Effects of plants with presumed cardiotonic properties on the decreased contractility of isolated guinea pig atria caused by acetylcholine: Implications for their clinical usefulness

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Abstract

Heart failure (HF) has been related to a chronic imbalance between autonomic sympathetic and parasympathetic activation. In the Republic of Suriname (South America), this condition is regularly treated with plant-derived preparations with presumed cardiotonic properties, mostly by traditional healers. In this study, aqueous extracts from Annona muricata (leaf), Mansoa alliacea (leaf), Momordica charantia (leaf and stem), Gossypium barbadensis (leaf), Artocarpus altulis (leaf), Chrysophyllum cainito (leaf), Solanum melongena (unripe fruit), and Stachytarpheta jamaicensis (leaf and stem) were evaluated at serial dilutions for their capability to reverse the decreased contractility and for their effects on the decreased beating frequency of isolated guinea pig atria caused by EC_{50} acetylcholine (10^{-7} M). The effects of the plant extracts alone were also investigated. Experiments were for 3 min with 2 x 2-min intervals in Ringer-Locke buffer, 100% O_{2}, and 30 °C. Results (g/sec and beats/min, means ± SDs; n ≥ 3) were expressed relative to those found with acetylcholine alone or buffer alone, and compared for statistically significant differences using one-way ANOVA (p < 0.05). None of the extracts reversed the decreased contractility and beating frequency of the atria caused by acetylcholine, but those from Mansoa alliacea (0.001 mg/mL) and Solanum melongena (0.001 and 0.01 mg/mL) lowered these activities by more than 50%. The latter extracts exerted similar effects on their own. Thus, the preparations did not display useful cardiotonic properties against parasympathetic abnormalities in HF, and those from Mansoa alliacea and Solanum melongena might even be cardiotoxic, warranting care when they are medicinally used.

Keywords: Heart Failure; Isolated Guinea Pig Atria; Cardiac Contractility; Cardiac Beating Frequency; Acetylcholine; Medicinal Plants; Suriname

1. Introduction

Heart failure (HF) is a cardiovascular condition characterized by the inability of the cardiac muscle to adequately pump and/or fill with blood to develop sufficient output to meet the metabolic needs of the body and properly discharge the venous return [1,2]. As a result, patients experience chronic tiredness and shortness of breath; edema in the lower body, around the stomach, and/or the neck; liver or kidney damage; pulmonary hypertension; and/or other heart conditions such as an irregular heartbeat, heart valve disease, and even sudden cardiac arrest [1,2]. HF can be caused by any disorder that impairs ventricular filling or ejection of blood to the systemic circulation, such as coronary heart disease, heart inflammation, hypertension, cardiomyopathy, or an irregular heartbeat [1,2].

Globally, an estimated 64 million individuals are now suffering from HF, and another 500,000 are added every year, mostly because of ageing of the world population [3]. Indeed, HF is the most common diagnosis in hospitalized patients older than 65 years of age [3]. The prevalence in adults in the USA based on self-reported data was approximately 25

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Treatment of HF is in general aimed at relieving symptoms and slowing down further damage to the heart, by correcting the imbalance between the decreased cardiac contractility on the one hand, and maintaining essential body functions on the other hand [6]. This mainly involves increasing the force of contraction using positive-inotropic agents such as β1-agonists, cardiac glycosides, and/or phosphodiesterase inhibitors, and/or relieving the cardiac workload using diuretics, inhibitors of the angiotensin-converting enzyme (ACE), β1-antagonists, and/or vasodilators [6]. Of note, these forms of treatment must go hand in hand with lifestyle changes such as smoking cessation and limited alcohol consumption, less intake of salt and caffeine, losing weight and improving physical condition, and reducing stress [6].

Thus, the primary effect of parasympathetic stimulation by acetylcholine is to decrease cardiac output by reducing both stroke volume and heart rate. However, autonomic imbalance with reduced parasympathetic activity has also been implicated in heart diseases, even though the role of parasympathetic signaling in these disorders is not fully understood [12]. For instance, parasympathetic withdrawal was substantially involved in the autonomic imbalance observed in HF in human subjects and a paced canine model of ventricular failure [13]; left ventricular dysfunction and an altered heart rate occurred together with changes in vagal nerve activity [14]; the early stages of HF coincided with a decrease in parasympathetic regulation [15]; and reduced vagal ganglionic transmission, altered muscarinic receptor density and composition, and decreased acetylcholinesterase activity have been reported in patients with HF [16].

