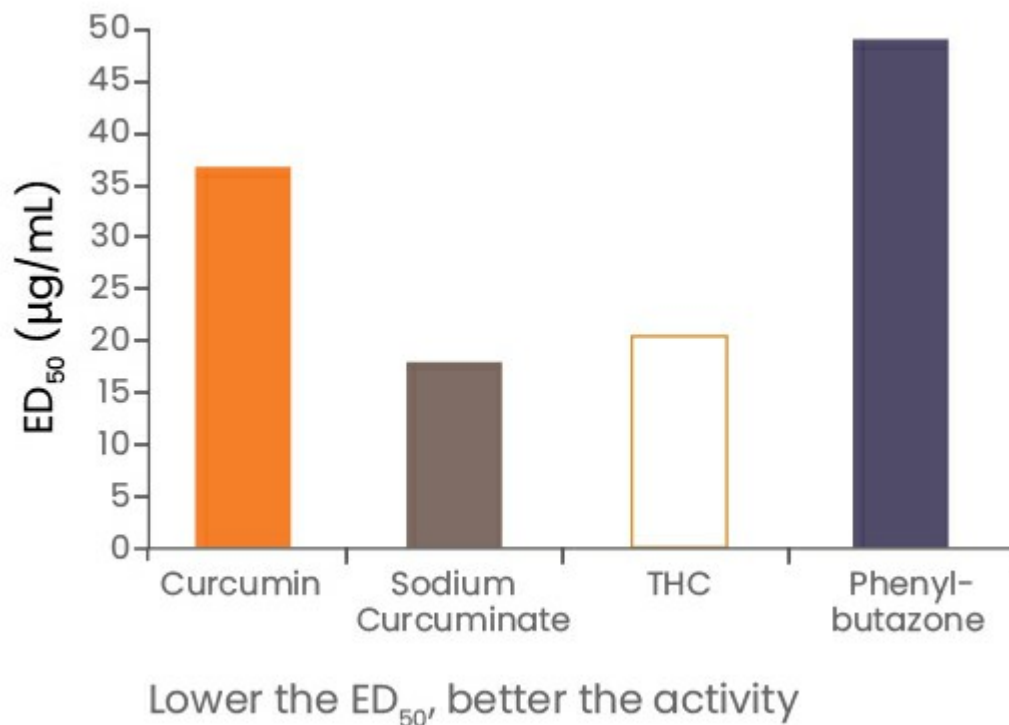


Anti-inflammatory potential

Tetrahydrocurcumin (THC) shows a potent anti-inflammatory activity similar to its parent compound – curcumin. In one of the studies, curcumin, sodium curcumin (NaC) and THC were evaluated for their anti-inflammatory activity in carrageenan-induced paw edema model in rats. The results have shown that THC was effective at almost half the dose of curcumin itself. The anti-inflammatory potency of the curcumin, THC, NaC and phenylbutazone (PB) were found to be in following order (Majeed *et al.*, 1995).

In a study on neuro-inflammation in (chronic as well as acute) animal models using Curcumin C3 Reduct®, (Begum *et al.*, 2008) reported for the first time that THC showed efficacy in preventing CNS oxidative damage.

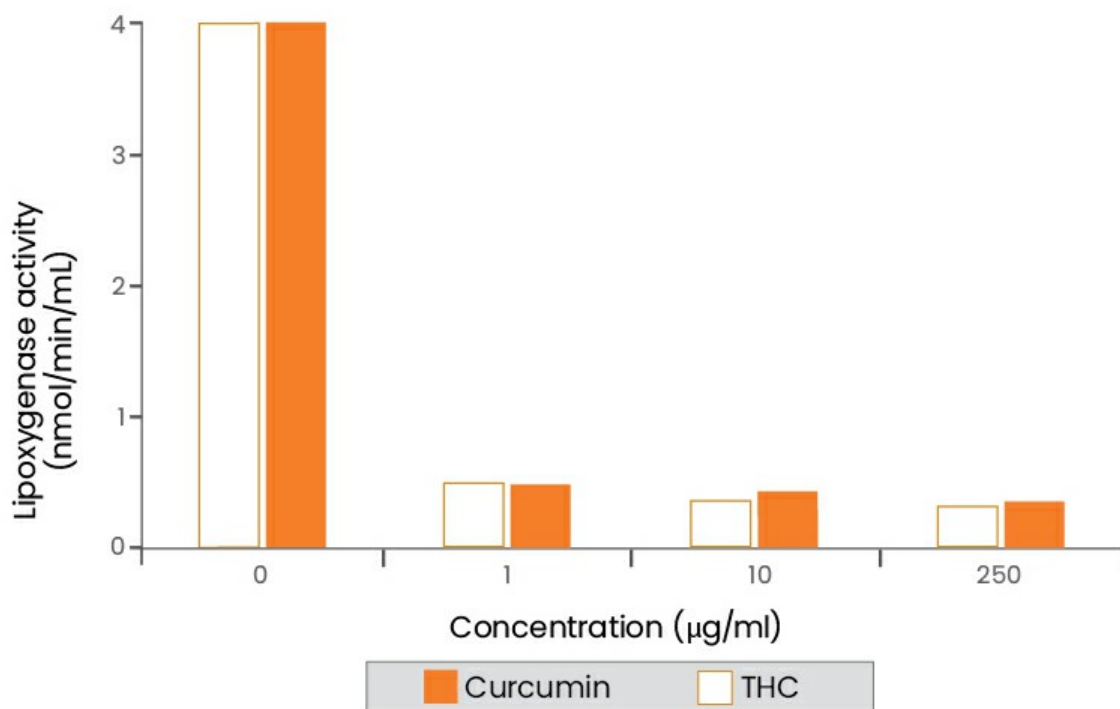
They showed that THC inhibited the brain inflammatory marker IL-1 β better than curcumin (EC_{50} = 1.286 μ M vs. 1.722 μ M, respectively) in the acute inflammation model. Similar efficacy was found in chronic model also.



