Research Article

Pharmacological Effects of Hydrocotyle bonariensis Comm. ex Lam (Araliaceae) Extract on Cardiac Activity

Kaboua Komla,1 Pakoussi Tcha,1 Mouzou Aklesso,1 Kadissoli Balakiyém,1 Assih Minede,1 Bois Patrick,2 and Chatelier Aurelien2

1Laboratory of Physiology-Pharmacology, FDS, University of Lomé, BP 1515, Lomé, Togo
2Laboratory of Signaling and Membrane Ion Transport, Pole Biosante, University of Poitiers, BP 86000, Poitiers, France

Correspondence should be addressed to Kaboua Komla; kaboua90@gmail.com

Received 15 July 2022; Revised 19 August 2022; Accepted 5 September 2022; Published 29 September 2022

Academic Editor: Woon-Man Kung

Copyright © 2022 Kaboua Komla et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Hydrocotyle bonariensis is one of the medicinal plants used in traditional medicine for the management of hypertension in Africa, Asia, and Latin America. However, the real impact of the traditional use of this plant on arterial hypertension has not yet been the subject of conclusive scientific information in the literature. This study aimed essentially to evaluate the potential cardiomodulatory effect of the hydroethanolic extract of Hydrocotyle bonariensis. In order to do so, the hydroethanolic extract of H. bonariensis was studied in vivo on the Wistar rat ECG and then in vitro on the isolated perfused Wistar rat heart using the Langendorff system. The extract was also tested on isolated guinea pig atria kept alive in the organ-specific vessel under physiological conditions similar to those of a living organism. At the cellular level, the effects of the extract were evaluated on the human cardiac sodium current INav1.5 and on the human cardiac pacemaker current If. We noted that the extract caused a decrease in P wave and T wave amplitudes and heart rate and an increase in the duration of the RR interval on the in vivo rat ECG. On the isolated perfused Langendorff heart as well as on the isolated atria, a decrease in the RR interval and in the heart rate was noted. The extract had no effect on human cardiac sodium current, but it did reduce human cardiac pacemaker current. In conclusion, the present study demonstrated that Hydrocotyle bonariensis, a medicinal plant traditionally used to prevent and treat hypertension, has an overall cardiomoderating effect. This effect would contribute to the reduction of blood pressure.

1. Introduction

Hypertension, a major cardiovascular risk factor, is known to shorten the lifespan of a significant proportion of the world’s population and considerably increase the number of annual deaths. It currently affects 1.28 billion people worldwide and contributes to the development of other cardiovascular diseases (WHO, 2021). This pathology sets in when a failure occurs in the normal regulation of blood pressure [1, 2]. In addition to peripheral arterial resistance, cardiac output is one of the two critical factors targeted by the development of hypertension. Cardiac function, therefore, remains a justified fundamental target of certain drugs and cardiovascular pharmacological research related to hypertension. Despite the efforts against cardiovascular diseases, hypertension spread remains persistent and increasing, with a heavy prevalence rate in the future [3]. This situation obliges scientists to deepen cardiovascular research while diversifying the sources of candidate molecules such as phytotherapy. Indeed, more than 80% of the African or even global population have always resorted to plants to relieve themselves or to overcome their various pathologies, including hypertension [4]. Hydrocotyle bonariensis, a semiaquatic herbaceous plant of the Araliaceae family, has interesting ethnobotanical data regarding its antihypertensive virtues. According to Burkill [5] and Monyn et al. [6], Hydrocotyle bonariensis is used by traditional medicine practitioners to treat high blood pressure. Our previous work has demonstrated its antiarrhythmic cardiac effects [7] as well as its safety by oral administration [8]. In order to further evaluate the antihypertensive potential of this plant, we set the objective in this study to...
further investigate experimentally its effects on cardiac function. Specifically, we test the hydroethanolic extract of the leaves of this plant on the electrocardiogram, isolated perfused heart, isolated atria, cardiac sodium current, and mammalian cardiac pacemaker current.

