Anti-inflammatory, Analgesic and Antipyretic Activity of *Terminalia arjuna* Roxb. Extract in Animal Models

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Background: *Terminalia arjuna Roxb. (family Combretaceae) is commonly known as 'Sa maw thet' in Thai. The fruit is used in traditional medicine as natural mild laxatives, carminative and expectorant.*
Objective: *This research aims to study the anti-inflammatory, analgesic and antipyretic activities of Terminalia arjuna extract by using animal models in comparison to the reference drugs.*
Material and Method: *The anti-inflammatory study was conducted by 2 experimental animal models namely ethyl phenylpropiolate (EPP)-induced ear edema and carrageenan-induced paw edema. The study of analgesic activity used 2 methods of pain induction including acetic acid and heat induced pain. In addition, the antipyretic activity study was performed by induced hyperthermia with yeast.*
Results: *The results showed that the oral administration of Terminalia arjuna extract possessed acute anti-inflammatory effect in carrageenan-induced paw edema. Terminalia arjuna extract showed the analgesic activity in acetic acid-induced writhing response and heat-induced pain. This indicated its peripheral effect by inhibiting the biosynthesis and/or release of some pain mediators and some mechanism through central nervous system. Moreover, Terminalia sp. extract at the dose of 1000 and 1500 mg/kg body weight showed the antipyretic activity, The effect could be due to the inhibition of prostaglandins synthesis.*
Conclusion: *The findings of this study indicated that the Terminalia arjuna extract possesses the anti-inflammatory, analgesic and antipyretic activities in animals.*

Keywords: *Terminalia arjuna extract, anti-inflammatory activity, analgesic activity, antipyretic activity*

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Terminalia arjuna Roxb. belongs to the family Combretaceae. The fruit of *T. arjuna* is used in traditional medicine as mild laxatives, carminative and expectorant. The stem bark of *T. arjuna* is widely used in Ayurveda in various cardiovascular conditions. The arabinogalactan is an essential component of *T. arjuna* stem bark that give an antitussive action[1]. Moreover, the pharmacological activity of the stem bark of *T. arjuna* is anti-ischemic, antihypertensive, antihypertrophic and antioxidant effects[2]. However, there have been no anti-inflammatory, analgesic and antipyretic activities reports regarding of this plant. The aim of this study was to evaluate the anti-inflammatory, analgesic and antipyretic activities of *T. arjuna* fruit extract in animal models.

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Material and Method

Animal and ethical considerations

Male ICR albino mice (30 to 40 g) and male Sprague Dawley (SD) rats (40 to 60 g, 100 to 120 g and 200 to 220 g) were obtained from the National Laboratory Animal Center, Nakhon Pathom, Thailand. The animals were housed in a temperature-controlled room (25±1°C) and provided with standardized pelleted feed and clean drinking water ad libitum. The study

had obtained the ethical clearance from the Animal Ethics Committee of Faculty of Medicine, Thammasat University, Pathumthani, Thailand (AE 002/2014).

Plant material and extract

The fruits of *T. arjuna* was identified by Associate Professor Dr. Noppamas Soonthorn-chareonnon, Department of Pharmacognosy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand. The voucher specimen has been kept at the Faculty of Pharmacy, Mahidol University, Bangkok, Thailand.

Thirty kilograms of dry fruits from *T. arjuna* were immersed in 100 L of water for 30 min, then boiled for 1 h and filtered to remove the residue. The water extract was spray dried to remove trace of solvent. The quality control of raw materials and the extract followed the Thai Herbal Pharmacopoeia (THP) including organoleptic examination, % loss on drying, extractive values, total ash and acid insoluble ash. The finger prints of the extract were standardized by thin-layer chromatography and high performance liquid chromatography (HPLC)[3].

Ethyl phenylpropiolate (EPP)-induced ear edema in rats[4]

Male SD rats (40 to 60 g) were divided into 3 groups (n = 3): group 1, vehicle control; group 2, positive control; group 3, *T. arjuna* extract treatment. The vehicle was prepared by mixing 10 mL of 5% dimethysulfoxide (5% DMSO) and 10 ml of acetone. Twenty microliters of vehicle (group 1) or 1 mg phenylbutazone (group 2), or 3 mg *T. arjuna* extract (group 3) were applied to animals' ears. The ear edema was induced by topical application of EPP (1 mg/20 mL/ear) to the inner and outer surface of both ears to all groups by using a microliter pipette. The ear thickness was measured by the vernier calipers at 0, 15, 30, 60, and 120 min after EPP induction.

