

# Evaluation of the Effects of An Aqueous Extract of *Senna alata* (L.) Roxb. (Fabaceae) on Cardiac Arrhythmia in Rabbits

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**Abstract** Heart rhythm problems also known as cardiac arrhythmias are one of the main causes of morbidity. The objective of this work is to evaluate the effects of an aqueous extract of *Senna alata* (Fabaceae) on cardiac arrhythmia in rabbits. To conduct this study, An electrocardiograph (Cam, Chim, China) is used to measure the electrical activity of the heart. The results of the extract on the normal rabbit ECG show that this substance, at low doses ( $5.10^{-3}$  to  $5.10^{-2}$  mg/kg BW) causes an increase in the amplitude of the P wave and the QRS complex and causes tachycardia. On the other hand, bradycardia is obtained for higher doses (greater than  $5.10^{-1}$  mg/kg BW, and up to 15 mg/kg BW), with also an increase in the amplitude of the P wave and the QRS complex. Thus, at low doses, the extract has adrenergic-type properties and, at high doses, digitalis-type properties. On rabbit ECG, this extract, at a dose of 10 mg/kg BW, corrects cardiac rhythm disturbances, which present in the form of tachycardia and arrhythmia induced by prior administration of Isoprenaline (0.1 mg/kg BW). These effects on cardiac arrhythmia show that this extract has antiarrhythmic properties. This justifies the use in traditional medicine of *Senna alata* (Fabaceae) in the treatment of heart diseases.

**Keywords:** Electrocardiogram, *Senna alata*, antiarrhythmic

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## 1. Introduction

Cardiovascular diseases are a group of problems that affect the heart and blood vessels. These diseases include high blood pressure, atherosclerosis, myocardial infarction, heart failure [1]. Heart rhythm problems, also known as cardiac arrhythmias or heart rate disorders, are caused by improper diet, lack of physical exercise, smoking, and excessive use of alcohol [2]. These diseases are one of the main causes of morbidity. When the heart beats irregularly, too slowly (bradycardia) or too quickly (tachycardia), it leads to cardiac arrhythmia. It should be emphasized that therapeutic treatments are expensive and often inaccessible to populations.

*Senna alata*, is a plant that is traditionally used in different regions of the world to treat various ailments [3]. Several previous studies have reported promising

biological activities associated with this plant, such as anti-inflammatory, antimicrobial, and antioxidant properties [4]. However, few studies have investigated the effect of *Senna alata* (Fabaceae) on cardiac activity. In this context, the objective of this work is to evaluate the effects of an aqueous extract of *Senna alata* (Fabaceae) on cardiac arrhythmia in rabbits.

## 2. Materials and Methods

### 2.1. Materials

#### 2.1.1. Animal Material

The rabbits used are of the species *Oryctolagus cuniculus* (Leporidae) and have an average weight of 2 kg. They come from private farms and were acclimatized for a week at the Biosciences Training and Research Unit for

pharmacological tests. All experimental protocols are conducted in accordance with the European directive of November 24, 1986 (86/609/EEC) and the decree of April 19, 1988 relating to the use of experimental animals in research [5].

### 2.1.2. Plant Material

The plant material consists of dried leaves of *Senna alata* (Fabaceae) harvested in the town of Bouaké in Ivory Coast, and sold in the Anono market in Abidjan. This plant was identified at the National Floristic Center (CNF).

## 3. Methods

### 3.1. Preparation of the Aqueous Extract of *Senna alata* Leaves (Fabaceae)

The aqueous extract of *Senna alata* (Fabaceae) leaves was prepared according to the method described by [6,7].

For the preparation of the aqueous extract of *Senna alata* (Fabaceae), 100 g of dry leaves of this plant are boiled in 2 liters of distilled water for 30 minutes after boiling. The decoction obtained was previously filtered twice through hydrophilic cotton and then once through Whatman No. 2 filter paper. The collected filtrate was dried in an oven for 72 hours at 40°C and the aqueous extract of *Senna alata* (EASa) is obtained. The product (EASa) obtained is used for pharmacological studies on arrhythmias in rabbits.

