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Research Paper

Effects of hippadine on the blood pressure and heart rate in male spontaneously hypertensive Wistar rats

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Chemical compounds studied in this article
Hippadine (PubChem CID: 100605)
Adrenaline (PubChem CID: 5816)
Atenolol (PubChem CID: 2249)
Prazosin hydrochloride (PubChem CID: 68546)
Pentobarbitone (PubChem CID: 4737)
Heparin (PubChem CID: 25244225)

ABSTRACT

Ethnopharmacological relevance: Hippadine is an alkaloid isolated from *Crinum macowanii*. *Crinum macowanii* is used in South Africa to treat oedema, 'heart disease', rheumatic fever, cancer and skin diseases, and belongs to the plant family Amaryllidaceae, assumed to have originated in the South African region. The aim of this study was to evaluate the effect of hippadine, an alkaloid extracted from *Crinum macowanii*, on the blood pressure (BP) and heart rate (HR) in anaesthetized male spontaneously hypertensive Wistar rats (SHR); and to find out if α_1 and/or β_1 adrenoceptors contribute to its effects.

Materials and methods: Hippadine (2.5–12.5 mg/kg), adrenaline (0.05–0.20 mg/kg), atenolol (0.5–40 mg/kg) and prazosin hydrochloride (100–500 μg/kg) were infused intravenously, and the BP and HR measured via a pressure transducer connecting the femoral artery and the PowerLab.

Adrenaline increased the systolic, diastolic and mean arterial BP, while hippadine, atenolol and prazosin respectively decreased the systolic, diastolic and mean arterial BP. Increases in HR were observed with both adrenaline and prazosin, while reductions in HR were observed with atenolol and hippadine. Infusion of adrenaline in rats pre-treated with atenolol (30 mg/kg), prazosin (400 μg/kg), and hippadine (10 mg/kg) led to similar increases in BP and HR in all groups. All changes in HR or BP were significant ($p < 0.05$) and dose dependent.

Conclusion: Hippadine decreases the BP and HR in SHR, and these effects may be due to α_1 and β_1 adrenoceptor inhibition.

1. Introduction

Hippadine is one of the alkaloids that have been isolated from *Crinum macowanii* (Boger and Wolkenberg, 2000; Nkanwen et al., 2009; Mugabo et al., 2012; Jin, 2013; Nair and van Staden, 2013) so far. *Crinum macowanii* has found extensive use in traditional medicines for the treatment of various illnesses such as oedema, gynaecological conditions, psychosis, wounds, rheumatic fever, cancer, skin diseases, and 'heart disease' (Duncan et al., 1999; Van Wyk et al., 2000; Van Wyk and Gericke, 2000; Elgorashi et al., 2001, 2002, 2003b; Van Wyk, 2011a, 2011b). *Crinum macowanii* belongs to the large plant family Amaryllidaceae which originates in the Southern African region, and has naturally been used extensively in the local traditional medicines in the region (Chattopadhyay et al., 1983; Boger and Wolkenberg, 2000; Koorbanally et al., 2000; Nair et al., 2000; Hiroya et al., 2004; Ganton and Kerr, 2005; Kissling et al., 2005; Mentzel et al., 2006; Nkanwen et al., 2009; Cheesman et al., 2012; Jin, 2013; Nair and van Staden, 2013, 2014). The medicinal properties of the family Amaryllidaceae are largely associated with the vast number of alkaloids that are produced by the plants in the family (Elgorashi et al., 2003a; Nkanwen et al., 2009; Cheesman et al., 2012; Refaat et al., 2012a, 2012b, 2012c, 2013a, 2013b; Nair and van Staden, 2013, 2014).

Recent scientific research has established the potency and selective inhibitory activity of galanthamine, an alkaloid obtained from the family Amaryllidaceae, against the enzyme acetylcholinesterase, an activity beneficial in the management of Alzheimer's disease. Pancratistatin is another alkaloid obtained from this family that has shown potent and cell line specific antiproliferative properties (Jensen et al., 2011; Nair and van Staden, 2013). Some other plants in this family, such as *Boophone disticha* and *Cyclamen purpurascens* have displayed novel, broad spectrum antibacterial activity (Cheesman et al., 2012) and may contain antibacterial agents which could be used in the treatment of typhoid fevers and urogenital infections respectively (Nkanwen et al., 2009). Some

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of the abundant alkaloids obtained from the family Amaryllidaceae are hypothesized to be responsible for various medicinal properties of the family (Chattopadhyay et al., 1983; Boger and Wolkenberg, 2000; Koorbanally et al., 2000; Nair et al., 2000; Elgorashi et al., 2003a; ; Osorio et al., 2010; Cheesman et al., 2012; Refaat et al., 2012a, 2012b, 2012c, 2013a, 2013bJin, 2013) and have shown cardiovascular activity (Mugabo et al., 2001; Andraws et al., 2005; Burger et al., 2009; Rostoff et al., 2010; Jayakumar and Sheu, 2011; Nair et al., 2011; Mugabo et al., 2012). Previously, we have reported positive inotropic effect, with no chronotropic effect (Mugabo et al., 2001) and negative inotropic and chronotropic effects (Mugabo et al., 2012) with crude extracts of the bulbs of *Crinum macowanii* and hippadine respectively, in isolated perfused rat hearts. Therefore, in this study we intend to determine the effects of hippadine on the blood pressure (BP) and heart rate (HR) in anaesthetized spontaneously hypertensive male Wistar rats (SHR) and to find out whether adrenoceptors contribute to this.

