Antispasmodic Effects of Curcuminoids on Isolated Guinea-Pig Ileum and Rat Uterus

CHANDHANEE ITTHIPANICHPONG, MSc*,
WANDEE KEMSRI, BSc*,
NIJSIRI RUANGRUNGSI, PhD**,
ANUGOOL SAWASDIPANICH, MSc*

Abstract

Curcuminoids, a yellow constituent isolated from *Curcuma longa* Linn. rhizomes was studied for its antispasmodic activity in isolated guinea-pig ileum and rat uterus. Curcuminoids at the concentration of 12 μg/ml significantly inhibited the ileum pre-contracted with acetylcholine (ACh) 5×10^{-7} M and histamine 5×10^{-7} M. (Force of contraction was 62.84 ± 4.66% and 75.60 ± 4.66% respectively) and the effects were prominently observed when the concentration of curcuminoids was increased to 36 μg/ml. (Force of contraction was 44.93 ± 4.33% and 42.79 ± 1.98%) In potassium depolarizing Tyrode solution, curcuminoids 4 μg/ml and 20 μg/ml reduced the contraction induced by calcium chloride ($CaCl_2$) 1.8 mM. (The contraction was 63.31 ± 1.80% and 36.87 ± 3.25%) In rat uterus smooth muscle preparation, curcuminoids 8 μg/ml and 16 μg/ml significantly reduced force and frequency of contraction induced by oxytocin 1×10^{-2} IU/ml. Curcuminoids 8 μg/ml produced 54.68 ± 3.34 per cent force of contraction and 79.09 ± 2.29 per cent frequency of contraction. Curcuminoids 16 μg/ml caused more relaxation of rat uterus smooth muscle. (Force of contraction was 43.38 ± 3.56%, frequency of contraction was 49.96 ± 5.20%). Curcuminoids 8 and 16 μg/ml significantly reduced force of contraction induced by KCl 50 mM. (Force of contraction was 54.10 ± 4.92% and 36.60 ± 2.99%). The results obtained from this study concluded that curcuminoids produced a smooth muscle relaxation effect on isolated guinea-pig ileum and rat uterus by receptor-dependent and independent mechanism.

Key word : Curcuminoids, Antispasmodic, Turmeric

ITTHIPANICHPONG C, RUANGRUNGSI N, KEMSRI W, SAWASDIPANICH A
J Med Assoc Thai 2003; 86 (Suppl 2): S299-S309

* Department of Pharmacology, Faculty of Medicine,
** Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand.

Turmeric rhizomes (*Curcuma longa* Linn Family Zingiberaceae) is known very well as "Kamin" in Thailand. It is widely used as a spice, coloring agent in several kinds of foods, such as curry and mustard. Insect-repellant, cosmatic and medical purposes are other uses of it[1-4]. In Thai folk remedies [5], Kamin is employed as a carminative, an anti-inflammatory substance. It is also used in the treatment of menstrual difficulty, hepatic disorder as well as biliary disorder. Active constituents of turmeric compose of curcuminoids which are yellow pigment accumulated in the parenchymal cells of cortex in turmeric rhizomes. There are 3 principle components in curcuminoids from turmeric: curcumin, demethoxycurcumin and bisdemethoxycurcumin as demonstrated in Fig. 1.

In vivo and *in vitro* evaluation of *Curcuma longa* L. revealed a variety of pharmacological actions including : scavenging of reactive oxygen species[6, 7], cancer chemoprevention[8-10], anti-inflammation [11,12], antiprotozoal activity[13,14], antibacterial activity[15], anti HIV effect[16] and antipeptic ulcer agents[17,18].

Even though advanced research of curcumin is evident, it is still essential to elucidate some important pharmacological aspects of this substance since it is commonly used in daily food. The present study aimed at evaluating the antispasmodic and relaxant effects of curcuminoids on isolated guinea-pig ileum and rat uterus.

MATERIAL AND METHOD

Plant material

The dried rhizome of turmeric (*Curcuma longa* Linn) was collected in Nakhon Pathom province. A voucher specimen of the plant material was deposited at the herbarium of the Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok Thailand.

Animals

Female wistar rats (200 g) and both sexes of guinea pigs were purchased from the National Laboratory Center, Salaya, Mahidol University, Nakhon Pathom province. All animals were kept in an air conditioned room at the Animal Facility Center of the Faculty. They were acclimatized for at least 1 week before beginning the experiment and fed with a standard diet (Zuellig Co). Water was allowed ad libitum.

Chemicals

Acetylcholine hydrochloride, histamine base, ethylene glycol bis (β-aminoethylether)-N,N,N′,N′-tetraacetic acid (EGTA) were obtained from Sigma Chemical Co, St.Louis USA. Oxytocin (syntocinon®) was purchased from Sandoz, Switzerland, Estradiol valerate (Progynon Depot®) was from Schering Germany. Others were from E. Merck, Darmstadt, Germany.

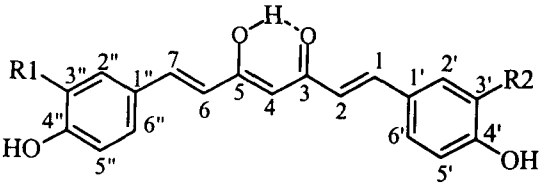
Apparatus

Organ bath for smooth muscle preparation with isometric transducer and recording system for physiograph. (Narcobiosystem USA)

Method

Plant preparation

The dried rhizome was ground into powder and the extraction process started with separation of volatile substance and fat compound from the powder by distillation in soxhlet apparatus for 6-8 h using petroleum ether as an extraction solvent, then the powder was macerated in 95 per cent ethanol for 48 h. The ethanolic extract was concentrated under reduced pressure to a semisolid mass. The compound was further purified using column chromatography containing silica gel as the stationary phase and eluted with chloroform. Yellow fraction of curcuminoids were collected, crystallization and drying. Identification of curcuminoids substance was performed for comparison with standard curcuminoids by thin layer chromatography (TLC) (Fig. 2). Appropriate concen-



R1, R2 = OCH_3 ; Curcumin
R1 = OCH_3, R2 = H ; Demethoxycurcumin
R1, R2 = H ; Bisdemethoxycurcumin

Fig. 1. Chemical structures of curcuminoids from turmeric rhizomes.

