Pharmaceutical Biology

ISSN: 1388-0209 (Print) 1744-5116 (Online) Journal homepage: informahealthcare.com/journals/iphb20

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To cite this article: Nkechi V. Offiah & Chidum E. Ezenwaka (2003) Antifertility Properties of the Hot Aqueous Extract of Guaiacum officinale, Pharmaceutical Biology, 41:6, 454-457, DOI: 10.1076/phbi.41.6.454.17823

To link to this article: https://doi.org/10.1076/phbi.41.6.454.17823

Pharmaceutical Biology
2003, Vol. 41, No. 6, pp. 454–457

1388-0209/03/4106-454$16.00

Antifertility Properties of the Hot Aqueous Extract of *Guaiacum officinale*

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Abstract

The hot aqueous extract of the aerial part (leaves, flowers, fruits and tender branches) of *Guaiacum officinale* Linn (Zygophyllaceae) was evaluated for antifertility effects. In over 50 trials, the extract caused abortion in mice and rats. The extract caused abortion in the second and third trimesters only. The abortion ED_{50} in pregnant mice was 320.50 ± 20.00 mg/kg, while the LD_{50} was 1280.13 ± 9.03 mg/kg. At a dose of 480.75 mg/kg, the extract significantly reduced the litter size in mice when given during the first trimester (day 5) of pregnancy. The extract did not produce contraction of either the primed or gravid uteri derived from these animals. Similarly, the extract did not cause contraction of the guinea-pig ileum. However, it potentiated the contractions caused by acetylcholine. These findings tend to support the utility of the hot water extract of *Guaiacum officinale* in folk medicine for antifertility purposes.

Keywords: *Guaiacum officinale,* abortion, contraction, antifertility, folk medicine.

Introduction

*Guaiacum officinal*e Linn (Zygophyllaceae) commonly known as *Lignum vitae,* is a small evergreen tree about 4–8 m in height when fully grown. It is native to the West Indies and Central America. *Guaiacum officinale* is the source of hard, dense wood and it was almost exterminated by the natives because of its medicinal use in venereal disease (Mabberley, 1997). The aerial part (leaves, flowers, fruits and tender branches) has a folk reputation for use as an antifertility agent, particularly for the expulsion of foetuses in early pregnancy. Other medicinal uses of the plant include molluscicidal properties (Mendes et al., 1993; Tania Maria de Almeida Alves et al., 1996) and anti-inflammatory activity (Duwiejua et al., 1994).

A review of the literature revealed no reported investigation on the antifertility effects of this plant. It was therefore considered of interest to investigate the effects of the hot aqueous extract of the aerial part of *Guaiacum officinale* on whole animals and on isolated guinea-pig ileum, gravid and non-gravid uteri of mice and rats.

Materials and methods

Plant material

The aerial part (leaves, flowers, fruits, and tender branches) of *Guaiacum officinale* was collected from The University of the West Indies, (U.W.I.) St. Augustine, Trinidad. The identity of the plant, also known as *Lignum vitae* (TRIN 28357), was established by Mrs. Yasmin S. Baksh-Comeau, curator of the National Herbarium, U.W.I. St. Augustine, Trinidad.

Animals

Albino mice and rats and guinea-pigs bred at the animal house, School of Veterinary Medicine, Faculty of Medical Sciences, U.W.I. St. Augustine, Trinidad were used. The animals had free access to water and were fed with standard livestock feeds (cubes for mice and rats and pellets for guinea-pigs). The guinea-pigs were also given green grass.

Preparation of the extract

The extract was prepared by boiling 100 g of the fresh aerial part of *Guaiacum officinale* in 200 ml of distilled water for

Accepted: April 17, 2003

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10 min (this is the method of preparation in folk medicine). After cooling and filtering, the solid content of the extract was determined (32.05 mg/ml). The extract was used fresh or frozen until needed.

Pharmacological methods

Pharmacological studies were performed with isolated guinea-pig ileum, gravid and non-gravid uteri of mice and rats, using standard procedures (Turner, 1965). The effects of (32.05 mg/ml) fresh extract of *Guaiacum officinale* in a 20 ml organ bath were compared to those of known effective concentrations of standard drugs, for example, acetylcholine (1–10 µg/ml), histamine (2–10 µg/ml) and oxytocin (0.05–0.4 IU/ml). The extract was added to the organ bath 5 min before each challenge with the standard drugs.

Effect of the extract on pregnant mice

Preliminary experiments were conducted on pregnant mice to establish the intraperitoneal effective dose (ED_{50}) and the lethal dose (LD_{50}) (Miller & Tainter, 1944; Lorke, 1983). Forty pregnant inbred albino mice weighing 30–50 g were randomly divided into five groups. Group A received 160.25 mg/kg of the extract, group B received 320.50 mg/kg of the extract, group C received 641.00 mg/kg of the extract, group D received 1282.00 mg/kg of the same extract and group E received 20 ml/kg of normal saline. All the drugs were administered intraperitoneally. The mice were observed for 24 h for vaginal bleeding, fetal discharge, death and any other adverse effects.