2. Material and Methods

2.1. Preparation of Hydrocotyle bonariensis Leave Hydroethanolic Extract. The leaves of Hydrocotyle bonariensis were collected from the botanical garden of the Faculty of Sciences of the University of Lomé. These leaves were identified at the Laboratory of Botany and Plant Ecology of the Faculty of Sciences of the University of Lomé and deposited in the herbarium under the identification number TG 15183. After harvesting, they were washed abundantly with tap water and then dried under air-conditioning at 20°C in the dark.

After 3 weeks of drying, the leaves of Hydrocotyle bonariensis (Araliaceae) were pulverised, and then 320 grams was macerated for 72 hours with intermittent stirring in a hydroethanolic solvent in an equal volume ratio (1:1). After maceration, the solution was filtered through filter paper and cotton. The filtrate obtained was evaporated under vacuum using a Rotavapor at 45°C. 68.28 grams of the extract was obtained, giving a yield of 21.34%. The extract obtained was kept cool for the preparation of the different concentrations to be used for the tests.

2.2. Testing of H. bonariensis Extract on the Electrocardiogram (ECG) of Wistar Rats In Vivo. Wistar Albino rats weighing between 180 and 250 g and guinea pigs between 220 and 300 g were used. The animals were reared in the animal house of the Physiology-Pharmacology Laboratory of the Faculty of Sciences (University of Lomé) under standard light (natural day/night cycle of 12h) and temperature (25°C). The rats were fed a standard diet. Principles of laboratory animal care as described in institutional guidelines and ethics of Laboratory of Physiology/Pharmacology of the University of Lomé, Togo (ref: 001/2012/CB-FDS-UL), were followed.

For electrocardiogram (ECG) recording, 16 male rats were anesthetized by intraperitoneal injection of sodium pentobarbital (Dolethal) 182 mg/kg and then fixed on the restraint table. The jugular vein was exposed and intubated with a thin polyethylene catheter attached to a syringe. The 0.9% heparinized 10% NaCl solution was injected at a rate of 0.1 ml/100 g body weight to prevent blood clotting. The axilla of both forelimbs and the groin of both hindlimbs were shaved and cleaned with alcohol. Four electrodes were attached at these sites according to the color/position relationship indicated in the recording system instructions [9].

ECG measurements were performed using an electrocardiogram transducer coupled to an acquisition system (PowerLab; ADInstruments, Castle Hill, NSW, Australia) connected to a computer driven by LabChart6.0 software (ADInstruments).

Rats were each administered with 0.1 ml/100 g body weight, 0.9% NaCl solution i.v. for control and hydroethanolic extract of H. bonariensis leaves diluted in 0.9% NaCl solution at 10, 20, 40, and 80 mg/kg i.v., respectively. The extract was administered to rats via the jugular vein at a dose of 0.1 ml/100 g after a blood pressure stabilization time of approximately 30 minutes. The effects of this extract on ECG were recorded continuously throughout the experiment.

2.3. Testing of H. bonariensis Extract on Isolated Perfused Wistar Rat Heart (In Vitro). The study of the effects of the extract on isolated heart was performed with the inspiration of the method of Carré et al. [10]. Four male rats were anesthetized as before. The rat heart was harvested after checking for the absence of vegetative reflex (paw pinch) under deep anesthesia. The animal was placed on its back, its 4 limbs were attached to the dissection stand, and the ventral part of the rat was moistened with alcohol to prevent hair dispersion. The excised heart was rapidly immersed in a bath of Krebs–Henseleit solution cooled to 4°C in a Petri dish with a Sylgard bottom (Krebs–Henseleit solution of, in mM, NaCl 118.5; KH2PO4 2.5; KCl 4.7; MgSO4 1.2; CaCl2 2.5; NaHCO3 25; glucose 11. The pH of the solution was adjusted to 7.40 with NaOH, conditions that allowed cannulation of the aorta with a metal cannula of suitable diameter (18 G). The cannulated heart was placed on the Langendorff system (EMKA Technology) and perfused retrogradely (perfusion is in the opposite direction of in vivo blood flow) through the coronary artery network with Krebs–Henseleit solution. The perfusion fluid was thermostated at 37°C using a water bath (GD120. Grant) and saturated with a carbogen-type gas mixture (95% O2 and 5% CO2).