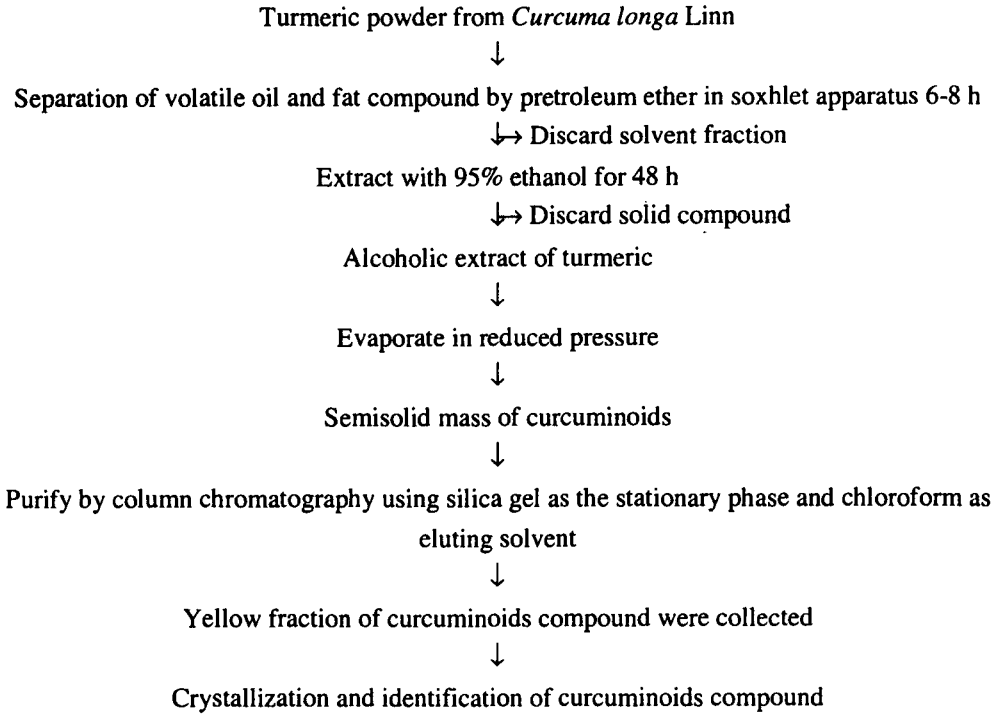


Fig. 2. Diagram demonstrates the extraction and purification process of curcuminoids compound from *Curcuma longa* Linn (turmeric).

tration of the extracts were prepared in 95 per cent ethanol and used in the experiment. The volume of 30 µl was added for each study concentration.

Antispasmodic activity of curcuminoids on histamine, acetylcholine and $CaCl_2$ induced contractile response of guinea-pig isolated ileum

After overnight fasting, the guinea pig was killed by a blow to the base of the skull and cervical dislocation, a piece of ileum (1 cm length) was suspended in an organ bath containing Tyrode solution (composition in g/L : NaCl 8.00, KCl 0.20, $NaHCO_3$ 1.00, $MgCl_2$ 0.21, NaH_2PO_4 0.05, $CaCl_2$ 0.26, glucose 1.00) at 37°C gassed with 95 per cent CO_2 and 5 per cent O_2. The tissue was allowed to equilibrate for 45 min (the physiological medium was changed every 20 min). The guinea-pig ileum was pre-contracted with acetylcholine 5 x 10^{-7} M or histamine 5 x 10^{-7} M (submaximal concentration which causes 60- 70 per cent of maximum contraction) for 15 min. When the contractile response was completely obtained, the guinea-pig ileum was rinsed with Tyrode solution every 20 min until tension returned to the baseline level. Then it was incubated in 95 per cent ethanol (curcuminoids dissolving solvent or curcuminoids 12 µg/ml or 36 µg/ml) for 5 min. The tissue was contracted again with acetylcholine 5 x 10^{-7} M or histamine 5 x 10^{-7} M. Comparison of ileal contraction was performed before and after exposure to 95 per cent ethanol, curcuminoids 12 and 36 µg/ml in a tissue bath.

$CaCl_2$ 1.8 mM induced ileal contration was performed in potassium depolarizing Tyrode solution for 30 min then curcuminoids 4, 20 µg/ml or solvent were added and recorded ileal contraction for 20 min. Relaxation of $CaCl_2$ induced-contraction was calculated after curcuminoids were applied.

