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Analgesic and anti-inflammatory effects of the aqueous extract of leaves of *Persea americana* Mill (Lauraceae)

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Abstract

The aqueous extract of *Persea americana* leaves produced a dose-dependent inhibition of both phases of formalin pain test in mice, a reduction in mouse writhing induced by acetic acid and an elevation of pain threshold in the hot plate test in mice. The extract also produced a dose-dependent inhibition of carrageenan-induced rat paw oedema. The results obtained indicate that the extract possesses analgesic and anti-inflammatory effects.

Keywords: *Persea americana*; Anti-inflammatory; Analgesic effects

1. Introduction

Persea americana, known as avocado or alligator pear, is an evergreen tree approximately 20 m high which originated in Central America but is now found in most tropical and subtropical countries. The bark, fruit and leaf are used in traditional medicine in South and Central America, West Indies and Africa for the treatment of various ailments such as menorrhagia [1], hypertension [2], stomach ache, bronchitis [3], diarrhoea and diabetes [4].

An infusion of the leaves is used in the treatment of inflammatory conditions, pain and fever (Jonah, N. 1999, personal communication).

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To determine the medicinal properties of *P. americana*, we investigated the analgesic and anti-inflammatory activities of the aqueous extract using different animal models.

2. Experimental

2.1. Preparation of plant extract

Fresh leaves of *P. americana* were collected from Mushin in Lagos State, Nigeria, in May 2000. Botanical authentication was confirmed by Prof. Dele Olowokudejo of the Department of Botany and Microbiology, Faculty of Science, University of Lagos, Lagos, Nigeria.

The fresh leaves (470 g) were boiled in 2 l of distilled water for 1 h, decanted and filtered. The filtrate was evaporated to dryness in an oven at 40 °C. The dried extract (yield: 7% w/w) was reconstituted in distilled water to a concentration of 400 mg/ml.

2.2. Phytochemical tests

Screening of the plant extract gave positive reactions for flavonoids, alkaloids, reducing sugars, tannins and saponins.

2.3. Animals

Swiss mice (18–22 g) and Wistar rats (130–150 g) of either sex kept at the Laboratory Animal Center of the College of Medicine, University of Lagos, Lagos, Nigeria were used. The animals maintained under standard environmental conditions had free access to standard diet (Pfizer feeds, PLC, Lagos) and water ad libitum.

2.4. Mouse writhing assay

The extract (200–1600 mg/kg, orally) or acetylsalicylic acid (100 mg/kg, sc) was administered to mice before intraperitoneal injection of acetic acid (0.6% v/v in normal saline, 10 ml/kg) [5]. The number of writhes was counted for 30 min.

2.5. Hot plate test

This was done using a modification of the method already described [6]. Mice were placed in a glass beaker on a hot plate (56 ± 1 °C) and the reaction time to thermal stimulus was observed with a cut-off time of 10 s.

The extract (200–1600 mg/kg, orally) and morphine (2 mg/kg, sc) were given 30 min before the test. Control animals received distilled water (10 ml/kg, orally).

2.6. Formalin test

Twenty microliters of 1% formalin was injected subcutaneously into the right hind paw of mice [7]. The time (in seconds) spent in licking and biting responses of the injected paw was taken as an indicator of pain response.

Responses were measured for 5 min (first phase) and 15–30 min (second phase) after formalin injection. Extract (200–1600 mg/kg, orally) or acetylsalicylic acid (100 mg/kg, sc) was administered 30 min before formalin injection. Control group was treated with distilled water (10 ml/kg).

2.7. Carrageenan-induced rat paw oedema

Inflammation was induced in rats by the injection of carrageenan (0.1 ml, 1% w/v in normal saline) into the sub-plantar tissue of the right hind paw [8]. The linear paw circumference was measured at hourly intervals for 6 h [9].

Extract (400–800 mg/kg) and indomethacin (10 mg/kg) were administered orally and subcutaneously, respectively, 1 h before induction of inflammation. Control animals received an equal volume of distilled water.

2.8. Acute toxicity

Mice were administered intraperitoneally and orally with the extract (1–10 g/kg). Mortality in each group was observed for 24 h.

2.9. Statistical analysis

Results are expressed as mean ± S.E.M. Student's *t*-test was used to analyse the significance of the results.

3. Results and discussion

The aqueous extract of *P. americana* leaves caused a significant ($P < 0.05$) and dose-dependent inhibition of the control writhes (Table 1). The inhibition by 1600 mg/kg extract was similar to that produced by 100 mg/kg of acetylsalicylic acid (57.2% and 58.0%, respectively). The extract increased the reaction time in the hot plate test (Table 2). The inhibition (87.2%) shown by 800 mg/kg of extract was same as morphine (2 mg/kg, 87.0%).

Table 3 shows the effect of the extract on formalin-induced pain. There was a significant ($P < 0.05$) and dose-dependent inhibition of both phases, by the extract.

A greater inhibition (77.1%) was produced by the extract (800 mg/kg) compared to acetylsalicylic acid (68%) in phase II of the test.

The aqueous leaf extract of *P. americana* (800 mg/kg) produced a significant ($P < 0.05$) inhibition of the swelling caused by carrageenan at 3 h (Fig. 1). This effect was similar to that produced by indomethacin at the same time.