The Republic of Suriname is located on the north-eastern coast of South America, near the Atlantic Ocean. The prevalence of HF in Latin America and the Caribbean has been estimated at 1% [17]. This approximation is in close accordance with the crude rate that could be derived from the number of 895 hospitalized patients with HF in 2015 [18] and Suriname’s population size of 575,475 in that year [19]. Suriname is renowned for its ethnic diversity, harboring native Amerindians as well as the descendants of enslaved people, indentured laborers, and immigrants from many parts of the world [19]. All the ethnic groups have largely adhered to their cultural customs including their particular forms of traditional medicine [20]. As a result, many Surinamese often treat their diseases including HF with (plant-based) traditional preparations instead of, or in conjunction with allopathic medications [20], despite the availability of affordable and accessible modern health care throughout the entire country [21].

So far, however, the scientific evidence to support the clinical efficacy of these preparations is scant. For this reason, we previously carried out a number of studies with plants that are traditionally used as cardiotonics using isolated organ models that are related to cardiovascular abnormalities involving HF [22-24]. Some of the plant preparations decreased the contractility of norepinephrine-stimulated isolated guinea pig atria without affecting the beating frequency [22], others increased the contractility of post-hypoxic isolated guinea pig atria [23], and still others decreased the tension of phenylephrine-stimulated guinea pig aorta rings [24]. In the current study, we explored whether some of these presumed plant-derived cardiotonics [25-28] were (also) able to improve the contractility and beating frequency of isolated guinea pig atria incapacitated by acetylcholine.

2. Materials and methods

2.1. Plants and preparation of plant extracts

The plant species investigated in the current study are given in Table 1. They were collected in rural areas outside Suriname’s capital city Paramaribo, in locations that had been free of herbicides or pesticides for at least the preceding six months. The plant collections took place in collaboration with the National Herbarium of Suriname (BBS) that is in the possession of a collection permit from the Surinamese Ministry of Physical Planning, Land and Forestry Management. None of the plants were on the International Union for Conservation of Nature’s Red List of endangered or threatened species [29]. They were authenticated with the help of published data on regional flora [30,31] and by comparing voucher specimens with identified herbarium collections at the BBS. The plant parts of interest (Table 1)
were first washed with tap water to remove adhering dirt, then twice with distilled water, air-dried, and macerated, and extracted by steeping for 45 min in hot distilled water. The thus obtained infusions were cooled, filtered, freeze-dried, and divided in aliquots of 3 g which were stored at a temperature of -20 °C until experiments. Plant material weighing between 500 and 1000 g typically yielded 15 to 20 g of extract.

2.2. Drugs and chemicals

The muscarinic receptor agonist acetylcholine and the specific muscarinic receptor antagonist atropine were from Sigma Chemical Co (St. Louis, MO, USA). Shortly before experiments, these compounds were dissolved in Ringer-Locke buffer and diluted with this buffer to the desired concentrations. Five liters of the Ringer-Locke buffer consisted of NaCl 45 g, KCl 2.1 g, CaCl2 1.2 g, NaHCO3 0.75 g, and glucose 5 g, and the pH was adjusted to 7.4 with concentrated phosphoric acid. These chemicals as well as all others used in the current study, were from our laboratory stock and were of the highest grade available.

2.3. Animals and preparation of isolated atria

Adult guinea pigs weighing 200 to 400 g were acquired from the Animal Facility of our institution. The animals were kept under standard conditions and had free access to food and water. On the day of an experiment, a guinea pig was anaesthetized with chloroform in a gassing chamber, the thoracic cavity was opened by a parasternal incision, and the heart was exposed. The major blood vessels were excised, after which the heart was quickly isolated, placed in ice-cold Ringer-Locke buffer, and the atria were carefully dissected from the rest of the heart.

