

SMOOTH MUSCLE ACTIONS OF SOME THAI HERBAL CARMINATIVES

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SUMMARY

Crude extracts from five Thai medicinal plants traditionally employed as carminatives, viz :- *Zingiber officinale*, *Zingiber cassumunar*, *Murraya paniculata*, *Ocimum sanctum* and *Allium ascalonicum* were studied on guinea pig ileum and rat uterus. Tonicity of guinea pig ileum was lowered by *Z. officinale*, *Z. cassumunar* and *A. ascalonicum*, unaffected by *O. sanctum*; and conversely, contraction was induced by *M. paniculata*. *Z. cassumunar* exhibited the most potent tonicity-reducing action. Effects of acetylcholine and histamine were depressed by all extracts, whose effects were reversible upon washing. *Z. officinale* exhibited the most powerful blocking effect. Rat uterus was not affected by *Z. officinale*, *Z. cassumunar* and *M. paniculata* alone; but contraction was produced by *O. sanctum* and *A. ascalonicum*. All extracts inhibited the contraction response to acetylcholine. The inhibiting effects were reversible with all extracts except *Z. cassumunar*. There may be multiple mechanisms associated to the carminative and emmenagogue actions of the plants studied. Spasmolytic property may be only a part of the actions.

Use of medicinal plants are being encouraged in developing countries as remedies for various diseases. The encouragement is concerned with the need for low cost treatment in conformity with the World Health Organization Primary Health Care Programme. The present study was conducted to determine whether five commonly used Thai medicinal plants, viz:- *Zingiber officinale*, *Zingiber cassumunar*, *Murraya paniculata*, *Ocimum sanctum* and *Allium ascalonicum* had any action on smooth muscle of the gastrointestinal tract and the uterus, which would warrant their use as carminatives and emmenagogues respectively.

Z. officinal Rosc. is generally known as ginger . Its rhizome is hot and diaphoretic and is used as a remedy for fever and diarrhea, as emmenagogue, and more commonly as carminative. Reported

constituents are zingiberol, zingiberene, gingerol and zingerone. The volatile oil consists mostly of terpenes, phellandrene, dextrocamphene, the sesquiterpene zingiberene, zingerone, resins and starch(1).

Z. cassumunar Roxb. is similar to *Z. officinale* in its texture. The rhizome is also used as antipyretic, antidiarrheal, laxative, emmenagogue and carminative.

Murraya paniculata L. leaves are used for tapeworm infestation, dysentery, diarrhea, flatulency, and to stimulate menstrual discharge. Reported constituents are a glycoside murrayin and an essential oil, the chief component of which is cadinene.

Ocimum sanctum L. is generally known as sacred basil. The leaves are used as expectorant in bronchitis, as carminative, for the treatment of peptic ulcer and sometimes for irregular menstruation. Reported constituents of the volatile oil are methyl chavicol, cineole; linalol, methyl homoanistic acid, caryophyllene, eugenol, eugenol methyl ether and carvaerol. The mucilage contains hexuronic acid, pentoses, and ash; on hydrolysis it was found to contain xylose(1).

Allium ascalonicum L. exists in the form of tubers of which the texture is similar to onion, but the size is smaller. The bulb is reported to be useful for colds, as diuretic, purgative, and also carminative.

MATERIALS AND METHODS

Guinea pigs were fasted overnight and the terminal ileum was dissected in length of 1.5-2 cm. Young female rats in the estrous phase, identified by the vaginal smear, were sacrificed, and uterus was taken for the experiment.

Physiological salt solutions to be used were:

Tyrode's solution for guinea pig ileum and Munsik's solution for rat uterus.

The organ bath was adjusted to a constant temperature of 37°C. Other equipments that were used included a mechano-electrical transducer, biogastab V, an amplifier for the transducer, and a multipen recorder.

Preparation of Extracts

Crude extracts of the plants were prepared as follows :-

1. *Z. officinale*. Five hundred grams of chopped rhizome were macerated in sufficient 95% ethyl alcohol for 24 hours. The filtered extract was evaporated to a syrupy consistency. Five hundred milligrams of the extract were dissolved in 10 ml. of distilled water for the experiment.

2. *Z. cassumunar*. The extract was prepared as in 4.1 . Concentration of 20 mg. per ml. was used.

3. *M. paniculata*. Ten grams of the leaves were chopped up, mixed with some water, ground and strained. The volume was made up to 40 ml. with water.

4. *O. sanctum*. Aqueous extract of the leaves was prepared as in 4.3; it was made up to a concentration of 10 g. in 40 ml.

5. *A. ascalonicum*. Extract of the tuber was prepared similarly to 4.3 . The concentration used was 750 mg. per ml.

