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INTRODUCTION

Muntingia calabura L., locally known as *Takhop farang* (Thai) and belonging to the Elaeocarpaceae family. It is a flowering plant native to southern Mexico, the Caribbean, Central America, and western South America. The tree grows very easily and is widespread, and in Malaysia, it is popularly known as "*Kerukup Siam*." Despite less attention given to its medicinal values in the Malay folklore medicine, *M. calabura* has been traditionally used by the Peruvian to treat various ailments (1, 2). Scientifically, the leaves of *M. calabura* have been reported to possess antitumour, antinociceptive, anti-inflammatory and antipyretic, antibacterial, antiproliferative and antioxidant (3,4). Its have been used in Thai traditional medicine for relief to alleviate headaches, colds, anti-inflammation and antispasmodic activity. Phytochemical screening of the leaves demonstrated the presence of flavonoids, saponins, tannins, triterpenes, and steroids, but no alkaloids (5), while the phytochemical analysis of methanol extract of *M. calabura* leaves (MEMC) revealed only the presence of flavonoids, saponins, and tannins (6). However, previous study on oral toxicity of ethanolic extract of this plant still has no found in Thailand. Thus, the objective of this study is to determine the safety of 95% ethanolic extract and its freeze-dried powder of *M. calabura* L. in rats.

MATERIAL AND METHOD

Animals: Male (250 ± 20 g) and Female (230 ± 20 g) Wistar rats were obtained from National Laboratory Animal Centre, Mahidol University, Salaya, Nakornpathom. They were kept in cages with sterilized wood shavings as bedding at 24 ± 2°C in 12 h light/dark cycle and feed with standard diets and tap water *ad libitum*. All rats were acclimatized for 7 days prior to the experiments.

Method: Acute oral toxicity test was carried out following the "Guideline No. 423: Acute oral toxicity-Acute toxic class method of the OECD Guidelines for Testing of Chemicals (7)". In brief, animals were divided into five groups and each group contains five rats of both sexes. Group 1 was served as a negative control which was received 0.5% CMC or distill water in equivolume to the test group. Group 2-3 were served as treatment groups which were received the extract at dose of 2,000 mg/kg and 15,000 mg/kg, respectively. Group 4-5 were served as treatment groups which were received its freeze-dried powder at dose of 2,000 mg/kg and 15,000 mg/kg, respectively. The rats were fasted for 16 hrs prior to dosing the test sample while drinking water was available *ad libitum*. And food was withheld for a further 3-4 hrs. Any toxic signs were immediately observed at ½, 1 and 3 hrs. The special care should be considered to animals that obviously showed toxic signs during the first 4 hrs after dosing and observed once daily thereafter for 14 days. Body weight was recorded weekly and at the end of the test. All survivors were euthanized by CO_2 asphyxiation and then performed necropsy finding. The mean of body weight gain of the animals in the test groups was calculated in comparison to the rats of the control group using Student's *t*-Test ($p \leq 0.05$).

RESULTS AND DISCUSSION

As shown in Table 1and 2. All groups of treated rats (2,000 mg/kg and 15,000) did not show any toxic sings and death through the observation period. The body weight gain of the rats showed no difference from the control group. Necropsy findings exhibited normal appearance and no macroscopic pathological lesions of visceral organ. Thus, LD_{50} (lethal dose) was estimated over than 15,000 mg/kg.

Table 1: Summary of mortality rate and gross pathology of control and treated rats

Treatment/Dose	[a]Mortality rate			Gross Pathology
	Male	Female	Total	
Control group 0.5% CMC equivolume to the treatment group	0/5	0/5	0/10	Normal
Treatment group "*Takhop farang* extract 2,000 mg/kg bw."	0/5	0/5	0/10	Normal
Treatment group "*Takhop farang* extract 15,000 mg/kg bw."	0/5	0/5	0/10	Normal
Control group Distill water equivolume to the treatment group	0/5	0/5	0/10	Normal
Treatment group "freeze-dried powder of *Takhop farang* 2,000 mg/kg bw."	0/5	0/5	0/10	Normal
Treatment group "freeze-dried powder of *Takhop farang* 15,000 mg/kg bw."	0/5	0/5	0/10	Normal

[a] Number of dead rats/number of rats tested

Table 2: Means of body weight gain of the control and treated rats recorded during experimentation and at termination

Sex	Treatment/Dose	*Mean of body weight gain (g)	
		Day 8	Day 15
Male	**Control group** 0.5% CMC	46.80 ± 2.32	79.40 ± 5.08
	Treatment group "*Takhop farang* extract 2,000 mg/kg b.wt."	44.00 ± 0.31	69.20 ± 2.45
	Treatment group "*Takhop farang* extract 15,000 mg/kg b.wt."	46.00 ± 2.94	68.80 ± 2.03
Female	**Control group** 0.5% CMC	28.20 ± 1.76	39.20 ± 1.85
	Treatment group "*Takhop farang* extract 2,000 mg/kg b.wt."	24.00 ± 2.27	36.80 ± 1.76
	Treatment group "*Takhop farang* extract 15,000 mg/kg b.wt."	29.80 ± 2.91	43.20 ± 2.79

* Data shown in the table are mean ± SEM

Table 2: Means of body weight gain of the control and treated rats recorded during experimentation and at termination (Cont.)

Sex	Treatment/Dose	* Mean of body weight gain (g)	
		Day 8	Day 15
Male	**Control group** Distill water	41.00 ± 1.26	75.80 ± 3.24
	Treatment group "freeze-dried powder of *Takhop farang* 2,000 mg/kg b.wt."	42.40 ± 4.69	61.00 ± 7.49
	Treatment group "freeze-dried powder of *Takhop farang* 15,000 mg/kg b.wt."	48.40 ± 3.43	73.80 ± 3.90
Female	**Control group** Distill water	18.00 ± 2.73	40.60 ± 2.47
	Treatment group "freeze-dried powder of *Takhop farang* 2,000 mg/kg b.wt."	19.00 ± 3.10	28.20 ± 3.75
	Treatment group "freeze-dried powder of *Takhop farang* 15,000 mg/kg b.wt."	16.40 ± 1.88	27.80 ± 3.39

* Data shown in the table are mean ± SEM

CONCLUSION

The LD_{50} of 95% ethanolic extract and freeze-dried powder of *Takhop farang* in rats are greater than 15,000 mg/kg body weight. Therefore, this study indicated that *Takhop farang* extract may be safe in use as material source for herbal drug development. However, the repeated dose toxicity evaluation of the extract is still necessary in further study.

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