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# Anticonvulsant and Analgesic Effects of *Harpephyllum caffrum* Bernh. ex C.F. Krauss [Anacardiaceae] Stem-Bark Aqueous Extract in Mice

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**Abstract:** This study was undertaken to evaluate the anticonvulsant and analgesic effects of *Harpephyllum caffrum* stem-bark aqueous extract (HCE) in mice. The anticonvulsant effect of the plant's stem-bark extract (HCE, 50-800 mg $kg^{-1}$ intraperitoneally) was examined against pentylenetetrazole (PTZ)- and picrotoxin (PCT)-induced seizures, while the analgesic effect of the extract (HCE, 50-800 mg $kg^{-1}$ I. p.) was evaluated by hot-plate and acetic acid analgesic test methods. *H. caffrum* stem-bark extract (HCE, 100-800 mg $kg^{-1}$ I. p.) dose-dependently and significantly delayed ($p<0.05$-$0.001$) the onset of the seizures and profoundly antagonized, PTZ- and PCT-induced seizures. Moreover, HCE (50-800 mg $kg^{-1}$ I. p.) produced dose-dependent, significant analgesic effects ($p<0.05$-$0.001$) against thermally and chemically-induced nociceptive pain in mice. The findings of the present study appear to suggest that *H. caffrum* stem-bark aqueous extract produces its anticonvulsant effect by enhancing GABAergic neurotransmission and/or action in the brain. The results also seem to suggest that *H. caffrum* stem-bark extract possesses centrally- and peripherally-mediated analgesic properties. Although the precise mechanisms of the anticonvulsant and analgesic actions of HCE could not be established, the findings of this laboratory animal study indicate that *H. caffrum* stem-bark aqueous extract possesses anticonvulsant and analgesic properties. These findings lend pharmacological credence to the suggested folkloric, ethnomedical uses of the plant as a natural supplementary remedy in the management or control of childhood convulsions and epilepsy, as well as in the treatment or management of painful conditions in some rural communities of South Africa.

**Key words:** *Harpephyllum caffrum*, stem-bark aqueous extract, anticonvulsant and analgesic properties

## INTRODUCTION

In South Africa, *Harpephyllum caffrum* (Bernh. ex C.F. Krauss) [family: Anacardiaceae] is commonly known as 'wild plum' or 'bush mango' in English Language; or 'umgwenya' in isiZulu language (Van Wyk *et al*., 2002; Dlamini, 2004). The natural distribution of *H. caffrum* is restricted to southern Africa. This ornamental garden tree is distributed throughout the eastern part of southern Africa; from the Eastern Cape Province of South Africa northwards through KwaZulu-Natal Province, Swaziland, southern Mozambique, Limpopo Province and then into Zimbabwe (Dlamini, 2004). *H. caffrum* is a large and attractive, single-stemmed, perennial, erect, terrestrial, evergreen deciduous tree that grows up to 15 m in height. It is commonly planted as a street tree in many South African towns and cities. The main stem of *H. caffrum* is clean and straight. The bark is smooth when young, becoming rough and dark grey-brown as it grows older (Van Wyk *et al*., 2002; Dlamini, 2004). Extracts from various morphological parts of *H. caffrum* have been reported to contain numerous polyphenolic compounds, protocatechuic acid, kaempferol and other flavonoids (Watt and Breyer-Brandwijk, 1962; El-Sherbeiny and El-Ansari, 1976; Van Wyk *et al*., 2002).

