BACKGROUND

Mitragynine, an indole alkaloid of *Mitragyna speciosa* commonly known as kratom was found to possess analgesic effects by binding partially to opioid receptors similar to morphine. Although mitragynine has structurally different from morphine, it was found to have broader spectrum of pharmacological properties. Mitragynine was reported to inhibit an *in vitro* inflammatory model by inhibiting cyclooxygenase enzyme-2 (COX-2) expression. Yet, no study has been done to identify the effective dose of mitragynine for the treatment of pain via this systemic anti-inflammatory pathway. Thus, the acetic acid writhing pain model was adopted to investigate the analgesic effects of mitragynine via anti-inflammatory pathway.

OBJECTIVES

1. To assess the effects of mitragynine on pain rat model by evaluating the writhing frequency and percentage of writhing inhibition.
2. To determine the mean effective dose (ED50) of mitragynine.

METHODOLGY

48 Sprague Dawley rats
(Male and female; body weight: 250-300g; 12:12-hours light-dark cycle; temperature: 25°C)

- Single dose administration [intraperitoneally (i.p.)]:
  - a) Vehicle 20% Tween 80; n=6
  - b) Indomethacin (1 mg/kg); n=6
  - c) Mitragynine (1, 5, 10, 12.5, 15 or 30 mg/kg); n=6/group

- 30 minutes after the treatment, 1 mL of 2% acetic acid was injected (i.p.)*

- Pain-like writhing behaviour response was recorded and counted within 1 hour

- Percentage of inhibition was calculated:
  - (Writhes of vehicle group – writhes of treated group) x 100
  - Writhes of vehicle group

- Dose response curve was generated and mean effective dose (ED50) was calculated from the curve

- All data were statistically analysed using SPSS

RESULTS

A) Total and percentage of inhibition of writhing behaviour
All mitragynine doses except 1 mg/kg significantly reduced the number of writhes (p<0.001). Mitragynine (15 and 30 mg/kg) demonstrated significantly higher percentage of inhibition than indomethacin (p<0.01 and p<0.05 respectively). The highest percentage of inhibition was mitragynine (30mg/kg)

![Percentage of inhibition of writhing behaviour](image)

B) Mean effective dose (ED50)

The mean effective dose (ED50) value was calculated from the graph and found to be 3.578 mg/kg.

![Dose response graph of percentage of inhibition](image)

CONCLUSION

Mitragynine alleviated pain-like behaviour and proven to possess analgesic effects via anti-inflammatory pathway at an effectively low doses.

REFERENCES

1. Taufik Hidayat, M., et al. (2020). Determination of Mitragynine Bound Opioid Receptors. Advances in Medical and Dental Sciences, 3(1), 65–70

All protocols were conducted with the approval of the Universiti Sains Malaysia Animal Ethics Committee. USM/1ACUC/2018(112)(917) This study was supported by Higher Education Excellence (HeCoS) special funding (3111-C82AH64401009) For more information please contact: Assoc. Prof. Dr. Zurina Hassan (zurina_hassan@usm.my) / Noorul Hamizah Mat (hamizah.mat@usm.my)