Vasorelaxant effect of isoquinoline derivatives from two species of *Popowia perakensis* and *Phaeanthus crassipetalus* on rat aortic artery

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**Abstract** Five bisbenzyl isoquinolines (1–5), three benzyl isoquinolines (6–8), four isoquinoline alkaloids (9–12), and two unclassified compounds (13 and 14) from *Popowia perakensis* and *Phaeanthus crassipetalus* were evaluated for their vasorelaxant effect on rat aortic arteries. In aortic rings pre-contracted with phenylephrine (PE, 0.3 μM), some of the bisbenzyl isoquinoline alkaloids, benzyl isoquinoline alkaloids, and isoquinoline alkaloids showed clearly vasorelaxant effects at 30 μM. The action of (−)-limacine (4) was deduced to be mediated through the increased release of NO from endothelial cells, and that of pecrassipine A (7) and backebergine (12) partly mediated by NO release. Further, the action of pecrassipine A (7) and backebergine (12) may be attributed to their inhibition of the voltage-dependent Ca²⁺ channel and receptor-operated Ca²⁺ channel.

**Keywords** *Popowia perakensis* · *Phaeanthus crassipetalus* · Vasorelaxant effect · Rat aortic artery · Isoquinoline alkaloids

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**Introduction**

Vasodilators are useful for treatment of cerebral vasospasm and hypertension, and for improvement of peripheral circulation. Several endothelium-dependent vasodilators, such as Bradykinin, acetylcholine, and histamine, have been reported to elevate Ca²⁺ levels in endothelial cells and activate NO release, leading to vasorelaxation [1, 2]. On the other hand, contractile response in smooth muscle is caused by Ca²⁺ influx through the voltage-dependent Ca²⁺ channel (VDC) and/or receptor-operated Ca²⁺ channel (ROC) [3]. The endothelium-independent vasodilators, such as nicardipine, nifedipine, diltiazem, and verapamil, have been reported to inhibit VDC and lead to a decrease in the intracellular Ca²⁺ concentration in smooth muscle, leading to vasorelaxation [3].

Two genera have been reported to be rich sources of alkaloids [4–9]. The genus *Popowia* (Annonaceae) is widely distributed in tropical Africa, Madagascar, South India, Burma, Siam, Indo, China, Malaysia, and Australia. In Malaysia, this genus is found in the dense forests of Maxwell’s Hill or Taiping Hill in Perak and Johore. There are seven species of *Popowia*; *P. pisocarpa* (P. ramosissima), *P. pauciflora*, *P. fusca*, *P. velutina*, *P. perakensis*, *P. tomentosa*, and *P. tomentosa* var. *cinerea* [10]. The genus *Phaeanthus* has 20 species distributed in South India, Lower Burma, Cambodia, Malay Peninsula to New Guinea and the Philippines [10]. In Malaysia, only two species are found; *P. crassipetalus* and *P. opthalmicus* [10, 11]. Fasihuddin et al. [11] have reported the occurrence of o xoaporphine and bisbenzylisoquinolines in *Phaeanthus crassipetalus* collected from Sabah (East Malaysia), which has been used by the locals in Sabah to treat wounds and high blood pressure.

During our search for bioactive natural products inducing vasorelaxation from medicinal plants [12–18], we...