Uterine relaxant effect of curcuminoids

Female Wistar rats were pretreated with estradiol valerate 0.1 mg/kg the body weight subcutaneously 24 h before starting the experiment to bring rat uterus into the estrous stage. The animal was sacrificed by a blow to the base of the skull. The

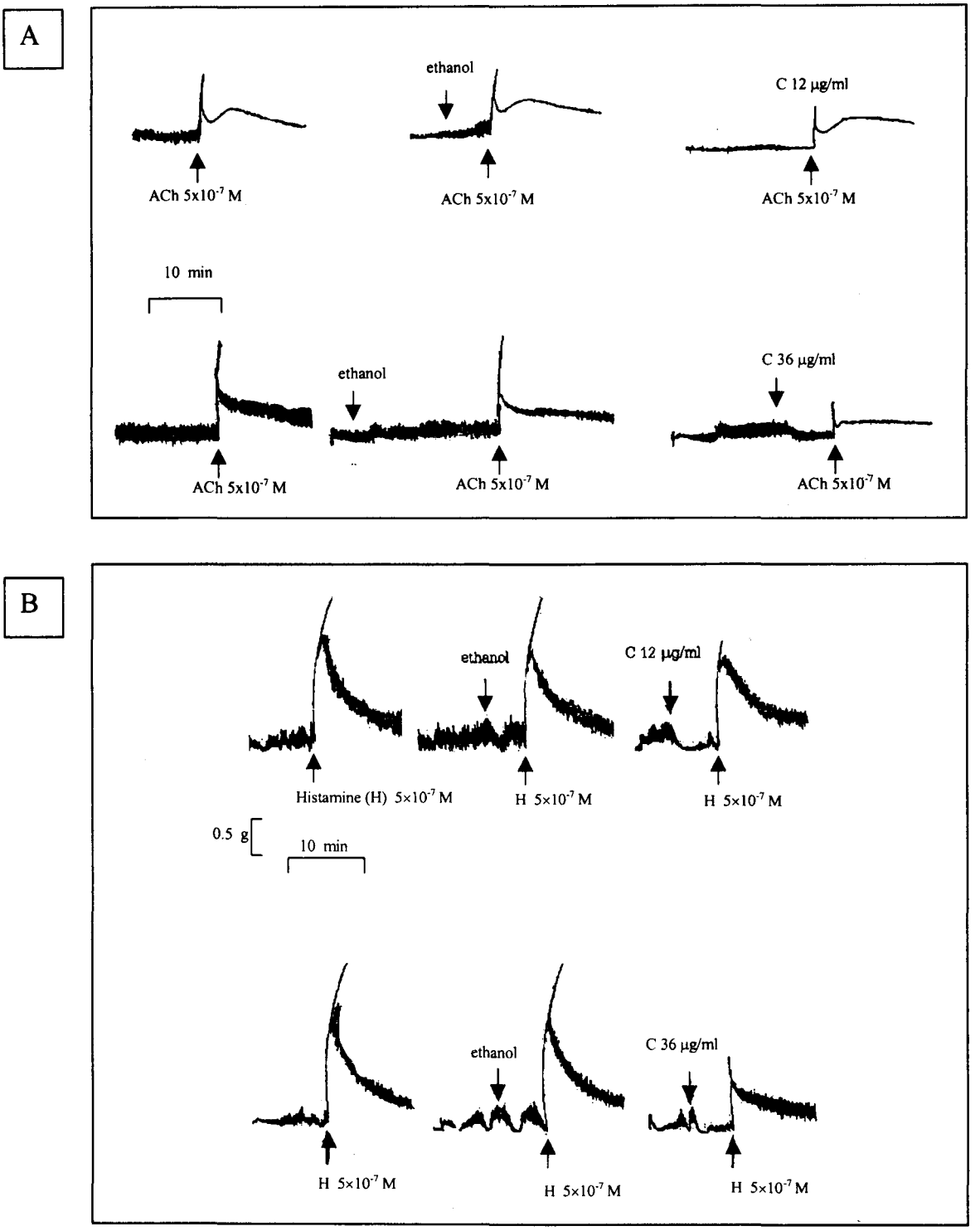


Fig. 3. Relaxation response of isolated guinea-pig ileum pre-contracted with ACh 5 x 10^{-7} M (A) Histamine 5 x 10^{-7} M (B) in Tyrode solution elicited by curcuminoids 12 and 36 µg/ml.

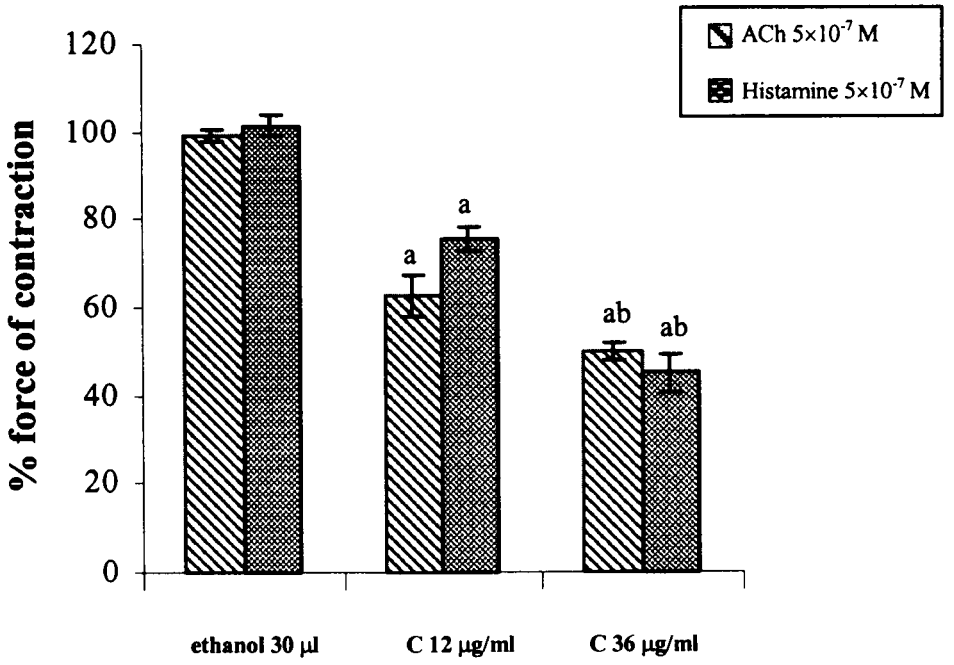


Fig. 4 **Inhibitory effect of curcuminoids (C) compound 12 and 36 µg/ml on isolated guinea-pig ileum pre-contracted with ACh 5 x 10^{-7} M and histamine 5 x 10^{-7} M in Tyrode solution. Each value represents mean ± SE of 7 experiments.**