The isolated atria were then transferred to an organ bath containing 40 mL of Ringer-Locke buffer that was kept at a temperature of 30 °C and gassed with pure oxygen. The tip of one atrium was attached to a fixed point in the organ bath, that of the other to a FT-302 force transducer (iWorx, Dover, USA). The preload was kept at 1 g during the entire experiment. The atria started to contract spontaneously as soon as the operating temperature had been reached, indicating that the sino-atrial node had remained intact during the dissection. The isolated atria were allowed to stabilize in Ringer-Locke buffer for at least 30 min before initiating the experiments. The buffer was regularly refreshed during that period. The Bioethics Committee of our institution had approved the design of these experiments.

2.4. Incubations, assessment of atrial responses, and data processing

The isolated guinea pig atria were exposed for 3 min to a plant extract, acetylcholine, or atropine, either alone or at certain combinations, after which they were washed twice for 2 min with fresh, pre-warmed Ringer-Locke buffer. The resulting forces of contraction of the atria were registered by the force transducer and processed by an ETH-260 Bio Amplifier (CB-Sciences, Dover, NH, USA) connected to a Powerlab 400 E series analog/digital converter (ADInstruments, Castle Hill, Australia). Signals were monitored with a desktop computer using the Chart 4.2.3 for Windows software (AD-Instruments, Castle Hill, Australia). The software also displayed the beating frequency of the atria in beats/min, and generated the relative contractility dF/dt in g/sec by differentiating forces of contraction (+dP/dtmax). All signals were saved on the hard disk of the computer, allowing off-line analyses. The relative contractility and beating frequency caused by acetylcholine, atropine, and/or a plant extract were derived from the average peak values of their respective readings, and were expressed with respect to average values recorded in the presence of Ringer-Locke buffer alone. The effects of the plant extracts on the contractility and frequency of the atria due to acetylcholine, were expressed relative to those caused by acetylcholine alone. Data presented are means ± SDs of at least three independent experiments performed in triplicate. P values < 0.05 were taken to indicate statistically significant differences according to one-way ANOVA with Tukey’s post hoc test.

3. Results

3.1. Responses of isolated guinea pig atria to acetylcholine in the absence or presence of atropine

The responses of the atria to six serial dilutions of acetylcholine between 10⁻⁹ and 5 x 10⁻⁷ M were determined in the absence or presence of atropine 10⁻⁸ M. In previous pilot studies, the latter compound was found to antagonize the acetylcholine-induced decrease in contractility and frequency of the atria at that concentration, without substantially affecting smooth muscle tone (data not shown). As depicted in Figures 1a and 1b, exposure of the atria to acetylcholine led to a progressive decrease in their contractility and beating frequency. From these dose-response curves, the half maximal effective concentration or EC₅₀ value of acetylcholine (the concentration of acetylcholine necessary to cause half of the maximum possible effect) was deduced at about 10⁻⁷ M. The effects of acetylcholine were clearly lower upon the addition of atropine 10⁻⁸ M (Figures 1a and 1b). These observations were in agreement with the well-known
negative-inotropic and negative-chronotropic effects of acetylcholine as well as the antagonizing effect of atropine on these phenomena [32], validating the usefulness of the model to carry out the current studies.

3.2. Effects of the plant extracts on the decreased contractility and beating frequency of the isolated guinea pig atria caused by acetylcholine

Next, the aqueous extracts from A. muricata leaf, M. alliacea leaf, M. charantia leaf and stem, G. barbadensis leaf, A. altillis leaf, C. cainito leaf, S. melongena unripe fruit, and S. jamaicensis leaf and stem were assessed for their ability to improve the reduced contractility of the atria caused by acetylcholine. The plant extracts were also assessed for their effects on the beating frequency of the atria. They were used at the concentrations of 0.001, 0.01, 0.1, and 1 mg/mL acetylcholine at the EC50 value of 10^{-7} M. Data have been expressed relatively to those found with acetylcholine 10^{-7} M alone.