Carrageenan-induced paw edema in rats[5]

Male SD rats (100 to 120 g) were divided into 5 groups of 6 animals each. *T. arjuna* extract and aspirin were prepared by dissolving in distilled water whereas 1% carrageenan was prepared by dissolving in saline solution. *T. arjuna* extract at the doses of 500, 1,000, 1,500 mg/kg, aspirin at the dose of 300 mg/kg and distilled water at the dose of 5 mL/kg were orally given 1 h prior to carrageenan injection. A volume of 0.05 ml of 1% carrageenan (in sterile normal saline solution, NSS) was injected intradermally into the plantar surface of the right hind paw of an unanesthetized rat restrained in a plastic cage. The paw edema volume was measured using a plethysmometer (model 7140, Ugo Basile, Italy) at 0, 1, 3 and 5 hours after carrageenan injection.

Acetic acid-induced writhing response in mice[6,7]

Male ICR mice (30 to 40 g) were used and divided into 5 groups of 6 animals each. *T. arjuna* extract and aspirin were prepared by dissolving in distilled water. *T. arjuna* extract at the doses of 500, 1,000, 1,500 mg/kg, aspirin at the dose of 300 mg/kg and distilled water at the dose of 5 mL/kg were orally given 1 h prior to 0.75% acetic acid injection at volume of 0.1 mL/10 g body weight into the peritoneal cavity. The number of writhes was counted by observing, the response of contraction of an abdominal wall, pelvic rotation and followed by hind limb extension per count. The counting was done through the continuous observation for 15 min. The starting point was at 5 min after acetic acid injection.

Tail-flick test in rats[8]

Male SD rats weighing 180 to 200 g were divided into 6 groups of 6 animals each. The amount of each substance in mg per kg body weight (mg/kg) was dissolved in distilled water. These substances were *T. arjuna* extract (500, 1,000, 1,500 mg/kg), aspirin (300 mg/kg), codeine (120 mg/kg) and distilled water (5 mL/kg). Each solution was orally given 1 h prior to placing the tail of rat (3 cm from tip) on a flush mounted photocell window of the tail-flick apparatus (model 7360, Ugo Basile, Italy). Heat was applied by the infrared lamp (50 W bulb) mounted in a reflector. When the rat felt pain flicked its tail moved away from the heat and the reaction time, presented on a digital display was observed. The voltage was adjusted to give a normal reaction time of 2 to 4 sec. The cut-off time of 10 sec was a maximum time for the rat that did not move its tail away from the heat to avoid tissue damage. The reaction time was determined before and at 1, 2, and 3 h after each test substance administration.

Yeast-induced hyperthermia[9]

Male SD rats (200 to 250 g) were used and divided into 5 groups of 6 animals. The hyperthermia was induced by subcutaneous injection of 25% yeast in sterile NSS each. The volume of an injection was 1 mL/100 g body weight. The rectal temperature (°C) was measured by using the twelve-channel electrical thermometer (LETICA, model TMP 812 RS, Panlab SL, Spain) connected with the probes which were inserted into the rectum about 5 cm depth. The basal rectal

temperature was recorded at 1 h after probe insertion. At 18 h after yeast injection, the rectal temperature was measured again and those rats that showed rises in rectal temperature ≥1°C were registering for the test. *T. arjuna* extract (500, 1,000, 1,500 mg/kg body weight), aspirin (300 mg/kg body weight) and distilled water (5 mL/kg body weight) were orally given and the rectal temperatures were then recorded at 30, 60, 90, 120 and 180 min.

Statistical analysis

Results were expressed as mean ± standard error of mean (SEM). Statistical significance was determined by one-way analysis of variance (ANOVA), Dunnett test and Student's t-test. The *p*-values less than 0.05 were considered significant.

Results

The percentage yield of *T. arjuna* extract was 13.33% weight of raw materials. The values of quality control and quantity of chemical compounds of the raw material and extract were remained within the normal ranges (Tables 1).