a = p < 0.05 *vs* ethanol 30 µl
b = p < 0.05 *vs* curcuminoids 12 µg/ml

abdomen was opened and the intestine was removed to reveal the uterus. Both horns of the uterus were dissected and transferred them to De Jalon solution (composition in g/L : NaCl 9.0, KCl 0.42, $CaCl_2$ 0.06, $NaHCO_3$ 0.5, glucose 0.5) aerated with 95 per cent CO_2 and 5 per cent O_2 and maintained at 37 ± 0.05°C. Each horn of the uterus was cut longitudinally and divided into four pieces of uterine muscle sheets. Each piece of uterine sheet was mounted in an organ bath in the same condition as described and allowed to equilibrate for 45 min. The medium was changed every 20 min. A change in isometric tension was measured with a force transducer. The uterus was pre-contracted with oxytocin 1 x 10^{-2} IU/ml (submaximal contraction which caused 70-80% maximal contraction). The uterus was washed several times with physiological medium, then 95 per cent ethanol (a solvent for dissolving curcuminoids), curcuminoids 8, 16 µg/ml were applied for 15 min. The uterus was contracted again with oxytocin 1 x 10^{-2} IU/ml. Change in contractile response and frequency of contraction were measured before and after exposure to 95 per cent ethanol, curcuminoids 8, 16 µg/ml.

The effect of 95 per cent ethanol, curcuminoids 8, 16 µg/ml were also evaluated on acetylcholine 1 x 10^{-5} M, KCl 50 mM pre-contracted uterus.

Statistical analysis

Contractile responses (force) or frequency of contraction were expressed as percentage of the maximal contraction (100%) induced by appropriate contractile stimuli before exposure to solvent or curcuminoids (mean ± SE)

Statistical differences between the treated and untreated control (95% ethanol) were analysed by student's unpaired *t*-test and one-way analysis of variance (ANOVA Bonferroni method). A probability level of less than 0.05 was regarded as statistical difference.

RESULTS

Total curcuminoids (yield) obtained was 11 per cent from this study.

Antispasmodic activity of curcuminoids on histamine, acetylcholine and $CaCl_2$ induced contractile response of guinea-pig isolated ileum

Exposure of the preparation for 5 min to a given solvent (95% ethanol 30 µl) did not alter the contraction induced by submaximal concentration of ACh 5 x 10^{-7} M, histamine 5 x 10^{-7} M and $CaCl_2$ 1.8 mM. However curcuminoids at the concentration of 12, 36 µg/ml significantly attenuated acetylcholine induced ileal contraction to 62.84 ± 4.66 per cent and 42.79 ± 1.98 per cent. Histamine (5 x 10^{-7} M) mediated contractile response was decreased significantly after exposure to curcuminoids 12, 36 µg/ml to 75.60 ± 2.77 per cent and 44.93 ± 9.33 per cent (Fig. 3, 4). In potassium depolarizing Tyrode solution (a calcium free medium, a depolarization condition) $CaCl_2$ induced ileal tonic contractile response. Curcuminoids 4, 20 µg/ml reduced response to $CaCl_2$ to 63.31 ± 1.80 per cent and 36.87 ± 3.25 per cent as shown in Fig. 5.

Uterine relaxant effect of curcuminoids

Curcuminoids 8 µg/ml significantly inhibited force and frequency of rat uterine pre-contraction

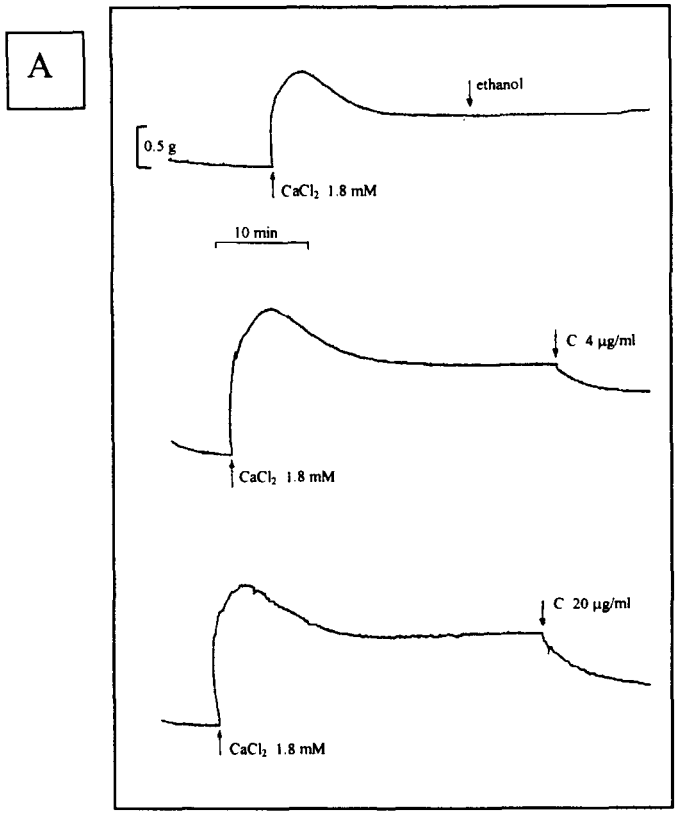


Fig. 5A. A decrease in sustained contractile response of isolated guinea-pig ileum induced by $CaCl_2$ 1.8 mM 30 min in depolarizing Tyrode solution after ethanol 95 per cent or curcuminoid 4 and 20 µg/ml exposure. Each value represents the mean ± SE of 7 experiments.

