



Effects of *Jasminum multiflorum* leaf extract on rodent models of epilepsy, motor coordination and anxiety

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ABSTRACT

Jasmine flowers and leaves are used extensively in folk medicine in different parts of the world to treat a variety of diseases. However, there are very few published reports on the neuropsychiatric effects of *Jasmine* extracts. Hence, the objectives of the present study were to examine the effects of an alcohol extract of *Jasminum multiflorum* leaves on topically-applied bicuculline (a model of acute simple partial epilepsy) and maximal electroshock (MES, a model of generalized tonic-clonic seizure) in male Sprague-Dawley rats. The objectives also included an examination of the anxiolytic properties of the extract using an elevated plus maze and the effect of the extract on motor coordination using a rotarod treadmill. Phytochemical analysis of the extract showed the presence of three flavonoids and four additional compounds belonging to the steroid, terpenoid, phenol or sugar classes of compounds. The *Jasmine* alcohol extract, diluted with water and given orally or intraperitoneally, reduced the number of bicuculline-induced epileptiform discharges in a dose-dependent manner. The extract did not cause a significant increase in the current needed to induce hind limb extension in MES experiments. The extract significantly affected motor coordination when injected at 500 mg/kg but not at 200 mg/kg. At the latter dose, the extract increased open-arm entries and duration in the elevated plus maze to a level comparable to that of diazepam at 2 mg/kg. We conclude that *Jasmine* leaf extract has a beneficial effect against an animal model of acute partial complex epilepsy, and significant anxiolytic effect at a dose that does not affect motor co-ordination.

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1. Introduction

Jasmines are well-known for their fragrant flowers and there are over 200 species that grow in temperate and tropical regions. *Jasminum multiflorum* Linn. (Family: Oleaceae) is a glabrous twining shrub that grows in several parts of the Caribbean. The leaves of *Jasminum multiflorum* (subsequently referred to as *Jasmine*) are mostly ternate or pinnate; the flower is white with a tubular five- or eight-cleft calyx, a cylindrical corolla-tube with a spreading limb and two stamens enclosed in the corolla-tube. *Jasmine* flowers and leaves are used extensively in folk medicine in different parts of the world to treat a variety of diseases e.g. dental caries, gastric ulcers and hepatitis B viral infection (Nagarajappa et al., 2013; Umamaheswari et al., 2007; Zhao et al., 2009). We have reported previously that an alcohol extract of *Jasmine* leaves promotes healing of skin wounds

in rats (Nayak and Mohan, 2007). *Jasmine* has been shown to have sedative (Kuroda et al., 2005) and potential anti-depressant effects (Ferrerres et al., 2014). The Epilepsy Society of UK has suggested that *Jasmine* has “a calming effect and may be helpful in improving seizure control”. Therefore, we set out to examine the possible anti-epileptic properties of *Jasmine* leaf extract in rat models of (1) acute simple partial seizure using topically applied bicuculline methobromide, and (2) generalized tonic-clonic seizure using maximal electroshock (MES) (Fisher, 1989). Some anti-epileptic drugs used clinically have anxiolytic effects and may affect motor coordination. Hence, we also examined possible anxiolytic effects of the *Jasmine* extract (using an elevated plus maze) and its effects on motor coordination using a rotarod treadmill.

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2. Materials and methods

2.1. Plant material

Jasmine leaves were collected locally and identified by the curator and plant taxonomist of the National Herbarium at the University of the West Indies. The voucher specimen was conserved under the reference number TRIN 40629.

2.2. Preparation of extracts

The leaves of the plant were air dried in the shade over a period of 6 weeks; they were then cut into small pieces and ground to a fine powder. The ground plant material (635 g) was soaked overnight in 3000 mL of methanol at room temperature and filtered. The residue was then suspended in 2000 mL of 95% ethanol over a 48 h period and filtered once again. The resultant methanol and ethanol filtrates were combined, and the solvent removed under reduced pressure at 40–50 °C using a rotary evaporator. A green semisolid residue was obtained of mass 92.5 g (14.5%). A portion of the dried green semisolid residue (11.1 g) was re-suspended in 100 mL methanol-water (2:8) mixture and extracted sequentially with 2 × 25 mL portions of petroleum ether 60–80 °C, chloroform, ethyl acetate and finally *n*-butanol. Each of these extracts was concentrated to dryness using a rotary evaporator at 40–50 °C under reduced pressure to yield petroleum ether (1.44 g), chloroform (0.194 g), ethyl acetate (0.134 g) and *n*-butanol (1.580 g) residues. A small portion (0.25 g approx.) of the crude green semisolid methanol-ethanol extract was dissolved in 0.5 mL methanol-ethanol (1:1) mixture for analysis by thin layer chromatography (TLC) as a preliminary assessment of plant metabolites. Additionally, a small portion (0.01 g) each of the chloroform and ethyl acetate extracts was dissolved in chloroform-methanol (1:1), and the *n*-butanol extract (0.01 g) was dissolved in methanol-water (9:1) for TLC analysis to detect the presence of metabolites.