The stem-bark of *H. caffrum* is commonly used in South African traditional medicine for the treatment, management and/or control of an array of human ailments, including childhood convulsions, epilepsy and painful conditions. It is usually applied in the forms of facial saunas and skin washes to treat acne, eczema and similar skin diseases. Decoctions of the stem-bark are also used

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as blood purifiers by people with 'bad blood' that results in pimples on the face. Powdered burnt stem-bark of the plant is applied to scarifications to treat sprains and bone fractures (Van Wyk *et al*., 2002; Dlamini, 2004). The tree's burnt stem-bark is also used for headaches (Van Wyk *et al*., 2002). Root decoctions of *H. caffrum* are traditionally taken for paralysis thought to have been contracted from walking over an area that has been 'poisoned' or polluted through sorcery in some parts of Eastern Cape Province of South Africa (Dlamini, 2004). Recent studies in our laboratories (Ojewole, 2006a) have shown that *H. caffrum* stem-bark aqueous extract possesses hypoglycaemic and hypotensive activities in laboratory animals. Some traditional health practitioners in KwaZulu-Natal Province of South Africa have claimed that decoctions and infusions of *H. caffrum* stem-bark are effective remedies in the management, control and/or treatment of childhood convulsions and epilepsy, as well as in the treatment of headaches and body pains. The core aim of the present study was, therefore, to evaluate the anticonvulsant and analgesic properties of *H. caffrum* stem-bark aqueous extract in mice experimental paradigms.

## MATERIALS AND METHODS

The experimental protocols and procedures used in this study were approved by the Ethics Committee of the University of KwaZulu-Natal, Durban 4000, South Africa and conform to the Guide to the Care and Use of Animals in Research and Teaching (published by the Ethics Committee of the University of Durban-Westville, Durban 4000, South Africa).

**Plant material:** Fresh stem-bark pieces of *Harpephyllum caffrum* (Bernh. ex C.F. Krauss) were collected on the Westville Campus of the University of KwaZulu-Natal, Durban, South Africa, between June and October, 2004. The plant was identified by Professor H. Baijnath, the Taxonomist/Curator of the former University of Durban-Westville's Department of Botany, as those of *Harpephyllum caffrum* (Bernh. ex C.F. Krauss) [family: Anacardiaceae]. Voucher specimen of the plant (S/N-OJ-005) has been deposited in the Herbarium of the University's Botany Department.

**Preparation of *H. caffrum* stem-bark aqueous extract:** Fresh pieces of *H. caffrum* stem-bark were air-dried at room temperature. One kilogramme of the air-dried stem-bark of the plant was milled into fine powder in a Waring commercial blender (Waring Instruments Inc., Springfield, Missouri, USA). The powdered stem-bark was macerated twice in distilled water on each occasion with 2.5 L of distilled water at room temperature for 48 h (with occasional shaking). The combined aqueous extract solubles were concentrated to dryness under reduced pressure at 60±1°C in a Heidolph® rotary evaporator (Heidolph Instruments, Schwabach, Germany). The resulting aqueous extract was freeze-dried in a Forma Scientific® freeze dryer (Forma Scientific Inc., Ohio, USA), finally giving 29.61 g [i.e., 2.961% yield] of a light brown, powdery crude aqueous stem-bark extract of *H. caffrum* (HCE). Without any further purification, aliquot portions of this crude extract residue were weighed and dissolved in distilled water for use on each day of our experiments.

**Animals:** Healthy, Balb C male and female mice (*Mus domesticus*) weighing 20-25 g were used. The animals were kept and maintained under laboratory conditions of temperature, humidity and light and were allowed free access to food (standard pellet diet) and water *ad libitum*. The animals were divided into plant extract- and drug-treated test and distilled water-treated control groups of 8-10 mice per group. All the animals were fasted for 16 h, but still allowed free access to water, before the commencement of our experiments.

**Acute toxicity testing:** The median lethal dose ($LD_{50}$) of *H. caffrum* stem-bark aqueous extract was determined in mice, using a modified method of Lorke (1983). Mice fasted for 16 h were randomly divided into experimental groups of 8 mice per group. Stepwise, escalated doses of *H. caffrum* stem-bark aqueous extract (HCE, 25, 50, 100, 200, 400, 800, 1600 and 3200 mg $kg^{-1}$) were separately administered intraperitoneally (i.p.) to the mice in each of the test groups. Each of the mice in the control group was treated with distilled water (3 mL $kg^{-1}$ i.p.) only. The mice in both the test and control groups were then allowed free access to food and water and observed over a period of 48 h for signs of acute toxicity. The number of deaths (caused by the extract) within this period of time was noted and recorded. Log dose-response plots were constructed for the plant's extract, from which the median lethal dose ($LD_{50}$) of the aqueous extract was determined.