### 3.2. Recording of the rabbit's electrocardiogram (ECG)

#### 3.2.1. Experimental Device

An electrocardiograph (Cam Chim, China) is used to measure the electrical activity of the heart. The electrodes are placed on the bare surface of each of the rabbit's leg roots (armpits and groins) and connected to the electrocardiograph.

#### 3.2.2. Rabbit ECG Recording Technique

The anesthetized rabbit is shaved and cleaned with 90° ethyl alcohol on the armpits of the two forelimbs and on the wing of the two hind limbs. A conductive gel (Ultrasound KONIX gel, USA) is used to insert these shaved limbs, and four electrodes are placed respectively in the shaved armpits and groins. The electrodes attached to the animal's body are each connected to the cable corresponding to the appropriate limb. Parameters such as speed (25 mm/s), bypasses, filter and amplification are set. These last two parameters can be adjusted during recording. The electrodes collect the potential fluctuations, transmit them to the electrocardiograph and the ECG recording is made on a thermosensitive ECG paper which unrolls at a determined speed. Each recording is automatically calibrated at the beginning and the recording parameters (derivation, speed, calibration and filter) are displayed on the traces.

### 3.2.3. Method of Studying the Effect of the Extract on the ECG

In this research, the extract or pharmacological substances are dissolved in a 9% NaCl solution and administered to rabbits using a saphenous vein connected to a syringe. The amounts of injected substances are measured in mg/kg BW. In order to analyze the dose response effect, the extract is administered in single, increasing doses every 15 minutes. The interaction is studied by first taking the pharmacological substance at a specific dose, and then the extract at an active dose. The experiment is repeated 5 times on different rabbits to confirm the results.

### 3.2.4. Phytochemical Screening of the Aqueous Extract of *Senna alata* Leaves

Phytochemical screening was carried out by tube tests using the appropriate reagents.

### 3.2.5. Physiological Solutions and Pharmacological Substances

9% NaCl saline solution is used for the processes of dissolution and dilution of extract and pharmaceutical substances. The chemicals used during this work are Thiopental Inresa 0.5g, Heparin Choay (5000 IU) and injectable isoprenaline.

### 3.2.6. Processing of Results

#### 3.2.6.1. Statistical Analyses

The computer program GraphPad Instat (San Diego, CA, USA) was used for statistical analysis of the results. Values are given as the mean, followed by the standard error of the mean (SEM). Statistical differences between results were determined using ANOVA analysis of variance, followed by the Tukey Kramer multiple comparison test. These differences were considered non-significant (NS) for a probability greater than 5% ( $p > 0.05$ ) or significant (\*) for  $p < 0.05$ ; (\*\*) for  $p < 0.01$ ; (\*\*\*) for  $p < 0.001$ .

#### 3.2.6.2. Graphics

The graphs are represented by GraphPad Prism 8 software (San Diego CA, USA) and then the sigmoid curves are plotted after converting the values of the abscissa axis into decimal logarithm.

## 4. Results and Discussion

### 4.1. Results

#### 4.1.1. Phytochemical Screening of the Aqueous Extract of *Senna alata* (Fabaceae)

The results of the phytochemical screening of the aqueous extract of *Senna alata* (Fabaceae) are presented in Table 1.

The tube tests performed on the aqueous extract of *Senna alata* (Sapindaceae) revealed the presence of sterols

and polyterpenes, polyphenols, flavonoids, catechol tannins, quinone compounds.

## 4.2. Pharmacological effects of *Senna alata* aqueous extract (EASa) on induced arrhythmia in rabbits

### 4.2.1. Dose-response Effects of EASa on Rabbit Electrocardiogram (ECG)

Figure 1 shows the effects of EASa on rabbit ECG, in lead DII. It appears that when a dose lower than  $5.10^{-2}$  mg/kg BW is administered to the rabbit, EASa has no effect on cardiac activity. Indeed, when EASa is administered to rabbits at a dose of  $5.10^{-3}$  mg/kg BW (Figure 1), the ECG presents a regular rhythm, with

