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Influence of β-Eudesmol on Blood Pressure

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Abstract – The present study was undertaken to investigate the effects of β-eudesmol, one of various ingredients isolated and identified from the bark of *Magnolia obovata* Thunberg, on arterial blood pressure and vascular contractile responses in the normotensve rats and to establish its mechanism of action. β-Eudesmol (30~300 μg/kg) given into a femoral vein of the normotensive rat produced a dose-dependent depressor response. These β-eudesmol-induced hypotensive responses were markedly inhibited in the presence of chlorisondamine (1.0 mg/kg, i.v.) or phentolamine (2.0 mg/kg, i.v.). Interestingly, the infusion of β-eudesmol (1.0 mg/kg/30min) into a femoral vein made a significant reduction in pressor responses induced by intravenous norepinephrine. Furthermore, the phenylephrine (10^{-5} M)-induced contractile responses were depressed in the presence of high concentrations of β-eudesmol (10~40 μg/ml), but not affected in low concentration of β-eudesmol (2.5~5 μg/ml). Also, high potassium (5.6×10^{-2} M)-induced contractile responses were greatly inhibited in the presence of β-eudesmol (10~40 μg/ml) in a dose-dependent fashion. Taken together, these results obtained from the present study demonstrate that intravenous β-eudesmol causes a dose-dependent depressor action in the anesthetized rat at least partly through the blockade of vascular adrenergic α_1-receptors, in addition to the some unknown mechanism of direct vasorelaxation.

Keywords – β-Eudesmol; Vasorelaxation; Adrenergic α_1-receptors blockade

Introduction

The bark of *Magnolia obovata* Thunberg (日厚朴), a medicinal plant, has been used for the treatment not only of gastrointestinal disorders but also of anxiety, which led us to consider that magnolia bark may influence the central and/or autonomic nervous systems. The Chinese traditional medical book mentions that magnolia bark itself has a tranquilizing action. Actually, the extract of magnolia bark has been shown to have depressant actions on the central nervous system (Watanabe *et al.*, 1973). Various ingredients have been isolated and identified from magnolia bark. They are β-eudesmol, α- and β-pinenes, and bornyl acetate, as essential oils; magnolol and honokiol, as diphenyl compounds; and magnocurarine and magnoflorine, as alkaloids. It also has been reported that some of these ingredients have pharmacological effects on nervous systems (Watanabe *et al.*, 1983; Chiou *et al.*, 1997). However, until now, there has been no evidence showing the influence of magnolia bark and its components on autonomic nervous systems and clarifying the relationship between the pharmacological effects of magnolia bark and those of its ingredients.

Recently, Lim and his co-workers (2003) have found that intravenous bornyl acetate, one of active components of magnolia bark, causes the depressor action in the anesthetized rat at least partly through the blockade of adrenergic α_1-receptors, and it also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic a_1-receptors. Moreover, it has been reported that the crude extract of magnolia bark, an herbal drug, inhibited the secretion of catecholamines from bovine adrenal chromaffin cells stimulated by acetylcholine (ACh) in a concentration-dependent manner (Tachikawa *et al.*, 2000). These results indicate that magnolia bark contains some effective components inhibiting the secretion of catecholamines from bovine adrenal chromaffin cells stimulated by ACh due to the antagonism of Na^+ and Ca^{2+} influxes into the cells. However, inhibition by the extract of magnolia bark seems to be attributable to honokiol and bornyl acetate (Tachikawa *et al.*, 2000). Despite of this report, there has been remarkably little evidence on cardiovascular system, especially on blood pressure. Therefore, the present study was attempted to examine the effects of β-eudesmol on blood pressure in the anesthetized normotensive rat and contractile responses of isolated aortic strips of the rat and to clarify the mechanism of action.

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Experimental

Experimental procedure – Mature male Sprague-Dawley rats, weighing 150 to 350 g, were used in the experiment. The animals were housed individually in separate cages, and food (Cheil Animal Chow) and tap water were allowed *ad libitum* for at least a week to adapt to experimental circumstances. On the day of experiment, a rat was anesthetized with thiopental sodium (40 mg/kg) intraperitoneally, and tied in supine position on fixing panel.

Isolation of aortic strips – The thorax was opened by a midline incision, and placing three-hook retractor exposed the heart and surrounding area. The heart and portion of the lung were not removed, but pushed over to the right side and covered by saline-soaked gauge pads in order to obtain enough working space for isolating aortic vessel. The aorta was isolated from the proximal part of the heart to the vicinity of liver and immediately immersed in cold Krebs solution. The blood within the aorta was rapidly removed. The aorta was cut into the ring of 4-5 mm length.

Preparation of arterial cannulation – The animal was tied in supine position on fixing panel to insert a T-formed cannula into the trachea for securing free air passage. The rectal temperature was maintained at 37-38°C by a thermostatically controlling blanket and heating lamp throughout the course of the experiment.