**Evaluation of anticonvulsant activity:** The mice used for anticonvulsant evaluation of the plant's extract were divided into eight experimental groups of 10 mice per group. The anticonvulsant testing method of Vellucci and Webster (1984), modified by Amabeoku and Chikuni (1993) and Mahomed and Ojewole (2006), was used to assess the anticonvulsant property of *H. caffrum* stem-bark aqueous extract (HCE) in the mice. Standard convulsant agents, pentylenetetrazole (PTZ, 90 mg $kg^{-1}$ i.p.) and picrotoxin (PCT, 10 mg $kg^{-1}$ i.p) were used to

induce convulsions (seizures) in the mice. Phenobarbitone (PBT, 20 mg $kg^{-1}$ i.p.) and diazepam (DZP, 0.5 mg $kg^{-1}$ i.p.) were used as reference anticonvulsant drugs for comparison. Following induction of convulsions in the test mice (with intraperitoneal injections of the convulsant agents), the animals were observed for 30 min for signs of neurological deficits, especially hind-limb tonic seizures or convulsions. Hind-limb tonic extensions of the mice were regarded as manifestations of seizures. The ability of the plant's extract (HCE, 50-800 mg $kg^{-1}$ i.p.) to prevent the seizures or delay/prolong the latency or onset of the hind-limb tonic extensions, was considered as an indication of anticonvulsant activity (Navarro-Ruiz *et al*., 1995; Amabeoku *et al*., 1998). Because the plant's extract and the reference drugs used in this study were dissolved in distilled water each day at the beginning of our experiments, distilled water (3 mL $kg^{-1}$ i.p.)-treated mice were used as control animals.

**Evaluation of analgesic activity:** The hot-plate (thermal) and acetic acid (chemical) analgesic test methods were used.

**Hot-plate test method:** The hot-plate (thermal) analgesic test method employed in this study was modified from those described in detail earlier by Eddy and Leimback (1953), Lanhers *et al.* (1992) and Williamson *et al.* (1996). A 600- mL glass beaker was placed on a Heidolph® MR 2002 (Heidolph Instruments, Schwabach, Germany) hot-plate (with adjustable temperature). The temperature of the hot-plate was then regulated to 45±1°C. Each mouse was separately placed in the glass beaker (on the hot-plate) in order to obtain the animal's response to electrical heat-induced pain (licking of the forepaws and eventually jumping out of the glass beaker). Jumping out of the beaker was taken as an indication of the animal's response to heat-induced pain. The time taken for each mouse to jump out of the beaker (i.e., reaction time) was noted and recorded in seconds. Each mouse served as its own control. Thus, before treatment, its reaction time was determined thrice at 1 h intervals. The mean of these three determinations constituted the initial reaction time i.e., reaction time before treatment of the mouse. The mean reaction times of all the mice used were pooled to obtain the final, control mean reaction time (Tb). Each of the test mice was thereafter treated with either distilled water, *H. caffrum* stem-bark aqueous extract (HCE), or morphine (MPN) intraperitoneally. Twenty minutes after treatment with distilled water, the plant's extract (HCE), or reference drug (morphine), the reaction time was again evaluated, but only once on this occasion. This reaction time value was pooled for the mice used in each treatment group and the final test mean reaction time value (Ta) for each treatment group was calculated. This final test mean reaction time value (Ta) represented after-treatment reaction time for each group of treated mice. This test mean reaction time value (Ta) was subsequently used to determine percentage thermal pain relief or protection, by applying the formula:

$$\text{Protection against thermal pain (\%)} = \frac{\text{(Test mean-Control mean)}}{\text{Control mean}} \times 100$$

The plant extract (HCE) was tested at doses of 50, 100, 200, 400 and 800 mg $kg^{-1}$ i.p., respectively. The reference drug, morphine (MPN) was used at a dose of 10 mg $kg^{-1}$ i.p. only. Treated control mice received distilled water (3 mL $kg^{-1}$ i.p.) only.

