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STUDY OF THE ACUTE TOXICITY AND CARDIOVASCULAR EFFECTS OF GINGER (ZINGIBER OFFICINALE ROSCOE)(การศึกษาพิษอย่างเฉียบพลันและผลต่อระบบหัวใจและหลอดเลือด...

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Original article

STUDY OF THE ACUTE TOXICITY AND CARDIOVASCULAR EFFECTS OF GINGER (ZINGIBER OFFICINALE ROSCOE)*

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ABSTRACT Hantrakul, M. and Tejasen, P, Study of the acute toxicity and cardiovascular effects of Ginger (Zingiber Officinale Roscoe).

Ginger extract causes both stimulant and depressant effects with additional changes in the autonomic profile after an intravenous injection into mice. Death results from severe convulsions. The LD 50 is found to be 1,500.00 (1,327.43–1,695.00) mg/Kg body weight.

The intravenous administration of Ginger extract into pentobarbital anesthetized dogs produces two phases of hypotension. The first phase is prompt and pronounced whereas the second one is minimal and may persist much longer. Bradycardia and variable changes in the electrocardiographic records are also noted. Studies in the isolated turtle's heart preparations and the nerve free isolated human arteries reveal a negative chronotropic and a negative inotropic effect on the heart as well as a depressor effect on vascular smooth muscle.

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The results of the comparative studies of the cardiovascular effects of K^+ equivalent to the K^+ content of Ginger extract in similar series of experiments indicate the K^+ is the active principle responsible for the cardiodepressant effect of Ginger extract. Another unidentified pharmocologically active compound possessing a prominent vasodilating effect is responsible for the hypotension.

INTRODUCTION

The pharmacological effect, confined to the cardiovascular system, of zingiberaceae plants has been studied by few investigators. In 1971, Veerasan (1) observed certain actions of Zingiber cassumunar (Plai) on turtle's atria and rat's ventricular stips. Later, Chantaratham and Tejasen (2) reported that an aqueous extract of Wan Ngu (Curcuma sp.) caused definite hypotension and bradycardia in pentobarbital anesthetized dogs. Therefore, pharmacological studies of ginger (Zingiber offcinale Roscoe), another member of the zingiberaceae family, become a subject of interest for further study.

Ginger is a perenial herb with digitately branched rhizomes containing 56 per cent of starch, 5–8 per cent of oleoresin and approximately 1–2 per cent of volatile oil (3, 4) It is widely used in many countries for both culinary and medical purposes (3, 5). As mentioned in the Thai Materia Medica, ginger has been used as an antiemetic, an anticolic, a carminative, and as cardiac and hypnotic–drugs (6, 7)

In 1920, gastrointestinal and other effects of Zingerone, the volatile substance isolated from the rhizome of ginger, was reported by Doi (8). Panthong (9) demonstrated that aqueous Ginger extract exerted a substantial effect on rat's gastrointestinal tract and as evidenced from further studied in dogs, she proposed that Ginger extract exhibited a direct effect on the smooth muscle of the gastrointestinal system.

These suggestive evidences led to the continuation of pharmacological studies of Ginger extract on other organ systems with particular interest in the cardiovascular effects. So the determination of acute toxicity and cardiovascular effects of Ginger extract are included in this investigation.

MATERIALS AND METHODS

Preparation of Ginger extract: Twenty and fifty per cent (W/V) aqueous extract of Ginger were used in this investigation. They were prepared by triturating for ten minutes Ginger powder with distilled water which was then filtered through gauze. The filtrate was centrifuged for one hour and the supernatant was decanted and kept as a stock solution (9).

Determination of K+ concentration in Ginger extract: The K^+ concentration in the 20 and 50 per cent (W/V) solutions of Ginger extract was determined by a Coleman Model 21 Flame Photometer and a Coleman Model 22 Gal-O-Meter following the method of Kanjanapothi and Tejasen (10).

Study of the acute toxicity of Ginger extract in mice: The acute toxicity of Ginger extract was studied (11) using the method described by Litchfield and Wilcoxon (12) and Tejasen et al (13). Twenty per cent Ginger extract in doses of 750, 1,000, 1,250, 1,500, 1,750 and 2,000 mg/Kg body weight were injected into the lateral tail vein of all mice. Changes in gross behavior were observed and all mice were kept for observtion for a period of 72 hours.

Preparation of isolated perfused turtle's heart: The heart of a field turtle was excised and prepared for perfusion with tyrode's solution and drugs by the method of Veerasarn (1) The aorta was cannulated with Syme's cannula; the ventricular apex and the left atrium were separtely connected to two Force-displacement transducer FT 03 by means of pulleys and their isotonic contractions were recorded on a Grass P-7 Polygraph.

Preparation of isolated turtle's heart strips: Atrial and ventricular strips of the field turtle were prepared for recording of contractions following the method of Veerasarn (1). One end of the strips was hooked to the active lead electrode which was attached to the stereotaxic instrument and another end was tied to the Force-displacement transducer FT 03. Their contractions were triggered by stimuli (rectangular pulses with an intensily of supramaximal voltage, a duration of 6 msec. with a frequency higher than the spontaneous rhythmicity of the atria) from S-5 Stimulator and were recorded on the Grass P-7 Polygraph.

Preparation of isoloted human umbilical arterial strips: Strips of umbilical arteries were prepared by a method described by Harnirattisai and Tejasen (15). A strip was placed in oxygenated modified Kreb-Henseleit solution; one end was attached to a hook fixed at the bottom of the smooth muscle chamber and the other end to a Force-displacement transducer FT 03. The isometric contraction was recorded on a Grass P-7 Polygraph.