The ear edema thickness of both control groups were gradually increased and peaked at 1 h after the EPP application, and slightly decreased after that. *T. arjuna* extract at the dose of 3 mg/ear did not reduce ear edema at all time-points. As a positive control, phenylbutazone (1 mg/ear) exhibited significant inhibitory activity on the ear edema formation at all time-points (Table 2).

The paw edema was gradually increased and peaked at 5 h after the carrageenan injection. Aspirin at the dose of 300 mg/kg and *T. arjuna* extract at doses of 1,000 and 1,500 mg/kg could significantly inhibit paw edema at all time-points (Table 3).

The writhing response was intensively produced in the control group. Aspirin at the dose of 300 mg/kg and *T. arjuna* extract at the doses of 500, 1,000 and 1,500 mg/kg possessed inhibitory effect on writhing response (Table 4).

The reaction time of the tail flick test in the control group was not different from their baseline values at all time-points. Aspirin (300 mg/kg) and codeine (120 mg/kg) could significantly increase test reaction time at 1 and 3 hour. *T. arjuna* extract at the doses of 500 and 1,500 mg/kg could significantly increase test reaction time at 3 hour. *T. arjuna* extract at the dose of 1,000 mg/kg could significantly increase test reaction time at 2 and 3 hour (Table 5).

At 18 h after yeast injection, the hyperthermia was generated and maintained at all time-points in the

Table 1. Monograph of *T. arjuna* extract

Physical appearance	The powder is brown
	
UV spectrum	max 219, 266 nm
IR spectrum	3385, 1718, 1611, 1310, 1199, 1031
Chemical compounds screening	Hydrolysable tannin
% Tannin	36.1
% Total carbohydrate	16.96
% Uronic acid	7.55
% Gallic acid (HPLC)	6.72
Microbial test	Not found (*Salmonella sp, Clostridium sp, Staphylococcus aureus)*
Aflatoxin test	Not found

Table 2. Effect of *T. arjuna* extract on EPP-induced ear edema in rats

Group	Time after topical application of EPP/ear edema (mm)			
	15 min	30 min	1 h	2 h
Acetone 20 ml/ear	121.67±5.43	161.67±4.77	168.33±7.03	143.33±5.58
5% DMSO 20 ml/ear	125.00±4.28	155.00±6.19	160.00±3.65	138.33±3.07
Phenylbutazone 1 mg/ear	48.33±6.01*	66.67±2.11*	70.00±3.65*	63.33±3.33*
T. arjuna extract 3 mg/ear	115.00±6.19	146.67±4.94	153.33±3.33	135.00±5.63

Values are expressed as mean ± SEM (n = 6)
*Statistically difference from the control group, $p<0.05$

Table 3. Effect of *T. arjuna* extract on carrageenan-induced hind paw edema in rats

Group	Edema volume (mL)		
	1 h	3 h	5 h
Control	0.26±0.03	0.43±0.03	0.47±0.02
Aspirin 300 mg/kg	0.07±0.01*	0.17±0.02*	0.23±0.02*
T. arjuna extract			
500 mg/kg	0.17±0.02*	0.38±0.02	0.40±0.03
1,000 mg/kg	0.16±0.02*	0.34±0.04*	0.37±0.04*
1,500 mg/kg	0.17±0.01*	0.32±0.02*	0.34±0.02*

Values are expressed as mean ± SEM (n = 6)
* Statistically difference from the control group, $p<0.05$

Table 4. Effect of *T. arjuna* extract on acetic acid-induced writhing response in mice

Group	Dose (mg/kg)	Number of writhes	% inhibition
Control	-	29.17±2.10	-
Aspirin	300	9.50±1.98*	67.78
T. arjuna extract	500	15.50±1.67*	47.21
	1,000	13.50±1.34*	54.06
	1,500	13.00±2.27*	55.78

Values are expressed as mean ± SEM (n = 6)
* Statistically difference from the control group, $p<0.05$

control group (no treatment). Aspirin at the dose of 300 mg/kg could significantly reduce hyperthermia at all time-points. *T. arjuna* extract, at the dose of 1,000 mg/kg, could significantly reduce hyperthermia at 90 and 120 min, and *T. arjuna* extract, at the dose of 1,500 mg/kg, could significantly reduce hyperthermia at 60, 90 and 120 min (Table 6).