The ECG recording electrodes (Ag-AgCl) were placed on the epicardium of the right atrium near the sinoatrial node and in opposition to the apex (lead II of the human ECG). The electrode array was connected to a standard ECG amplifier and an analog-to-digital converter (EMKA Technologies, France). The signal was digitized with a sampling rate of 1 kHz. The heart was stabilized 15 minutes before the start of recording. The parameters of the cardiac activity were recorded continuously by a computer system dedicated to the acquisition with the IOX 2.9.5.43 software (EMKA Technologies, France).

After 15 minutes of stabilization in standard perfusion condition (Krebs–Henseleit), H. bonariensis extract was continuously perfused in increasing doses (1.56; 3.125; 6.25; 12.5; 25; 50 mg/ml) every 3 minutes. After each range, the heart was flushed with Krebs–Henseleit solution to measure reversibility.

2.4. Test of H. bonariensis Extract on Isolated Guinea Pig Auricles. The test of the effects of the extract on the isolated auricles of guinea pigs was carried out according to the method of Bonnah et al. Four male guinea pig was anesthetized as before. The heart was isolated as quickly as possible and placed in a physiological Krebs–Henseleit solution. The two atria were separated from the ventricles. The ends of the atria taken together were attached with wires. The preparation was then mounted in an isolated organ tank.
maintained at 37°C containing Mac Ewen’s solution. Organ contraction was recorded using LabChart V6 software (ADI Instruments). After stabilization for 30 min, volumes of extract corresponding to final concentrations of 0.05, 0.1, 0.2, 0.4, and 0.8 mg/ml of *H. bonariensis* extract were injected into the vessel every 10 min, and the effects were recorded.

2.5. Testing of *H. bonariensis* Extract on Human Cardiac Sodium Current I Nav1.5. Recording of sodium current (I Nav1.5) was performed on human cardiac Nav1.5 channels transiently expressed in HEK 293 cells. Cells were cultured in Dulbecco’s modified Eagle’s medium (DMEM, HyClone, Logan, UT, USA) and 10% (v/v) fetal bovine serum (FBS, Gibco, Gaithersburg, MD, USA) in a humidified atmosphere at 37°C with 5% CO 2-enriched air. Cells were subcultured every 2-3 days using brief trypsin treatments and seeded on 35 mm kneaders for 24–48 hours before patch-clamp experiments.

For I Nav1.5 recording, we used a pipette solution containing the following (in mM): 100 NaCl, 100 CsCl, 120.0 CsF, 1.0 MgCl2, 1.0 CaCl2, 10.0 EGTA, and 10.0 HEPES (pH adjusted to 7.2 with CsOH). We also used an extracellular bath solution with the composition (in mM/L) of 30.0 NaCl, 110.0 choline chloride, 5.0 CsCl, 1.2 MgCl2, 2.0 CaCl2, 10.0 HEPES, and 10.0 glucose (pH adjusted to 7.4 with NaOH).

Cells on coverslips were transferred to a continuously perfused recording chamber mounted on the stage of an inverted microscope and perfused with 10 ml of bath solution at a flow rate of approximately 1 ml/min for electrophysiological recording. The current signal was filtered at 5 kHz and sampled at 10 kHz. The capacitance and resistance of the entire cell were compensated, and leakage currents were subtracted. The currents were recorded 5 min after the whole-cell patch-clamp configuration was completed.

Sodium currents were generated by clamping the cell membrane from a holding potential of −120 mV to potentials ranging from −100 mV to 40 mV for 50 ms in 10 mV increments, with 3-second intervals between stimuli. Cells were superfused with vehicle until stabilization and then with 0.5 mg/ml *H. bonariensis* extract (n = 6) until steady state, followed by a washout period with vehicle.

Fast and slow decay time constants were obtained by fitting the current traces with a double exponential equation. The voltage dependence of activation was determined from the relative membrane conductance versus potential using the formula GNa = INa/(Vm − Vrev), where GNa is the peak conductance and INa is the peak sodium current for the test potential Vm. Vrev is the estimated sodium current reversal potential obtained by extrapolating the current-voltage relationship. The resulting sodium ion conductance was normalized to the maximum response for each cell. The activation data were fitted with Boltzmann’s equation: G/Gmax = 1/(1 + exp((V − V_{1/2})/k)), where Gmax represents the maximum conductance and V_{1/2} and k represent the half-maximum activation voltage and Boltzmann slope coefficient, respectively.

