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Effects of Mastoparan on a Vascular Contractility in Rabbit Aorta

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Mastoparan is an amphiphilic tetradecapeptide derived from wasp venom which activates G-proteins. Several secondary effects have been attributed to this peptide, including activation of phospholipase and phosphatidylinositol kinase. The aim of the present study was to investigate the effects of mastoparan on vascular contractility. Rabbit aortic rings were cut and mounted on a force transducer to record isometric tension on a polygraph. The effects of mastoparan were then investigated on the contractile responses in the isolated rabbit aorta with or without endothelium.

The results were summarized as follows;

1. Mastoparan caused biphasic response, a transient relaxation followed by a further contraction, in norepinephrine (NE)-precontracted ring with endothelium. These effects were not observed in the aorta in the absence of endothelium.

2. Mastoparan-induced transient relaxation was significantly inhibited by treatment with a N-ω-nitro-L-arginine or methylene blue.

3. When an inhibitor of phospholipase C, neomycin was added to the precontracted aortic ring with NE, the transient relaxation induced by mastoparan was inhibited, but sustained contraction was not inhibited.

4. When an inhibitor of phospholipase A_2, quinacrine and inhibitor of the cyclooxygenase pathway, indomethacin, were added to a precontracted ring with NE, the transient relaxation induced by mastoparan was not inhibited, but sustained contraction was inhibited.

5. Mastoparan induced a contraction of the aorta either with or without endothelium. Indomethacin and nifedipine inhibited mastoparan-induced contraction.

From the above results, we concluded that mastoparan acts on the endothelium and modifies the release of endothelium-derived relaxing factors such as nitric oxide and also endothelium-derived contracting factors such as metabolites of arachidonic acid.

Key Words: Mastoparan, vascular contractility, rabbit aorta

Furchgott and Zawadzki (1980) first reported the crucial role of the endothelium in the regulation of vascular tones in various vasodilators, and it soon became obvious that the vascular endothelial cells release a vasodilator termed endothelium-derived relaxing factor (EDRF) in response to various stimuli (Bolton & Clapp, 1986; Chen *et al.* 1988). It is now well established that EDRF relaxes the blood vessels by activating the guanylate cyclase and increases the production of cGMP (Taylor *et al.* 1988), which decreases the cytosolic Ca^{2+} concentration of smooth muscle cells (Lincoln

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et al. 1990; Lincoln & Cornwell, 1991). The nature of EDRF has been identified as nitric oxide (NO) (Ignarro *et al.* 1987; Myers *et al.* 1990). Production of NO is induced by increase in the cytosolic Ca^{2+} concentration of endothelial cells; the elevated Ca^{2+} stimulates the enzyme, nitric oxide synthase, to form NO from L-arginine (Moncada & Higgs, 1990).

Wasp venom contains pharmacologically active amines (Habermmann, 1972), enzymes such as hyaluronidase, phospholipid and polypeptides such as mastoparan (Argiolas & Pisano, 1983). Mastoparan, an amphiphilic tetradecapeptide, has the potent effect of causing rat peritoneal mast cell degranulation and histamine release (Mousli *et al.* 1989). This polypeptide is isolated, characterized, and chemically synthesized (Hirai *et al.* 1979). Recent studies suggest that mastoparan activates G-proteins such as G_i and G_o (Higashijima *et al.* 1990; Higashijima *et al.* 1988; Weingarten *et al.* 1990). Several secondary effects are also been attributed to this peptide, including activation of phospholipases (Argiolas & Pisano, 1983; Okano *et al.* 1985) and phosphatidylinositol kinases (Eng & Lo, 1990). In addition, mastoparan may inhibit phosphoinositide turnover in some systems as well as impair renal Na^+/K^+-ATPase (Eng *et al.* 1990) and calmodulin activity (Barnette *et al.* 1983). To determine whether mastoparan induces EDRF production or release from endothelial cell, we investigated the effects of mastoparan on vascular contractility and the mechanism(s) of change in contractility induced by mastoparan.