**Acetic acid test method:** The acetic acid analgesic test method used in this study was adopted from those described in detail earlier by Williamson *et al.* (1996), Koster *et al.* (1959), Zakaria *et al.* (2001) and Silva *et al.* (2003). The mice used were divided into two broad experimental groups of test and control animals. There were two separate (A and B) groups of control mice. Group A control mice were not pretreated with anything at all and the 8 mice in this Group A served as the untreated control animals for the mice in all the other groups. Each of these untreated Group A mice was however, treated with intraperitoneally administered 0.2 mL of a 3% w/v acetic acid solution (Koster *et al*., 1959). Each mouse in the control Group B was pretreated with distilled water (3 mL $kg^{-1}$ i.p.) only. Diclofenac (DIC, 100 mg $kg^{-1}$ i.p.) was used as the reference drug for comparison. Each mouse in the treated control Group B and in the other test groups, was treated with either distilled water (3 mL $kg^{-1}$ i.p.), diclofenac (DIC, 100 mg $kg^{-1}$ i.p.), or a graded dose of *H. caffrum* stem-bark aqueous extract (HCE, 50, 100, 200, 400 and 800 mg $kg^{-1}$ i.p.). Twenty minutes after treatment with distilled water, reference drug (DIC), or a dose of the plant's extract (HCE), 0.2 mL of a 3% w/v acetic acid solution was injected (i.p.) to each of the treated mice (Koster *et al*., 1959). The numbers of writhes (i.e., abdominal contractions and stretches) that occurred within the first 20 min following acetic acid administration were counted and recorded. The recorded numbers of acetic acid-induced writhes that occurred in the HCE, DIC and distilled water pretreated mice were compared with those in the untreated Group A control mice.

**Data analysis:** Experimental data obtained are presented as means (±SEM). Data from distilled water-treated control mice were used as baseline values. The differences between the data obtained with the plant's extract and

reference anticonvulsant drug-treated test mice and the data obtained with distilled water-treated control animals, were subjected to one-way analysis of variance (ANOVA; 95% confidence interval), followed by Scheffe's multiple range comparison test. The proportion of mice convulsing was analysed by Chi-Squared test (Bienvenu *et al*., 2002). In all cases, values of $p \leq 0.05$ were taken to imply statistical significance.

## RESULTS

Intraperitoneal administrations of graded doses of *H. caffrum* stem-bark aqueous extract (HCE) in mice gave an $LD_{50}$ value of 1345±108 mg $kg^{-1}$. This finding probably suggests that the plant's stem-bark aqueous extract is relatively safe.

**Effect of *H. caffrum* stem-bark aqueous extract (HCE) on pentylenetetrazole (PTZ)-induced seizures:** Pentylenetetrazole (PTZ, 90 mg $kg^{-1}$ i.p.) produced hind-limb tonic seizures in all the 10 mice used. *H. caffrum* stem-bark aqueous extract (HCE, 100-800 mg $kg^{-1}$ i.p.) produced dose-related, significant protection ($p<0.05$-$0.001$) of the mice against PTZ-induced seizures (Table 1). The plant's extract (HCE, 100-800 mg $kg^{-1}$ i.p.) significantly delayed ($p<0.05$-$0.001$) the onset of the seizures and antagonized, PTZ-induced seizures. The reference anticonvulsant drugs used, phenobarbitone (PBT, 20 mg $kg^{-1}$ i.p.) and diazepam (DZP, 0.5 mg $kg^{-1}$ i.p.), also profoundly delayed ($p<0.001$) the onset of and significantly antagonized, PTZ-induced seizures (Table 1).