Discussion

The EPP-induced ear edema model was used for screening and evaluating the anti-inflammatory activity of the extract[4]. EPP causes acute inflammatory response by inducing pro-inflammatory mediator releases (e.g., histamine, serotonin, kinins and prostaglandins (PGs)[10] which causes vascular changes, including vasodilatation, and increasing in vascular permeability leading to ear edema formation[10,11]. Topical application of *T. arjuna* extract at the dose of 3 mg/ear did not reduce ear edema at all assessment time points. However, carrageenan-induced paw edema model was found that the oral administration of *T. arjuna* extract at the dose of 500, 1,000 and

Table 5. Effect of *T. arjuna* extract on tail flick test in rats

Group	Reaction time (h)			
	Baseline	1 h	2 h	3 h
Control	3.07±0.18	2.71±0.22	3.05±0.20	2.51±0.16
Aspirin 300 mg/kg	3.10±0.22	3.75±0.27*	3.78±0.33	3.94±0.23*
Codeine 120 mg/kg	3.10±0.08	3.75±0.32*	3.89±0.29	4.07±0.35*
T. arjuna extract				
500 mg/kg	3.02±0.26	3.11±0.13	3.26±0.26	3.52±0.22*
1,000 mg/kg	3.14±0.17	3.56±0.21	4.01±0.15*	3.93±0.19*
1,500 mg/kg	3.15±0.16	3.31±0.30	3.78±0.21	3.49±0.23*

Values are expressed as mean ± SEM (n = 6)
* Statistically difference from the control group, $p<0.05$

Table 6. Effect of *T. arjuna* extract on yeast-induced hyperthermia in rats

Group	18 h after yeast injection	Rectal temperature (°C)			
		30 min	60 min	90 min	120 min
Control	38.83±0.22	38.70±0.18	38.55±0.24	38.43±0.21	38.45±0.22
Aspirin 300 mg/kg	38.57±0.15	38.02±0.15*	37.47±0.16*	37.22±0.16*	37.13±0.14*
T. arjuna extract					
500 mg/kg	38.73±0.08	38.40±0.12	38.10±0.16	37.93±0.16	37.83±0.16
1,000 mg/kg	38.62±0.14	38.22±0.15	37.90±0.16	37.72±0.16*	37.60±0.18*
1,500 mg/kg	38.60±0.11	38.13±0.17	37.70±0.24*	37.45±0.24*	37.20±0.21*

Values are expressed as mean ± SEM (n = 6)
* Statistically difference from the control group, $p<0.05$

1,500 mg/kg showed anti-inflammatory activity. The carrageenan-induced paw edema model was used to evaluate the acute anti-inflammatory activity, especially COX inhibitors[5]. Carrageenan causes biphasic phase of paw edema. The first phase (0 to 2.5 h after carrageenan injection) results from the release of histamine, serotonin, and kinins, whereas the second phase (2.5 to 6 h) is correlated with PGs, oxygen-derived free radicals, and the local neutrophil infiltration[12-15]. In the present study, the *T. arjuna* extract possessed anti-inflammatory activity similar to aspirin (reference drug). Thus, *T. arjuna* extract may act via COX inhibition and reduced PGs biosynthesis. In addition, it may also inhibit the release and/or infiltration activity of these pro-inflammatory mediators.

The acetic acid-induced writing response was a model to screen and evaluate whether a substance could act as both central and peripheral analgesic activity or not[16]. Being an irritant, acetic acid would enhance the synthesis and release of pro-inflammatory mediators such as bradykinin, serotonin, histamine, PGs and substance P, which irritate the pain nerve endings or nociceptors[6,7]. The result indicated that, *T. arjuna* extract had both centrally and peripherally acting analgesic activity. Moreover, this study found that *T. arjuna* extract exerted the centrally analgesic acting as shown by significantly inhibiting the tail flicking induced by heat. The flick of tail is explained by regulation of reflex arc in spinal cord which is modulated via the descending pathway mechanism[8]. These results suggest that the mechanism of analgesic effects of *T. arjuna* extract may be due to the inhibition of the synthesis and/or release of inflammatory pain mediators such as PGs and other mediators at peripheral nociception sites.