a = $p < 0.05$ *vs* ethanol 30 µl
b = $p < 0.05$ *vs* curcuminoids 4 µg/ml

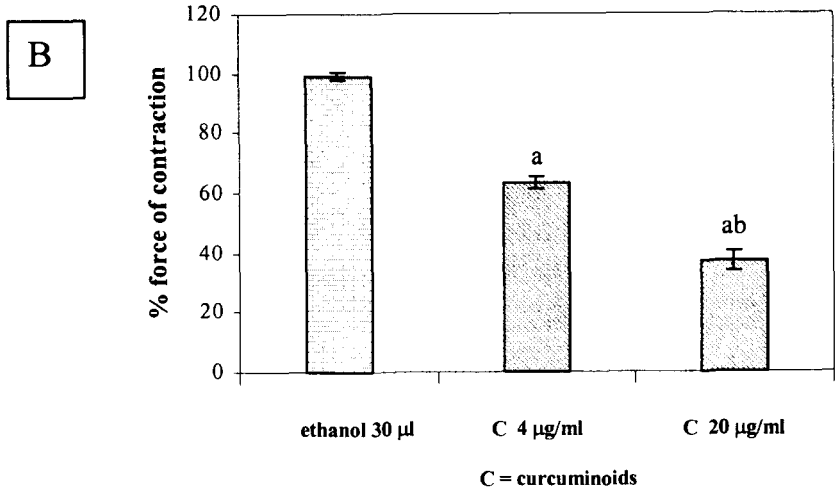


Fig. 5B Relaxant effect of curcuminoids 4 and 20 µg/ml on $CaCl_2$ induced guinea-pig ileal contraction. Each value represents the mean ± SE of 7 experiments.

a = $p < 0.05$ *vs* ethanol 30 µl
b = $p < 0.05$ *vs* curcuminoids 4 µg/ml

produced by oxytocin 1 x 10^{-2} IU/ml, ACh 2 µg/ml and the attenuation in force and frequency of contraction were more prominent when uterine tissue was exposed to curcuminoids 16 µg/ml. Exposure to curcuminoids also elicited relaxation of uterine smooth muscle precontracted with KCl 50 mM. (Table 1, Fig. 6)

DISCUSSION

The result from the present study has shown that curcuminoids, a yellow compound isolated from *C. longa* in the concentration at 12 µg/ml elicited relaxation of ileum pre-contracted with ACh 5 x 10^{-7} M and histamine 5 x 10^{-7} M to 62.84 per cent and 75.60 per cent respectively and these effects were more clearly found after exposure to curcuminoids 36 µg/ml (42.79% and 44.93%). Control of tension in gastrointestinal smooth muscle is in large part dependent on the intracellular Ca^{2+} concentration(20). In general, there are two types of excitation-contraction coupling based on the type of mechanism responsible for change in Ca^{2+} concentration. Electromechanical coupling requires changes in membrane potential which activate voltage-dependent Ca^{2+} channel to trigger an influx of Ca^{2+}. The others are pharmacomechanical coupling, in which chemical agents act *via* specific receptors and can bring both excitatory and inhibitory in nature.

Impaired histamine and acetylcholine induced guinea-pig ileal contraction through H_1 and M_3 receptor were obtained after curcuminoids exposure might be the result of inhibition through receptor-mediated contraction. However, curcuminoids also provided a non-receptor mediated mechanism for ileal contraction since its compound (4 and 20 µg/ml) exerted an inhibitory effect on ileal pre-contracted with $CaCl_2$ 1.8 mM in potassium depolarizing Tyrode solution (Ca^{2+} free medium). Curcuminoids impaired ileal smooth muscle contraction was partly due to interfering with Ca^{2+} influx *via* voltage-sensitive calcium channel(21).

As uterine contraction is triggered by increases in cytosolic Ca^{2+} concentration which arises from several mechanisms. Entry through the surface membrane calcium channel or Ca^{2+} release from the sarcoplasmic reticulum (SR) is responsible for its contraction mechanism(22). Uterine contractant such as oxytocin, acetylcholine (through oxytocin and M_3

receptors) increase force and frequency of uterine contraction by increasing influx and release from intracellular Ca^{2+} store secondary to phospholipase C (PLC) activation[23] curcuminoids 8 μg/ml decreased force and frequency of uterine contraction after pre-contraction with oxytocin 1 x 10^{-2} IU/ml and ACh 2 μg/ml to 54.68 and 73.01 per cent (force) and 79.09 and 76.33 per cent (frequency) respectively. The uterine relaxation was more prominent when a higher concentration of curcuminoids (16 μg/ml) was applied. Relaxation of the pre-contracted rat uterus with oxytocin and histamine by curcuminoids in the present study may imply alteration of regulatory phosphorylation mechanism and produced change in intracellular Ca^{2+}. KCl (depolarizing stimulant) triggers smooth muscle contraction by promoting Ca^{2+} influx through