MATERIALS AND METHODS

Aortic ring preparations

The preparation of each aortic ring was similar to that originally described by Furchgott & Zawadzki (1980). Briefly, adult rabbits weighing 2~3 kg were killed by stunning and exsanguination. The descending thoracic aorta was then removed. After excision, the aorta was immersed in Krebs-Henseleit solution (KH solution: mM: NaCl, 118; KCl, 4.8; $CaCl_2$, 2.5; $MgSO_4$, 1.2; KH_2PO_4, 1.2; $NaHCO_3$, 24; glucose, 11; EDTA, 0.03; aerated with 95% O_2 + 5% CO_2, pH 7.4). Adventitial fat and connective tissue were trimmed carefully and cut into rings 2~3 mm in width under a disecting microscope. Special care was taken to avoid damage to the endothelial layer for endothelium intact preparation. In some preparations, the endothelium were removed mechanically by gently rubbing the intimal surface with a moist cotton ball to ensure endothelium free preparation. The integrity of the endothelial cells was checked by the method of Furchgott & Zawadzki (1980).

Tension recording

The aortic rings were mounted for recording of isometric tension in 5 ml organ baths filled with KH solution at 37℃. The bath solution was continuously aerated with 95% O_2+ 5% CO_2. The preparations were attached to a force transducer (Grass FT03) and isometric tension was recorded on a polygraph (Grass Inc). A resting tension of 2 g was maintained throughout the experiments. Tissues were allowed to equilibrate for 90 min before each experiment.

Each aortic ring was made to contract isometrically with norepinephrine (NE; 10^{-7}M). This challenge was repeated to insure that the response was stable. Thereafter, when the contraction reached a plateau at the third or fourth challenge, acetylcholine (ACh; 10^{-6}M) or mastoparan (100 μg/ml) was added to the bath.

In some experiments mastoparan was incubated with N-ω-nitro-L-arginine (N-Arg; 100 μM), methylene blue (MB; 10^{-5}M), neomycin (5×10^{-4}M), quinacrine (2×10^{-4}M) or indomethacin (10^{-5}M).

Drugs and chemicals

Drugs used included: l-arterenol bitartrate (NE), ACh, mastoparan, N-arg, MB, neomycin, quinacrine and indomethacin from Sigma Chemicals Co, St Louis, MO, USA.

Statistics

Results were expressed as the mean±SEM. The effect of mastoparan was expressed as percent peak amplitude of NE-induced con-

traction. Significance tests were performed by Student's paired t test. P values of less than 0.05 were considered significant.

RESULTS

Effects of mastoparan on vascular contractility

Fig. 1 illustrates the effects of mastoparan on NE-precontracted or basal contractility. As shown in Fig. 1, mastoparan (100 μg/ml) caused a biphasic response, a transient relaxation followed by a further contraction to reach a new steady-state of tension, in NE (10^{-7}M)-precontracted rings with endothelial cells (Fig. $1A_2$). However, in endothelium-denuded rings, mastoparan had no appreciable effect on the NE-contracted ring (Fig. $1B_2$). Mastoparan slightly increased basal contractility in both the presence and absence of endothelial cells (Fig. $1A_3$ & B_3).

Effects of N-arg and MB on mastoparan-induced transient relaxation

Fig. 2A illustrates the effects of N-arg on mastoparan-induced relaxation. In the control experiment, mastoparan (100 μg/ml) induced transient relaxation followed by a sustained contraction in the NE-precontracted ring (Fig. $2A_1$). However N-arg (100 μM) significantly inhibited mastoparan-induced transient relaxation (Fig. $2A_2$) (control group: % of contraction $=54.8\pm6.9$, N-arg treated group: % of contraction $=112.2\pm9.6$, $p<0.05$) although a mastoparan-

