BMC Pharmacology

BioMed Central

Research article

Tetrandrine and thapsigargin release arachidonic acid from cells in culture and stimulate prostacyclin production in rat liver cells, but may do so by different pathways

Lawrence Levine*

Address: Department of Biochemistry, Brandeis University, Waltham, MA 02454, USA

Email: Lawrence Levine* - llevine@brandeis.edu

* Corresponding author

Published: 24 June 2005

BMC Pharmacology 2005, **5**:12 doi:10.1186/1471-2210-5-12

Received: 26 January 2005

Accepted: 24 June 2005

This article is available from: http://www.biomedcentral.com/1471-2210/5/12

Abstract

Background: Tetrandrine inhibits tumor cell proliferation and demonstrates chemoprevention in cancer models. Speculation on the association between its effects on K^+ and Ca^{2+} channels and cancer chemoprevention has been made. Thapsigargin also affects K^+ and Ca^{2+} conductance. Thapsigargin, however, is a weak tumor promoter in the two-stage model of mouse skin carcinogenesis, yet it can induce apoptosis in androgen-independent prostatic cancer cells. I have postulated that arachidonic acid release from cells in culture is associated with cancer chemoprevention. The effects of tetrandrine and thapsigargin on arachidonic acid release from human colon carcinoma and rat liver cells and prostacyclin production by rat liver cells are compared in the current studies.

Results: Tetrandrine and thapsigargin stimulate arachidonic acid release from human colon carcinoma and rat liver cells and prostacyclin production in rat liver cells. The stimulation by tetrandrine is not affected by incubation with actinomycin D, 100 mM KCl, the $[Ca^{2+}]_i$ chelator, 1,2-*bis* (*o*-amino-5-fluorophenoxy) ethane-*N,N,N',N'*,-tetraacetic acid tetraacetoxymethylester (BAPTA/AM) or in the absence of extracellular Ca^{2+}. In contrast, stimulation by thapsigargin *is* inhibited by incubation with actinomycin D, 100 mM KCl, BAPTA/AM or in the absence of extracellular Ca^{2+}.

Conclusion: Both tetrandrine and thapsigargin stimulate arachidonic acid release, but based on the different results obtained in the presence of actinomycin D, the $[Ca^{2+}]_i$ chelator, 100 mM KCl and in the absence of extracellular Ca^{2+}, the mechanisms leading to this release and pathways leading to apoptosis and/or cancer chemoprevention may be different. Stimulations by tetrandrine may be mediated by activation of a secretory phospholipase A_2, whereas thapsigargin's stimulations may be mediated by the cytoplasmic Ca^{2+}-dependent phospholipase A_2.

Background

Tetrandrine (TET), a bisbenzylisoquinoline (Fig. 1a), isolated from the root of the plant *Stephania tetrandra* has a number of potential medicinal properties. These include blockage of voltage-gated Ca^{2+} channels [1], large-conductance Ca^{2+} activated K^+ (BK) channels, and intracellular Ca^{2+} pumps [1-6]. TET also has anti-inflammatory [2,7] and anti-cancer activities [8,9]. TET stimulates