**Effect of *H. caffrum* stem-bark aqueous extract (HCE) on picrotoxin (PCT)-induced seizures:** Picrotoxin (PCT, 10 mg $kg^{-1}$ i.p.) produced hind-limb tonic seizures in all the 10 mice used. *H. caffrum* stem-bark aqueous extract (HCE, 100-800 mg $kg^{-1}$ i.p.) produced dose-related, significant protection ($p<0.05$-$0.001$) of the mice against PCT-induced seizures (as in the PTZ-induced tonic seizures Table 2). Moreover, the plant's extract (HCE, 100-800 mg $kg^{-1}$ i.p.) significantly delayed ($p<0.05$-$0.001$) the onset of the seizures and antagonized, PCT-induced seizures. The reference anticonvulsant drugs used, phenobarbitone (PBT, 20 mg $kg^{-1}$ i.p.) and diazepam (DZP, 0.5 mg $kg^{-1}$ i.p.), profoundly delayed ($p<0.001$) the onset of the seizures and significantly antagonized, PCT-induced seizures (Table 2).

**Effects of *H. caffrum* stem-bark aqueous extract (HCE) on thermally- and chemically-induced pain:** In the experimental animal paradigms used, *H. caffrum* stem-bark aqueous extract (HCE, 50-800 mg $kg^{-1}$ i.p.) produced dose-related and significant analgesic effects ($p<0.05$-$0.001$) against thermally- and chemically-induced pain (Table 3 and 4). *H. caffrum* stem-bark aqueous extract (HCE, 50-800 mg $kg^{-1}$ i.p.) dose-dependently and significantly delayed ($p<0.05$-$0.001$) the reaction times of the mice used in the hot-plate analgesic test method (Table 3). In the same hot-plate analgesic test method, morphine (MPN, 10 mg $kg^{-1}$ i.p.) profoundly delayed ($p<0.001$) the reaction times of the animals. Moreover, the plant's extract (HCE, 50-800 mg $kg^{-1}$ i.p.) dose-dependently and significantly inhibited ($p<0.05$-$0.001$) acetic acid-induced writhing in mice (Table 4). Similarly, diclofenac (DIC, 100 mg $kg^{-1}$ i.p.) markedly and significantly reduced ($p<0.001$) acetic acid-induced writhes in the mice.

## DISCUSSION

The high $LD_{50}$ value (of 1345±108 mg $kg^{-1}$ i.p.) obtained in this study for *Harpephyllum caffrum* stem-bark aqueous extract probably suggests that the plant extract is relatively safe in and/or non-toxic to, mice.

In South Africa, febrile convulsion among infants and young children is a common phenomenon, especially in the rural communities. Some of the infantile and/or childhood convulsions often result in death. Although there are a number of synthetic, pharmaceutical anticonvulsant drugs currently available for use in the management, control and/or treatment of individuals with convulsion or epilepsy, most of these synthetic anticonvulsant drugs are not only inaccessible and unaffordable, but they also possess many adverse effects.

Table 1: Effects of *Harpephyllum caffrum* stem-bark aqueous extract (HCE), phenobarbital (PBT) and diazepam (DZP) on pentylenetetrazole (PTZ)-induced seizures in mice

| Treatment dose (mg $kg^{-1}$) | | | | No. convulsed/ | % Animals not convulsed | Latency of tonic |
|---|---|---|---|---|---|---|
| PTZ | HCE | Phenobarbital | Diazepam | No. used | (i.e., % animals protected) | convulsion (min) |
| 90 | - | - | - | 10/10 | 0 | 8.50±0.71 |
| 90 | 100 | - | - | 7/10 | 30 | 12.28±1.30* |
| 90 | 200 | - | - | 6/10 | 40 | 15.30±1.65* |
| 90 | 400 | - | - | 5/10 | 50 | 18.46±2.12** |
| 90 | 800 | - | - | 3/10 | 70 | 22.35± 2.34*** |
| 90 | - | 20 | - | 0/10[c] | 100 | ∞*** |
| 90 | - | - | 0.5 | 0/10[c] | 100 | ∞*** |