Control agents

5.1 Acetylcholine in concentrations ranging from 1 : 2,000 to 1 : 400,000 was used selectively according to the response of the smooth muscles to 0.2 ml. of the agent solution, i.e., the concentration which was sufficient to exhibit control submaximal contraction.

5.2 Histamine in the concentrations of 1 : 2,000 to 10,000. was used.

Procedure

The general scheme of study was prepared as describe elsewhere(2). In short, control submaximal contractions of the smooth muscle were first elicited by using 0.2 ml. of appropriate concentration of acetylcho-

line and /or histamine solution. An extract was administered into the tissue bath in serial volumes. One minute later, 0.2 ml. of acetylcholine or histamine was applied, and any change in response was observed. The tissue was then washed with physiological salt solution. Equal intervals of three minute were allowed after each set administration of control drug and/or extract.

RESULTS

Effects on Guinea Pig Ileum

Z. officinale

Tonicity of the ileum was slightly lowered by the extract of *Z. officinale*. The responses were dose-related. When the extract was administered one minute prior to acetylcholine or histamine, the contraction responses of the ileum to these latter agents were lessened. After pretreatment with 0.2 ml. of the extract, the average amplitudes of contraction exhibited by acetylcholine and histamine were approximately 38% and 36% of the control respectively. The depressing effect was reversible upon washing but not completely.

Z. cassumunar

Tonicity of the ileum was apparently diminished by the extract of *Z. cassumunar* (figure 1). Compared to the effect of *Z. officinale*, *Z. cassumunar*, in spite of the lower concentration, exhibited more potent tonicity-lowering effect. Effects of acetylcholine and histamine were also diminished by the extract. After pretreatment with 0.2 ml. of the extract, the average amplitudes of contraction were 75% for acetylcholine and 89% for histamine as compared to control contractions. The blocking effects were completely reversible upon washing.

M. paniculata

The extract of *M. paniculata*, in contrast to others, stimulated contraction of the intestine in a dose-related manner (figure 2). Nevertheless, the contraction responses to acetylcholine and histamine were

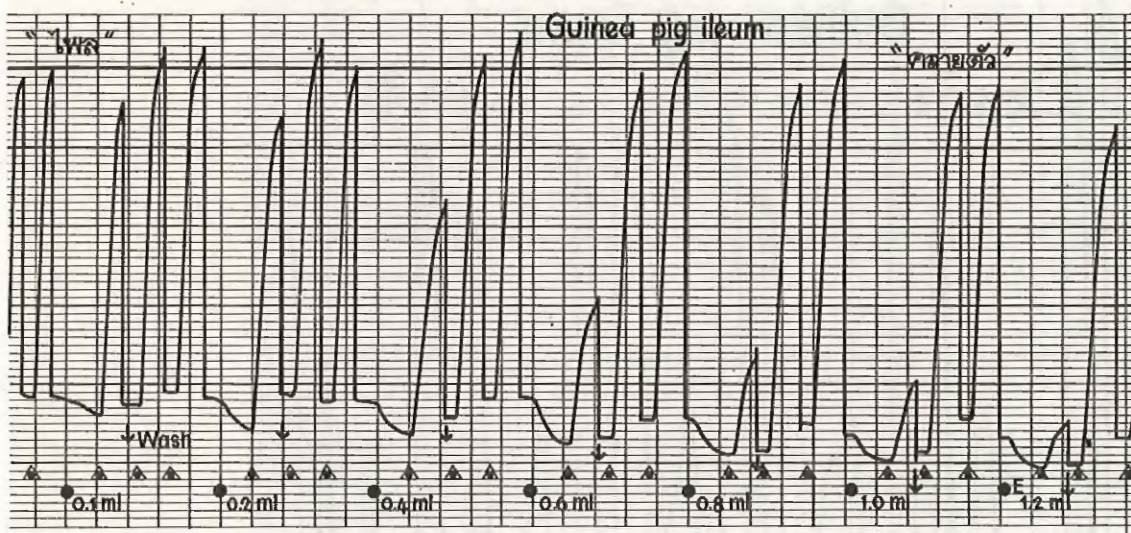


Fig. 1 The effect of Zingiber cassumunar on guinea pig ileum
 ▲ = Histamine; ● = Extract of Z. cassumunar

lowered by the extract. The contractions were lessened to about 36% and 84% of the control respectively; the inhibiting actions were reversible.

O, sanctum

The extract possessed no activity on the ileum, but blocked the spasmogenic action of acetylcholine and histamine which were given afterwards. The average amplitudes of contraction elicited by acetylcholine and histamine after pretreatment with O, sanctum extract were 81% and 30% of the control respectively. The blocking actions of the extract were completely reversible.