Table 1
Effect of *Persea americana* aqueous leaf extract on acetic acid-induced writhing in mice

Group	Doses (mg/kg)	No. of writhings (per 15 min)	% Inhibition
Control	–	126.63 ± 7.36	–
P. americana	200	100.33 ± 2.72*	20.77
	400	95.50 ± 6.90*	24.58
	800	74.33 ± 3.48**	41.300
	1600	54.17 ± 3.86**	57.22
Acetylsalicylic acid	100	53.17 ± 4.86**	58.01

Values are mean ± S.E.M. *$P < 0.05$, **$P < 0.01$ significantly different from control (Student's *t*-test).

Table 2
Effect of *Persea americana* aqueous leaf extract on the hot plate test in mice

Group	Dose (mg/kg)	Reaction time (mean ± S.E.M.)	% Inhibition
Control		1.00 ± 0.24	–
P. americana	200	2.25 ± 0.63*	55.55
	400	3.67 ± 0.67*	72.75
	800	7.83 ± 0.76**	87.23
	1600	6.42 ± 1.13**	84.42
Morphine	2	7.75 ± 0.46**	87.01

Values are mean ± S.E.M.; *$P < 0.05$, **$P < 0.01$ significantly different from control (Student's *t*-test).

Table 3
Effect of *Persea americana* aqueous extract on formalin-induced pain

Group	Doses (mg/kg)	0–5 min	% Inhibition	15–30 min	% Inhibition
Control		85.00 ± 2.26	–	91.83 ± 8.11	–
P. americana	200	66.17 ± 2.67**	22.15	70.17 ± 2.64*	23.59
	400	52.17 ± 1.31**	38.62	62.50 ± 1.38*	31.94
	800	51.33 ± 2.44**	39.61	21.00 ± 1.77**	77.13
	1600	50.33 ± 3.37**	40.79	38.17 ± 1.73**	58.43
Acetylsalicylic acid	100	83.17 ± 3.72**	2.15	29.40 ± 9.86**	67.98

Values are mean ± S.E.M. *$P < 0.05$, **$P < 0.01$ significantly different from control (Student's *t*-test).

Administration of the extract up to 1 g/kg (intraperitoneally) and 10 g/kg (orally) did not produce signs and symptoms of toxicity in mice.

The results of the study show that at all dose levels used, the extract significantly reduced acetic acid-induced writhing which suggests that its analgesic effects could

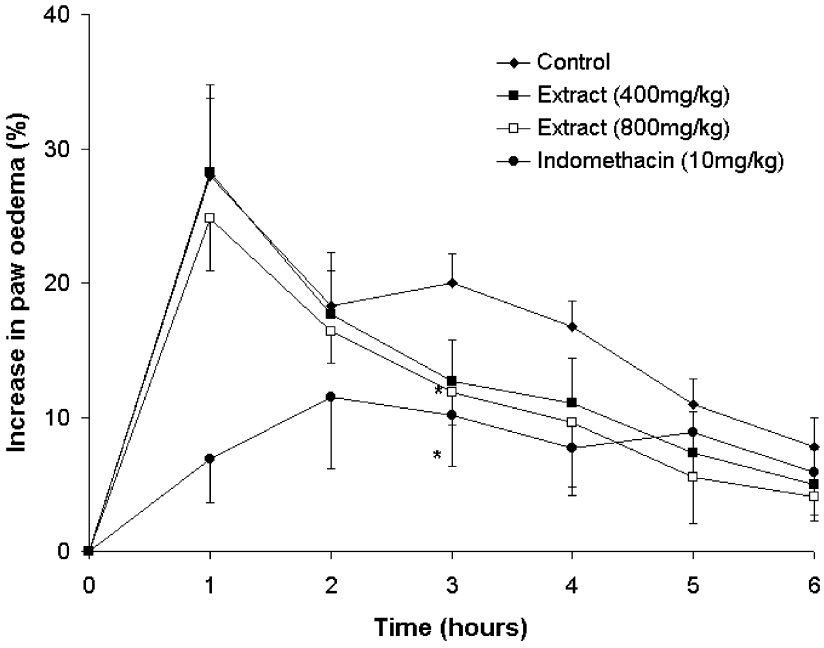

Fig. 1. Effect of *Persea americana* on carrageenan-induced oedema. Each point represents mean ± S.E.M. ($n = 5$) $^*P < 0.05$.

be peripherally mediated. The increase in the reaction time, by the extract to the thermal stimulus in the hot plate test indicates that the extract also possesses a central analgesic effect. The inhibition of both phases of formalin-induced pain, observed with the extract, confirms that its analgesic effects are mediated both centrally and peripherally [9,10,11].

Effect of the extract on carrageenan-induced paw oedema was most pronounced at the third hour of inflammatory response, which corresponds to the phase of prostaglandin release [12]. The results obtained show that *P. americana* possesses anti-inflammatory activity, which is consistent with its ability to inhibit prostaglandin synthesis in platelets [13].

The ability of the extract, in this study, to reduce the number of writhes, elevate the pain threshold to heat, inhibit both phases of formalin-induced pain confirms its analgesic and anti-inflammatory properties which may account for its use in traditional medicine.

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