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Comparison between the Analgesic effects of heated and unheated flower hydroalcoholic extract of female *Cannabis sativa* in rats.

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Purpose: Today production and applications of anti-nociceptive medicines have been attended to cure different kinds of pains with fewer side effects, especially chronic pains due to cancers and MS. This investigation designed to compare the effects of heated and unheated flower hydroalcoholic extract on thermal and chemical pain.

Methods: Heated and unheated extracts of flower top of female cannabis plant were prepared. A solution of Saline and DMSO were used as vehicle. 28 male wistar rats weighting 200-250g in four groups including: control, sham, heated flower extract and unheated flower extract (i.p. injected with 50 mg/kg) were tested by Tail flick to measure thermal pain threshold and formalin test for pain sensation as score of pain.

Results: Heated extract showed more anti-nociceptive effects on pain in acute phase of formalin test ($p < 0.05$) and unheated extract showed more effects on pain in inflammatory phase ($p < 0.05$) of formalin test. None of the extracts showed anti-nociceptive effects in thermal pain at Tail flick test.

Conclusion: While cannabinoids are heated they turn to decarboxylated form. Cannabinoid receptors (CB1 and CB2) and noncannabinoid receptors TRPVs, present in the pain pathways and central nervous system, have more affinity to decarboxylated form, so maybe this form significantly decreased the acute phase of pain. Carboxylated cannabinoids in unheated extract perhaps act as non-steroid anti-inflammatory drugs which have a carboxyl group and have strong inhibitory effects on cyclooxygenase 1 and 2, so it make them possibly able to decrease pain in inflammatory phase of formalin test.

Keywords: Pain, Cannabinoids, female, *Cannabis sativa*, flower top