As shown in Tables 2a and 2b, the extracts from A. muricata, M. charantia, G. barbadensis, A. altillis, C. cainito, and S. jamaicensis did not statistically significantly affected the decreased contractility and beating frequency of the atria caused by acetylcholine (p values ≥ 0.724, ANOVA). The extracts from M. alliacea (at 1 mg/mL) and S. melongena (at 0.1 and 1 mg/mL) even lowered the acetylcholine-induced decrease in contractility with more than 50% (p values ≤ 0.008, ANOVA) and abolished the beating frequency almost completely (p values ≤ 0.002). These observations suggest that preparations from G. barbadensis, M. cochinchenis, S. jamaicensis, C. cainito, A. muricata, and A. altillis might not possess meaningful cardiotonic properties and that those from M. alliacea and S. melongena might weaken a failing heart even more.

3.3. Effects of plant extracts on the contractility and beating frequency of isolated guinea pig atria in the absence of acetylcholine

The plant extracts were also assessed on their own (i.e., in the absence of acetylcholine) for their effects on the contractility and beating frequency of the isolated guinea pig atria. The results from these experiments are given in Tables 3a and 3b. Under these conditions, the extracts from G. barbadensis, M. cochinchenis, S. jamaicensis, C. cainito, A. muricata, and A. altillis also did not statistically significantly affect the contractility and the beating frequency of the atria (p values ≥ 0.700, ANOVA). On the other hand, those from M. alliacea (at 1 mg/mL) and S. melongena (at 0.1 and 1 mg/mL) also substantially and statistically significantly decreased the contractility and the beating frequency of the atria, i.e., with more than 50% (p values ≤ 0.007 and ≤ 0.002, respectively; ANOVA). These observations suggest that preparations from these plants may harm a normal heart, supporting their above-mentioned potential detrimental effect on a failing heart.

4. Discussion

The pathophysiology of HF has been associated with disturbances in parasympathetic signaling [12-16]. In the current study, preparations from plants that are traditionally used as cardiotonics in Suriname, have been assessed for their ability to restore the decreased contractility and counteract the lowered beating frequency of isolated guinea pig atria incapacitated by acetylcholine. The preparations studied were aqueous extracts from A. muricata leaf, M. alliacea leaf, M. charantia leaf and stem, G. barbadensis leaf, A. altillis leaf, C. cainito leaf, S. melongena unripe fruit, and S. jamaicensis leaf and stem [25-28]. The results obtained indicated that none of the plant samples statistically significantly affected the acetylcholine-decreased contractility and beating frequency of the isolated atria, and that those from M. alliacea and S. melongena even exacerbated the damping effects of acetylcholine. These observations do not support the alleged cardiotonic effects of the plants and discourage the use of the latter two plants against HF.

The apparent absence of an effect of the extracts from A. muricata, M. charantia, G. barbadensis, A. altillis, C. cainito, and S. jamaicensis on the contractility of the isolated guinea pig atria suggest that these samples did not increase the force of contraction of the heart muscle [6]. That the plants are, nevertheless, used against HF may be due to their potential to relieve the cardiac workload [6]. Indeed, previous studies reported that an aqueous extract from A. muricata fruit displayed ACE inhibitory activity and blood pressure-lowering effects in vitro [33]; preparations from M. charantia leaf, whole plant, and seed extracts lowered blood pressure in laboratory rats [34-36]; and those from C. cainito fruit pulp and leaf elicited antihypertensive activity in isolated rat aortic rings and salt-induced hypertensive rats [37-39]. In addition, A. muricata leaf extracts relaxed blood vessels and decreased blood pressure in both normotensive and hypertensive laboratory rats, presumably by blocking calcium ion channels [40,41]. And C. cainito leaf extracts caused vasodilation through nitric oxide following the release of prostaglandins [42] by nicotinic acid [43].