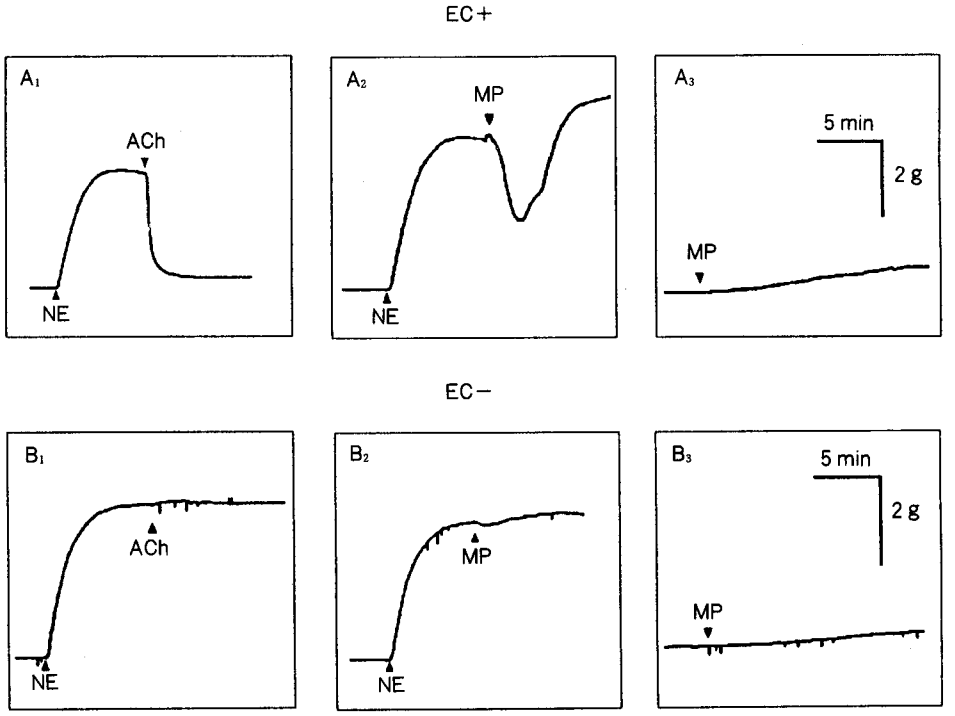

Fig. 1. *Effects of mastoparan on precontracted or basal vascular contractility.*
A_1-A_3: Original recordings represent the effects of mastoparan(100 μg/ml) on NE-precontracted or basal contractility with endothelial cells.
B_1-B_3: Original recordings represent the effects of mastoparan(100 μg/ml) on NE-precontracted or basal contractility without endothelial cells.
NE: norepinephrine (10^{-7}M), ACh: acetylcholine (10^{-6}M), MP: mastoparan

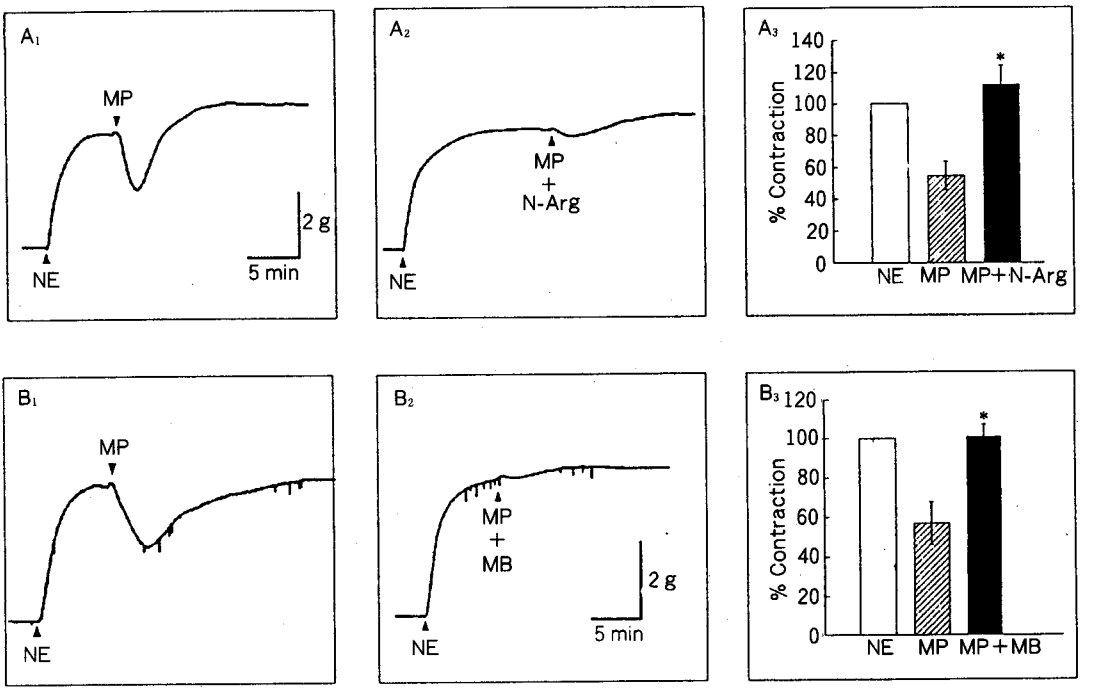

Fig. 2. *Effects of N-Arg and MB on mastoparan-induced transient relaxation.*
A_1-A_2: Original recordings represent the effects of N-Arg (100 μM) on mastoparan-induced transient relaxation.
*A_3: Mastoparan-induced relaxations with or without N-Arg was expressed as the percent of peak amplitude at precontraction. Data are means±SEM of values from 5 arterial rings. *: $p<0.05$ compared to control group (mastoparan- induced relaxation).*
B_1-B_2: Original recordings represent the effects of MB (10^{-5}M) on mastoparan-induced transient relaxation.
*B_3: Mastoparan-induced relaxations with or without MB are expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 5 arterial rings. *: $p<0.05$ compared to control group (mastoparan-induced relaxation).*
N-Arg: N-ω-nitro-L-arginine (100 μM), MB: methylene blue (10^{-5}M)