A, ascalonicum

Usually the crude extract of A, ascalonicum relaxed the guinea pig ileum. Occasionally, high doses of the extract stimulated the tissue. The responses were dose-related. Acetylcholine and histamine activities were inhibited by preceding administration of the extract which reduced the responses to the two agents to approximately 68% and 80% of the control respectively. These actions were reversible.

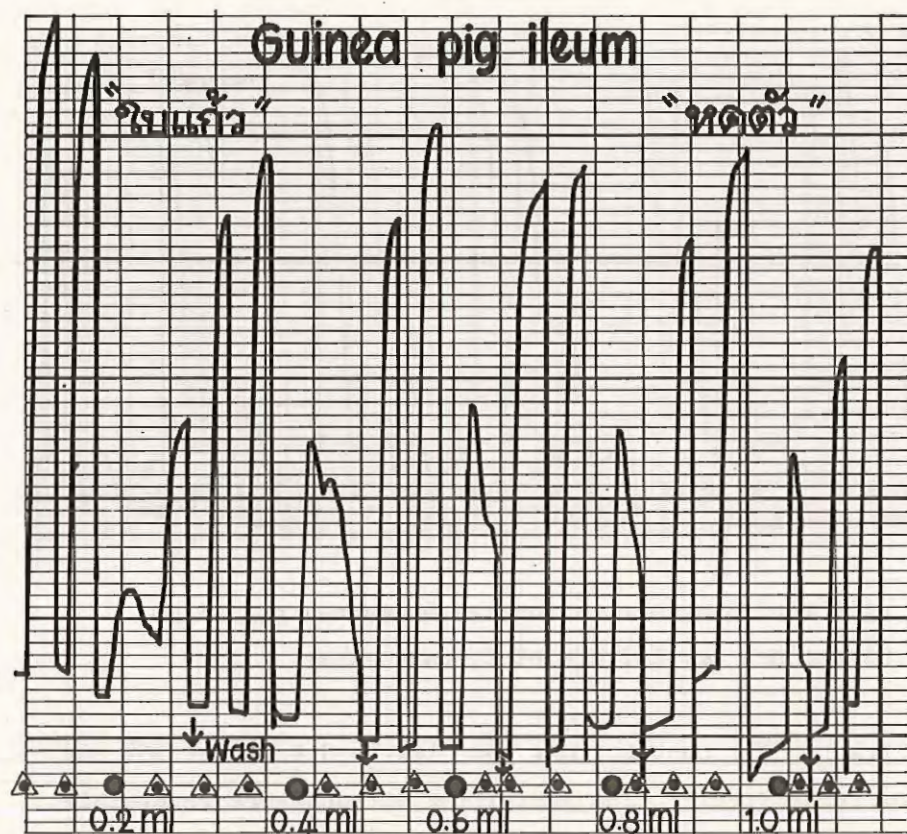


Fig. 2 The effect of *Murraya paniculata* on guinea pig ileum
 ▲ = Histamine; ● = Extract of *M. paniculata*

Effects on Rat Uterus

Extracts of *Z. officinale*, *Z. cassumunar* and *M. paniculata* when given alone exhibited no effect on rat uterus (figure 3). When 0.2 ml. of acetylcholine was dropped into the tissue bath one minute after dosing of either extract, contractions were induced but with reduced amplitudes as compared to acetylcholine alone. The depressing effects of *Z. officinale* and *Z. cassumunar* were irregularly related to dose. The average amplitudes of contraction produced by 0.2 ml. of the extracts of *Z. officinale*, *Z. cassumunar* and *M. paniculata* were 65%, 76% and 50% of the control respectively. The actions were partially reversible in the case of *Z. officinale* and *M. paniculata*, but irreversible in *Z. cassumunar*.