RESULTS

SECTION 1. Study of the acute toxicity of Ginger extract in mice.

Twenty per cent of Ginger extract in doses of 750, 1,000, 1,250, 1,500, 1,750 and 2,000 mg/Kg body weight were injected intravenously. Most of the animals developed clonic convulsious and respiratory arrest resulting in death preceded by symptoms of asphyxia, urination, salivation, and exophtalmos. In survived mice, initial stimulation followed by depression were observed with additional symptoms of piloerection, increased respiratory rate, salivation, and urination. The LD 50 obtained by the method of Litchfield and Wilcoxon (12) was found to be 1,500.00 (1,327.43-1,695.00) mg/Kg body weight, as shown in Fig. 1.

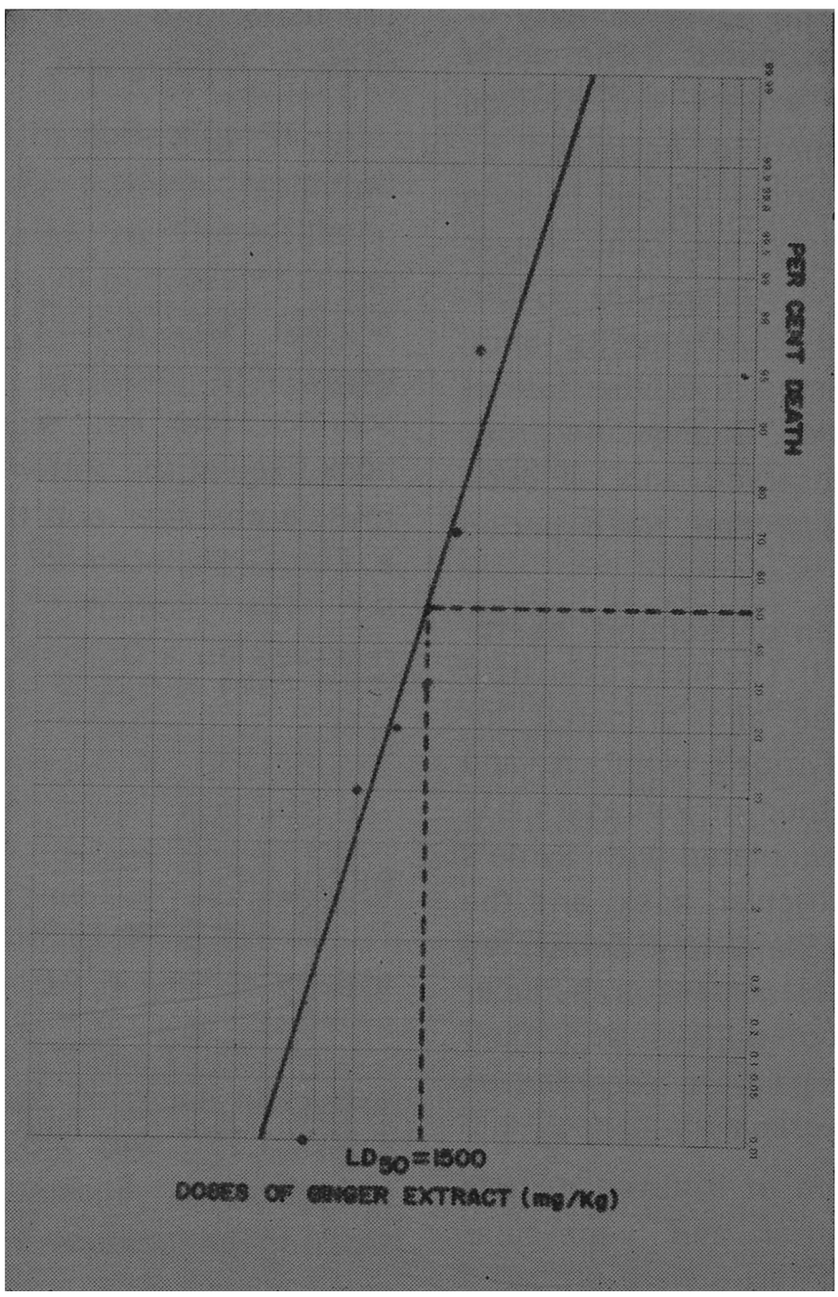

Fig. 1 The results of intravenous administration in mice of various doses (750, 1,000, 1,250, 1,500, 1,750 and 2,000 2,000 mg/Kg body weight) of Ginger extract.

SECTION 2. Study of the effects of Ginger extract on the cardiovascular system in dogs.

Intravenous administration of Ginger in doses of 5.0, 6.5, 7.5, 8.5, 10.0, 25.0, 50.0, 100.0 and 200.0 mg/Kg body weight were performed in pentobarbital anesthetized dogs. Hypotension, decrease in pulse pressure and a transient bradycardia in all experimental dogs were observed as summarized in Table 1. When the dose of Ginger extract was higher than 10 mg/Kg body weight, the