The yeast-induced hyperthermia model was used for the investigation of antipyretic activity of the extract. High body temperature involves the production

of pro-inflammatory cytokines such as IL-1β, IL-6, IFN-α and TNF-α which enter the hypothalamic circulation and stimulate the release of local PGs, leading to the reset of the hypothalamic thermal set point[17]. In the present study, the high dose of *T. arjuna* extract (1,500 mg/kg) showed antipyretic activity by decreasing body temperature of hyperthermic rats induced by brewer's yeast injection at 60, 90 and 120 min of assessment times. The antipyretic activity of *T. arjuna* extract may be due to the inhibition of the synthesis and/or release of local PGE_2 into the hypothalamus.

Conclusion

The present study conducted in animal models suggested that *T. arjuna* extract possesses anti-inflammatory analgesic, and antipyretic activities. It is preferably effective in acute inflammation. It possesses analgesic effect mainly via peripheral mechanism and partly centrally acting. The Antipyretic effect of that *T. arjuna* extract is probably due to its inhibition of PG synthesis/release in hypothalamus.

What is already known on this topic?

Terminalia arjuna is one of the most useful medicinal plants for the treatment of a wide variety of diseases. Ethnopharmacological properties include antioxidant, antihypertensive, anti-inflammatory, anti-cancer, and gastroprotective effect.

What this study adds?

This study reveals the mechanisms of anti-inflammatory, antipyretic, and analgesic effects of *Terminalia arjuna* in animal models. The oral administration of *Terminalia arjuna* extract possessed acute anti-inflammatory and antipyretic effects potentially through the inhibition prostaglandins and proinflammatory mediators. The analgesic activity of *Terminalia arjuna* was mediated by both peripheral and central nervous system.

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Potential conflicts of interest

None.

References

1. Sivova V, Bera K, Ray B, Nosal S, Nosalova G. Cough and Arabinogalactan Polysaccharide from the Bark of *Terminalia arjuna*. Adv Exp Med Biol 2016; 935: 43-52.
2. Meghwani H, Prabhakar P, Mohammed SA, Seth S, Hote MP, Banerjee SK, et al. Beneficial effects of aqueous extract of stem bark of *Terminalia arjuna* (Roxb.), An ayurvedic drug in experimental pulmonary hypertension. J Ethnopharmacol 2017; 197: 184-94.
3. Department of Medical Sciences, Ministry of Public Health. Thai herbal pharmacopoeia, Volume II. Nonthaburi, Thailand: Prachachon; 2000.
4. Brattsand R, Thalen A, Roempke K, Kallstrom L, Gruvstad E. Influence of 16 alpha, 17 alpha-acetal substitution and steroid nucleus fluorination on the topical to systemic activity ratio of glucocorticoids. J Steroid Biochem 1982; 16: 779-86.
5. Winter CA, Risley EA, Nuss GW. Carrageenin-induced edema in hind paw of the rat as an assay for antiiflammatory drugs. Proc Soc Exp Biol Med 1962; 111: 544-7.
6. Collier HO, Dinneen LC, Johnson CA, Schneider C. The abdominal constriction response and its suppression by analgesic drugs in the mouse. Br J Pharmacol Chemother 1968; 32: 295-310.
7. Nakamura H, Shimoda A, Ishii K, Kadokawa T. Central and peripheral analgesic action of non-acidic non-steroidal anti-inflammatory drugs in mice and rats. Arch Int Pharmacodyn Ther 1986; 282: 16-25.
8. D'Amour F, Smith D. A method for determining loss of pain sensation. J Pharmacol Exp Ther 1941; 72: 74-9.
9. Teotino UM, Friz LP, Gandini A, Bella DD. Thio Derivatives of 2,3-Dihydro-4H-1,3-benzoxazin-4-one. Synthesis and pharmacological properties. J Med Chem 1963; 6: 248-50.
10. Carlson RP, O'Neill-Davis L, Chang J, Lewis AJ. Modulation of mouse ear edema by cyclooxygenase and lipoxygenase inhibitors and other pharmacologic agents. Agents Actions 1985; 17: 197-204.
11. Murphy H, Ward P. Inflammation. In: Rubin E, editor.Rubin's pathology: clinicopathologic foundations of medicine.4th ed. Philadelphia: Lippincott Williams &Wilkins; 2005: 40-83.
12. Di Rosa M, Sorrentino L. The mechanism of the inflammatory effect of carrageenin. Eur J Pharmacol 1968; 4: 340-2.
13. Vinegar R, Schreiber W, Hugo R. Biphasic development of carrageenin edema in rats. J Pharmacol Exp Ther 1969; 166: 96-103.

