The neuromuscular blockade produced by pure alkaloid, mitragynine and methanol extract of kratom leaves (*Mitragyna speciosa* Korth.)

Somsmorn Chittrakarn\textsuperscript{a,\*}, Niwat Keawpradub\textsuperscript{b}, Kitja Sawangjaroena\textsuperscript{a}, Supaporn Kansenalaka\textsuperscript{a}, Benjamas Janchaweea\textsuperscript{a}

\textsuperscript{a} Department of Pharmacology, Faculty of Science, Prince of Songkla University, 15 Kanchanavanich, Hat-Yai, Songkhla 90112, Thailand

\textsuperscript{b} Department of Pharmacognosy and Pharmaceutical Botany, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand

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**ABSTRACT**

**Aim of the study:** The effects of pure alkaloid, mitragynine and a methanolic extract of kratom leaves were investigated on neuromuscular junction and compound nerve action potential.

**Materials and methods:** Wistar rats were killed by cervical dislocation and decapitated. The phrenic nerve–hemidiaphragms, hemidiaphragms and sciatic nerve were isolated.

**Results:** Kratom methanolic extract present at 0.1–1 mg/mL and mitragynine (0.0156 mg/mL) decreased the muscle twitch on the isolated phrenic nerve–hemidiaphragm and hemidiaphragm preparation. Muscle relaxation caused by kratom extract (1 mg/mL) was greater than the effect of mitragynine. Pancuronium and succinylcholine potentiated the effect of kratom extract. It also had a direct relaxation effect on the hemidiaphragm muscle. The muscle relaxation caused by kratom extract was not antagonized by neostigmine, tetraethylammonium and calcium chloride. High concentrations of kratom extract (10–40 mg/mL) and mitragynine (2 mg/mL) blocked the nerve conduction, amplitude and duration of compound nerve action potential.

**Conclusions:** The mechanism of action of kratom extract might not act as a competitive antagonist of acetylcholine yet its dominant effect was at the neuromuscular junction and not at the skeletal muscle or somatic nerve.

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1. Introduction

Kratom (*Mitragyna speciosa* Korth.) is a tall leafy tree, in the family Rubiaceae, and is native to Southeast Asia. It grows in hot, wet tropical areas such as Thailand, where it is generally called kratom. It grows mostly in the southern regions of this country. The leaves have long been for “medicinal purposes” and as a narcotic drug. It was also classified in Category V of a five category classification of narcotics by the Thai government enacted the Narcotics Act B.E. 2522, placing kratom along with marijuana. This means that it is illegal to buy, sell, import, or growing and harvesting. This law makes planting the tree illegal and requires existing trees to be cut down. However it is not fully effective, since the tree is indigenous to the country and native people prefer to use them. Hence, kratom remains a popular drug in Thailand, especially in southern regions.

Kratom has been traditionally used in Thailand, and there are also reports of some use in Malaysia. There are two kinds of kratom, distinguished by the color of veins in the leaf, red or green. Local people prefered to use both of them. In addition to being used, in its own right, as a narcotic drug, it is often used as a substitute for opium when opium is unavailable, or to moderate opium addiction. Kratom has been reported to be a central nervous system stimulant, and also depressant. It helps to increase work efficiency and tolerance to hard work under a scorching sun (Suwanlert, 1975). It also uses to treat muscle ache and fatigue (Chucheun, 2005).

Over 25 alkaloids have been isolated from kratom leaves with mitragynine being the most dominant (Chitrakarn et al., 2005). Other alkaloids are mitraphylline, speciogynine, 7-hydroxymitragynine, etc. Mitragynine has an antinociceptive action through the supraspinal opioid receptors and descending noradrenergic and serotonergic systems (Matsumoto et al., 1996). Mitragynine inhibited the vas deferens contraction elicited by nerve stimulation, probably through its blockage of neuronal Ca\textsuperscript{2+} channels (Matsumoto et al., 2005). Mitragynine inhibits guinea-pig ileum contraction in vitro via the opioid receptor (Watanabe et al., 1997). 7-Hydroxymitragynine has a more potent analgesic activity than that of morphine (Matsumoto et al., 2004). In folk medicine, it has been used to treat diarrhea. It was found that methanolic extract of kratom had the antidiarrheal activity and decreased...