*$p<0.05$, **$p<0.01$, ***$p<0.001$vs pentylenetetrazole (PTZ, 90 mg $kg^{-1}$ I p.) control, [c]$p<0.001$ vs pentylenetetrazole (PTZ, 90 mg $kg^{-1}$ i.p.) control; Chi-Squared test

Table 2: Effects of *Harpephyllum caffrum* stem-bark aqueous extract (HCE), phenobarbital (PBT) and diazepam (DZP) on picrotoxin (PCT)-induced seizures in mice

| Treatment dose (mg kg$^{-1}$) | | | | | | |
|---|---|---|---|---|---|---|
| PCT | HCE | Phenobarbitone | Diazepam | No. convulsed/ No. used | (%) Animals not convulsed (i.e., % animals protected) | Latency of tonic convulsion (min) |
| 10 | - | - | - | 10/10 | 0 | 8.46±0.66 |
| 10 | 100 | - | - | 7/10 | 30 | 13.50±1.35* |
| 10 | 200 | - | - | 6/10 | 40 | 16.40±1.78* |
| 10 | 400 | - | - | 5/10 | 50 | 19.33±2.10** |
| 10 | 800 | - | - | 3/10 | 70 | 24.48±2.36*** |
| 10 | - | 20 | - | 1/10[c] | 90 | 28.56*** |
| 10 | - | - | 0.5 | 1/10[c] | 90 | 29.24*** |

*p<0.05, **p<0.01, ***p<0.001, vs picrotoxin (PCT, 10 mg kg$^{-1}$ i.p.) control, [c]p<0.001 vs picrotoxin (PTZ, 10 mg kg$^{-1}$ i.p.) control; Chi-Squared test

Table 3: Effects of *Harpephyllum caffrum* stem-bark aqueous extract (HCE, 50-800 mg kg$^{-1}$ i.p.) and morphine (MPN, 10 mg kg$^{-1}$ i.p.) on electrical heat-induced pain

| Group | Dose (i.p.) | Mean reaction time (sec) | Protection (%) |
|---|---|---|---|
| Control Group A (untreated) | 0 | 10.78±1.50 | 0.00 |
| Control Group B (distilled water-treated) | 3 mL kg$^{-1}$ | 10.82±1.44 | 0.37 NS |
| HCE | 50 mg kg$^{-1}$ | 12.15±1.40* | 12.71* |
| HCE | 100 mg kg$^{-1}$ | 13.08±1.42* | 21.34* |
| HCE | 200 mg kg$^{-1}$ | 14.45±1.43** | 34.04** |
| HCE | 400 mg kg$^{-1}$ | 16.78±1.46*** | 62.72*** |
| HCE | 800 mg kg$^{-1}$ | 18.57±1.48*** | 80.29*** |
| Morphine (MPN) | 10 mg kg$^{-1}$ | 21.35±2.05*** | 98.05*** |

NS = p>0.05; *p<0.05; **p<0.01; ***p<0.001 vs control, Each value represents the mean (±SEM) of 8 observations

Table 4: Effects of *Harpephyllum caffrum* stem-bark aqueous extract (HCE, 50-800 mg kg$^{-1}$ i.p.) and diclofenac (DIC, 100 mg kg$^{-1}$ i.p.) on acetic acid-induced writhes

| Group | Dose (i.p.) | No. of writhes (contractions) in 20 min | Inhibition (%) |
|---|---|---|---|
| Control Group A (untreated) | 0 | 42.36±5.40 | 0.00 |
| Control Group B (distilled water-treated) | 3 mL kg$^{-1}$ | 42.16±5.36 | 0.47 NS |
| HCE | 50 mg kg$^{-1}$ | 33.38±4.11* | 21.20* |
| HCE | 100 mg kg$^{-1}$ | 24.45±3.18** | 42.28** |
| HCE | 200 mg kg$^{-1}$ | 15.43±2.05** | 63.57** |
| HCE | 400 mg kg$^{-1}$ | 10.33±1.20*** | 75.61*** |
| HCE | 800 mg kg$^{-1}$ | 6.40±0.65*** | 84.89*** |
| Diclofenac (DIC) | 100 mg kg$^{-1}$ | 3.12±0.30*** | 92.63*** |

NS = p>0.05; *p<0.05; **p<0.01; ***p<0.001 vs control, Each value represents the mean (±SEM) of 8 observations

There is, therefore, a dire need for the development of cheap, effective and safe anticonvulsant agents from plants and other natural sources.

