Antiulcer Activity of Methanol Extract of *Melastoma malabathricum* Leaves in Rats

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Key Words

Melastoma malabathricum leaves • Melastomaceae •
In vivo • Antiulcer activity • Methanol extract

Abstract

Objective: To determine the potential antiulcer activity of methanol extract of *Melastoma malabathricum* leaves (MEMM) using various established rat models. **Materials and Methods:** Ten groups of rats were used and orally administered 10% DMSO (negative control), 100 mg/kg ranitidine (positive control) or MEMM (50, 250 and 500 mg/kg) followed by gastric ulcer induction either using ethanol or indomethacin. The stomachs were collected and subjected to macroscopic and microscopic analyses. **Results:** MEMM exhibited significant ($p < 0.05$) antiulcer activity in the ethanol, but not in the indomethacin-induced gastric ulcer model. The percentage of antiulcer activity for 50–500 mg/kg MEMM ranged between 3 and 75%, respectively. The gross observations were supported by histological findings. MEMM also aggravated the indomethacin-induced gastric ulcer, leading to an increase in ulcer area formation and ulcer score. **Conclusion:** The *M. malabathricum* leaves showed antiulcer activity, which could be attributed to their antioxidant and anti-inflammatory activities. This requires further in-depth studies.

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Introduction

Gastric ulcer, a serious gastrointestinal disorder that develops due to erosion on the inside lining of the stomach [1], is thought to be due to an imbalance between aggressive and protective factors [2]. Although treatment of gastric ulcer can be achieved via the use of proton pump inhibitors, prostaglandins analogs, histamine receptor antagonists and cytoprotective agents, these drugs also produce several adverse reactions which include toxicities and tolerance [1, 3]. Thus, interest and effort have been shifted towards medicinal plants as new sources of gastroprotective agents [3]. *Melastoma malabathricum* L. Smith (family Melastomaceae), a small shrub that is native to tropical and temperate Asia, is locally known to the Malay as ‘Senduduk’ [4]. The leaves of *M. malabathricum*, in particular, have been traditionally used to treat various ailments including gastric ulcers [4]. The leaves extracts exhibited various pharmacological activities (i.e. antinociceptive, antioxidant and antiproliferative) [4]. However, to the best of our knowledge no attempt has been made to study the antiulcer potential of *M. malabathricum* leaves. Thus, our aim was to determine the antiulcer activity of methanol extract of *M. malabathricum* leaves (MEMM) using various animal models.

Fig. 1. Histological evaluation of antiulcer activity of MEMM against ethanol-induced gastric lesions in rats. **a** Stomach of a negative control rat. **b** Stomach of a positive control rat. **c** Stomach of

a rat treated with 50 mg/kg MEMM. **d** Stomach of a rat treated with 250 mg/kg MEMM. **e** Stomach of a rat pretreated with 500 mg/kg MEMM.

Table 1. Effect of various doses of MEMM and ranitidine on ethanol- and indomethacin-induced gastric lesions in rats

Model	Pre-treatment	Dose, mg/kg	Ulcer area, mm ²	Ulcer score, U
Absolute ethanol	10% DMSO	–	21.67 ± 5.42	2.75 ± 0.36
	ranitidine	100	12.00 ± 2.26*	1.33 ± 0.17*
	MEMM	50	22.33 ± 4.34	2.67 ± 0.42
		250	20.20 ± 7.10	1.75 ± 0.53
		500	8.67 ± 4.41*	0.75 ± 0.34*
Indo-methacin	10% DMSO	–	3.67 ± 0.70	0.42 ± 0.04
	ranitidine	100	2.33 ± 0.42 [#]	0.58 ± 0.02 [#]
	MEMM	50	3.00 ± 0.07	0.50 ± 0.07
		250	5.00 ± 0.06 [#]	0.75 ± 0.05 [#]
		500	9.33 ± 0.76 [#]	1.00 ± 0.21 [#]

Values are mean ± SEM (n = 6/group).

* Data differed significantly ($p \leq 0.05$) when compared against the 10% DMSO-pretreated group in the absolute ethanol-induced group.

[#] Data differed significantly ($p \leq 0.05$) when compared against the 10% DMSO-pretreated group in the indomethacin-induced group.

Materials and Methods

The leaves of *M. malabathricum* were collected from their natural habitat in Serdang, Selangor, Malaysia from August to September 2010 and a new voucher specimen, ACP 0017, was deposited at the Herbarium of IBS, UPM. The ground dried leaves (40 g) were soaked in methanol 1:20 (w/v) three times at room temperature for 24 h and the methanol supernatant was evaporated (40°C) under reduced pressure to dryness resulting in a yield of 12.8 g dried and sticky methanol extract (percentage yielded was ≈ 32%).

Seventy adult male Sprague-Dawley rats weighing 180–200 g were used in the present study and approval was obtained from the Animal Ethics Committee, UPM with reference No. UPM/FPSK/PADS/BR-UUH/00382 as described by Zakaria et al. [5]. The acute toxicity (n = 10) study of MEMM was performed in a single dose administration of 5,000 mg/kg p.o. as described by

Mohamed et al. [6]. The ethanol- and indomethacin-induced gastric ulcer models were carried out according to the method described by Zakaria et al. [5]. Ten groups of 48-hour fasted rats were divided into two subgroups, of which each (n = 6) received (orally) once daily 10% DMSO (10 ml/kg), ranitidine (100 mg/kg) or MEMM (50, 250 and 500 mg/kg) for 7 consecutive days. On the 8th day, ulcer was induced using 1 ml/200 g body weight absolute ethanol or 100 mg/kg indomethacin. Fifteen minutes or 4 h later, the rats, induced either with absolute ethanol or indomethacin, were anesthetized using diethyl ether and then euthanized by cervical dislocation, respectively. The stomachs were removed and opened along the greater curvature. All the stomachs were gently rinsed with water to remove the gastric contents and blood clots prior to the macroscopic analysis. The macroscopic (ulcer area and ulcer score) and histopathological evaluations were determined according to the method described in Zakaria et al. [5]. The results are presented as mean ± SEM, and analyzed using the one-way analysis of variance (ANOVA) test with Dunnet post-hoc test with $p < 0.05$ as the limit of significance.