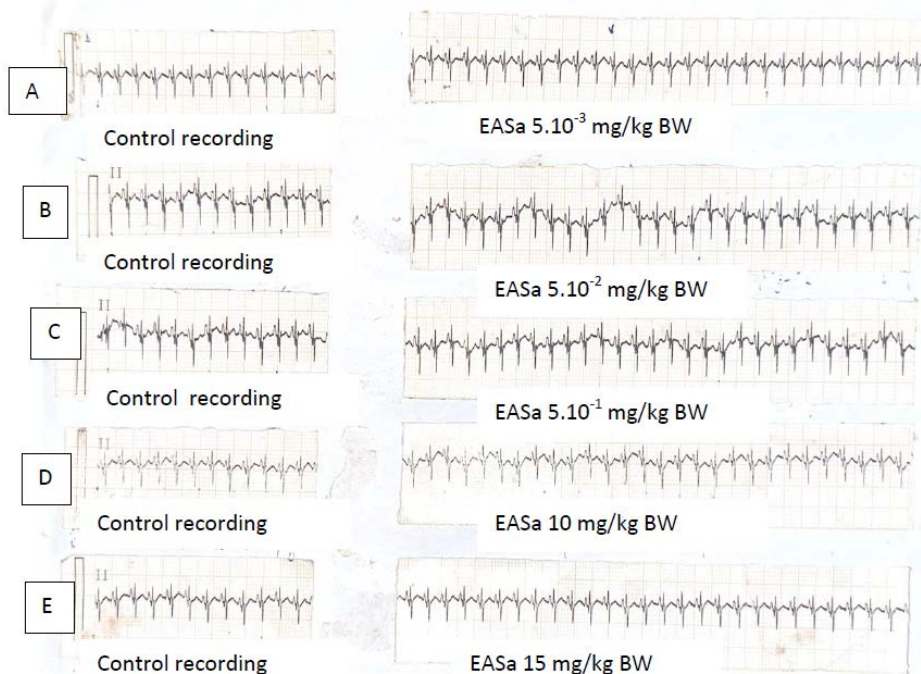
the amplitudes of the P, T waves and the QRS complex identical ( $p > 0.05$ ) to those of the control ECG. Also, EASa has no significant effects ( $p > 0.05$ ) on the durations of PR, QT intervals and ST segment. However, at low doses ranging from  $5.10^{-2}$  to  $5.10^{-1}$  mg/kg BW, EASa causes a decrease in the amplitudes of the P, T waves and the QRS complex, while the frequency increases. Beyond the dose of  $5.10^{-1}$  mg/kg BW, and up to the dose of 15 mg/kg BW, EASa induces a decrease in the frequency and an increase in the amplitude of these waves. At these doses, the effects of EASa are dose-dependent. It should be noted that beyond 15 mg/kg BW, EASa induces disturbances in cardiac activity. Table 2 shows, for a typical series of experiments, the ECG of the rabbit, before and after treatments with the different doses of EASa.

Table 1. Results of phytochemical screening of the aqueous extract of *Senna alata* (Fabaceae)

| Chemical compounds sought |                           | Reactions / Reagents         | Results |
|---------------------------|---------------------------|------------------------------|---------|
| Polyphenols               |                           | Reaction to ferric chloride  | +       |
| Sterols and polyterpenes  |                           | Liebermann-Bouchard reaction | +       |
| Flavonoids                |                           | Reaction to cyaniding        | +       |
| Saponins                  |                           | Vigorous agitation           | -       |
| Quinonic Compounds        |                           | Borntraeger's reaction       | +       |
| Alkaloids                 |                           | Dragendorff's reagent        | -       |
|                           |                           | Bouchardat's reagent         | -       |
| Catechetical              | Stiasny's reagent         | Stiasny's reagent            | +       |
|                           | Hydrochloric acid reagent | Hydrochloric acid reagent    | +       |

+: Presence of the compound (Positive test)

–: Absence of the compound (Negative test)



A: Control recording, then effect of EASa at  $5.10^{-3}$  mg/kg BW

B: Control recording, then effect of EASa at  $5.10^{-2}$  mg/kg BW

C: Control recording, then effect of EASa at  $5.10^{-1}$  mg/kg BW.

D: Control recording, then effect of EASa at 10 mg/kg BW.