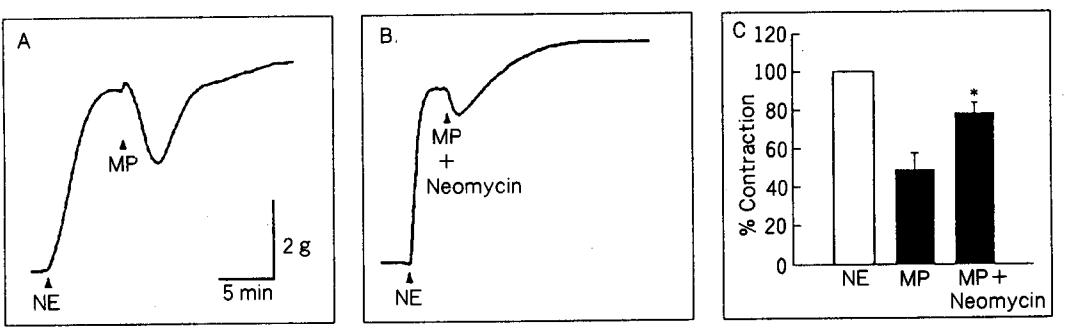

Fig. 3. *Effects of neomycin on mastoparan-induced transient relaxation.*
A & B: Original recordings represent the effects of neomycin on mastoparan-induced transient relaxation.
*C: Mastoparan-induced relaxations with or without neomycin (5×10^{-4}M) were expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 6 arterial rings. *: $p<0.05$ compared to the control group (mastoparan-induced relaxation).*

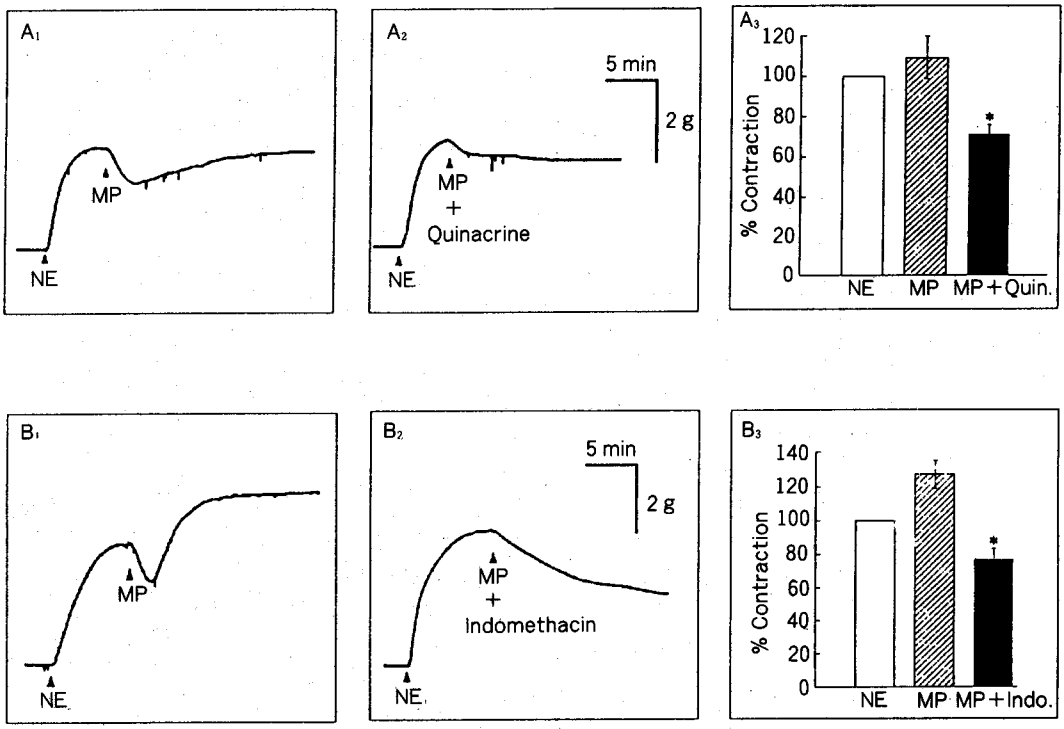

Fig. 4. *Effects of quinacrine and indomethacin on mastoparan-induced sustained contraction.*

A_1-A_2: Original recordings represent the effects of quinacrine (2×10^{-4}M) on mastoparan-induced sustained contraction.

