

Anti-allergic activity of compounds from *Kaempferia parviflora*

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Abstract

Kaempferia parviflora is one of the plants in the Zingiberaceae family, locally known in Thai as kra-chai-dam. In Thai traditional medicine, the decoction of *Kaempferia parviflora* powder with alcohol has been reported to cure allergy, asthma, impotence, gout, diarrhea, dysentery, peptic ulcer and diabetes. Therefore, the present study aimed to investigate anti-allergic substances from this plant. Bioassay-guided fractionation led to the isolation of seven methoxyflavone derivatives (1-7) from *Kaempferia parviflora* extract and they were identified on the basis of spectroscopic methods. Among the compounds tested, 5-hydroxy-3,7,3',4'-tetramethoxyflavone (5) possessed the highest anti-allergic activity against antigen-induced beta-hexosaminidase release as a marker of degranulation in RBL-2H3 cells with an IC(50) value of 8.0 microM, followed by 5-hydroxy-7-methoxyflavone (2, IC(50)=20.6 microM) and 5-hydroxy-7,4'-dimethoxyflavone (4, IC(50)=26.0 microM), whereas others showed moderate activities (IC(50)=37.5-66.5 microM). Structure-activity trends of 7-methoxyflavone derivatives on anti-allergic activity can be summarized as follows: (1) substitution with vicinal methoxyl groups at positions 3' and 4' conferred higher activity than only one methoxylation, (2) methoxylation at position 3 reduced activity and (3) methoxylation at position 5 showed higher activity than hydroxylation. Compounds 2, 4 and 5 were also determined for their mechanisms on ionomycin-induced beta-hexosaminidase release. The results indicated that the mechanism on inhibition of cell degranulation of compounds 2 and 5 mainly involve the inhibition of Ca(2+) influx to the cells, whereas that of 4 may be partly due to this inhibition. In regards to the active constituents for anti-allergic activity of *Kaempferia parviflora*, 5-hydroxy-3,7,3',4'-tetramethoxyflavone (5), 5-hydroxy-7-methoxyflavone (2) and 5-hydroxy-7,4'-dimethoxyflavone (4) are responsible for anti-allergic effect of this plant. The findings support the traditional use of *Kaempferia parviflora* rhizomes for treatment of allergy and allergy-related diseases.

Introduction

Kaempferia parviflora is one of the plants in the Zingiberaceae family, locally known in Thai as kra-chai-dam. The rhizome of this plant has been used for treatment of allergy, gastrointestinal disorders, fungal infection and impotence

(Pengcharoen, 2002). This plant has been known as Thai ginseng. *Kaempferia parviflora* has recently been reported to possess antimycobacterial, antiplasmodial (Yenjai et al., 2004), anti-peptic ulcer (Rujjanawate et al., 2005) and anti-viral protease effects (Sookkongwaree et al., 2006) as well as modulators of multidrug resistance in cancer cells (Patanasethanont et al., 2007). The wine preparation of this plant is increasingly used in Thailand as a tonic and as an aphrodisiac. In Thai traditional medicine, the decoction of *Kaempferia parviflora* powder with alcohol has been reported to cure allergy, asthma, impotence, gout, diarrhea, dysentery, peptic ulcer and diabetes. Previously, we reported anti-allergic effects of the selected Zingiberaceous plants using RBL-2H3 cell line model (Tewtrakul and Subhadhirasakul, 2007). It was found that the rhizome of *Kaempferia parviflora* exhibited the most potent activity ($IC_{50} = 10.9 \mu\text{g/ml}$). The present study therefore aimed to investigate the active principles of this plant, which are responsible for anti-allergic effect.

Section snippets

Reagents

Minimum Essential Medium Eagle (MEM) and anti-DNP-IgE (Monoclonal anti-DNP) were purchased from Sigma; fetal calf serum (FCS) was purchased from Gibco; dinitrophenylated bovine serum albumin was prepared as described previously (Tada and Okumura, 1971). Other chemicals were obtained from Sigma. 24-well and 96-well plates were purchased from Nunc.

Plant materials

Kaempferia parviflora rhizomes, locally grown in Loei province, were bought from a Thai traditional drug store in Songkhla province, Thailand in the

Results and discussion

Bioassay-guided fractionation led to the isolation of seven methoxyflavone derivatives, the structures of these compounds are shown in Fig. 1. The effect of these compounds on anti-allergic activity indicated that 5-hydroxy-3,7,3',4'-tetramethoxyflavone (**5**) possessed the highest anti-allergic activity with an IC_{50} value of $8.0 \mu\text{M}$, followed by 5-hydroxy-7-methoxyflavone (**2**, $IC_{50} = 20.6 \mu\text{M}$) and 5-hydroxy-7,4'-dimethoxyflavone (**4**, $IC_{50} = 26.0 \mu\text{M}$), whereas others showed moderate activities ($IC_{50} = 37.5\text{--}66.5$

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