The G. barbadensis, A. altillis, and S. jamaicensis samples might also relieve the workload of the heart muscle rather than increase its contractility. For instance, a study with laboratory rats suggested that a G. barbadensis leaf extract decreased heart rate and relaxed blood vessels, accomplishing a hypotensive effect through a mechanism comparably to the
centrally acting $\alpha_2$-adrenergic agonist clonidine [44]. On the other hand, an aqueous leaf extract of *A. altillis* leaf counteracted the contractions of isolated rat aortic rings caused by the $\alpha_1$-adrenergic receptor agonist phenylephrine, and exerted hypotensive and negative-chronotropic activities in normotensive Sprague-Dawley rats [45], suggesting that it might antagonize the $\alpha_1$-adrenoceptor rather than the $\alpha_2$-adrenoceptor. Notably, an aqueous *A. altillis* leaf extract decreased the tension of isolated guinea pig aorta rings stimulated with phenylephrine, supporting its apparent antagonism of the $\alpha_1$-adrenoceptor [24]. In the case of *S. jamaicensis*, aqueous leaf preparations decreased blood pressure and heart rate in anesthetized normotensive male rabbits - presumably due to negative-chronotropism or a direct effect on vascular smooth muscle [46] - and produced a decrease in plasma sodium concentrations and an increase in plasma potassium concentrations in normal rabbits [47]. These effects might partly be attributed to the glycoside verbascoside in the leaf [48] that stimulated the formation of the vasodilating eicosanoid prostacyclin from arachidonic acid [49].

The deterioration of the contractility and beating frequency of the isolated guinea pig atria - both in the presence and the absence of acetylcholine - following exposure to the extracts from *M. alliacea* leaf and *S. melongena* unripe fruit cannot readily be explained. A tentative pharmacological explanation for the findings with the *M. alliacea* leaf sample might involve its content of, among others, the naphthoquinone 9-methoxy-$\alpha$-lapachone [50]. This compound acted as a positive allosteric modulator of the muscarinic receptor (*i.e.*, the $m_2$ muscarinic receptor subtype) [51], changing the receptor’s conformation and enhancing its affinity and responsiveness to acetylcholine and in this way, the potency and efficacy of acetylcholine [52]. Notably, allosteric modulators themselves may also produce an agonistic effect, as has been described for the anti-Alzheimer drug galantamine, that acts both as an inhibitor of acetylcholinesterase and as an allosteric agonist of the nicotinic acetylcholine receptor [53]. Whether such a mechanism may account for the current observations with the *M. alliacea* extract must be examined in greater detail.

As far as the *S. melongena* preparation is concerned, this plant - as well as many other members from the plant genus *Solanum* - produces several defensive substances such as the bitter-tasting steroidal glycoalkaloids solanine and solanidine [54]. The steroidal glycoalkaloids are potent inhibitors of acetylcholinesterase activity [55], preventing the breakdown of acetylcholine in synaptic clefts, increasing both the level and the duration of its action. This may eventually result in a greater decrease in the contractility and beating frequency of the atria than that caused by acetylcholine alone, as observed in the current study. Furthermore, *S. melongena* contains the flavonoids kaempferol and quercetin [56,57], the vasodilating properties of which may help lower the peripheral resistance, also reducing cardiac workload [58]. Incidentally, should this sample indeed elicit vasodilation, it may have some positive effect in HF by lowering pre- and afterload. Clearly, all these hypotheses about the *S. melongena* extract as well as those about the *M. alliacea* sample also need further investigation.

Summarizing, although the eight plants evaluated in the current study are attributed cardiodynamic properties [25-28], none of them increased the contractility of the isolated guinea pig atria incapacitated by acetylcholine. Furthermore, preparations from *S. melongena* and *M. alliacea* may deteriorate a heart weakened by parasympathetic abnormalities and must be used with care until more definitive data on their safety are available. Thus, the current data do not support the traditional use of the plants as cardiotonics, at least, not in cases of HF involving parasympathetic abnormalities. However, when taking into account the previously published data cited above, the samples may decrease cardiac workload through various other mechanisms, particularly those involved in decreasing blood pressure. It is also possible that the relevant constituents in the samples are pro-drugs that must undergo metabolic conversion into pharmacologically active substances; if so, their effects were, obviously, not detectable with the current use of an isolated organ model.

In any case, given the widespread traditional use of the plants [25-28], more comprehensive investigations are necessary in order to definitely determine their value for patients with HF, particularly those whose disease involves parasympathetic abnormalities. Preclinical studies in this area may involve the use of a guinea pig heart lung preparation that has the advantage of a constant pre-and afterload, heart rate, and temperature [59]. And subsequent human studies must take into consideration the results from a meta-analysis of randomized controlled trials that did not find evidence for an antihypertensive activity of *M. charantia* preparations, but presented indications for antihypertensive activity in younger adults and in short-term interventions upon subgroup analyses [60].
Table 1 Relevant characteristics of the plants investigated in the current study and literature references about their traditional use as cardiotonics