Doses mg/Kg	No.of dogs	% decrease in mean arterial B.P.		% decrease in pulse pressure		maximum change in heart rate	
		E_1	E_2	E_1	E_2	E_1(% increase)	% decrease
5.0	7	18.29 ± 11.90	3.32 ± 3.08	17.26 ± 11.15	6.55 ± 5.29	7.53 ± 3.63	13.04 ± 1.26
6.5	5	9.01 ± 2.55	37.51 ± 9.47	53.00 ± 8.14	27.68 ± 14.39	5.11 ± 2.27	11.82 ± 5.97
7.5	15	31.91 ± 7.76*	17.81 ± 5.44	23.28 ± 5.08*	19.80 ± 7.04*	5.47 ± 7.04*	9.48 ± 5.18
8.5	5	5.48 ± 2.79	11.86 ± 3.81	4.54 ± 8.04	15.32 ± 6.05	7.71 ± 1.93	12.78 ± 3.29
10.0	8	62.67 ± 3.35*	43.12 ± 3.27*	42.88 ± 6.88*	45.83 ± 6.79*	9.97 ± 3.39	16.20 ± 9.79
25.0	6	72.90 ± 4.58*	22.45 ± 4.99*	49.74 ± 3.81*	29.65 ± 8.50*	9.76 ± 3.79	19.71 ± 5.18
50.0	7	76.85 ± 6.39*	41.91 ± 11.59*	60.13 ± 6.99*	21.18 ± 6.74*	5.35 ± 7.91	22.73 ± 5.87
100.0	6	84.35 ± 7.96*	42.26 ± 5.83*	53.36 ± 6.49*	18.51 ± 9.33	7.75 ± 3.43	22.97 ± 3.27
200.0	8	83.34 ± 5.44*	45.25 ± 5.75*	34.92 ± 1.59*	17.79 ± 6.74	9.57 ± 3.02	18.11 ± 6.23

Table 1 Summary of the effects of various doses of Ginger Extract on the cardiovascular system in dogs.***

*** the results are expressed as Mean ± S.E.

E_1 represents the responses during the period of maximum hypotensive response caused by the administration of Ginger Extract.

E_2 represents the responses at the end of the experiment (3 hours after the administration of Ginger Extract).

** represents the maximum decrease in heart rate after the maximum hypotensive response.

* represents the significant change, $P < 0.05$

degree of hypotension appeared to be dose dependent. The maximum effective dose for the hypotensive response was found to be 100.0 mg/Kg body weight (Fig. 2.). The alteration in electrocardiographic record including changes of PR and QT intervals, P waves, the QRS complex and T waves were also evident but were variable and did not correlate with the dose of Ginger extract given.

Potassium ion (120±2.84 mFq/L) in an amount equivalent to the potassium content of Ginger extract (100 mg/Kg body weight) produced no significant change in the arterial blood pressure, pulse pressure, heart rate, and electrocardiogram in dogs.

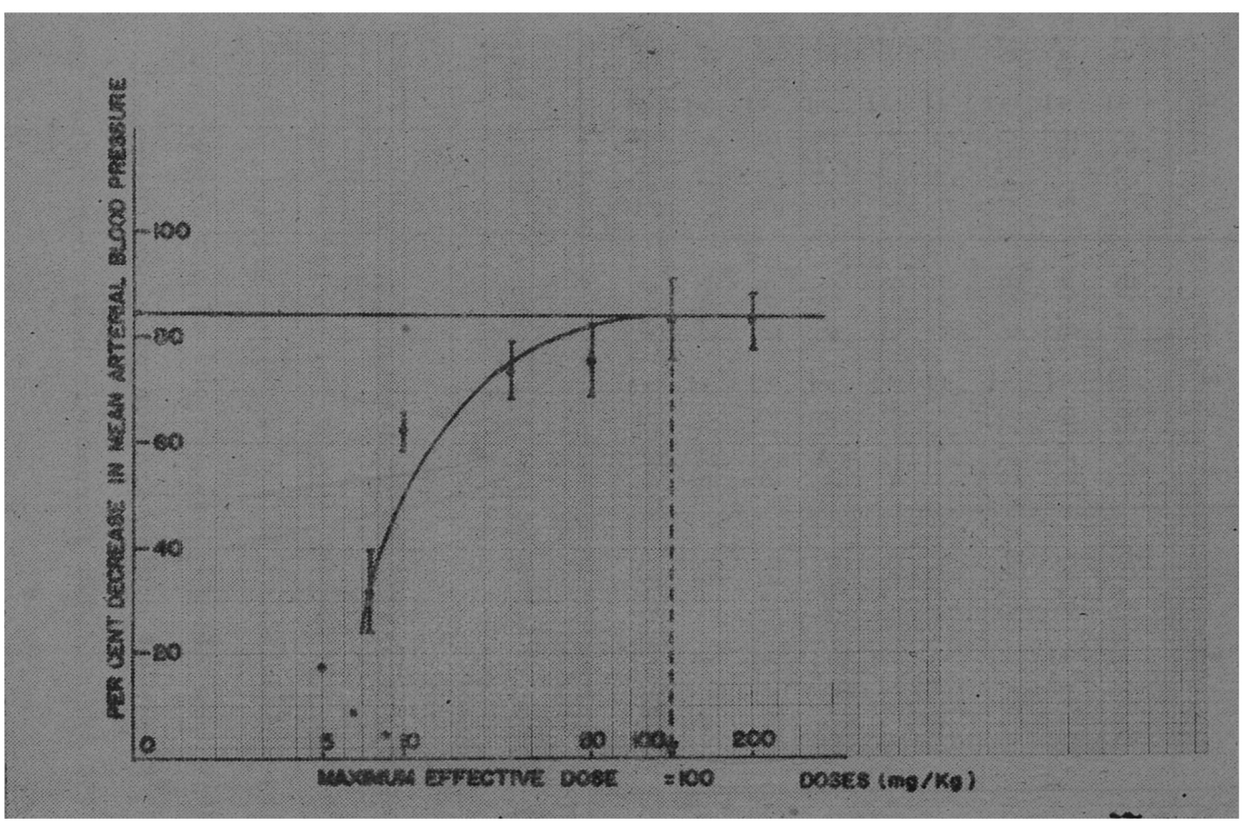

Fig. 2 Effects of intravenous administration of various doses (5.0, 6.5, 7.5, 8.5, 10.0, 25.0, 50.0, 100.0, and 200.0 mg/Kg body weight) of Ginger extract on mean arterial blood pressure in dogs.