Results

Gross pathological studies of the stomachs removed from ethanol- but not indomethacin-induced rats revealed a significantly ($p < 0.05$) dose-dependent reduction in ulcer formation characterized by decrease in the ulcer area and ulcer score (table 1). These findings were further supported by the histopathological observations (fig. 1). As for the indomethacin-induced group, pretreatment with MEMM significantly ($p < 0.05$) aggravated the ulcer formation (table 1).

Discussion

The present study demonstrated the antiulcer potential of MEMM against ethanol-, but not indomethacin-induced gastric ulcer in rats. Ethanol-induced gastric ulcer is regarded as a suitable model to study the cytopro-

protective activity of screened compounds. The ability of any compounds to enhance the synthesis of prostaglandins will stimulate the production of mucus and bicarbonate that will help protect the gastric mucosa from ulcer formation indicating the compounds' cytoprotective action. In addition, upon its rapid penetration into the gastric mucosa, ethanol can either cause lipid peroxidation or metabolize to form superoxide anion and hydroxyl radicals in the gastric mucosa [5] that can react with most of the cell components or be involved in other processes that ultimately result in oxidative damage [5], leading to gastric mucosal injury. Thus, the ability of MEMM to exhibit antiulcer activity is believed to be attributed to the extract's antioxidant and antiproliferative potentials reported recently [7]. Furthermore, the antiulcer activity of MEMM could be associated with its phytochemical contents, which contain flavonoids, saponins and tannins [7]. These compounds have been reported to exert antiulcer activity [8–10] and, thus, justify the present findings. Other than that, the failure of MEMM to attenuate indomethacin-induced gastric ulcer warrants some explanation and could be attributed to its anti-inflammatory activity [4]. Indomethacin is known to induce gastric ulcer

through its ability to directly suppress arachidonic acid-induced prostaglandin synthesis [5], and it is suggested that the MEMM, instead of exerting antiulcer effect, helps to suppress prostaglandin synthesis due to its strong anti-inflammatory effect.

Conclusion

The present study demonstrated that *M. malabathricum* leaves contain antiulcer-bearing compounds that were effective against ethanol-, but not indomethacin-, induced gastric ulcer and, thus, requires further extensive studies.

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References

- Galani VJ, Goswami SS, Shah MB: Antiulcer activity of *Trichosanthes cucumerina* Linn. against experimental gastro-duodenal ulcers in rats. *Orient Pharm Exp Med* 2010;10: 222–230.
- Alkofahi A, Atta AH: Pharmacological screening of the antiulcerogenic effects of some Jordanian medicinal plants in rats. *J Ethnopharmacol* 1999;65:341–345.
- Gregory M, Vithalrao KP, Franklin G, Kalichelavan V: Anti-ulcer (ulcer-preventive) activity of *Ficus arnottiana* Miq. (Moraceae) leaf methanolic extract. *Am J Pharmacol Toxicol* 2009;4:89–93.
- Joffry SM, Yob NJ, Rofiee MS, Affandi MM, Suhaili Z, Othman F, Akim AM, Desa MN, Zakaria ZA: *Melastoma malabathricum* (L.) Smith ethnomedicinal uses, chemical constituents, and pharmacological properties: a review. *Evid Based Complement Alternat Med* 2012;2012:258434.
- Zakaria ZA, Abdul Hisam EE, Rofiee MS, Norhafizah M, Somchit MN, Teh LK, Salleh MZ: Antiulcer activity of the aqueous extract of *Bauhinia purpurea* leaf. *J Ethnopharmacol* 2011a;137:1047–1054.
- Mohamed EA, Lim CP, Ebriki OS, Asmawi MZ, Sadikun A, Yam MF: Toxicity evaluation of a standardised 50% ethanol extract of *Orthosiphon stamineus*. *J Ethnopharmacol* 2011;133:358–363.
- Zakaria ZA, Rofiee MS, Mohamed AM, Teh LK, Salleh MZ: In vitro antiproliferative and antioxidant activities, and total phenolic contents of the extracts of *Melastoma malabathricum* leaves. *J Acupunct Meridian Stud* 2011;4:248–256.
- Izzo AA, Di Carlo G, Mascolo N, Capasso F, Autore G: Antiulcer effect of flavonoids. Role of endogenous PAF. *Phytother Res* 1994;8: 179–181.
- Yeşilada E and Takaishi Y: A saponin with anti-ulcerogenic effect from the flowers of *Spartium junceum*. *Phytochem* 1999;51:903–908.
- Souza SM, Aquino LC, Milach AC Jr, Bandeira MA, Nobre ME, Viana GS: Anti-inflammatory and antiulcer properties of tannins from *Myracrodruon urundeuva* Allemão (Anacardiaceae) in rodents. *Phytother Res* 2007;21:220–225.