A055 1-(2,3,4-trimethoxyphenyl)-3-(3-(2-chloroquinolinyl)-2-propen-1-one, a chalcone derivative with immunosuppressive and anti-inflammatory effects

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Chalcones are natural products which have been reported to possess anti-inflammatory and antioxidant properties (1, 2). Recently, a series of 2-chloroquinolinyl chalcone derivatives have been studied as inhibitors of human neutrophil functions and modulators of NO and prostaglandin E_2 production *in vitro* and *in vivo* (3) (4). In the present study, the synthetic chalcone derivative 1-(2,3,4-trimethoxyphenyl)-3-(3-(2-chloroquinolinyl)-2-propen-1-one (TQ) was evaluated for its immunomodulatory and anti-inflammatory efficacy *in vitro* and *in vivo*. TQ inhibited elastase release (IC_{50} 1.4 μM), superoxide generation (IC_{50} 5.9 μM) and leukotriene B_4 production (58% at 10 μM) in human neutrophils stimulated with cytochalasin B/fMLP, TPA and ionophore A23187, respectively. This compound also inhibited in a concentration-dependent manner, the PHA-induced ^3H thymidine incorporation into human lymphocytes (IC_{50} 1.4 μM). In RAW 264.7 macrophages stimulated with lipopolysaccharide, TQ reduced the production of NO (IC_{50} 1.1 μM) and prostaglandin E_2 (IC_{50} 6.6 μM). Oral administration of TQ (20 mg/kg) in the 24h zymosan-stimulated mouse air pouch model, inhibited cell migration, as well as NO and prostaglandin E_2 levels in exudates. In the delayed-type hypersensitivity response to 2,4-dinitrofluorobenzene in mice, TQ significantly inhibited ear swelling and leucocyte infiltration determined as myeloperoxidase activity. In addition, this compound displayed analgesic effects on the phenylbenzoquinone induced writhings as well as the early and the late phases of the nociceptive response to formalin in mice. Our findings indicate the potential interest of TQ in the treatment of some immune and inflammatory conditions.

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A056 Identification of a 5-LOX inhibitor from *Xanthium spinosum* L.

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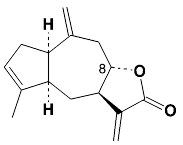
Extracts of four herbal medicines, namely *Acanthus mollis* L. (Acanthaceae), *Achillea ligustica* All. (Asteraceae), *Echeveria pumila* Hortex Baker var. *glauca* (Crassulaceae), and *Xanthium spinosum* L. (Asteraceae), were screened for their inhibitory effect on 5-lipoxygenase (5-LOX) activity.

The production of LTB_4 by intact cells in presence of the extracts and/or their constituents was measured by HPLC-DAD. This metabolite was released by rat peritoneal polymorphonuclear leukocytes from endogenous arachidonic acid following the addition of Ca^{2+} and ionophore A23187 (1). The extracts and products were not cytotoxic at the assayed doses when tested in the MTT assay.



Methanol extracts of *Achillea ligustica* and *Xanthium spinosum* inhibited LTB_4 release by nearly 100% when tested at 200 μg/ml. Their MeOH extracts were fractionated with solvents of increasing polarity and tested for their *in vitro* activity. The hexane fraction of *X. spinosum* showed the strongest activity, with a IC_{50} = 5.6 μg/ml (r = 0.993). It was further subjected to solid-phase extraction and a sesquiterpene lactone was isolated and identified as 3,10(14),11(13)-guaiatrien-12,8-olide (ziniolide) by spectroscopy. Ziniolide reduced LTB_4 release, with an IC_{50} value of 69 μM (r = 0.9768). These results are in agreement with the previously reported *in vivo* and *in vitro* anti-inflammatory activity of related 12,8-guaianolides (2).

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