I represents the standard error where significant change occurs.

SECTION 3. Determination of the sites of action of Ginger extract on the cardiovascular system.

Part A. Study of the effect of Ginger extract on isolated perfused turtle's heart.

A fifty per cent Ginger extract in graded doses of 5, 10, 20, 30 and 40 mg/ml decreased the amplitude of contraction and heart rate of the isolated perfused turtle's heart in an orderly fasion. Most of the negative

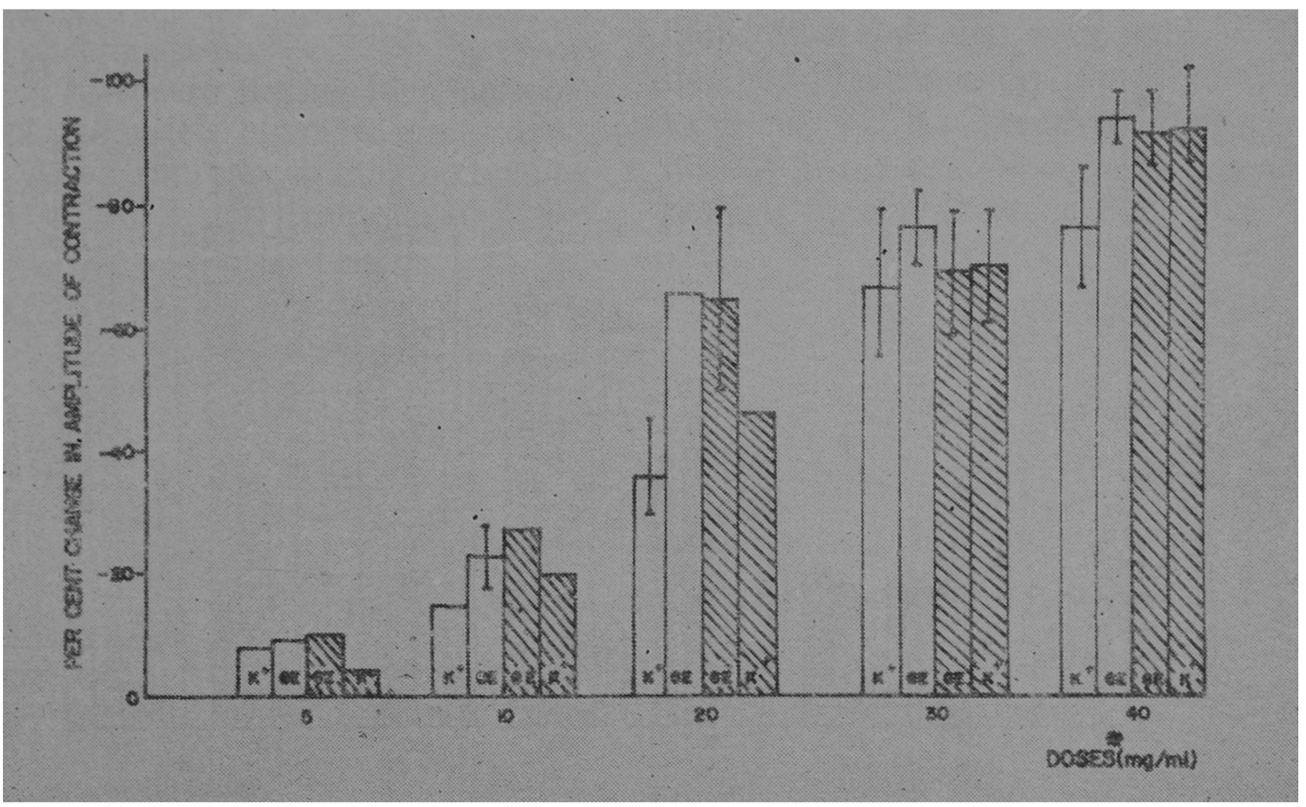

Fig. 3. Histogram comparing the results of various doses (5, 10, 20, 30 and 40 mg/ml) of 50 per cent Ginger extract and the equivalent potassium ion of these on isolated perfused turtle's heart.

K^+ represents potassium ion

GE represents Ginger extract

* represents equivalent doses of 50 per cent Ginger extract.

□ represents the responses of atria

▨ represents the responses of ventricles

I represents the standard error where significant change occurs.

inotropic responses were statistically significant whereas the negative chronotropic responses were not. Both atrial and ventricular tissues were identically sensitive to the Ginger extract,

Furthermore, in similar experiments, instead of Ginger extract, graded concentrations of equivalent potassium ion were employed. As the doses of potassium chloride solution were increased the amplitude of contractien was