2.6. Testing of the Extract on the Human Cardiac Pacemaker Current If ("Funny Current"). Recording of the If current was performed on the Chinese hamster ovary (CHO) cell-derived stable line expressing the HCN1 gene encoding the f channel. CHO cells were grown in DMEM (Dulbecco’s Modified Eagle’s Medium) culture medium supplemented with 1% antibiotics (100 IU/ml penicillin-G-Na; 50 IU/ml streptomycin sulfate), 1 nM insulin, and 10% fetal calf serum. Cells were seeded on 35 mm Petri dishes precoated with laminin (Invitrogen) and maintained at 37°C in a 5% CO 2 atmosphere. Seeding density was approximately 2.0 × 104 cells/cm 2, allowing cells to reach confluence in 2 to 3 days. The cell cultures were reseeded after trypsinization. Patch-clamp experiments were performed within 24 hours of culture progression.

We used Tyrode’s extracellular bath solution (in mM) of NaCl 140; KCl 25; CaCl2 1; MgCl2 1.2; D-glucose 5.5; HEPES-NaOH 5 (pH = 7.4); BaCl2 1; MnCl2 2; and 4 aminoptyridine 0.5. The intrapipette solution is composed of (in mM) KCl 40; NaCl 10; MgATP 2; GTP 0.3; CaCl2 1; EGTA 11; HEPES-KOH 10 (pH = 7.2). 10 μM cAMP was added to the pipette solution to amplify the current. Intracellular diffusion of CAMP is monitored immediately after membrane rupture under the patch clamp. After rupture of the seal and dialysis of the intracellular medium with CAMP, the If current increases rapidly to reach the steady state.

For current recording, the cells were superfused with Tyrode’s solution. The cell membrane capacitance was measured by applying a low amplitude (±10 mV) voltage pulse from −40 mV. We applied a hyperpolarizing voltage pulse between −40 and −140 mV for 2.5 seconds from a holding potential of −40 mV to verify the presence of If current. Cells were superfused with vehicle until stabilization and then with *H. bonariensis* extract 0.5 mg/ml (n = 6) until steady state, followed by a washout period with vehicle.

3. Results

3.1. Effects of *H. bonariensis* Extract on the Electrocardiogram (ECG) of the Wistar Rat In Vivo. Injection of increasing amounts of the hydroethanolic extract of the leaves of *H. bonariensis* caused effects on the recorded ECG, P wave, T wave, RR interval, and the heart rate of Wistar rats (Figure 1). Table 1 shows that, at 80 mg/kg, the extract caused a significant decrease in P wave and T wave amplitudes of 29.06% and 41.54%, respectively, compared with the control. The extract did not impact either the QRS wave amplitude or the QT interval duration at the tested doses. However, from 20 mg/kg onwards, it induced a progressively significant increase in the duration of the RR interval as well as a significant proportional decrease in the heart rate of Wistar rats. The *H. bonariensis* extract thus induced a dose-dependent slowing down of the cardiac activity in Wistar rats.

3.2. Effects of *H. bonariensis* Extract on the Isolated Perfused Wistar Rat Heart (In Vitro). The effects of *H. bonariensis*
extract were evaluated on some electrocardiogram parameters such as heart rate, QRS wave amplitude, and RR interval duration. Figure 2 shows that the hydroethanolic extract of *H. bonariensis* leaves at 50 mg/kg causes a non-significant decrease in heart rate in the isolated perfused heart. In addition to a very slight nonsignificant increase in QRS amplitude, the extract, almost without effect from 1.56 to 25 mg/ml, causes a significant increase in RR interval duration from 192 ms (control) to 530.33 ms (at 50 mg/ml).

### 3.3. Effects of *H. bonariensis* Extract on Isolated Guinea Pig Atria

The hydroethanolic extract of *H. bonariensis* leaves causes, approximately one minute after its injection into the organ tank containing the isolated atria in full contraction, a progressively significant decrease in the frequency of contraction of the ears as the concentration of the injected extract increases. This decrease in the frequency of contraction is 97.64% at the concentration of 0.8 mg/kg compared to the control. This extract causes a significant increase in atrial contraction amplitude at the same concentrations from 0.2 mg/mL onward. The increase in amplitude which is 68.91% at 0.2 mg/ml compared to control reverses from 0.4 mg/ml (Figure 3).

