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The activation of CXCR1/2 has been implicated in the genesis of inflammatory and postoperative pain. Here, we investigated a novel orally acting allosteric inhibitor of CXCR1/2 (DF2755A) and evaluated its antinociceptive effect in several models of inflammatory and post-operatory pain. DF2755A was tested in vitro for efficacy in the chemotaxis assay, selectivity and toxicity. In vivo, C57Bl/6 mice were treated orally with DF2755A and the following experiments were performed: pharmacokinetic profile; inflammatory hyperalgesia models using electronic pressure meter test; neutrophil migration assay assessed by myeloperoxidase assay. DF2755A selectively inhibited neutrophil chemotaxis induced by CXCR1/2 ligands without effect on CXCL8 binding to neutrophils. A single mutation of the allosteric site at CXCR1 abrogated the inhibitory effect of DF2755A on CXCL8-induced chemotaxis. DF2755A given orally was well absorbed (88.2%), and it was able to reduce, in a dose (3-30mg/kg)-dependent manner, inflammatory hyperalgesia induced by carrageenan, LPS and CXCL1/KC as well as neutrophil recruitment and IL-1β production. In addition, DF2755A was able to reduce post-incisional nociception. Therapeutic treatment with DF2755A reduced CFA-induced inflammatory hyperalgesia even when injected intrathecally. The present results indicate that DF2755A is a novel selective allosteric inhibitor of CXCR1/2 with a favorable oral pharmacokinetic profile. Furthermore, the results might suggest that DF2755A might be a candidate of a novel therapeutic option to control inflammatory and post-operative pain.