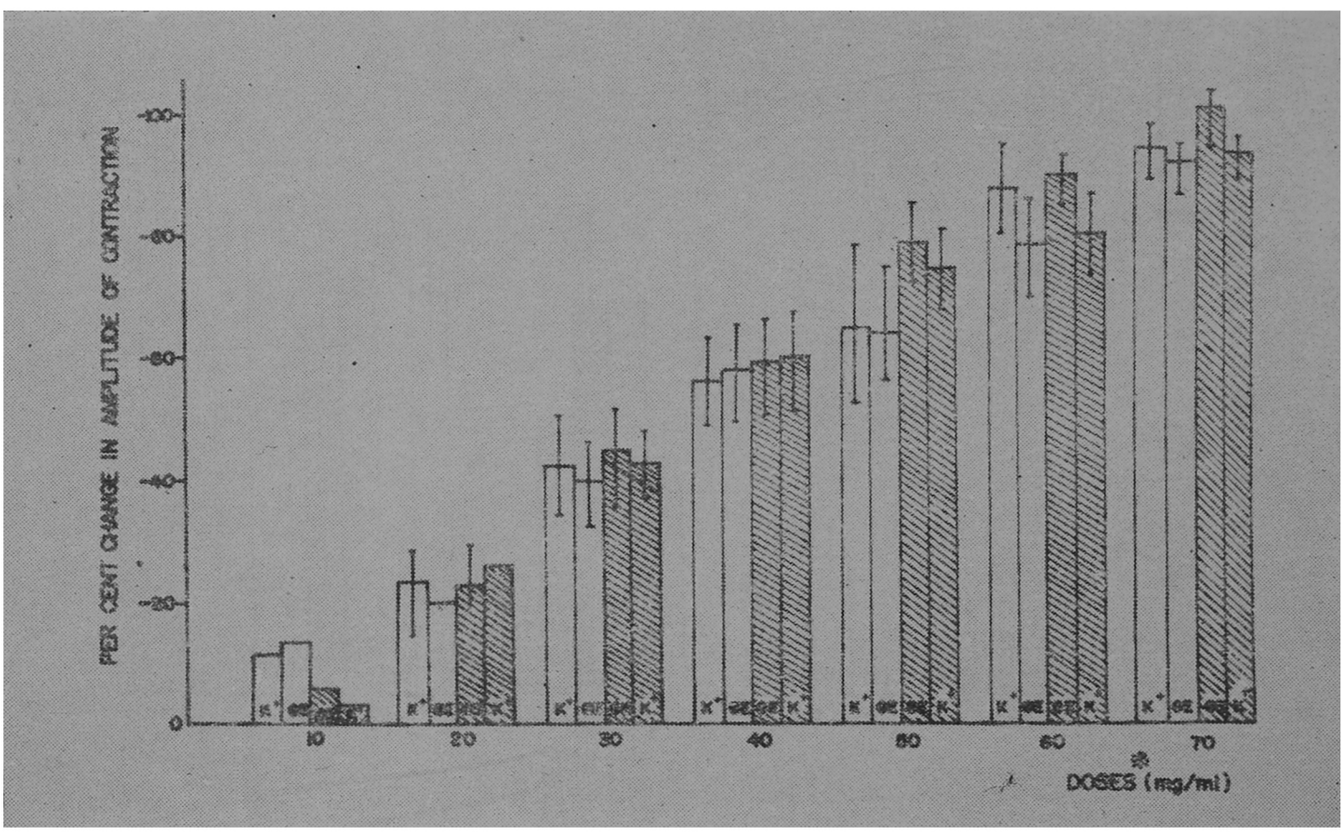

Fig. 4 Histogram comparing the results of various doses (10, 20, 30, 40, 50, 60 and 70 mg/ml) of 50 per cent Ginger extract with doses of an equivalent potassium ion concentration on turtle's atrial and ventricular strips.

K^+ represents potassium chloride

GE represents Ginger extract

* represents equivalent doses of 50 per cent Ginger extract

□ represents the responses of atrial strips

▨ represents the responses of vantricular strips

I represents the standard error where significant change occurs.

lowered progressively, The results of the negative inotropic effect of potassium chloride solution compared with those of Ginger extract are illustrated in Fig. 3.

Part B. Study of the effect of Ginger extract on turtle's atrial and ventricular tissues.

To ensure the negative inotropic effect on turtle's heart, Ginger extract was serially introduced into the bathing fluid of atrial and ventricular strips whose contractions were triggered regularly by stimuli supplied by an S-5 Stimulator. Cumulative doses of Ginger extract of 10, 20, 30, 40, 50, 60 and 70 mg/ml in the bathing fluid lowered progressively the amplitude of both atrial and ventricular strips. The degree of depression of atrial and ventricular strips produced by Ginger extract in the same concentration was not statistically different,