*A_3: Mastoparan-induced relaxations with or without quinacrine are expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 6 arterial rings. *: $p<0.05$ compared to control group (mastoparan-induced contraction).*

B_1-B_2: Original recordings represent the effects of indomethacin (10^{-5}M) on mastoparan-induced sustained contraction.

*B_3: Mastoparan-induced relaxations with or without indomethacin are expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 5 arterial rings. *: $p<0.05$ compared to the control group (mastoparan-induced contraction).*

induced sustained contraction was demonstrated.

Fig. 2B illustrates the effects of MB on mastoparan-induced transient relaxation. The effects of MB (10^{-5}M) were similar to those of N-arg (control group: % of contraction = 57 ± 8.5, MB treated group: % of contraction = 101 ± 4.8, $p<0.05$).

Effects of neomycin on mastoparan-induced transient relaxation

The effects of neomycin on mastoparan-induced transient relaxation are shown in Fig. 3. As shown in Fig. 3, neomycin (5×10^{-4}M) significantly inhibited mastoparan-induced transient relaxation (Fig. $3A_2$) (control group: % of contraction = 48.8 ± 7.0, N-arg treated group: % of contraction = 78.3 ± 4.5, $p<0.05$) but a mastoparan-induced sustained contraction was also demonstrated.

Effects of quinacrine and indomethacin on mastoparan-induced sustained contraction

Fig. 4A illustrates the effects of quinacrine

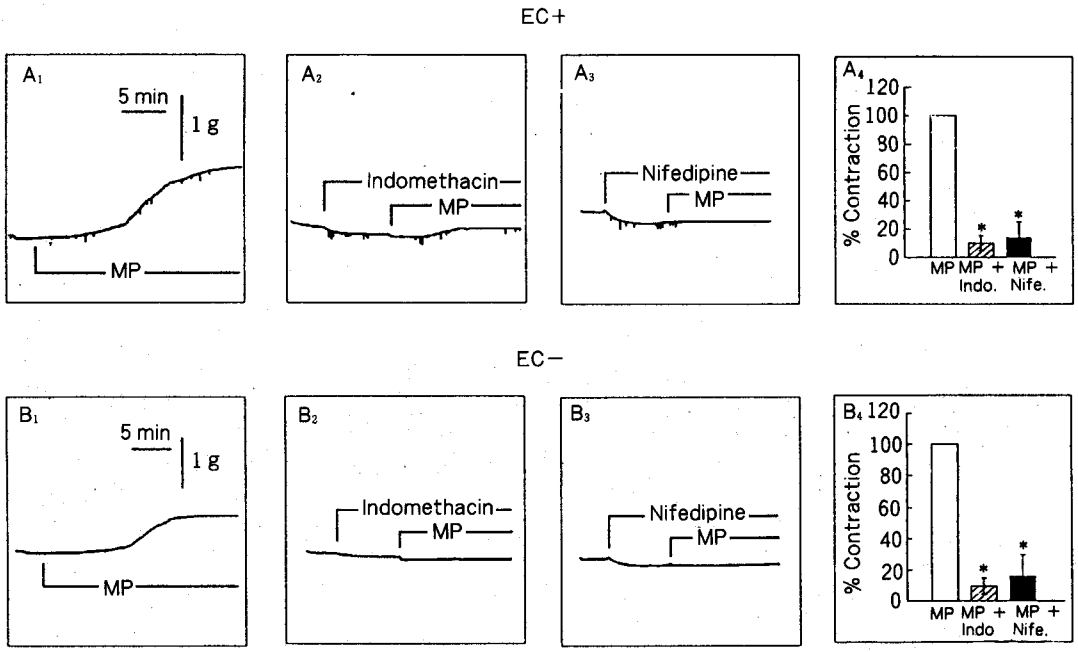

Fig. 5. *Effects of mastoparan on basal contractility.*

A_1-A_3: Original recordings represent the effects of indomethacin (10^{-5}M) or nifedipine (5×10^{-7}M) on basal contractility with endothelial cells.

*A_4: In the presence of endothelial cells, the effect of indomethacin or nifedipine treatment are expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 5 arterial rings. *: $p<0.05$ compared to the control group (mastoparan-induced contraction).*

B_1-B_3: Original recordings represent the effects of indomethacin (10^{-5}M) or nifedipine (5×10^{-7}M) on basal contractility without endothelial cells.