<table>
<thead>
<tr>
<th>Plant family</th>
<th>Plant species (vernacular name in English; Surinamese)</th>
<th>Plant part(s) used</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annonaceae</td>
<td>Annona muricata L. (Soursop; zuurzak)</td>
<td>Leaf</td>
<td>32-34</td>
</tr>
<tr>
<td>Bignoniaceae</td>
<td>Mansoa alliacea (Lam.) A.H. Gentry. (Garlic vine; konofroku tetey)</td>
<td>Leaf</td>
<td>33;35</td>
</tr>
<tr>
<td>Cucurbitaceae</td>
<td>Momordica charantia L. (Wilde sopropo; busi sopropo)</td>
<td>Leaf and stem</td>
<td>32;33</td>
</tr>
<tr>
<td>Malvaceae</td>
<td>Gossypium barbadensis L. (Sea Island cotton; redi katun)</td>
<td>Leaf</td>
<td>32-34</td>
</tr>
<tr>
<td>Moraceae</td>
<td>Artocarpus altilis (S. Parkinson) Fosb. (Breadfruit; bredebon)</td>
<td>Leaf</td>
<td>35</td>
</tr>
<tr>
<td>Sapotaceae</td>
<td>Chrysophyllum cainito L. (Star apple; sterappel)</td>
<td>Leaf</td>
<td>35</td>
</tr>
<tr>
<td>Solanaceae</td>
<td>Solanum melongena L. (Eggplant; boulanger)</td>
<td>Unripe fruit</td>
<td>32-34</td>
</tr>
<tr>
<td>Verbenaceae</td>
<td>Stachytarpheta jamaicensis (L.) Vahl (Jamaica vervain; isri wiwiri)</td>
<td>Leaf and stem</td>
<td>32-34</td>
</tr>
</tbody>
</table>

Figure 1 Effects of acetylcholine in the absence (■) or presence (▼) of atropine $10^{-8}$ M on the contractility (A) and beating frequency (B) of isolated guinea pig atria. Data are expressed with respect to average values recorded in the presence of Ringer-Locke buffer alone.
Table 2a Effects of plant extracts on the contractility of the isolated guinea pig atria in the presence of acetylcholine. Results (means ± SDs; n ≥ 3) are EC\textsubscript{50} values of acetylcholine in the presence of the plant extracts relative to that of acetylcholine alone. The latter value was set at 1

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Concentration (mg/mL)</th>
<th>Concentration (mg/mL)</th>
<th>Concentration (mg/mL)</th>
<th>Concentration (mg/mL)</th>
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</thead>
<tbody>
<tr>
<td>A. muricata</td>
<td>1.0 ± 0.0</td>
<td>0.9 ± 0.0</td>
<td>1.0 ± 0.1</td>
<td>1.2 ± 0.0</td>
</tr>
<tr>
<td>M. alliacea</td>
<td>0.9 ± 0.1</td>
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<td>0.9 ± 0.0</td>
<td>0.3 ± 0.1\textsuperscript{a}</td>
</tr>
<tr>
<td>M. charantia</td>
<td>1.0 ± 0.0</td>
<td>0.9 ± 0.0</td>
<td>0.9 ± 0.0</td>
<td>0.7 ± 0.2</td>
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<tr>
<td>G. barbadensis</td>
<td>1.0 ± 0.0</td>
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<td>1.0 ± 0.1</td>
<td>1.1 ± 0.1</td>
</tr>
<tr>
<td>A. altillis</td>
<td>1.0 ± 0.0</td>
<td>0.9 ± 0.0</td>
<td>0.9 ± 0.0</td>
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</tr>
<tr>
<td>C. cainito</td>
<td>1.2 ± 0.5</td>
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<td>0.9 ± 0.0</td>
</tr>
<tr>
<td>S. jamaicensis</td>
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<tr>
<td>S. melongena</td>
<td>0.9 ± 0.0</td>
<td>0.9 ± 0.1</td>
<td>0.2 ± 0.2\textsuperscript{a}</td>
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</table>

\textsuperscript{a}Statistically significantly different from values found for acetylcholine alone (p values ≤ 0.008, ANOVA)