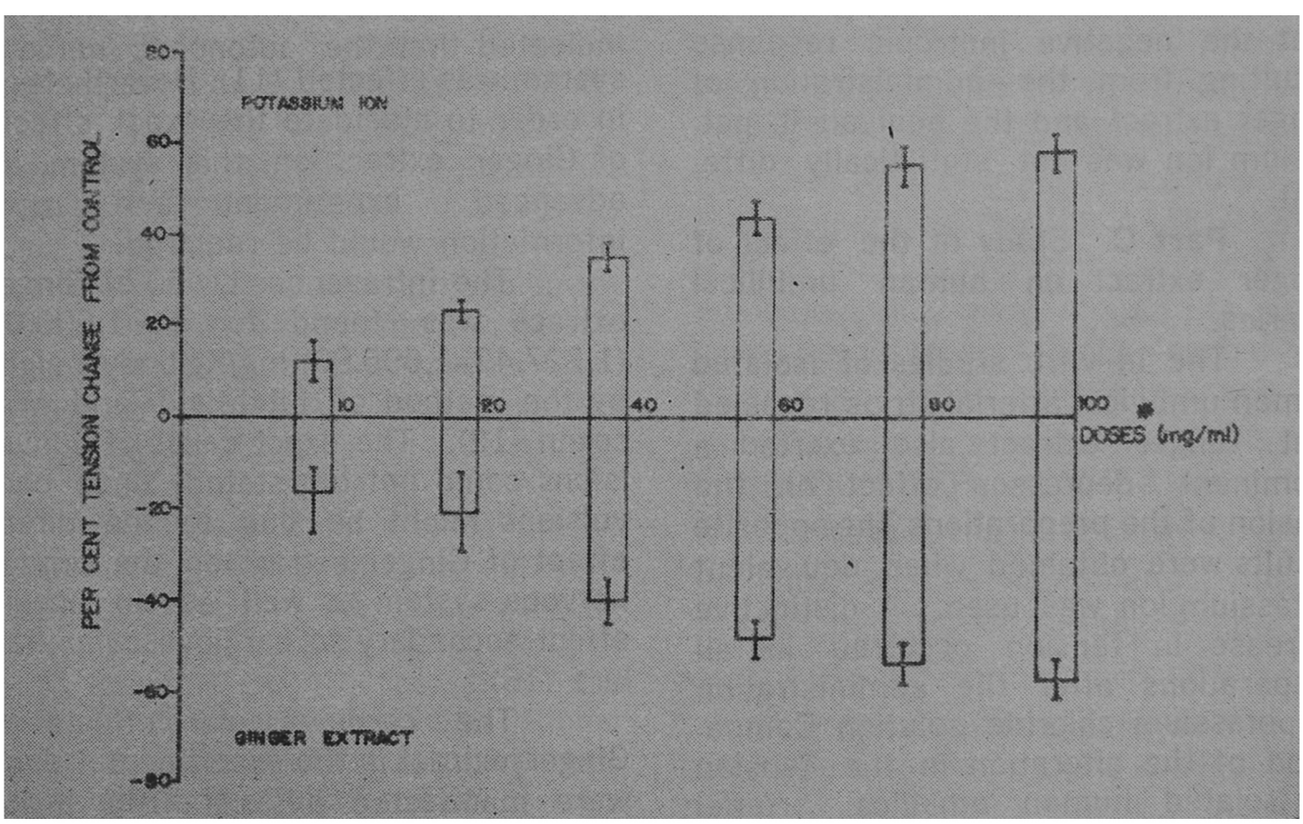

Fig. 5 Histogram comparing the results of various doses 10, 20, 40, 60, 80 and 100 mg/ml) of 50 per cent Ginger extract with doses of an equivalent potassium ion concentration on tension of isolated human umbilical arterial strips

* represents equivalent doses of 50 per cent Ginger extract.

I represents the standard error where significant change occurs.

Effects of the dilution of bathing fluid by distilled water and the effects of equivalent potassium ion were studied in the same manner. The results were: the dilution exhibited no detectable results whereas equivalent potassium ion created a marked decrease in amplitude of atrial and ventricular contractile force. Degree of atrial depression produced by various doses of Ginger extract resembled those of ventricular strips. The comparative results illustrated in Fig. 4 show that the negative inotropic response resulting from the administration of Ginger extract and the equivalent potassium ion was not statistically different.

Part C. Study of the effect of Ginger extract on human umbilical arteries.

The in vitro studies of isolated human umbilical arterial strips revealed that Ginger extract also exerted a prominent depressor effect on the tension of the preparations The opposite results were obtained when equivalent potassium ion was used. A distinctive increase in tension occurred in all preparations after the administration of potassium chloride solution Comparison of the alteration in the tension of isolated human umbilical arterial strips produced by Ginger extract and equivalent potassium ion is shown in Fig. 5.

DISCUSSION

The finding in this study suggests that Ginger extract has a serious effect on the cardiovascular system. The effects on the central and autonomic nervous system require further study.

Profound changes in the behavior of those groups of survived mice characterized by an initial stimulation followed by a depression suggested that Ginger extract possessed both central nervous system stimulant and depressant effects. Moreover, the evidence for central nervous system excitation was convincing by the incidence of severe convulsions which resulted in death in other groups of mice. in addition, autonomic effects of Ginger extract revealed by the presence of piloerction, salivation, urination, and exophthalmos in mice indicated that the autonomic nervous system was affected (11). Nevertheless, in order to elucidate the exact effects of Ginger extract on this system, an advanced experiment and more information would be required.

The intravenous LD 50 of Ginger extract was found to be 1,500.00 (1,327.43–1,695.00) mg/Kg body weight by the method of Litchfield and Wilcoxon (12). The exact cause of convulsions could not be stated since convulsions might be due to the direct effect of Ginger extract on the central nervous system as well as an anoxic effect secondary to cardiovascular failure (16).

The cardiovascular effects of Ginger extract in the experimental dogs were manifested by a fall in blood pressure, changes in heart rate, decrease in pulse pressure, and alterations in electrocardiographic records as previously mentioned in "Results".

Hypotension could be induced by various drugs that exerted their pharmacological effects upon the following potential sites of action: the central vasomotor center, the autonomic ganglia, the heart, and the vascular smooth muscle (17, 18). One or more pharmacologic sites could be responsible for the resultant hypotensive effect.

For example, the hypotensive effect of veratrum alkaloids was found to be the result of depression of the central vasomotor mechanism as well as due to the effects upon the carotid sinus baroreceptor, chemoreceptors and nodose ganglion (19, 20). Hexamethonium, a ganglionic blocking agent, was a prototype hypotensive drug which caused primary loss of vasoconstrictor tone together with a reduction in circulatory blood volume and cardiac output in the non-failing heart (21). Dipalma (21) also proposed that profound hypotension induced by the injection of quinidine was due mostly to peripheral vasodilatation but that a depression of cardiac contractility could not be ruled out. Papaverine was found to produce hypotension by relaxing the vascular smooth muscle particularly those of the coronary and pulmonary arteries. Additional moderate quinidine-like effect on the myocardium have been shown (22).

