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Ardisia crispa roots inhibit cyclooxygenase and suppress angiogenesis

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Abstract

Background: In our previous studies conducted on *Ardisia crispa* roots, it was shown that *Ardisia crispa* root inhibited inflammation-induced angiogenesis *in vivo*. The present study was conducted to identify whether the anti-angiogenic properties of *Ardisia crispa* roots was partly due to either cyclooxygenase (COX) or/and lipoxygenase (LOX) activity inhibition in separate in vitro studies.

Methods: Benzoquinonoid fraction (BQ) was isolated from hexane extract by column chromatography, and later analyzed by using gas chromatography–mass spectrometry (GC-MS). Anti-angiogenic effect was studied on mouse sponge implantation assay. *Ardisia crispa* ethanolic rich fraction (ACRH), quinone-rich fraction (QRF) and BQ were screened for COX assay to evaluate their selectivity towards two isoforms (COX-1 and COX-2), The experiment on soy lipoxygenase (LOX) inhibitory assay was also performed to determine the inhibitory effect of ACRH, QRF and BQ on soy LOX.

Results: BQ was confirmed to consist of 2-methoxy-6-undecyl-1,4-benzoquinone, when compared with previous data. Antiangiogenesis study exhibited a reduction of mean vascular density (MVD) in both ACRH and QRF, compared to control. In vitro study showed that both ACRH and QRF inhibited both COX-1 and COX-2, despite COX-2 inhibition being slightly higher than COX-1 in BQ. On the other hand, both ACRH and QRF were shown to have poor LOX inhibitory activity, but not BQ.

Conclusions: In conclusion, ACRH and QRF might possibly exhibit its anti-angiogenic effect by inhibiting cyclooxygenase. However, both of them were shown to possess poor LOX inhibitory activity. On the other hand, BQ displayed selectivity to COX-2 inhibitory property as well as LOX inhibitory effect.

Keywords: *Ardisia crispa*, COX inhibitor, LOX inhibitor, Soy lipoxygenase assay

Background

Angiogenesis is a fundamental process of new capillary formation which is physiologically important in wound healing and reproduction [1]. Under normal physiologic circumstances, the body controls angiogenesis by producing a precise balance of pro-angiogenic and anti-angiogenic factors [2]. The imbalance of these factors will result in excessive or insufficient angiogenesis. Excessive angiogenesis for instance, contributes to initiation, progression, and prognosis of numerous diseases, such as cancer, arthritis, and cardiovascular diseases [3].

Cyclooxygenase (COX), also known as prostaglandin endoperoxide synthase, is a rate-limiting enzyme that catalyzes the transformation of arachidonic acid into prostaglandin H_2 (PGH_2), which eventually leads to the biosynthesis of other prostanoids (i.e. prostaglandins, prostacyclin and thromboxane) [4]. There are two isozymes identified in the COX family, which are COX-1 and COX-2. Whilst the COX-1 expression is constitutive in most tissue and exhibit physiological roles in the body, COX-2 expression is inducible upon a wide spectrum of stimuli, such as inflammatory responses [5].

Whilst COX-2 is important in catalyzing prostaglandin biosynthesis during inflammation, it also contributes to angiogenesis by upregulating VEGF level [6]. COX-2 is shown to be induced not only in the endothelial cells

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