2.3. Phytochemical screening

A preliminary survey of the metabolites of the plant was performed on silica gel TLC plates (Sigma-Aldrich) of the dried green semisolid crude extract in methanol-chloroform (1:9) solvent mixture. The plate was air dried and the chromatogram viewed under UV₂₅₄ and UV₃₆₅ nm light. The presence of flavonoids in the chloroform, ethyl acetate and *n*-butanol extracts was determined by TLC on silica gel TLC plates (Sigma-Aldrich) in methanol-chloroform (3:7) solvent. The chromatogram was first visualized under UV₂₅₄ and UV₃₆₅ nm light and then viewed a second time under both wavelengths of UV light following spraying of the TLC plate with a 1% ethanolic solution of aluminium chloride and air drying. Flavonoids showed up as yellow fluorescent spots under UV₃₆₅ nm light.

Detection of phenols, sugars, steroids, and terpenes was carried out on silica gel TLC plates (Sigma-Aldrich) of the chloroform, ethyl acetate and *n*-butanol extracts by development in methanol-chloroform (1:9) solvent. The chromatogram was viewed under UV₂₅₄ and UV₃₆₅ nm light before spraying with a freshly prepared solution of 0.5 mL *p*-anisaldehyde in a mixture of 100 mL glacial acetic acid and 2 mL 97% sulfuric acid (9.8:0.2) followed by air drying and heating at 105 °C until visualization of spots was maximized. Blue, violet, green, grey and red spots were indicative of the presence of steroids, terpenoids, sugars and phenols.

2.4. Animals

The animal experiments were approved by the institutional ethics committee for use of animals. Male Sprague-Dawley rats

were maintained in the animal care facility of the university's veterinary hospital. The rats were exposed to a 12 h light/dark cycle and had free access to food and water.

2.5. Bicuculline-induced epileptiform discharges on electrocorticogram

The experimental procedure used for recording epileptiform discharges has already been reported (Addae et al., 2007; Addae et al., 2012). Briefly, rats weighing 200–300 g were anaesthetized with urethane at 1.5–1.7 g/kg i.p., mounted in a stereotaxic frame and the body temperature maintained by means of a heating blanket and a rectal thermistor. The atlanto-occipital membrane was punctured to prevent brain oedema. A burr hole of approximately 6 mm diameter was made and the dura removed to expose the parietal cortex. A cortical cup of paraffin wax was constructed around the cortex to facilitate topical application of compounds. The cup also allowed for washing of the cortex with pre-gassed (95%O₂/5%CO₂) artificial cerebrospinal fluid (aCSF) with the following composition (in mM): NaCl 115.0; KCl 2.0; KH₂PO₄ 2.2; NaHCO₃ 25.0; D-Glucose 10; MgSO₄ 1.2 and CaCl₂ 2.5.

The electrocorticogram (ECoG) was recorded using a Caldwell Sierra system with a band pass filter of 0.32–200 Hz and amplification 500X. The recording was an adaptation of the method described by Kent et al. (Kent and Webster, 1986). The active electrode was a silver ring that was placed on the exposed cortex. The reference electrode was placed over the exposed frontal bone, whilst the ground electrode was placed in the neck muscle.

The green semisolid alcohol extract of *Jasmine* was dissolved in distilled water for oral administration or normal saline for i.p. administration at a concentration of 100 mg/ml. *Jasmine* was given orally to a conscious rat 30 min before it was anesthetized with urethane; this translated to 90 min before induction of epileptiform discharges with the GABA-A antagonist, bicuculline methobromide, which was applied topically at 50 μM to the exposed cortex for 5 min. When given i.p., *Jasmine* was injected 30 min before the induction of epileptiform discharges. The number of epileptiform discharges in rats that had been given *Jasmine* were compared to those from rats in the control groups that had received distilled water orally or saline injection.

2.6. Maximal electroshock seizure threshold (MES-T) test

The method for determining maximal electroshock seizure threshold (MES-T) has been described in previous reports (Addae et al., 2012; Fischer et al., 2016). Briefly, MES-T was effected with an electroconvulsive unit using a pair of corneal electrodes (Ugo Basile, Italy). The electroconvulsive unit had the following settings: pulse frequency of 8 Hz, pulse width of 1 ms and shock duration of 1 s. The corneas were anaesthetized with lidocaine 30 min before application of the electrodes. For each rat, the initial stimulation current was sub threshold and increased in steps of 2 mA until there was full extension of the hind limbs; the current at this level was taken as the effective threshold MES current for the animal.

2.7. Rotarod treadmill

An accelerating rotarod (Ugo Basile) which automatically increased rotation slowly from 4 to 40 rpm over 5 min was used to test for motor coordination (Addae et al., 2012). Each rat was placed on the rotarod and the duration for which it stayed on the rotating rotarod was taken as a measure of the extent to which it could maintain motor balance and coordination.

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