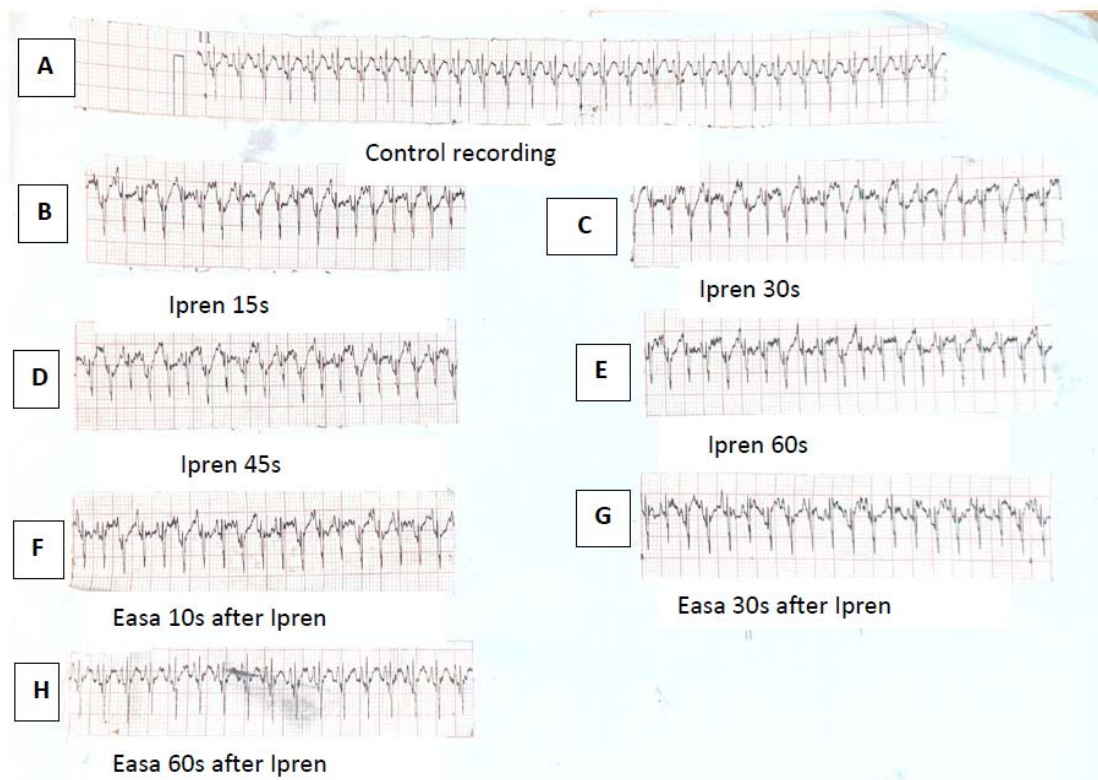
E: Control recording, then effect of EASa at 15 mg/kg BW.

Calibration: 20 mm/mV; Speed: 25mm/s

Figure 1. Dose-response effects of *Senna alata* aqueous extract (EASa) on rabbit ECG

**Table 2. Dose-response effects of *Senna alata* aqueous extract (EASa) on rabbit ECG**

| Dose of EASa Effects (mg/kg BW) |                   | P wave (mV) | QRS complex (mV) | T wave (mV) | Frequency in beats per minute (bpm) |
|---------------------------------|-------------------|-------------|------------------|-------------|-------------------------------------|
| 5.10 <sup>-3</sup>              | Control recording | 0,1         | 0,4              | 0,05        | 228                                 |
|                                 | Effects           | 0.1         | 0.4              | 0.05        | 229                                 |
| 5.10 <sup>-2</sup>              | Control recording | 0.1         | 0.5              | 0.1         | 216                                 |
|                                 | Effects           | 0.15        | 0.55             | 0.1         | 228                                 |
| 5.10 <sup>-1</sup>              | Control recording | 0.13        | 0.45             | 0.09        | 216                                 |
|                                 | Effects           | 0.13        | 0.5              | 0.09        | 240                                 |
| 10                              | Control recording | 0.1         | 0.38             | 0.05        | 240                                 |
|                                 | Effects           | 0.15        | 0.45             | 0.07        | 216                                 |
| 15                              | Control recording | 0.09        | 0.4              | 0.075       | 279                                 |
|                                 | Effects           | 0.1         | 0.45             | 0.1         | 265                                 |



A-Control recording

B, C, D and E- Effects of Isoprenaline (Ipren) at 0.1 mg/kg BW, 15 s (B), 30 s (C), 45 s (D) and 60 s (E) after its injection

F, G and H- Effects of EASa at a dose of 10 mg/kg BW, 10 s (F), 30 s (G) and 60 s (H) after the effects of Isoprenaline (Ipren).