*B_4: In the absence of endothelial cells, the effects of indomethacin or nifedipine treatment are expressed as the percent of peak amplitude of precontraction. Data are means±SEM of values from 5 arterial rings. *: $p<0.05$ compared to the control group (mastoparan-induced contraction).*

on mastoparan-induced contraction. In the control experiment, mastoparan (100 μg/ml) induced transient relaxation followed by a sustained contraction in the NE-precontracted ring (Fig. 4A_1). However, in the presence of quinacrine (2×10^{-4}M), a mastoparan-induced contraction was not demonstrated (Fig. 4A_2) (control group: % of contraction=119.3±8.7, quinacrine treated group: % of contraction=57.3±7.7, $p<0.05$). Fig. 4B illustrates the effects of indomethacin on a mastoparan-induced sustained contraction. The effects of indomethacin (10^{-5}M) were similar to those of quinacrine (control group: % of contraction=127.6±6.3, indomethacin treated group: % of contraction=70±9.0, $p<0.05$).

Effects of mastoparan on basal contractility

As shown in Fig. 5, mastoparan caused contraction in the basal state ring with (Fig. 5A_1) and without (Fig. 5B_1) endothelial cells. Pretreatment with indomethacin (10^{-5}M) significantly inhibited the mastoparan-induced contraction with (Fig. 5A_2) and without (Fig. 5B_2) endothelial cells. Moreover, the effects of pretreatment with nifedipine (5×10^{-7}M) were similar to those of indomethacin.

DISCUSSION

Mastoparan, an amphiphilic tetradecapeptide, has a potent effect causing rat peritoneal mast cell degranulation and histamine release (Mousli *et al.* 1989). Recent studies suggest that mastoparan activates G-proteins such as G_i and G_o in endothelial cells (Higashijima *et al.* 1990; Higashijima *et al.* 1988; Weingarten *et al.* 1990). To determine whether mastoparan induces EDRF production or release from endothelial cells, the present study investigated the effects of mastoparan on vascular contractility.

As shown in Fig. 1, mastoparan (100 μg/ml; effective dose resulted in dose-response curve) caused a biphasic response, a transient relaxation followed by a further contraction reaching a new steady-state tension, in NE(10^{-7}M)-precontracted ring with endothelial cells. However, in endothelium-denuded rings, mastoparan had no appreciable effect on the NE-precontracted ring. Mastoparan-induced transient relaxation was significantly inhibited by treatment with an inhibitor of NO synthase, N-Arg (Fukuto *et al.*, 1990) or inhibitor of guanylate cyclase, MB (Murad *et al.*, 1978: Fig. 2). Neomycin significantly inhibited mastoparan-induced relaxation (Fig. 3). Neomycin is a well known inhibitor of phospholipase C (Cockcroft & Gomperts, 1985) and Ca^{2+} channel blockers (Liu *et al.*, 1994). These results indicate that mastoparan increase intracellular Ca^{2+} concentration and production of EDRF in the endothelial cell, after which concentration of cGMP in the smooth muscle cell is increased.

It has been reported that mastoparan is able to elicit Ca^{2+} release from an intracellular store of endothelial cells, and this effect might be associated with the activation of G-proteins (Tracey & Peach, 1993). Brock *et al.* (1988) reported that mastoparan increases fura-2 fluorecence in the endothelial cell and this effect might be asspciated with release of Ca^{2+} from intracellular Ca^{2+} store in the endothelial cell.

Mastoparan elicits a significant influx of Ca^{2+} into endothelial cells from the extracellular fluid and interact with/perturb membrane structure (Higashijima *et al.* 1983; Katsu *et al.* 1990). In our study, we did not demonstrate the effect of mastoparan on Ca^{2+} influx across the cell membrane and action site of mastoparan.

However, mastoparan also induced sustained contraction in NE-precontracted ring and the contraction was only demonstrated in those rings with endothelium (Fig. 1). Mastoparan-induced sustained contraction was significantly inhibited by quinacrine or indomethacin (Fig. 4). Quinacrine and indomethacin are inhibitors of phospholipase A_2 (Riemle & Vanhoutte, 1983) and inhibitors of the cyclooxygenase pathway (Kalsner, 1976), respectively. Phospholipase is a well known enzyme which produces arachidonic acid, the precursor of prostaglandin and leukotrienes. Therefore, our results suggest that mastoparan-induced sustained contraction in the precontracted ring is induced by metabolite(s) of the cyclooxygenase pathway produced in endothelial cells.