The results of the present study provide evidence in favour of the anticonvulsant activity of *H. caffrum* stem-bark aqueous extract in the experimental animal model used. In general, the average onset and duration of convulsions were markedly delayed and reduced, respectively. These findings appear to suggest that *H. caffrum* stem-bark aqueous extract might have inhibited and/or attenuated PTZ- and PCT-induced seizures of the mice used by enhancing, or in some ways interfering with, GABAergic neurotransmission and/or action in the brain.

The results obtained in the analgesic test experiments also appear to suggest that *H. caffrum* stem-bark aqueous extract possesses centrally- and peripherally-mediated analgesic properties. The peripheral analgesic effect of the plant's extract may be mediated through inhibition of cyclo-oxygenases and/or lipoxygenases (and other inflammatory mediators), while the central analgesic action of the plant's extract may be mediated via inhibition of central pain receptors. This hypothesis is in consonance with those of Eddy and Leimback (1953), Williamson *et al.* (1996) and Koster *et al.* (1959) who postulated that acetic acid-induced writhing and hot-plate test methods are useful techniques for the evaluation of peripherally and centrally-acting analgesic drugs, respectively.

The exact mechanisms of the anticonvulsant and analgesic actions of HCE could not be established in this study. We were also unable to identify with certainty, the chemical constituent/s of HCE that might be responsible for the observed anticonvulsant and analgesic effects of the extract. However, a number of investigators have shown that tannins and other polyphenolic compounds (e.g., coumarins), flavonoids, triterpenoids and a host of other secondary plant metabolites possess analgesic, anti-inflammatory, anticonvulsant, hypoglycaemic and antihypertensive properties in various experimental animal models (Asongalem *et al.*, 2004; Dongmo *et al.*, 2003; Taesotiku *et al.*, 2003; Adzu *et al.*, 2003; Jäger *et al.*, 1996; Akah and Okafor, 1992; Mahomed and Ojewole, 2006; Ojewole, 2004; 2005b; 2006b; 2007). *H. caffrum* is known to contain numerous polyphenolic compounds, protocatechuic acid, kaempferol and other flavonoids (Watt and Breyer-Brandwijk, 1962; El-Sherbeiny and El-Ansari, 1976; Van Wyk *et al.*, 2002). It is not unreasonable, therefore, to speculate that some of the polyphenolic compounds and flavonoids present in the plant are probably responsible for the observed anticonvulsant and analgesic effects of the plant's aqueous extract.

Our previous pharmacological exploration of the Anacardiaceae family has revealed that many members of the family possess analgesic, anti-inflammatory,

anticonvulsant and hypoglycaemic properties (Ojewole, 2003a, b, 2004, 2005a, 2006a, 2007). It is, therefore, not surprising that *H. caffrum*, another member of the Anacardiaceae family, possesses anticonvulsant and analgesic activities. However, the pharmacological actions of HCE unveiled in the present study appear to provide some rational explanations and justifications for the ethnomedical uses of the plant in anecdotal, folkloric, African traditional medicines. In summary, the experimental evidence obtained in the present laboratory animal study indicates that *H. caffrum* stem-bark aqueous extract (HCE) possesses anticovulsant and analgesic properties. These findings lend pharmacological credence to the suggested folkloric, ethnomedical uses of *H. caffrum* as a natural supplementary remedy for the management and/or control of childhood convulsions and epilepsy, as well as for general painful body conditions in some rural communities of South African.

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