Effect of the extract on pregnant rats

Thirty pregnant rats weighing 250–300 g were randomly divided into five groups and treated with the extract as described above for the pregnant mice. The same dosages per kg were used. The animals were observed for 24 h for vaginal bleeding, fatal discharge, death and any other adverse effects.

Effect of the extract on litter size in mice

Twenty mice in their first trimester of pregnancy (weighing 29–35 g) were randomly divided into three groups. Group A received 300 mg/kg of the extract, group B received 480.75 mg/kg of the extract and group C received 20 ml/kg of normal saline. The drugs were administered intraperitoneally. The animals were observed for vaginal bleeding, fatal discharge, death or any other adverse effects, until they pupped after a gestation period of 20–22 days.

Drugs

The following drugs were used: acetylcholine chloride (Sigma), histamine dihydrochloride (Sigma), oxytocin (Sanofi), diethylstilbestrol and 5-hydroxytryptamine creatinine sulphate (Sigma).

Statistical analysis

Data were analysed using the general linear model procedure of SAS (1985).

Results

Effect of the extract on isolated tissues

Addition of up to 40.00 mg of the extract to a 20 ml organ bath did not induce contractions of the guinea-pig ileum. However, the addition of 1.6×10^{-3} mg of the extract potentiated acetylcholine-induced (1.1×10^{-8} M) contractions of the guinea-pig ileum (Table 1). Higher doses of the extract (0.08–0.65 mg to a 20 ml bath) inhibited acetylcholine-induced contractions and shifted the dose-response curve to the right. The maximal responses were raised (Fig. 1). On rat and mice isolated non-gravid and gravid uteri, the extract did not produce contraction at concentrations up to 32.05 mg; contractions caused by acetylcholine and oxytocin were inhibited.

Effect of the extract on whole animals

Table 2 shows the *in vivo* effects of the extract of *G. officinale* on pregnant mice. The data on pregnant rats showed similar effectiveness of the extract in causing fetal discharge. The fetuses were expelled encased within the placental membrane together with the caruncles. The expulsion of the fetuses was simultaneous with vaginal bleeding which was

Table 1. Effect of *G. officinale* on acetylcholine (1.1×10^{-8} M)-induced contraction of the guinea-pig ileum.

Treatment	Responses to acetylcholine in cm*	Percentage of control
Control	3.05 ± 0.01	100
Extract 0.4×10^{-3} mg	3.65 ± 0.21	119.67
Extract 0.8×10^{-3} mg	4.26 ± 0.33	139.67
Extract 1.6×10^{-3} mg	4.42 ± 0.12	144.92

* The values are mean ± SEM; n = 5.