**Figure 2.** Effects of *Senna alata* aqueous extract (EASa) and Isoprenaline (Ipren), as a function of time, on rabbit ECG

#### 4.2.2. Effects of EASa on Isoprenaline-induced Arrhythmia in Rabbits

Figure 2 shows the normal rabbit ECG in lead DII, with the P wave of 0.15 mV, the QRS complex of 0.65 mV and the T wave of 0.1 mV. Its frequency is 192 bpm.

Isoprenaline, administered at a dose of 0.1 mg/kg BW, does not cause effects on the amplitudes of the P, T waves, and the QRS complex, but causes an increase in frequency (Figure 2), followed by an arrhythmia characterized by variations in frequency that go from 192 bpm to 252 bpm after 30 s, then to 228 bpm after 45 s, and finally to 245 bpm after 60 s. When, following this arrhythmia, the aqueous extract of *Senna alata* is injected at a dose of 10 mg/kg BW, the frequency gradually decreases over time until reaching a rhythm of 198 bpm, statistically identical ( $p > 0.05$ ) to the normal rhythm (192 bpm), after 60 s (Figure 2). The injection of EASa also leads to a regulation of the rhythm and, at the same time, the isoelectric line,

disturbed with the appearance of arrhythmia, also gradually becomes normal.

## 5. Discussion

The pharmacological study of the effects of EASa shows that intravenous administration of this extract at doses ranging from 5.10<sup>-3</sup> to 15 mg/kg BW has no significant impact on the durations of the PR, QT intervals and the ST segment. However, at low doses of EASa, between 5.10<sup>-2</sup> and 5.10<sup>-1</sup> mg/kg BW, tachycardia and a slight increase in the amplitude of the P wave and the QRS complex appear. For higher doses (above 5.10<sup>-1</sup> mg/kg BW, and up to 15 mg/kg BW), EASa always causes an increase in the amplitude of the P wave and the QRS complex, accompanied by bradycardia. Since EASa has no notable effects on the intervals separating the different waves, this bradycardia induced by this extract



would be of sinus origin, because the electrocardiogram shows a normal-looking trace with a slowed rhythm [8,9]. Also, the observed tachycardia would also be of sinus origin. The effects of EASa at low doses ( $5.10^{-3}$  to  $5.10^{-2}$  mg/kg BW), i.e., an increase in P wave and QRS complex amplitude and frequency, indicate that this extract contains adrenergic-like substances [10]. In addition, the extract exhibits at high doses (greater than  $5.10^{-1}$  mg/kg BW, and up to 15 mg/kg BW) cardiotonic and bradycardic effects similar to those of digitalis-type substances [6,11,12,13]. The negative chronotropic effect would be associated with an increase in potassium outflow, which would lead to a decrease in the excitability of the cardiac muscle [14]. Given this potential "digitalis-like" effect, it is possible that EASa is a cardioprotective substance, which is justified by its antioxidant potential and by the presence of polyphenols identified in this extract by phytochemical screening. After induction of cardiac arrhythmia and tachycardia by Isoprenaline administered at a dose of 0.1 mg/kg BW, administration of the EASa dose at 10 mg/kg BW results in a significant decrease in heart rate and a gradual return to normal heart rate. This effect makes EASa an antiarrhythmic substance.

## 6. Conclusion

Pharmacological tests on the effects of EASa on normal rabbit ECG reveal that this substance, at low doses, causes an increase in the amplitude of the P wave and the QRS complex and causes tachycardia. In contrast, bradycardia is obtained for higher doses with the same effects on P waves and the QRS complex. Thus, at low doses, EASa has adrenergic-type properties and, at high doses, digitalis-type properties. In rabbit ECG, EASa corrects cardiac rhythm disturbances, which presented as tachycardia and arrhythmia induced by prior administration of Isoprenaline. These effects of EASa on cardiac arrhythmia show that this extract has antiarrhythmic properties. This justifies the use of *Senna alata* (Fabaceae) as a traditional medicine to treat heart diseases.

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