### 3.4. Effects of *H. bonariensis* Extract on Human Cardiac Sodium Current *I_{Nav1.5}*

We studied the effect of *Hydrocotyle bonariensis* leaf hydroethanolic extract (0.5 mg/mL) on *I_{Nav1.5}*. Sodium currents with transiently transfected HEK 293 cell lines (Figure 4). Cells were perfused with control until stabilization and then with *H. bonariensis* extract at 0.5 mg/ml until steady state, followed by a washout period with control. *H. bonariensis* extract at 0.5 mg/ml, as shown in Figure 4, has no effect on the amplitude of *I_{Nav1.5}*. Recording of the IV current in the presence of the 0.5 mg/mL *H. bonariensis* extract showed no difference from its recording under control conditions. Thus, the hydroethanolic extract of *H. bonariensis* has no effect on human cardiac sodium current.

### 3.5. Effects of *H. bonariensis* Extract on Human Cardiac Pacemaker Current *I_{f}*

We evaluated the effect of hydroethanolic extract of *Hydrocotyle bonariensis* leaves (0.5 mg/ml) on *I_{f}* current with CHO cells expressing the human cardiac *I_{f}* channel. Figure 5 shows that *H. bonariensis* extract at 0.5 mg/ml inhibits the *I_{f}* current to reach a steady state. This inhibitory effect is partially reversible and is estimated to be 24.55% (*p* < 0.05; *n* = 4).

The effect of *H. bonariensis* extract on the current-voltage relationship of the *I_{f}* channel was estimated by normalizing the current values plotted against the test potential in the absence of the extract. Normalized currents were obtained from the maximum current amplitudes in response to depolarizing pulses in the range of −40 to −140 mV (Figure 6). Analysis of the activation curves indicates a significant decrease in maximum conductance of 37.82% at −40 mV.

### 4. Discussion

The first step in studying the effects of the *H. bonariensis* leaves extract on cardiac activity was to test this extract on the electrocardiogram of the Wistar rat. The results of this study showed that this extract transiently causes a significant decrease in heart rate, *P* wave, and *T* wave amplitude, followed by a significant increase in the duration of the RR interval. The *T* wave corresponds to the final phase of ventricular repolarization; thus, the decrease in its amplitude would imply that this extract would inhibit ventricular repolarization of the heart. The *P* wave materializes the atrial
depolarization, and its decrease suggests that this extract would act on the muscarinic receptors. Indeed, the activation of muscarinic receptors is translated on the ECG by a decrease or an inversion of the P wave, a lengthening of the PR space, and an atrioventricular dissociation [11]. Similar effects with the aqueous extract of *Averrhoa carambola* on guinea pig hearts were observed [12], suggesting that the hydroethanolic extract contains cholinomimetic substances.

The lengthening of the RR interval would translate slowing down of the cardiac contractions induced by this extract as it was shown by Adnet et al. [13]. This result is confirmed by the decrease in heart rate observed after intravenous administration of the hydroethanolic extract to normotensive rabbits. These results generally reflect a decrease in electrical activity and cardiac conduction, effects that could be induced by cholinomimetic substances. These effects could...
Figure 4: Effects of *H. bonariensis* extract on human cardiac sodium current I\_Nav1.5. Comparison of the amplitudes of cardiac sodium currents recorded on HEK 293-I\_Nav1.5 cells in control and 0.5 mg/kg *H. bonariensis* extract-treated conditions ((a) *t*-test + Mann–Whitney test). The effect of *H. bonariensis* extract on the current-voltage relationship of the I\_Nav1.5 channel was estimated by normalizing the current values plotted against the test potential in the absence and presence of the extract ((b) ANOVA + Sidak’s multiple comparisons test). No change in I\_Nav1.5 current is observed in the presence of the extract. \( n = 10 \).

Figure 5: Continued.
also be induced by the anticalcics contained in the extract. Indeed, anticalcics block L-type voltage-dependent calcium channels in the vessels and heart, thus preventing the release of intracellular calcium necessary for contraction [9, 14–16].