14. Crunkhorn P, Meacock SC. Mediators of the inflammation induced in the rat paw by carrageenin. Br J Pharmacol 1971; 42: 392-402.
15. Di Rosa M. Biological properties of carrageenan. J Pharm Pharmacol 1972; 24: 89-102.
16. Koster R, Anderson M, De Beer EJ. Acetic acid-induced analgesic screening. Federation Proceedings 1959; 18: 412.
17. Dalal S, Zhukovsky DS. Pathophysiology and management of fever. J Support Oncol 2006; 4: 9-16.

ฤทธิ์ต้านการอักเสบ ระงับปวด และลดไข้ของสารสกัดสมอเทศในหนูแรท

ลินดา จุฬาโรจน์มนตรี, ณัฏฐกานติ์ จิรัณธนัฐ, กาญจนา ใจจ้อย, ปิยนุช โรจน์สง่า, สืบบูรณ์ สิรีรัฐวงศ์

ภูมิหลัง: *Terminalia arjuna Roxb. (วงศ์ Combretaceae) รู้จักกันในภาษาไทยว่า "สมอเทศ" ผลของสมอเทศ ถูกนำมาใช้เป็นยาระบายอย่างอ่อน ขับลมและขับเสมหะ*

วัตถุประสงค์: *เพื่อศึกษาฤทธิ์ต้านการอักเสบระงับปวดและลดไข้ของสารสกัดสมอเทศโดยใช้แบบจำลองในสัตว์ ทดลองเปรียบเทียบกับยามาตรฐาน*

วัสดุและวิธีการ: *การศึกษาฤทธิ์ต้านการอักเสบโดยใช้ 2 การทดลอง คือ การเหนี่ยวนำการบวมของใบหูหนูด้วยสาร ethyl phenylpropiolate (EPP) และการเหนี่ยวนำการบวมของอุ้งเท้าด้วยคาร์ราจิแนน การศึกษาฤทธิ์ระงับปวดใช้การเหนี่ยวนำความเจ็บปวดด้วยกรดอะซิติกและความร้อน ส่วนการศึกษาฤทธิ์ลดไข้ใช้การเหนี่ยวนำให้เกิดไข้ด้วยยีสต์*

ผลการศึกษา: *ผลการทดลองพบว่าการป้อนสารสกัดสมอเทศทางปากสามารถลดการบวมของอุ้งเท้าหนูแรท จากการกระตุ้นด้วย carrageenan ได้ สารสกัดสมอเทศสามารถระงับความเจ็บปวดที่เกิดจากการเหนี่ยวนำ ด้วยกรดอะซิติกและกระตุ้นด้วยความร้อนได้ ซึ่งแสดงให้เห็นว่าสารสกัดสมอเทศมีฤทธิ์ระงับปวดผ่านระบบประสาท ส่วนปลายโดยการยับยั้งการสร้างและ/หรือการหลั่งของสารสื่อกลางที่เกี่ยวข้องกับความเจ็บปวด และฤทธิ์ระงับปวดมีกลไกบางส่วนผ่านทางระบบประสาทส่วนกลาง นอกจากนี้สารสกัดสมอเทศขนาด 1,000 และ 1,500 มิลลิกรัม ต่อกิโลกรัมน้ำหนักตัวสามารถลดไข้ ซึ่งแสดงได้ว่าสารสกัดสมอเทศมีฤทธิ์ลดไข้โดยอาจเป็นผลจากการยับยั้ง การสังเคราะห์สารพรอสตาแกรนดินส์*

สรุป: *ผลการวิจัยในครั้งนี้สามารถสรุปได้ว่าสารสกัดสมอเทศมีฤทธิ์ต้านการอักเสบระงับปวดและลดไข้ในสัตว์ทดลองได้*