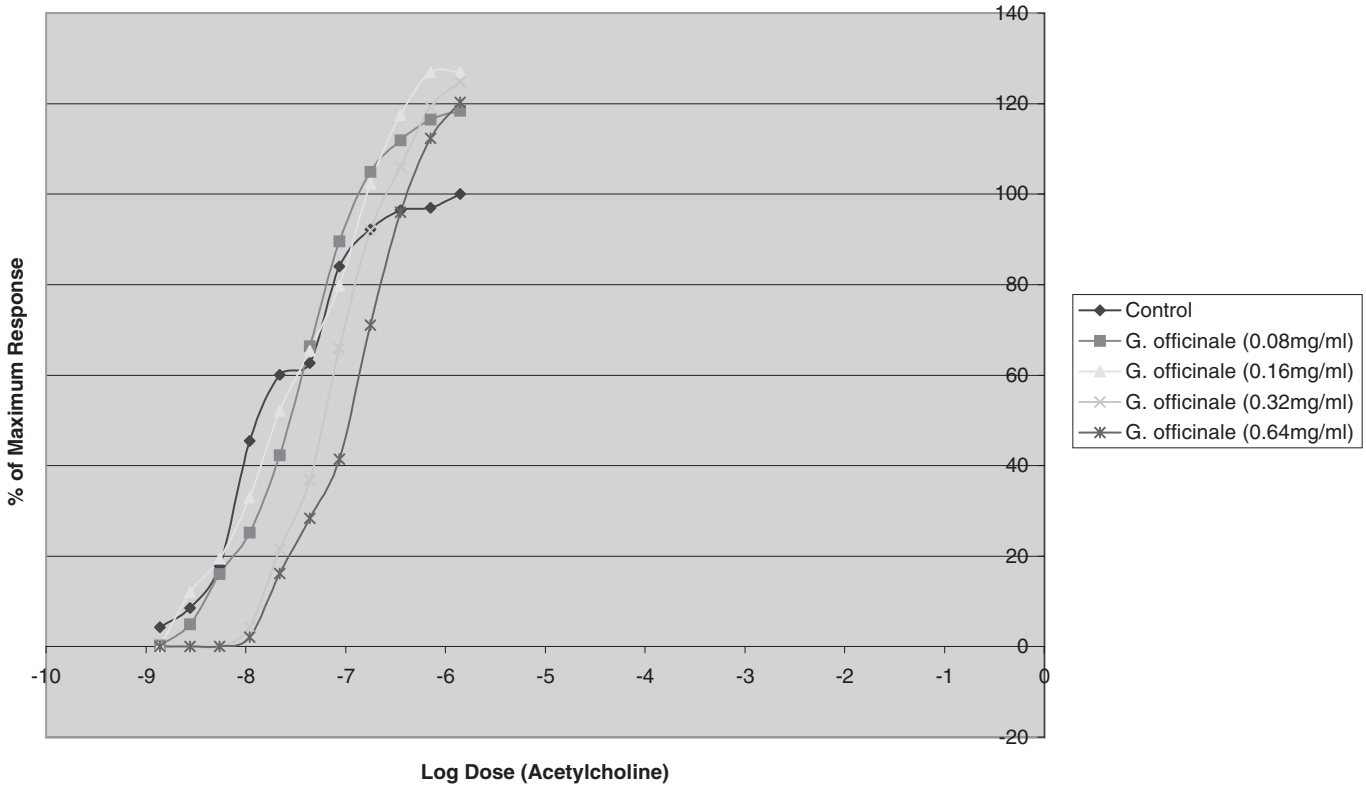

Figure 1. Effects of *Guaiacum officinale* on acetylcholine-induced contractions of the Guinea pig ileum.

Table 2. Effect of intraperitioneal administration of *Guaiacum officinale* in pregnant mice.

Treatment/Dose (mg/kg)	No. of mice	No. of animals that aborted			Total no. of fetuses aborted
		Day 1	Day 2	Day 3	
G. officinale 160.25	8	–	2	2	32
G. officinale 320.50	8	4	2	–	56
G. officinale 641.00	8	6	–	–	64
G. officinale 1282.00	8	4*	–	–	46
N. Saline 20 mg/kg	8	–	–	–	–

* Three of the animals died on day 1 before aborting.

profuse in some animals. The fetuses were expelled at the second and third trimesters only. Postmortem examinations of the animals that did not abort showed that they were either not pregnant or on their first trimester of pregnancy. Twenty percent of the mice that aborted died in less than 48 h after abortion, while 50% of rats died less than 48 h after abortion.

In all of the treated animals, there were visible signs of spasm, minutes after the administration of the extracts. Some animals started bleeding from the vagina between 30 and 75 min after receiving the extract. The abortion ED_{50} in pregnant mice was 320.5 ± 20.00 mg/kg while the LD_{50} was 1280.13 ± 9.03 mg/kg.

Effect of the extract on litter size in mice

At a dose of 300 mg/kg, the extract significantly reduced the litter size in mice when administered in the first trimester of pregnancy (Table 3), while the pregnancy did not progress in the mice that received 480.75 mg/kg. Postmortem examination of the uteri in animals in group B showed signs of regression.

Discussion

The hot aqueous extract of the aerial part (leaves, flowers, fruits, and tender branches) of *Guaiacum officinale* was

Table 3. Effect of *G. officinale* (300 mg/kg) on litter size in mice.

Rat	Treatment	Dose	Litter Size	Mean Litter Size V S.E.M.
1	N. Saline	20 ml/kg	9	10.75 ± 0.53*
2			9	
3			10	
4			10	
5			11	
6			12	
7			12	
8			13	
1	*G. officinale*	300 mg/kg	2	4.50 ± 0.65
2			2	
3			4	
4			4	
5			5	
6			6	
7			6	
8			7	

* $P < 0.001$.

observed in more than 50 occasions to induce abortion in rats and mice. The extract, at a dose of 300 mg/kg, significantly ($P < 0.001$) reduced the litter size in mice when administered during the first trimester, while at a dose rate of 480.75 mg/kg, the extract caused regression of pregnancy. It was observed that the extract did not cause contraction of either primed or gravid uteri derived from these animals, even though spasms were observed when the extract was given *in vivo*. This interesting observation supports the work of Offiah and Anyanwu (1989), which illustrates clearly that *in vitro* results do not necessarily represent the *in vivo* situation. The results suggest that the extract may be acting by the release of an endogenous substance that is not found in the uterus per se. The reduced litter size may be due to resorption of some of the fetuses, as a result of maternal rejection of the implanting embryo (Passey et al., 1999).

The *in vitro* results do not suggest the mechanism by which the extract produces abortion. Alves et al. (1996) isolated four saponins from the pericarp of *Guaiacum officinale*. These saponins may be contributing to the abortifacient activity of the extract. However, the whole animal study tends to support the antifertility effects and the use of the hot aqueous extract of the aerial parts of *G. officinale* in traditional medicine for expulsion of the fetuses and placentae.

Acknowledgments

Thanks to Mr. Gerard Ramirez for his technical assistance, to Mr. S. Williams for introduction to the plant and Ms. Colette Gall for her secretarial assistance.

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