The second step of the study of the effects of the extract on cardiac activity consisted of testing it on isolated organs such as the isolated perfused rat heart and the isolated guinea pig atria. Our results showed that the extract has a dose-dependent negative chronotropic effect as well as a transient positive inotropic effect on the mechanical activity of the atria. Inhibition of the atrial contraction rate by the extract could result in a decrease in electrical activity and cardiac conduction as explained above. This negative chronotropic action on the atria could also imply an interference of the bioactive compounds of the extract in the regulation of cardiac automatism. These effects are similar to those obtained by other authors who tested the effects of plants on isolated guinea pig atria [17, 18].

The third step in the study of the effects of the hydroethanolic extract of *Heliotropium bonariensis* leaves on cardiac function is cellular and was focused on human cardiac ionic electrophysiology. Indeed, the cardiac action potential is an
electrical phenomenon finely regulated by modifications of the membrane voltage generated by the opening of various ion channels (sodium, calcium, chloride, and potassium) present at the surface of cardiomyocytes. The transfer of ions across the membrane via these channels generates currents that can be measured by the patch-clamp technique. Therefore, cardiac electrical activity is the result of a balance of different ion flows that can also be modulated by the sympathetic and parasympathetic systems to allow adaptation of the heart rhythm [19]. The extract is tested on some of these ionic currents strongly involved in cardiac physiology and pathophysiology, such as sodium, potassium, and cardiac pacemaker currents.

We examined the effect of the extract on the cardiac subunit of the human sodium current (NaV1.5) in order to verify if this extract would influence the electrical activity of the heart via these channels. Divided into rapid (INa peak) and sustained (INaL) phases which respectively intervene in the excitability and duration of an AP (plateau phase), the sodium current (INa) is responsible for the initiation of action potentials (AP) and modulates its duration. It, therefore, plays a major role in cardiac excitability and electrical impulse conduction. Because of this, a change in the biophysical properties of INa during pathophysiological conditions can generate rhythm modulation [20, 21]. The results of our voltage-gated work on INa revealed that this extract has no influence on the cardiac subunit of sodium current. No effect is observed on either the amplitude or the current-voltage relationship of human cardiac sodium channels. The mechanism of action of this extract would not, therefore, involve the sodium channels.

In addition to the test on cardiac sodium current, we studied the impact of the hydroethanolic extract of Hydrocotyle bonariensis leaves on cardiac rhythmicity by evaluating its effects on the human cardiac pacemaker current If.

The If current, called “funny current,” modulating the heart rate, was also a target of our study of the effects of the extract of H. bonariensis on cardiac rhythmicity. This current activated by membrane hyperpolarization is particularly present in sinus cells with pacemaker activity (automatic and regulating the cardiac rhythm). It controls slow diastolic depolarization at the sinus node, exclusively regulating the heart rate [22]. In this study, we have shown that the extract of H. bonariensis at the concentration of 0.5 mg/ml significantly decreases the amplitude of the If current while decreasing the current-voltage relationship (curve IV). The extract reduces the conductance of the channels without altering their kinetics. The bioactive compounds in the extract would, therefore, partially block the If channel pore. The effect of the extract is partially reversible. This partial reversibility would be the binding of the bioactive compounds on different sites of one or more subunits of the If channel. Furthermore, it is plausible that these sites have a variable affinity towards the different components present in the extract, further explaining the partial reversibility. These results are similar to other studies performed on the pharmacology of If channels, leading to cardiac therapeutic molecules against stable angina and myocardial ischemia [23, 24]. This If current produced by specific If ischemia and playing an essential role in the depolarization of the sinus node is today the target of some therapeutic molecules. It is specifically and selectively inhibited by a benzocyclobutene compound called ivabradine. This is a bradycardia-inducing molecule that does not affect other currents present in the cells of the sinus node. The hydroethanolic extract of the leaves of H. bonariensis, like ivabradine, has the property of slowing down the heart rate by inhibiting the If current, the regulatory current of the cardiac pacemaker.

5. Conclusion

The hydroethanolic extract of the leaves of Hydrocotyle bonariensis has an overall inhibitory effect on cardiac activity. Cardioinhibition is one of the causes of the reduction of blood pressure figures due to the reduction of systolic ejection volume and heartbeat cycles. This would justify its use in the traditional management of hypertension.