Because of this information, we studied the possible sites of action of Ginger extract on the cardiovascular system in SECTION 3, using isolated preparations. On the basis of the findings in this section that Ginger extract exhibited both a negative chronotropic effect without statistical significance and a prominent negative inotropic effect, it might be assumed that Ginger extact contains one or more cardiodepressive active principles.

Next, the direct effect of Ginger extract on vascular smooth muscle was studied in narve free human umbilical arteries as suggested by von Euler (23) and Somlyo et al (24). A significant reduction of tension of these preparations indicated that Ginger extract exerted a direct vasodilating effect on vascular smooth muscle which was at least in part responsible for the hypotension observed in the experimental dogs in SECTION 2.

As evidenced from the forgoing studies on the indigenous plants, K^+ was found to be one of their active principles (1, 25, 26), so the amount of K^+ content of 20 and 50 per cent Ginger extract was determined and the cardiovascular effects were studied. In SECTION 2, K^+ equivalent to the amount of K^+ in the maximum effective dose of Ginger extract caused no appreciable change in the experimental dogs except an occasional alteration of the electrocardiogram. According to the comparative results in SECTION 3 (Part A and B), various amounts of equivalent K^+ were found to exert cardiodepressant effects similar to those produced by Ginger extract. However, opposite results were obtained in SECTION 3 (Part C). The equivalent K^+ increased the tension of human umbilical arteries significantly, therefore it could be implied that K^+ possesses a vasoconstrictive property.

These results suggested that the K^+ component in Ginger extract was responsible for the cardiodepressant effect. Besides K^+, Ginger extract might contain other pharmacologically active principle which possess a strong and substantial enough vasodilating effect to overcome the vasoconstrictive property of K^+.

On the basis of the present results, it may be concluded that:

1. Cardiovascular effects of Ginger extract observed from this investigation are:

a) Ginger extract contains at least two pharmacologically active principles
   - K^+ component which appears to be responsible for the cardiodepressant effect
   - another unidentified component possessing a direct vasodilating effect seems to be responsible for the hypotensive effect.

b) In the experimental dogs, the tachycardia occurred concurrently with a fall in blood pressure as a reflex response and the transient bradycardia, decrease in pulse pressure, and some variable changes in electrocardiogram presumable are due to the high concentration of K^+ reaching to heart.

2. The direct effect of Ginger extract on the central nervous system and/or anoxia secondary to cardiovascular failure plays an important role in acute toxicity.

REFERENCES

1. Veerasarn, V. and Komalahiranya, A. : Observations of certain cardiac actions of an indigenous drug : Zingiber cassumunar roxb. Chiang Mai Med. Bull. 10 : 9 – 16, 1971.
2. Chantaratham, A. and Tejasen, P. : Studies of pharmacological action of Wan Ngu on the neuromuscular junction and the cardiovascular and respiratory systems. Chiang Mai Med. Bull. 11 : 103 – 109, 1972.
3. Youngken, H.W. : Textbook of Pharmacognosy, 6th ed. The Blakiston Company, Philadelphia, U.S.A. pp. 183 – 186, 221 – 222 and 227, 1950.
4. Nelson, A. : Medical Botany. E & S Livingstone, Ltd. Edinburgh, pp. 401 – 402, 1951.
5. Krishnamurthy, N. ; Nambudiri, E. S. and Lewis, Y. S. : Essential oil of Ginger. Central Food Technological Research Institute, Mysore – 2 A., Personal Communication, 1974.
6. Association of Thai Medical School : Collection of therapeutic use of Thai Medicine. Vol. 1, pp. 158 – 160, 188 and 189, 1970.
7. Pongse – Boonrod, S. : Foreign Thai Medicine and Materia medica, pp. 91 – 95, 113 and 114, 1971.
8. Doi, R. The pharmacological study of Zingerone. Tohoku J. Exp. Med. 1 : 96 – 101, 1920.
9. Panthong, A. and Sivamogstham, P. : Pharmacological study of the action of Ginger (Zingiber officinale roscoe) on the gastrointestinal tract. Chiang Mai Med. Bull. 13 : 41 – 54, 1974.
10. Kanjanapothi, D. and Tejasen, P. : A pharmacological study of certain diuretic action of Mimusops elengi (Pikhun). Chiang Mai Med. Bull. 9 : 89 – 103, 1970.
11. Turner, R. A. : Screening Methods in Pharmacology. Academic Press, New York, U.S.A. p. 26, 1965.
12. Litchfield, J. T. and Wilcoxon, F. : A simplified method of evaluating dose–effect experiments. J. Pharmacol. Exp. Therap. 96 : 99 – 113, 1949.
13. Tejasen, P. : Chantaratham, A. and Kanjanapothi D. : The antagonistic effect of a medicinal plant (Curcuma sp. Zingiberaceae) to Thailand cobra venom (Naja naja siamensis). Part II. Chiang Mai Med. Bull. 8 : 229 – 236, 1969.