As shown in Fig. 5, mastoparan caused contraction in the basal state ring with and without endothelial cells, but the amplitude of the contraction was very small. Pretreatment with indomethacin significantly inhibited mastoparan-induced contraction with and without endothelial cell. Moreover, the effects of pretreatment with the Ca^{2+} channel blocker, nifedipine (Hottenstein *et al.* 1984) were similar to those of indomethacin. Therefore, our results suggest that mastoparan-induced contraction in the resting ring may be caused by metabolite(s) of the cyclooxygenase pathway such as prostaglandin $F_{2\alpha}$ and then metabolite (s) of the cyclooxygenase pathway may facilitate the Ca^{2+} influx through cell membrane. Riemle and Vanhoutte (1983 & 1984) report that cyclooxygenase or lipoxygenase products may facilitate the Ca^{2+} entry into vascular smooth muscle cells. However, in this study, we did not demonstrate the existence of specific receptors for mastoparan. Furthermore, the present data provide no identification of the mechanism of the action of mastoparan on cyclooxygenase pathway. Further work is required to examine the mechanism(s) of

action of mastoparan on cyclooxygenase pathway.

In summary, this report demonstrated that mastoparan induced a biphasic response of vascular contractility through two distinct processes. The first pathway was via mastoparan increased intracellular Ca^{2+} concentration, and after release of EDRF in the endothelial cell, the concentration of cGMP in the smooth muscle cell increased. The second pathway was via a mastoparan increased concentration of metabolites into the cyclooxygenase pathway in the endothelial cell.

REFERENCES

Argiolas A, Pisano JJ: Facilitation of phospholipase A_2 activity by mastoparans, a new class of mast cell degranulating peptides from wasp venom. *J Biol Chem 258: 13697-13702, 1983*

Barnette MS, Daly R, Weiss B: Inhibition of calmodulin activity by insect venom peptides. *Biochem Pharmacol 32: 2929-2933, 1983*

Bolton TB, Clapp LH: Endothelial-dependent relaxant actions of carbachol and substance P in arterial smooth muscle. *Br J Pharmacol 87: 713-723, 1986*

Brock TA, Dennis PA, Griendling KK, Diejl TS, Davies PF: GTP,S loading of endothelial cells stimulates phospholipase C and uncouples ATP receptors. *Am J Physiol 255: C667-C673, 1988*

Chen G, Suzuki H, Weston AH: Acetylcholine releases endothelium-derived hyperpolarizing factor and EDRF from rat blood vessels. *Br J Pharmacol 95: 1165-1174, 1988*

Cockcroft S, Gomperts BD: Role of guanine nucleotide binding protein in the activation of polyphosphoinositide phosphodiesterase. *Nature 314: 534-536, 1985*

Eng SP, Clough DL, Lo CS: Mastoparan inhibits rat renal Na/K ATPase activity. *Life Sci 47: 2451-2458, 1990*

Eng SP, Lo CS: Mastoparan increases membrane bound phosphatidylinositol kinase and phosphatidylinositol 4-monophosphate kinase activities in Madin-Darby canine kidney cells. *Life Sci 46: 273-279, 1990*

Fukuto JM, Wood KS, Byrns RE, Ignarro LJ: N^G-amino-L-arginine: A new potent antagonist of L-arginine mediated endothelium-dependent relaxation. *Biochem Biophys Res Commun 168: 458-465, 1990*

Furchgott RF, Zawadzki JV: The obligatory role of endothelial cells in the relaxation of arterial smooth muscle by acetylcholine. *Nature 288: 373-376, 1980*

Habermann E: Bee and wasp venoms : The biochemistry and pharmacology of their peptides and enzyme are reviewed. *Science 177: 314-322, 1972*

Higashijima T, Burnier J, Ross EM: Regulation of G_i and G_o by mastoparan, related amphiphilic peptides, and hydrophobic amines, Mechanism and structural determinants of activity. *J Biol Chem 265: 14176-14186, 1990*

Higashijima T, Uzu S, Nakajima T, Ross EM: Mastoparan, a peptide toxin from wasp venom, mimics receptors by activating GTP-binding regulatory proteins (G proteins). *J Biol Chem 263: 6491-6494, 1988*

Higashijima T, Wakamatsu K, Takemitsu M, Fujino M, Nakajima T, Miyazawa T: conformational change of mastoparan from wasp venom on binding with phospholipid membrane. *FEBS Lett 152: 227-230, 1983*