In addition to the study of the effects of the extract of this plant on cardiac activity, the mammalian vascular system would be a complementary target to study its antihypertensive effects.

Data Availability

The data used to support the findings of this study are included in the article.

Additional Points

(i) Hydrocotyle bonariensis decreases heart rate in all tested ECG study models. (ii) Hydrocotyle bonariensis partially blocks human if current but has no effect on human cardiac INav1.5 current. (iii) Hydrocotyle bonariensis has a cardiomodulating effect.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

K. Kaboua, A. Mouzou, P. Bois, Aurelien Chatelier, and T. Pakoussi conceived the project and defined research methodology; K. Kaboua, B. Kadissoli, Aurelien Chatelier, and M. Assih performed the experiments; K. Kaboua, P. Bois, T. Pakoussi, B. Kadissoli, and K. and A. Mouzou wrote the paper.

Acknowledgments

The authors would like to thank J. Bescond and D. Aboudoulatif for their expertise. The work was supported by Campus France and La Fondation Pierre Fabre.

References

[1] American Heart Association, What Is High Blood Pressure?, South Carolina State Documents Depository, 2017.
Evidence-Based Complementary and Alternative Medicine

[2] C. D. A. Goonasekera and M. J. Dillon, “Current topic: measurement and interpretation of blood pressure,” Archives of Disease in Childhood, vol. 82, no. 3, pp. 261–265, 2000.

[3] J. J. Noubiap, J. J. Bigna, J. R. Nansseu et al., “Prevalence of dyslipidaemia among adults in Africa: a systematic review and meta-analysis,” The Lancet Global Health, vol. 6, pp. e998–e1007, 2018.

[4] J. Addo, L. Smeerth, and D. A. Leon, “Hypertension in sub-Saharan Africa: a systematic review,” Hypertension, vol. 50, no. 6, pp. 1012–1018, 2007.

[5] H. M. Burkhill, The Useful Plants of West Tropical Africa, Royal Botanic Gardens, Richmond, England, 1985.

[6] E. D. Monyn, A. Bakayoko, F. H. Tra Bi, K. Yao, and M. W. Kone, “Niveau de connaissance et composition minérale de hydrocotyle bonariensis lam. (araliaceae), une plante utilisée dans les ménages du district d’abidjan (côte d’ivoire),” International Journal of Brain and Cognitive Sciences, vol. 10, no. 5, pp. 2046–2061, 2017.

[7] K. Kaboua, A. Mouzou, T. Pakoussi et al., “Hydrocotyle bonariensis comm ex lam (Araliaceae) leaves extract inhibits IKs not IKr potassium currents: potential implications for anti-arrhythmic therapy,” Journal of Traditional and Complementary Medicine, vol. 12, no. 4, pp. 330–334, 2022.

[8] K. Kaboua, T. Pakoussi, A. Mouzou et al., “Toxicological evaluation of hydrocotyle bonariensis comm. ex lam (Araliaceae) leaves extract,” Beni-Suef University Journal of Basic and Applied Sciences, vol. 10, no. 1, pp. 69–77, 2021b.

[9] G. M. Bleu, N. F. Bakou, Z. F. Kpahé, and A. Semi, “Effets pharmacologiques de Passiflora foetida (Passifloraceae) sur le système cardiovasculaire de rat et de lapin,” Journal of Applied Biosciences, vol. 155, pp. 15960–15973, 2020.

[10] G. Carré, H. Carreyre, M. Ouedraogo et al., “The hypotensive agent donodene inhibits L-type Ca2+ current with negative inotropic effect on rat heart,” European Journal of Pharmacology, vol. 728, pp. 119–127, 2014.

[11] A. R. Houghton and D. Gray, Maîtriser l’ECG: de la Théorie à la Clinique, p. 274, Elsevier Masson, Amsterdam, Netherlands, 2005.

[12] C. M. L. Vasoncelos, M. S. Araújo, and E. A. Conde-Garcia, “Electrophysiological effects of the aqueous extract of Averrhoa carambola L. leaves on the Guinea pig heart,” Phytotherapy, vol. 13, no. 7, pp. 501–508, 2006.

