

Antinociceptive Activities of Aqueous and Ethanol Extracts of *Piper betle* Leaves in Rats

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Abstract

Leaves of *Piper betle* Linn (Piperaceae) possess a broad spectrum of pharmacological and therapeutic properties. However, its antinociceptive activity has not been investigated so far. The aim of this study therefore, was to examine the antinociceptive activity of hot water extract (HWE) and cold ethanol extract (CEE) of *P. betle* leaves using rats and three models of nociception (tail flick, hot plate, and formalin tests). Different concentrations of HWE (125, 200, 300, 500 mg/kg) and CEE (125, 200, 300, 500 mg/kg) were made and orally administered to rats, and the reaction times were determined. The results showed that the extracts have marked antinociceptive activity when evaluated in the hot plate and the formalin tests but not in the tail-flick test. The overall antinociceptive effect of CEE was higher than that of HWE. The antinociceptive effect was mediated via opioid mechanisms.

Keywords: Antinociception, opioid receptor, *Piper betle* leaves.

Introduction

Piper betle Linn (Piperaceae) is a perennial dioecious, semi-woody climber. Stems strongly swollen at the nodes, papillose when young. Leaves alternate, simple, and yellowish green to bright-green in color. Leaves of fertile branches with a petiole 1–2 cm long, 1.2–1.8 mm thick when dry, and glabrous at maturity. Flowers are naked, unisexual, dioecious in dense cylindrical spikes, male spikes not seen, female spikes 2.5–5 cm long, pendulous. Bracts peltate, orbicular to obovate, broadly stipitate with a membranous margin (Jayaweera, 1982;

Dassanayake & Fosberg, 1987). *P. betle* is cultivated in Sri Lanka, India, Malay Peninsula, the Philippines, and East Africa (Dassanayake & Fosberg, 1987). The chief constituent of the leaves of this plant is a volatile oil known as betel oil. The volatile oil is a bright-yellow to dark-brown liquid possessing a clove-like flavor and consists of terpenes and phenols (Anonymous, 1992).

In Asian countries, betel leaves are used for chewing and are credited with many medicinal properties such as digestive, stimulative, carminative, and aphrodisiac (Anonymous, 1992). However, Sri Lankan betel inhibits male sexual behavior in rats and possesses antiaphrodisiac activity (Ratnasooriya & Premakumara, 1996). Further, betel juice is given to children for cough and administered to the eye for night blindness in adults. It is used to treat catarrh and diphtheria. The leaves are given for gastric and lung disorders in children and applied to purulent ulcers (Jayaweera, 1982). Experimentally, leaves of *P. betle* are shown to possess antimicrobial (Tewari & Nayak, 1991), gastroprotective (Majumdar et al., 2003), wound healing (Santhanam & Nagarajan, 2002), hepatoprotective (Saravanan et al., 2002), antioxidant (Choudhary & Kale, 2002; Saravanan et al., 2002; Santhakumari et al., 2003), antifertility on male rats (Ratnasooriya & Premakumara, 1997), and antimotility effects on washed human spermatozoa (Ratnasooriya et al., 1990). According to available literature, antinociceptive activity of *P. betle* is not scientifically investigated yet. However, it is possible that *P. betle* leaves may possess antinociceptive properties, as *P. longum* (Vedhanayaki et al., 2003) a close relative of the plant, was shown to have antinociceptive properties. Therefore, this study was undertaken to examine whether extracts of leaves of *P. betle* possess antinociceptive