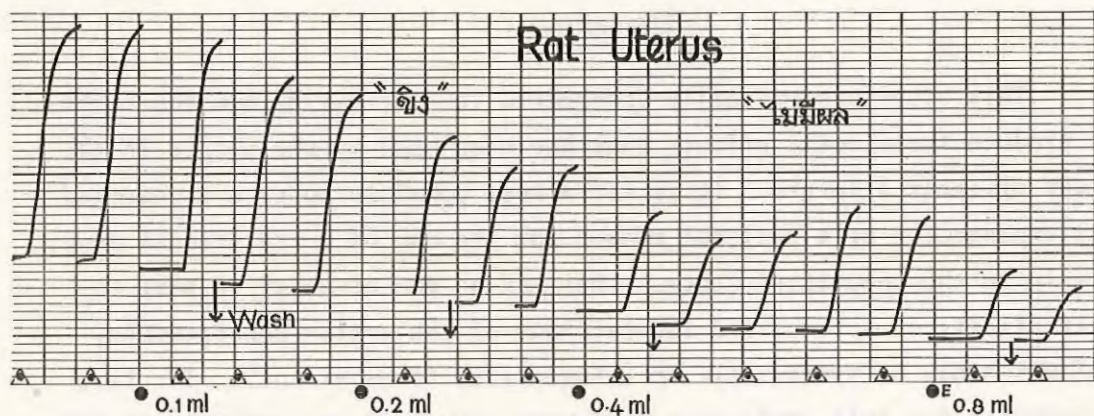


Fig. 3 The effect of *Zingiber officinale* on rat uterus

▲ = Acetylcholine; ● = Extract of *Z. officinale*

Conversely, extracts of *O. sanctum* and *A. ascalonicum* stimulated contractions of rat uterus (figure 4). The effects were regularly related to dose. Moreover, the effects of acetylcholine on the uterus were also blocked by both extracts given previously.

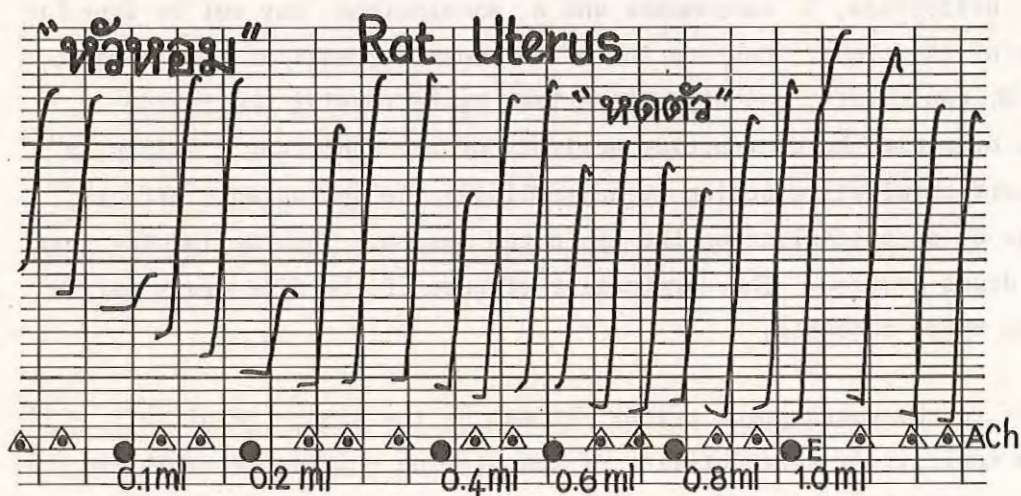


Fig. 4 The effect of *Allium cepa* on rat uterus

▲ = Acetylcholine; ● = Extract of *A. cepa*

DISCUSSION

This study was primarily interested in elucidating how the herbs act to produce therapeutic effects that has been used by the people in the treatment of their ailments. It is not always possible to give a pharmacological explanation or a rational reason for the use of a traditional drug, especially in the unpurified state. This may be due at least in part to the multiplicity of actions and interactions of the active constituents, some of which may be synergistic or antagonistic to each other. The five drugs selected for this study have been popularly used as carminatives and emmenagogues for hundreds of years, and all still enjoy a very good reputation.

This study showed that *Z. officinale*, *Z. cassumunar* and *A. ascalonicum* relaxed the guinea pig ileum, while *M. paniculata* contracted. *O. sanctum* was inactive. There were discrepancies in these effects, and yet all are efficacious carminatives. This finding indicated a multiplicity of the mechanisms of action of carminative drugs. The textbook explanation that relief of tympanites results from the carminative relaxing the cardiac sphincter, and so allowing the accumulated gases to escape, as seen in the cases of *Z. officinale*, *Z. cassumunar* and *A. ascalonicum*, may not be true for all members of the class. Contraction of the muscular wall of the stomach, such as by *M. paniculata*, may also be effective, by increasing the inside pressure to overcome the obstructing activity of the sphincter. Lastly, a drug may exert carminative action by neutralising the spasmogenic effects of histamine or acetylcholine on the sphincter muscle. This action was seen in all the drugs studied. The carminative effects of the five drugs may be explained on these concepts.

As to the emmenagogue effect, it may be the simple result of increase in tonicity or contractility of the uterine muscle, as exhibited by *O. sanctum* and *A. ascalonicum*. Antihistamine and anti-acetylcholine actions may be helpful in spasmodic dysmenorrhea. This line of activity has been found in all five drugs.

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