Hirai Y, Kuwada M, Yasuhara T, Yoshida H, Nakajima T: A new mast cell degranulating peptide homologus to mastoparan in the venom of Japanes hornet (Vespa Xanthoptera). *Chem Pharm Bull (Tokyo) 27: 1945-1946, 1979*

Hottenstein O, Mitzner R, Bierkamper C: *Nitrendine blocks calcium-dependent depolarization induced by hopoxia in rat main pulmonary artery.* In Nitrendipine ed, by Scriabine A, Vanos S, Deck K, Baltimore, *1984*

Ignarro LJ, Byrns RE, Buga GM, Wood KS: Endothelium-derived relaxing factor from pulmonary artery and vein possesses pharmacologic and chemical properties identical to those of nitric oxide radical. *Circ Res 61: 866-978, 1987*

Kalsner S: Intrinsic prostaglandins release. A mediator of anoxia-induced relaxation in an isolated coronary artery preparation. *Blood Vessels 13: 155-166, 1976*

Katsu T, Kuroko M, Morikawa T, Sanchika K, Yamanaka F, Shinoda S, Fujita Y: Interaction of wasp venom mastoparan with biomembranes. *Biochim Biophys Acta 1027: 185-190, 1990*

Lincoln TM, Cornwell TL, Taylor AE: cGMP-dependent protein kinase mediates the reduction of Ca^{2+} in vascular smooth muscle cells. *Am J Physiol 258: C399-C407, 1990*

Lincoln TM, Cornwell TL: Towards an under-

standing of the mechanism of action of cyclic AMP and cyclic GMP in smooth muscle relaxation. *Blood Vessels 28: 129-137, 1991*

Liu G, Abramson JJ, Zable AC, Pessach IN: Direct evidence for the existence and functional role of hyperreactive sulfhydryls on the ryanodine receptor-triadin complex selectively labeled by the coumarin maleimide 7-diethyl(amino-3-(4'-maleimidylphenyl)-4-methylcoumarin. *Mol Pharmacol 45: 189-200, 1994*

Moncada S, Higgs EA: *Nitric oxide from L-arginine:* a bioregulatory system. Amsterdam, Elveiser, *1990*

Mousli M, Bronner C, Bueb JL, Tschirhart E, Gies JP, Landry Y: Activation of rat peritoneal mast cells by substance P and mastoparan. *J Pharmacol Exp Ther 250: 329-335, 1989*

Murad F, Mittal CK, Armold WP, Katsuki S, Kimura H: Guanylate cyclase: activation by azide, nitrocompounds, nitric oxide and hydroxyl radical and inhibition by hemoglobin and myoglobin. *Adv Cyclic Nucleotide Res 9: 145-158, 1978*

Myers PR, Minor RL Jr, Guerra R Jr, Bates JN, Harrison DG: Vasorelaxant properties of the endothelium-derived relaxing factor more closely resemble S-nitro-cysteine than nitric oxide. *Nature 345: 161-163, 1990*

Okano Y, Takagi H, Tohmatsu T, Nakashima S, Kuroda Y, Saito K, Nozawa Y: A wasp venom mastoparan-induced polyphosphoinositide breakdown in rat peritoneal mast cells. *FEBS Lett 188: 363-366, 1985*

Riemle TJ, Vanhoutte PM: Effects of inhibitors of arachidonic acid metabolism and calcium entry on responses to acetylcholine, potassium and norepinephrine in the isolated canine saphenous vein. *J Pharmacol Exp Ther 225: 720-728, 1983*

Riemle TJ, Vanhoutte PM: Effects of inhibitors of arachidonic acid metabolism and calcium entry on hypoxic contractions of the isolated canine coronary artery, in Calcium Antagonists: *Mechanism of Action on Cardiac Muscle and Vascular Smooth Muscle,* Sperelakis N and Canfield JB Eds., Martinus Nijhoff, The Hague, *1984, 303*

Taylor SG, Southerton JS, Weston AH, Baker JRJ: Endothelium-dependent effects of acetylcholine in rat aorta: A comparison with sodium nitroprusside and cromakalim. *Br J Pharmacol 94: 853-863, 1988*

Tracey WR, Peach MJ: Mechanism of mastoparan-induced EDRF release from pulmonary artery endothelial cells. *J Vasc Res 30: 68-72, 1993*

Weingarten R, Ransnas L, Mueller H, Sklar LA, Bokoch GM: Mastoparan interacts with the carboxyl terminus of the α-subunit of Gi. *J Biol Chem 265: 11044-11049, 1990*