

Research Article

Cardiovascular Activity of Labdane Diterpenes from *Andrographis paniculata* in Isolated Rat Hearts

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The dichloromethane (DCM) extract of *Andrographis paniculata* Nees was tested for cardiovascular activity. The extract significantly reduced coronary perfusion pressure by up to 24.5 ± 3.0 mm Hg at a 3 mg dose and also reduced heart rate by up to 49.5 ± 11.4 beats/minute at this dose. Five labdane diterpenes, 14-deoxy-12-hydroxyandrographolide (1), 14-deoxy-11,12-didehydroandrographolide (2), 14-deoxyandrographolide (3), andrographolide (4), and neoandrographolide (5), were isolated from the aerial parts of this medicinal plant. Bioassay-guided studies using animal model showed that compounds (2) and (3) were responsible for the coronary vasodilatation. This study also showed that andrographolide (4), the major labdane diterpene in this plant, has minimal effects on the heart.

1. Introduction

Andrographis paniculata Nees, family Acanthaceae, has been used since time immemorial in Ayurvedic medicine, mainly for liver problems and dysentery [1]. The plant is also known as "Indian Echinacea" and "King of bitter." Phytochemical screening on this herbal plant showed that it contains a lot of flavonoids and terpenoids while moderate in alkaloids and tannins compounds [2]. This plant has been featured in at least 26 Ayurvedic formulae, whereas in traditional Chinese medicine, *A. paniculata* is an important "cold property". In Malaysia, *A. paniculata* is more commonly known as "hempedu bumi" and is widely used in traditional medicine, especially for the treatment of cardiovascular disorders.

Previous researches have shown that *A. paniculata* extract and its labdane diterpenes have a broad range of pharmacological effects such as the ability to inhibit replication of the HIV virus [3, 4], prevent common cold [5–7], antimalarial [8], prevent diarrhea [9], antibacterial [10], anti-inflammatory [11–13], antihyperglycemic effect [14, 15],

suppress various cancer cells [16–18], and antifertility and pregnancy-terminating effects [19].

In earlier cardiovascular studies, *A. paniculata* extracts significantly reduced atherosclerotic artery stenosis and lowered restenosis rates after angioplasty in rabbits [20] decreases platelet aggregation *in vitro* [21] and were reported to be antihypertensive in rats [22]. Nevertheless, the scientific basis for the use of *A. paniculata* in treating "heart problems" is still unclear. To our knowledge, its direct effects on the isolated heart of an animal model are not known. Therefore, in this study, the dichloromethane (DCM) extract of *A. paniculata* was tested against coronary vessels, cardiac muscle contractility, and heart rate in Langendorff perfused rat hearts. Our preliminary study showed that the dichloromethane extract caused coronary vasodilatation, reduced heart rate while not affecting the cardiac contractility of isolated perfused rat hearts. Further isolation work was performed on the dichloromethane extract in order to identify the active compound(s) responsible for the cardiovascular activity observed.