In vitro vasoactivity of novel natural leads from Vietnamese medicinal plants

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Vietnam, a tropical Southeast Asian country, contains more than 10,000 vascular plants belonging to hundreds of families (Banskota *et al*., 2003). More than 4,000 plants have been popularly used so far in its unique traditional medicine system. Natural products continue to play a highly significant role in drug discovery and development processes (Kingston, 2011). Therefore, extracts and pure compounds isolated from Vietnamese plants belonging to the *Rutaceae* family were assessed for their effects on isolated vascular preparations in the search for novel chemical scaffolds leading to potential antihypertensive agents. In fact, the *Rutaceae* family comprises about 30 genera, and species such as *Clausena, Glycosmis*, *Micromelum*, *Zanthoxylum*, and *Murraya* are widely distributed throughout the country. *Murraya* species, considered to have potential therapeutic applications (Nhu *et al*., 2004), has led to the isolation and characterization of indol akaloids (Wu *et al*., 1989), polymethoxylated flavonoids (Zhang *et al*., 2011), essential oils (Rout *et al*., 2010), and a number of coumarins (Ito *et al.,* 1987; Raj *et al.*, 1976; Wu, 1988).
Whole-cell L-type Ca^{2+} currents were recorded in single tail artery or aorta myocytes, and contractile responses were measured from aorta rings.
The methanol extract of *Murraya paniculata* leaves relaxed more markedly rat aorta rings stimulated with 60 mM K^+ rather than with phenylephrine, the presence of endothelium further decreasing its spasmolytic activity. Two coumarins were isolated from the extract: the novel kimcuongin, and the already known murracarpin. Both compounds showed vasorelaxing activity with IC_{50} values of 37.7 and 139.3 μM respectively.
A new sulphur containing indole alkaloid, N-demethylglypetelotine, along with two known compounds, glypetelotine and the carbazol alkaloid murrayafoline A, were isolated from the leaves of *Glycosmis petelotii* Guilt and from the dried powdered roots of *Glycosmis stenocarpa*. The vasorelaxing effect of glypetelotine was more marked on aorta rings stimulated with phenylephrine (IC_{50} values of 20 μM). The presence of endothelium reduced murrayafoline A vasodilatory potency. The vasorelaxing effect of glypetelotine was more marked on rings stimulated with 25/30 mM than with 60 mM K^+. At low concentrations (< 10 μg/ml), murrayafoline A increased the response of the preparations to both phenylephrine and 30 mM K^+. All drugs but murrayafoline A, reduced significantly the Ca^{2+}-induced contraction in rings depolarized with high K^+. Phenylephrine-stimulated influx of extracellular Ca^{2+} was significantly inhibited when tissues were pre-treated with N-demethylglypetelotine and murrayafoline A. In single vascular myocytes, murrayafoline A stimulated vascular L-type Ca^{2+} channel currents, whereas glypetelotine and N-demethylglypetelotine antagonised it.
In conclusion Vietnamese medicinal plants represent a rich source of novel vasoactive agents able to modulate L-type Ca^{2+} channel currents.

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