14. Tejasen, P. ; Chantaratham, A. and Kanjanapothi, D. : The antagonistic effect of a medicinal plant (Curcuma sp. Zingiberaceae) to Thailand cobra venom (Naja naja siamensis). Part I. Chiang Mai Med. Bull. 8 : 165 – 178, 1969.
15. Harnirattisai, P. and Tejasen, P. : Comparative study on the mechanism of the initial depressor etfect of guanethidine and reserpine. Chiang Mai Med. Bull. 14 : 233 – 247, 1975.
16. Paget, G. E. : Methods in Toxicology. F. A. Davis Company, U.S.A. pp. 74 – 75, 1970.
17. Nodine, J. K. and Siegler, P. E. : Animal ahd clinical pharmacologic techniques in drug evaluation. Year Book Publisher Inc., U.S.A. pp. 148 – 149, 1964.
18. Domer, F. R. : Animal experiments in pharmacological analysis. Charles C. Thomas Publisher, Springfield, Illinois, U.S.A. pp. 56, 64, 437 and 445, 1971.
19. Krayer, O.; Wood, E. H. and Montes, G. : Studies on veratrum alkaloids. IV. The sites of the heart rate lowering action of veratridine. J. Pharmacol. Exp. Therap. 79 : 215 – 224, 1943.
20. Wang, S. C.; Ngai, S. H. and Grossman, R. G. : Mechanism of vasomotor action of veratrum alkaloids : Extravagal sites of action of verloid, protoveratrine, genitrine, neogermitrine, germitrine, veratridine, and veratramine. J. Pharmacol. Exp. Therap. 113 : 100 – 114, 1955.
21. DiPalma, J.R. : Drill's pharmacology in Medicine. 4th ed. New York, McGraw–Hill Book Company, pp. 837 – 838, 1971
22. McEachern, C. G.; Smithi F.H. and Manning, G. W. : The effect of intravenous injection of papaverine HCl upon the mortality resulting from sudden occlusion of coronary arteries in dogs. Am. Heart J. 21: 25 – 30, 1941.
23. Von Euler, U. S. : Action of adrenaline, acetylcholine add other substances on nerve–free vessels (human placenta). J. Physiol. (London) 93 : 129 – 143, 1938
24. Somlyo, A. V.; Woo, C. Y. and Somlyo, A. P. : Responses of nerve free vessels to vasoactive amines and polypeptides. Am. J. Physiol. 208 : 784 – 753, 1965.
25. Srinualchai, P. and Tejasen, P. : Investigation of the diuretic effect of Mimusops elngi (Pikhnn) in dogs and rats. Chiang Mai. Bull. 13: 5 – 21, 1974.
26. Naparatt, B. and Tejasen, P. : Investigatinn of the cardiovascular. respiratory and gastrointestinal effects of Leucaena Glauca(Kathin) Chiang Mai Med. 13 : 55 – 70 1974

การศึกษาพิษอย่างเฉียบพลันและผลต่อระบบหัวใจและหลอดเลือดของน้ำคั้นหัวขิง

มยุรี หาญตระกูล และ พาณี เตชะเสน

บทคัดย่อ

ในหนูถีบจักรที่ถูกฉีดน้ำคั้นหัวขิงขนาดต่าง ๆ เข้าทางช่องท้อง จะพบการเปลี่ยนแปลงทั้งในการกระตุ้น และกดต่อระบบประสาทส่วนกลาง ร่วมด้วยอาการบางอย่าง ซึ่งแสดงให้เห็นถึงการเปลี่ยนแปลง ของการทำงานของระบบประสาทอัตโนมัติ อาการพิษที่ทำให้หนูตายคือ การชักอย่างรุนแรง ขนาดของน้ำคั้นหัวขิง ที่ทำให้หนูครึ่งหนึ่งของการทดลองตาย คือ 1,500 (1327 43-1695.00) ม.ก/ก.ก. น้ำหนักตัว

หลังจากที่ให้น้ำคั้นหัวขิง เข้าทางเส้นเลือดดำของสุนัข ที่ถูกทำให้สลบด้วย เพนโต-บาร์บิตาล พบว่าความดันโลหิตลดลงเป็นสองช่วง ในช่วงแรกจะลดลงอย่างรวดเร็ว และเห็นได้ชัด ส่วนในช่วงหลัง จะลดลงเพียงเล็กน้อย แต่จะลดอยู่นานกว่าช่วงแรก อัตราการเต้นของหัวใจจะลดลง พร้อมทั้งพบการเปลี่ยนแปลงบางอย่าง ในการบันทึกของกระแสไฟฟ้าจากหัวใจ,จากการบันทึกผลของน้ำคั้นหัวขิงต่อหัวใจของเต่าที่แยกออกจากตัว และต่อหลอดเลือดแดง ที่ปราศจากเส้นประสาทมาเลี้ยงของคน พบว่าน้ำคั้นหัวขิงจะออกฤทธิ์กดการทำงานของหัวใจ และทำให้กล้ามเนื้อเรียบของเส้นเลือดหย่อนตัว เมื่อนำเอาโปแตสเซี่ยมในปริมาณเท่ากับที่มีอยู่ใน น้ำคั้นหัวขิง มาทำการทดลอง ในลักษณะเดียวกัน ก็ได้ผลการทดลองซึ่งบ่งให้เห็นว่า โปแตสเซี่ยมในน้ำคั้นหัวขิง เป็นสารออกฤทธิ์สำคัญที่ออกฤทธิ์กดการทำงานของหัวใจ ส่วนผลในการลดความดันโลหิตนั้น สืบเนื่องมาจากการขยายตัวของหลอดเลือดแดง ซึ่งเกิดจากผลของสารออกฤทธิ์สำคัญชนิดอื่นในน้ำคั้นหัวขิง

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