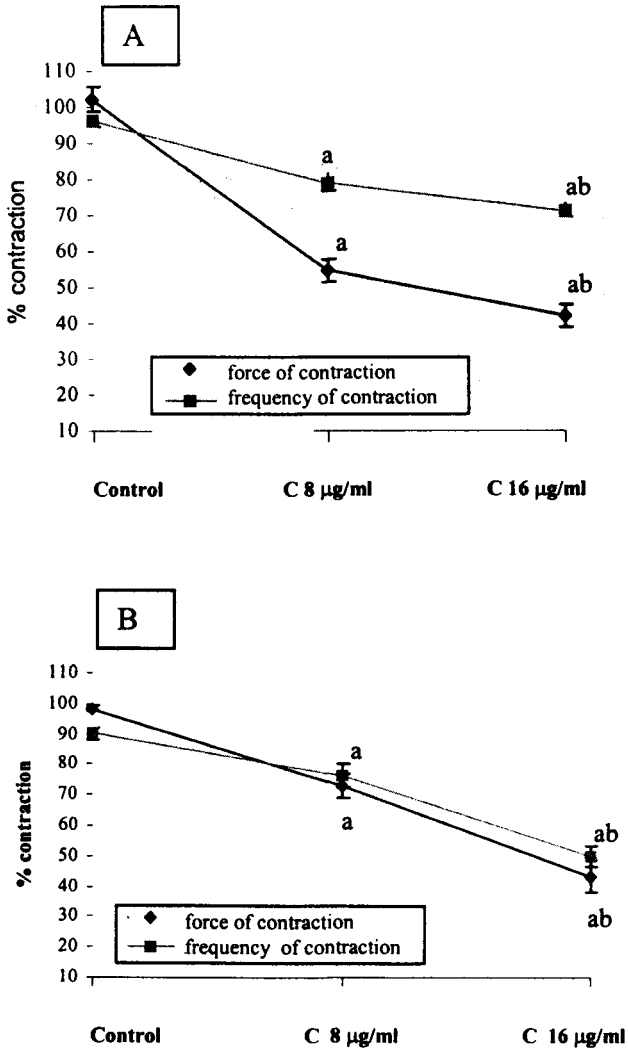


Fig. 6. Antispasmodic effects of curcuminoids 8 and 16 μg/ml on isolated rat uterus pre-contracted with oxytocin 1 x 10^{-2} IU/ml (A) ACh 2 μg/ml (B) and KCl 50 mM (C). Each value represents the mean ± SE of 7 experiments

a = $p < 0.05$ *vs* ethanol 30 μl
b = $p < 0.05$ *vs* curcuminoids 8 μg/ml

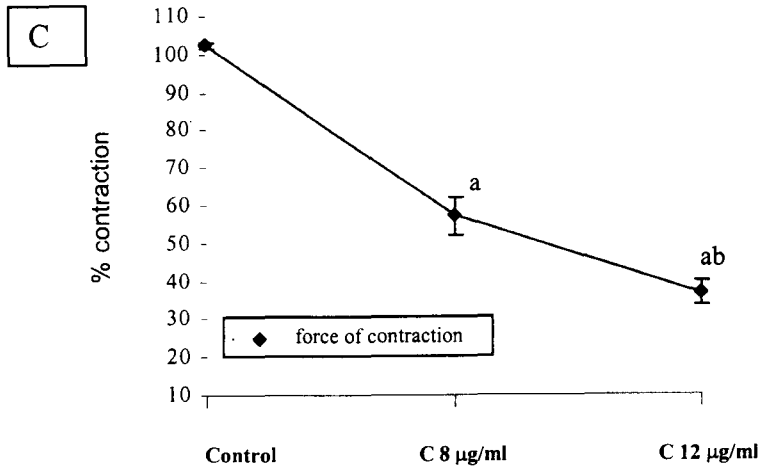


Fig. 6. Antispasmodic effects of curcuminoids 8 and 16 µg/ml on isolated rat uterus pre-contracted with oxytocin 1 x 10^{-2} IU/ml (A) ACh 2 µg/ml (B) and KCl 50 mM (C). Each value represents the mean ± SE of 7 experiments

a = $p < 0.05$ *vs* ethanol 30 µl
b = $p < 0.05$ *vs* curcuminoids 8 µg/ml

Table 1. Relaxant effect of curcuminoids 8,16 µg/ml on force and frequency of rat uterine contraction induced by oxytocin 1 x 10^{-2} IU/ml, ACh 2 µg/ml, KCl 50 mM. The results have been expressed as the per cent of maximum response to standard agonist prior exposure to curcuminoids. Values shown are mean ± SE (n = 7) a = significant difference from ethanol 30 µl, b = significant difference from curcuminoids 8 µg/ml treated group. ($p < 0.05$)

Standard agonist on uterine smooth muscle	95% ethanol 30 µl		Curcuminoids 8 µg/ml		Curcuminoids 16 µg/ml	
	Force of contraction	Frequency of contraction	Force of contraction	Frequency of contraction	Force of contraction	Frequency of contraction
Oxytocin 1 x 10^{-2} IU/ml	102.34 ± 3.57	96.35 ± 1.52	54.68 ± 3.34[a]	79.09 ± 2.29[a]	42.34 ± 3.16[ab]	71.18 ± 1.89[ab]
ACh 2 µg/ml	98.40 ± 1.97	90.29 ± 0.71	73.01 ± 4.10	76.33 ± 3.94[a]	43.38 ± 3.56[ab]	49.96 ± 5.20[ab]
KCl 50 mM	102.33 ± 0.68	-	57.10[a] ± 4.92	-	36.60 ± 2.99[ab]	-

voltage-sensitive calcium channel that are readily activated by membrane depolarization[24]. KCl also increases intracellular Ca^{2+} released from the calcium store in sarcoplasmic reticulum[25]. Curcuminoids 8, 16 µg/ml attenuated KCl 50 mM induced uterine contraction to 57.10 and 36.60 per cent. Therefore, extracellular Ca^{2+} influx through voltage-sensitive calcium channel is thought to be inhibited by the study compound. Inhibition of uterine pre-contracted with oxytocin 1 x 10^{-2} IU/ml, ACh 2 µg/ml and KCl 50 mM suggested that curcuminoids impaired uterine contraction likely through receptor and voltage ion channel mechanism.