[13] F. Adnet, F. Lapostolle, and T. Petrovic, ECG en urgence: Cas Clinique, Analyse ECG, Stratégie Thérapeutique, p. 271, Arnette Blackwell, 2003.

[14] A. E. Ossibi, R. D. G. E. Itou, J. Nzoni et al., Effets de l’Extrait Aqueux de Lippia Multiflora Moldenke (Verbenaceae) Sur la Pression Artérielle, la Fréquence Cardiaque et Les Ondes de l’Electrocardiogramme, 2014.

[15] F. Traoré, A.-L. Adjoungoua, A. Koffi, and F. Diafouka, “Effets pharmacologiques de Ziziphus mauritiana Lam. (Rhamna-ceae) sur le cœur isolé et l’aorte de mammifères,” Phytothérapie, vol. 6, no. 5, pp. 276–281, 2008.

[16] O. S. Zahoui, S. A. Nene-Bi, T. Y. Soro, and F. Traoré, “Etude des effets pharmacologiques de l’extrait aqueux de heliotropium indicum linn. (Boraginaceae) sur le cœur isolé de rat et l’aorte isolée de cobaye,” International Journal of Biological and Chemical Sciences, vol. 4, no. 5, pp. 1610–1620, 2010.

[17] B. Bonnah, K. A. Aklilokok, K. Akpagana, and M. Gbeassor, “Contribution à l’étude des propriétés pharmacologiques des extraits hydro-alcooliques des graines de parkia biglobosa. Sciences et Médecine,” Revue CAMS, vol. 4, pp. 12–15, 1998.

[18] G. E. A. Conde, V. T. Nascimento, and A. B. Santiago Santos, “Effets inotropes d’extraits de feuilles de psidium guayava L. (goyave) sur l’oreillette du cobaye,” Journal brésilien de recherche médicale et biologique, vol. 36, pp. 661–668, 2003.

[19] B. I. E. T. Michaël, Rôle et Implication du Courant Sodique Cardiaque Dans la Genèse des Phénomènes Arthymogéniques en Conditions Physiopathologiques, 2014.

[20] L. M. Ballou, R. Z. Lin, and I. S. Cohen, “Control of cardiac repolarization by phosphoinositide 3-kinase signaling to ion channels,” Circulation Research, vol. 116, no. 1, pp. 127–137, 2015.

[21] M. Matamoros, M. Perez-Hernandez, G. Guerrero-Serna et al., “Nav1.5 N-terminal domain binding to α1-syntrophin increases membrane density of human Kir2.1, Kir2.2 and Nav1.5 channels,” Cardiovascular Research, vol. 110, no. 2, pp. 279–290, 2016.

[22] P. Bois, R. Guinamard, A. E. Chemaly, J. F. Faviaire, and J. Bescond, “Molecular regulation and pharmacology of pacemaker channels,” Current Pharmaceutical Design, vol. 13, no. 23, pp. 2338–2349, 2007.

[23] G. Andrikopoulos, C. Dasopoulou, D. Sakellariou et al., “Ivabradine: a selective if current inhibitor in the treatment of stable angina,” Recent Patents on Cardiovascular Drug Discovery, vol. 1, no. 3, pp. 277–282, 2006.

[24] P. Lancellotti, “Le médicament du mois. Ivabradine (Procoralan),” Revue médicale, vol. 63, no. 4, pp. 220–224, 2008.

[25] B. Kadissoli, A. P. Mouzou, E. Tekaou, A. Aklilokokou, and M. Gbeassor, “Effet de l’extrait semi-éthanolique des feuilles de trema guineensis (celtidaeae) sur la musculature lisse du rat wistar,” International Journal of Brain and Cognitive Sciences, vol. 6, no. 3, pp. 985–994, 2012.

[26] OMS, “Hypertension,” 2021, https://www.who.int/fr/news-room/fact-sheets/detail/hypertension.

[27] R. Déhou, V. Dognon, P. Athède et al., “Étude phytoci- mique et toxiciologique de cassia italica, momordica balsamina et ocimum gratissimum, trois plantes utilisées contre la gale au sud-Bénin,” Revue Ivoirienne des Sciences et Technologie, vol. 32, pp. 286–297, 2018.