Table 2b Effects of plant extracts on the beating frequency of the isolated guinea pig atria in the presence of acetylcholine. Results (means ± SDs; n ≥ 3) are EC\textsubscript{50} values of acetylcholine in the presence of the plant extracts relative to that of acetylcholine alone. The latter value was set at 1

<table>
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<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>M. alliacea</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.3</td>
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</tr>
<tr>
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<tr>
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</tr>
<tr>
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<tr>
<td>C. cainito</td>
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<tr>
<td>S. jamaicensis</td>
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</tr>
<tr>
<td>S. melongena</td>
<td>0.8 ± 0.4</td>
<td>0.7 ± 0.6</td>
<td>0.1 ± 0.1\textsuperscript{a}</td>
<td>0.1 ± 0.1\textsuperscript{a}</td>
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</tbody>
</table>

\textsuperscript{a}Statistically significantly different from values found for acetylcholine alone (p values ≤ 0.002, ANOVA)

Table 3a Effects of plant extracts alone on the contractility of the isolated guinea pig atria. Results (means ± SDs; n ≥ 3) have been expressed relative to those found with Ringer-Locke buffer alone. The latter values were set at 1

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Concentration (mg/mL)</th>
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<td>A. muricata</td>
<td>1.0 ± 0.1</td>
<td>1.0 ± 0.1</td>
<td>1.2 ± 0.2</td>
<td>1.6 ± 0.7</td>
</tr>
<tr>
<td>M. alliacea</td>
<td>1.2 ± 0.2</td>
<td>1.3 ± 0.4</td>
<td>1.0 ± 0.1</td>
<td>0.1 ± 0.1\textsuperscript{a}</td>
</tr>
<tr>
<td>M. charantia</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.2</td>
<td>1.0 ± 0.1</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>G. barbadensis</td>
<td>1.2 ± 0.2</td>
<td>1.0 ± 0.2</td>
<td>1.1 ± 0.2</td>
<td>1.5 ± 0.6</td>
</tr>
<tr>
<td>A. altillis</td>
<td>1.0 ± 0.1</td>
<td>0.7 ± 0.3</td>
<td>0.8 ± 0.3</td>
<td>1.4 ± 0.7</td>
</tr>
<tr>
<td>C. cainito</td>
<td>0.8 ± 0.1</td>
<td>0.8 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>1.2 ± 0.2</td>
</tr>
</tbody>
</table>
Table 3b Effects of plant extracts alone on the beating frequency of the isolated guinea pig atria. Results (means ± SDs; n ≥ 3) have been expressed relative to those found with Ringer-Locke buffer alone. The latter values were set at 1

<table>
<thead>
<tr>
<th>Plant species</th>
<th>Extract concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.001 mg/mL</td>
</tr>
<tr>
<td>A. muricata</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>M. alliacea</td>
<td>1.0 ± 0.0</td>
</tr>
<tr>
<td>M. charantia</td>
<td>1.1 ± 0.1</td>
</tr>
<tr>
<td>G. barbadensis</td>
<td>1.4 ± 0.6</td>
</tr>
<tr>
<td>A. altilis</td>
<td>1.1 ± 0.1</td>
</tr>
<tr>
<td>C. cainito</td>
<td>0.9 ± 0.0</td>
</tr>
<tr>
<td>S. jamaicensis</td>
<td>1.0 ± 0.1</td>
</tr>
<tr>
<td>S. melongena</td>
<td>1.0 ± 0.1</td>
</tr>
</tbody>
</table>

*Statistically significantly different from values found for acetylcholine alone (p values ≤ 0.007, ANOVA)

Conclusion

The results from this study indicate that preparations from parts of *A. muricata*, *M. alliacea*, *M. charantia*, *G. barbadensis*, *A. altilis*, *C. cainito*, *S. melongena*, and *S. jamaicensis* did not improve the contractility of isolated guinea pig atria incapacitated by acetylcholine. The *M. alliacea* and *S. melongena* samples might even worsen this phenomenon. These findings speak against the traditional use of these plants as cardiotonics as well as their clinical efficacy against HF, and warrant care when they are medicinally used.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The experiments described in this publication have been approved by the Ethics Committee of our institution.

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