The ileal and uterine smooth muscle relaxant effect of curcuminoids from C longa might support its folk use as a medicinal plant for the treatment of

some gastrointestinal disorders and menstrual difficulty. It could be beneficial in patients suffering from a peptic ulcer(17,18).

In summary, the result obtained from the present study suggested that curcuminoids isolated from turmeric rhizomes exerted a relaxant effect on guinea-pig ileum pre-contracted with several contractile stimuli (ACh 5 x 10^{-7} M, histamine 5 x 10^{-7} M and $CaCl_2$ 1.8 mM) as well as uterine smooth muscle pre-contracted with oxytocin1 x 10^{-2} IU/ml, ACh 2 µg/ml and KCl 50 mM through receptor dependent and independent mechanism.

ACKNOWLEDGEMENT

This research work was supported by Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University.

(Received for publication on April 21, 2003)

REFERENCES

1. Helen CF. Isolation, purification and characterization of insect repellants from *Curcuma longa*. J Agric Food Chem 1982; 30: 290.
2. Tewtrakul S, De-Eknamkul W, Ruangrungsi N. Stimulataneous determination of individual curcuminoids in tumeric by TLC-densitometric method. Thai J Pharm Sci 1992; 16: 251-9.
3. Lin JK, Lin-Shiau SY. Mechanism of cancer chemoprevention by curcumin. Proc Natl Sci Counc ROC (B) 2001; 25: 59-66.
4. Ammon HP, Wahl MA. Pharmacology of *Curcuma longa*. Planta Med 1991; 57: 1-7.
5. Pongboonrord S. Mai-tet-muang-Thai. Bangkok: Kasem Bannakit Press; 1966: 92-3.
6. Kunchandy E, Rao MNA. Oxygen radical scavenging activity of curcumin. Int J Pharm 1990; 38: 239-40.
7. Subramanian M, Sreejayan Rao MNA, Devasagyam TPA, Singh BB. Diminution of singlet oxygen-induced DNA-damage by curcumin and related antioxidants. Mutat Res 1994; 311: 249-55.
8. Rao CV, Kawamori T, Hamid R, Reddy B. Chemoprevention of colonic aberrant crypt foci by an inducible nitric oxide synthase selective inhibitor. Carcinogenesis 1999; 20: 641-4.
9. Zhang F, Altorki NK, Mestre JR, Subbaaramaiah K, Dannenberg AJ. Curcumin inhibits cyclooxygenase-2 transcription in bile acid and phorbal ester-treated human gastrointestinal epithelial cells. Carcinogenesis 1999; 20: 445-51.
10. Inano H, Onoda M, Inofuku N, et al. Chemoprevention by curcumin during the promotion stage of tumorigenesis of mammary gland in rats irradiated with γ-rays. Carcinogenesis 1999; 20: 1011-8.
11. Mukophadhyay A, Basu N, Ghatak N, Gujral PK. Anti-inflammatory and irritant activities of curcumin analogues in rats. Agents and Action 1982; 12: 508-15.
12. Srimal RC, Dhawan BN. Pharmacology of diferuloyl methane (curcumin), a non-steroidal anti-inflammatory agent. J Pharm Pharmacol 1973; 25: 447-52.
13. Araujo CAC, Alegrio LV, Castro D, Lima MEF, Leon LL. *Leishmania amazonensis*: *In vivo* experiments with diarylheptanoids from Leguminosae and Zingiberaceae plants. 1 Mem Inst Oswaldo Cruz 1998; 93 (Suppl II): 306
14. Rasmussen HB, Christensen SB, Kvist LP, Karazmi A. A simple and efficient separation of the curcumins, the antiprotozol constituents of *Curcuma longa*. Planta Med 2000; 66: 396-8.
15. Bhavani Sankar TN, Murthy S. Effect of turmeric (*Curcuma longa*) fractions on the growth of some intestinal and pathogenic bacteria *in vitro*. Indian J Exp Biol 1979; 17: 1363-6.
16. Mazumber A, Raghavan K, Weinstein J, Kohn KW, Pommer Y. Inhibition of human immunodeficiency virus type-1 integrase by curcumin. Biochem Pharmacol 1995; 49: 1165-70.
17. Prucksunand C, Indrasukhsri B, Leethochawalit M, Hungspreugs K. Phase II clinical trial on effect of the long turmeric (*Curcuma longa* Linn.) on healing of peptic ulcer. Southeast Asian J Trop Med Public Health 2001; 32: 208-15.
18. Kositchaiwat J. *Curcuma longa* Linn in the treatment of gastric ulcer comparison to liquid antacid : A control clinical trial. J Med Assoc Thai 1993; 76: 601-5.
19. Perry WLM. Pharmacological experiments on isolated preparations. In : Porry WLM. Eds. London: E&S Livingstone; 1970: 92-5.
20. Pasricha PJ. Prokinetic agent, antiemetics, and agents used in Irritable Bowel Syndrome. In Hardman JG, Limbird LE, Gilman AG. eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York : McGraw-Hill Companies; 2001: 1021-36.
21. Martin HB, McCallum M, Stofer WD, Eichinger MR. Kavain attenuates vascular contractility through inhibition of calcium channels. Planta Med 2002; 68: 784-9.