Effect of curcumin derivatives and phenylbutazone on carrageenan-induced paw edema in rats
(Adapted from Itokawa *et al.*, 2008)

The THC was more effective than curcumin in lowering the brain lipid peroxidation products namely F2 isoprostanes with EC₅₀ value of 0.501 µM compared to curcumin's 1.067 µM.

In a recent study, Novaes *et al.*, (2017) investigated the anti-inflammatory properties of curcumin and THC in rats upon oral administration. Both curcumin and THC inhibited lipoxygenase activity at concentrations as low as 1 µg/mL compared to the untreated control.



The inhibition of lipoxigenase by THC and curcumin displayed as lipoxigenase activity in nmol/min/mL at the listed concentrations of curcumin.

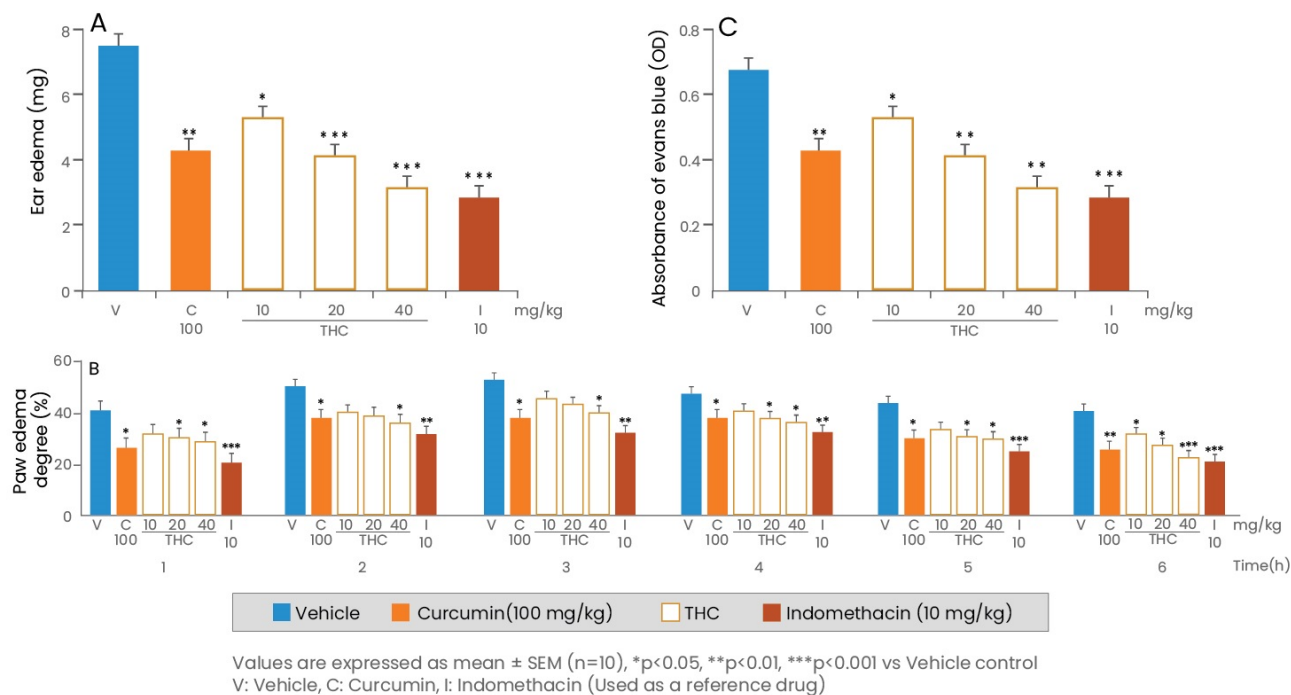
Anti-inflammatory effects of THC and curcumin

(Adapted from Novaes *et al.*, 2017)

Recently, Zhang *et al.*, (2018) compared the *in vivo* anti-inflammatory effects of THC and curcumin using three common inflammatory animal models, namely

- (→) Xylene-induced ear edema
- (→) Carrageenan-induced paw edema
- (→) Acetic acid-provoked vascular permeability

The results indicated that THC in a dose-dependent manner suppressed the formation of ear edema induced by xylene, paw edema provoked by carrageenan and inhibited the Evans blue dye leakage in peritoneal cavity elicited by acetic acid.



Effect of THC on (A) Xylene-induced ear edema, (B) Carrageenan-induced paw edema and (C) Acetic acid-induced vascular permeability in mice
(Adapted from Zhang *et al.*, 2018)

The authors also describe that THC possessed a better safety profile than curcumin with an LD₅₀ value greater than 10,000 mg/kg. Also, THC suppressed the tissue levels of IL-1 β , IL-6, TNF- α and PGE₂, indicating that THC could alleviate acute inflammation by mitigating the production of pro-inflammatory mediators. In addition, THC significantly inhibited the expression of COX-2, while it exerted no obvious influence on the expression of COX-1. Importantly, THC showed superior effects in inhibiting the levels of pro-inflammatory mediators and suppressing the expression of COX-2, when compared with curcumin. The results suggest that THC might possess a better effect than curcumin in selectively inhibiting the COX-2 activity.

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