2. Materials and methods

2.1. Study design

The study was designed as an experimental model investigating the effects of the unknown drug (hippadine) and that of the standard drugs (atenolol or prazosin) on the BP and HR in male SHR.

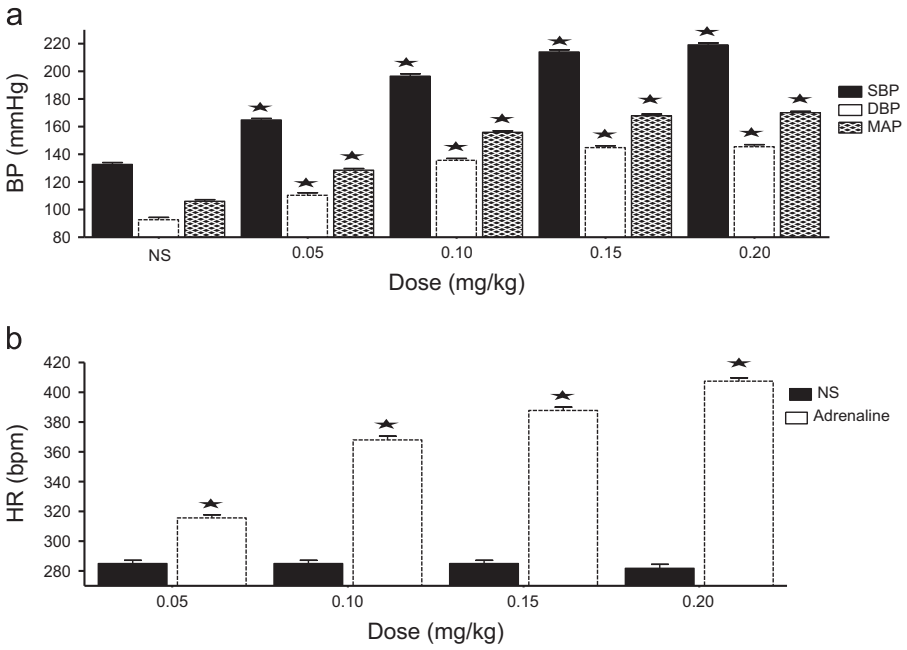

Fig. 1. Effect of adrenaline (0.05–0.20 mg/kg) on BP (a) and HR (b). Values are presented as mean ± SEM. * indicates statistical significance.

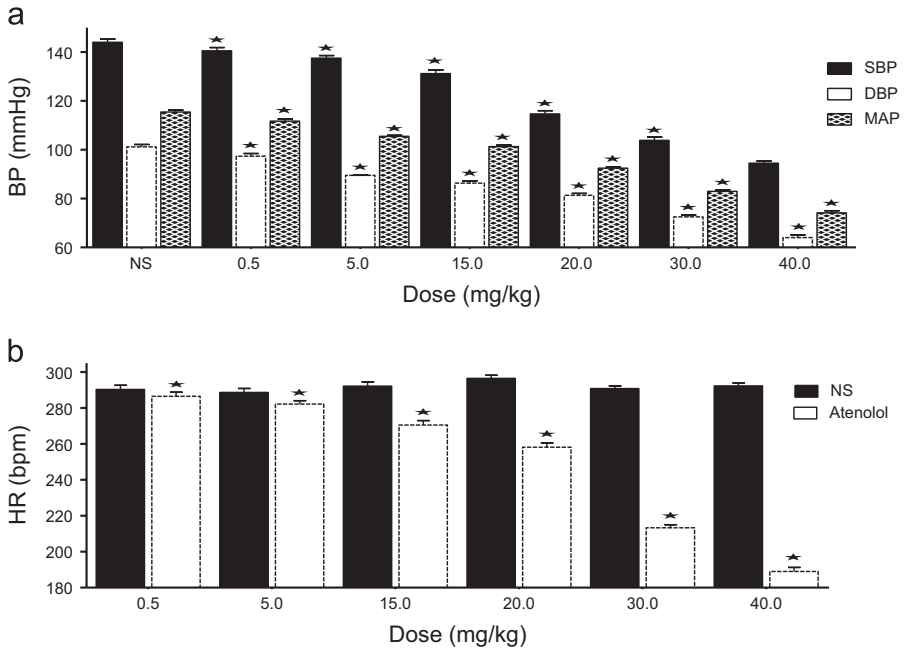

Fig. 2. Effect of atenolol (0.5–40 mg/kg) on BP (a) and HR (b). Values are presented as mean ± SEM. * indicates statistical significance.