22. Shmigol A, Eisner DA, Wray S. Properties of voltage-activated [Ca^{2+}] transients in single smooth muscle cell isolated pregnant rat uterus. J Physiol 1998; 511: 803-11.
23. Sanborn BM, Dodge K, Monga M, Qian A, Wang W, Yue C. Molecular mechanisms regulating the effects of oxytocin on myometrial intracellular calcium. Edv Exp Med Biol 1998; 449: 277-86.
24. Wong IYF, Huang Y, He ZD, Lau CW, Chen ZY. Relaxing effects of Ligstrum purpurascens extract and purified acetoside in rat aortic rings. Planta Med 2001; 67: 317-21.
25. Mironneau J. Uterine smooth muscle electrophysiology and pharmacology. In Szekeres L, Papp JG. eds. Pharmacology of smooth muscle. Berlin: Springer-Verlag; 1994: 445-63.

ฤทธิ์คลายการหดตัวของสารเคอร์คิวมินอยด์ต่อกล้ามเนื้อเรียบลำไส้เล็กหนูตะเภาและกล้ามเนื้อเรียบมดลูกหนูขาว

จันทนี อิทธิพานิชพงศ์, วทม, นิจศิริ เรืองรังษี, ปรด**, วันดี เข็มศรี, วทบ*, อนุกูล สวัสดิพาณิชย์, วทม**

การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาฤทธิ์คลายการหดตัวของสาร curcuminoids ที่แยกได้จากเหง้าขมิ้นชัน ผลการศึกษาพบว่าสาร curcuminoids 12 μg/ml สามารถยับยั้งการหดตัวของกล้ามเนื้อเรียบลำไส้เล็กหนูตะเภาส่วน ileum ที่เกิดจากการกระตุ้นด้วย acetylcholine 5 x 10^{-7} M และ histamine 5 x 10^{-7} M ได้อย่างมีนัยสำคัญทางสถิติ (แรงหดตัวเป็น 62.84 ± 4.66% และ 75.60 ± 4.66% ตามลำดับ) และฤทธิ์ยับยั้งการหดตัวนี้จะเพิ่มมากขึ้น (แรงหดตัวเป็น 44.93 ± 4.33% และ 42.79 ± 1.98% ตามลำดับ) เมื่อใช้สาร curcuminoids 36 μg/ml สาร curcuminoids 4และ 20 μg/ml สามารถทำให้การหดตัวของกล้ามเนื้อเรียบลำไส้เล็กหนูตะเภาส่วน ileum ลดลงเป็น 63.31 ± 1.80% และ 36.87 ± 3.25% เมื่อได้รับสารกระตุ้นการหดตัว CaCl2 1.8 mM ในน้ำยา potassium depolarizing Tyrode solution ส่วนผลต่อกล้ามเนื้อเรียบมดลูกหนูขาว พบว่า curcuminoids 8 และ 16 μg/ml สามารถลดแรงหดตัวและความถี่ของการหดตัวที่เกิดขึ้นจากการกระตุ้นด้วย oxytocin 1 x 10^{-2} IU/ml อย่างมีนัยสำคัญทางสถิติ โดย curcuminoids 8 μg/ml ทำให้แรงหดตัวเป็น 54.68 ± 3.34% และความถี่ของการหดตัวเป็น 79.09 ± 2.29% และ curcuminoids 16 μg/ml ทำให้แรงหดตัวลดลงมากขึ้นเป็น 42.34 ± 3.16% และความถี่การหดตัวเป็น 71.18 ± 1.89% ($p < 0.05$) และเมื่อใช้สารกระตุ้นเป็น acetylcholine 2 μg/ml พบว่า curcuminoids 8 μg/ml ทำให้แรงหดตัวและความถี่ของการหดตัวลดลงเป็น 73.01 ± 4.10% และ 76.33 ± 3.94% และถ้าใช้ curcuminoids 16 μg/ml แรงหดตัวและความถี่จะลดลงมากขึ้นอีกเป็น 43.38 ± 3.56% และ 49.96 ± 5.20% เมื่อใช้สารกระตุ้นการหดตัวเป็น potassium chloride 50 mM แรงหดตัวลดลงตามขนาดของ curcuminoids ที่ใช้คือขนาด 8 μg/ml แรงหดตัวลดลงเป็น 57.10 ± 4.92% และขนาด 16 μg/ml เป็น 36.60 ± 2.99% ซึ่งผลจากการศึกษาอาจสรุปได้ว่าสาร curcuminoids มีฤทธิ์ยับยั้งการหดตัวกล้ามเนื้อเรียบลำไส้เล็กส่วน ileum ของหนูตะเภา และกล้ามเนื้อเรียบมดลูกหนูขาว โดยกลไกที่ผ่านการทำงานของรีเซฟเตอร์และไม่ผ่านการทำงานของรีเซฟเตอร์

คำสำคัญ : เคอร์คิวมินอยด์, ฤทธิ์คลายการหดตัว, ขมิ้นชัน

จันทนี อิทธิพานิชพงศ์, นิจศิริ เรืองรังษี,
วันดี เข็มศรี, อนุกูล สวัสดิพาณิชย์
จดหมายเหตุทางแพทย์ ฯ 2546; 86 (ฉบับพิเศษ 2): S299–S309

* ภาคเภสัชวิทยา, คณะแพทยศาสตร์,
** ภาคเภสัชเวท, คณะเภสัชศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330