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Cardiotonic mechanisms of the n-butanol extract and purified compounds isolated from stems of *Tinospora crispa* in the left atria of rat

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Extracts from *Tinospora crispa* have been used in Thai folk medicine for many purposes including cardiotonic activity. We aimed to identify the active constituents present in the extract and determine their mechanisms. Ground dried stems of *T. crispa* were extracted with hot water and partition extracted with n-butanol, the n-butanol extract was fractionated by column chromatography and semi-preparative C_{18} reversed phase HPLC. The isolated compounds were characterized by mass spectroscopy and ^{1}H and ^{13}C NMR spectroscopy. The effects and mechanisms of the active compounds were studied in isolated left atria from normal and reserpinized female Wistar rats (220-250 g, 6 rats/group/each experiment) in Krebs Heinseleit solution. Differences for which $P<0.05$ were considered significant. Drugs were dissolved in distilled water or 10 % DMSO. The left atria were mounted in a 20-ml organ bath, one end was fixed at the bottom and the other end connected to a force-displacement transducer (FT03C) connected to a Grass polygraph, under a basal tension of 1 g. Electrical stimulation of the normal and reserpized left atrium produced isometric forces of 0.36 ± 0.03 g and 0.79 ± 0.11 g, respectively. The *T. crispa* extract (TS) caused an increase in these responses in a concentration dependent manner. This was inhibited by propranolol and atenolol. The positive inotropic effect of TS was potentiated in reserpinized left atria and abolished by propranolol. Twelve pure compounds were isolated from TS. Of these, five (adenosine, uridine, salsolinol, higenamine and tyramine) showed cardiotonic activities on isolated left atria. Higenamine caused an increase in force of the atrial contraction and this effect was significantly inhibited by ICI-118,551 and atenolol, but not by phentolamine. Similar results were found on the left atria isolated from reserpinized rats. Salsolinol at low concentrations caused a slight increase in the force of the atrial contraction, but higher concentrations caused a decrease. Atropine (10^{-6} M) and/or yohimbine (10^{-6} M) inhibited the negative inotropic effects of salsolinol, and similar results were found in the left atria isolated from reserpinized rats. Tyramine caused a positive inotropic effect, and this effect was inhibited by propranolol or by reserpinized pretreatment. Adenosine and uridine caused a decrease in force of contraction of the left atria. In conclusion these 5 compounds from *T. crispa* affected cardiac contractility. Higenamine, salsolinol and tyramine acted via adrenergic receptors to increase the force of the left atrial contraction, whereas salsolinol acted indirectly by stimulating the release of acetylcholine and adenosine and uridine acted via non-adrenergic and non-cholinergic pathways to cause negative inotropic effects on the isolated atria.