Xylopic acid (XA) is an isolate of a Ghanaian traditional spice, Xylopia aethiopica. This spice is used locally for the treatment of various conditions including pain - rheumatism, headache, neuralgia and colic pain. In this study, xylopic acid was investigated for the possibility of causing tolerance or dependence when administered alone or in combination with morphine.

Adult male Sprague-Dawley rats (200-250 g) received xylopic acid (10-100 mg/kg, p.o.) or morphine (10 mg/kg, i.p.) twice daily for 14 days to induce analgesic tolerance. To develop dependence, another group of rats were given escalating doses of xylopic acid (10-300 mg/kg) or morphine (2.5-40 mg/kg, i.p.) for 7 days. To determine the effect of xylopic acid on the development of morphine tolerance and dependence, xylopic acid (10-100 mg/kg) was administrated orally before morphine. The tail-withdrawal assay and naloxone precipitation test were used to assess the extent of tolerance and dependence, respectively.

Rats that received chronic morphine administration displayed tolerance to its analgesic effect and developed morphine dependence. Xylopic acid (10-100 mg/kg) significantly (p<0.001) prevented the development of morphine tolerance. Additionally, xylopic acid inhibited some naloxone-induced withdrawal signs (weight loss, diarrhoea and jumping). Chronic administration of xylopic acid did not produce tolerance or dependence. The inhibitory effect of XA on withdrawal jumps in morphine-dependent mice was blocked by pretreatment with α2-adrenoceptor antagonist, yohimbine, but not by α1-adrenoceptor antagonist, prazosin. The membrane expression of α2A-adrenoceptors in the brainstem was decreased in morphine withdrawn animals. The reduction was prevented by repeated administration of XA. These results suggest that XA inhibits morphine tolerance and dependence, and this is due partly to the prevention of the decreased membrane expression of the α2A-adrenoceptor in the brainstem.