Recording of mechanical activity – The ring segment of aorta was mounted in a muscle bath by sliding the ring over two parallel stainless-steel hooks (0.15 mm in diameter). The lower hook was fixed on bottom of the bath and the upper was connected to isometric transducer (Grass FT. 03). The signal from the transducer was displayed on a polygraph (Grass Instruments Model 79). The volume of bath was 25 ml and the bath solution was saturated with 95% O_2 and 5% CO_2 at 37°C (Fig. 1). The composition (mM) of Krebs was: NaCl, 118.4; KCl, 4.7; $CaCl_2$, 2.5; $MaCl_2$, 1.18; $NaHCO_3$, 25; KH_2PO_4, 1.2; glucose, 11.7. The final pH of the solution was maintained at 7.4 - 7.5. During equilibration period of 2 hours, the resting tension was adjusted to 0.5 g. After the equilibration period, the ring was challenged with 35 mM KCl two times, and if it responded with contraction, the proper experiment was started. Vasoconstrictors were administered into the bath in order to obtain dose-response curves. In the subsequent experiments, under the presence of green tea extract, some vasoconstrictors were administered, respectively. The data were expressed as % of the control tension.

Measurement of blood pressure – In order to observe the change of arterial pressure, one of the common carotid arteries or of the femoral arteries was catheterized with polyethylene tubing [outside diameter (o.d.): 0.5 mm]. The tubing was connected to a pressure transducer (Gould Co., U.S.A.) and pulse of mean arterial blood pressure was recorded on a biological polygraph (Grass Co., U.S.A.) continuously. The chart speed was adjusted to 2 cm per minute. The artery tubing was filled with heparin solution (400 I.U.) to prevent the blood coagulation during the experiment. Another cannulation with polyethylene tubing (o.d.: 0.3 mm) was made into a femoral vein for the administration of drugs and supplemental anesthetic agents as needed to maintain light surgical anesthesia. Each rat was left undisturbed for at least 30 minutes after completion of the operative procedures to permit cardiovascular parameters to be stabilized and drugs under investigation were administered at intervals of 20~30 minutes.

Statistical analysis – The statistical significance between groups was determined by the Student's *t*- and *ANOVA*-tests. A P-value of less than 0.05 was considered to represent statistically significant changes unless specifically noted in the text. Values given in the text refer to means and the standard errors of the mean (S.E.M.). The statistical analysis of the experimental results was made by computer program described by Tallarida and Murray (1987).

Drugs and their sources – The following drugs were used: β-eudesmol (Wako Pure Chemical Industry Ltd., Japan), phenylephrine hydrochloride, potassium chloride, and norepinephrine bitartrate (Sigma Chemical Co., U. S. A.), chlorisondamine chloride and phentolamine mesylate (CIBA Co., U.S.A.), thiopental sodium and heparin sodium (Daehan Choongwae Pharm. Co., Korea). Drugs were dissolved in distilled water (stock) and added to the normal Krebs or saline solution as required. However, β-eudesmol was dissolved in dimethyl sulfoxide. The concentration of dimethyl sulfoxide in the aortic bath was less than 1%, which had no effect on the vascular contractility and blood pressure under the conditions employed in this study. Concentrations of all drugs used are expressed in terms of molar base and gram.

Results

Effects of intravenous β-eudesmol on arterial blood pressure in the anesthetized rats – When cardiovascular parameters were stabilized for 30 min before the experimental protocols were initiated, the administration of physiological saline solution in a volume of 0.2 ml into a femoral vein did not cause any changes in both arterial

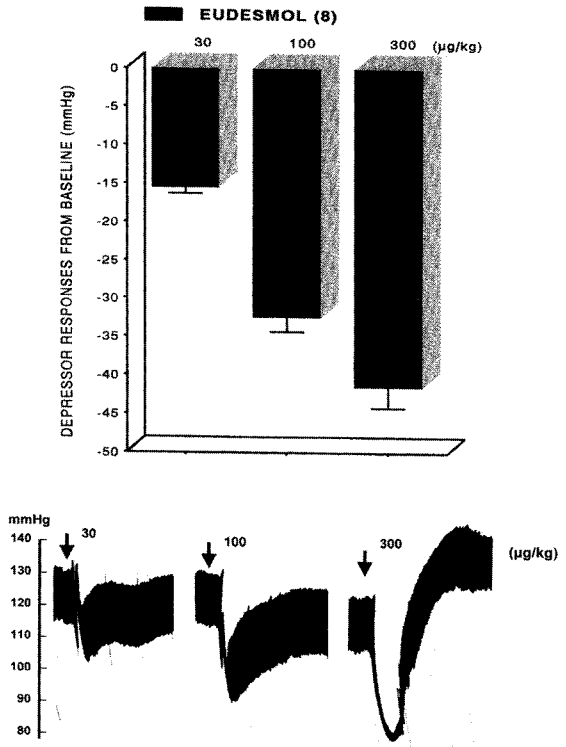

Fig. 1. Upper: Influence of intravenous β-eudesmol on arterial blood pressure in the thiopental-anesthetized rats. Ordinate: changes of arterial blood pressure in mmHg from 8 rats. Abscissa: intravenous doses of β-eudesmol in μg/kg. Vertical bar on each column indicates standard error of mean (S.E.M.). There was statistically significant difference in changes of arterial pressure responses induced by β-eudesmol from pre-injection level. Numeral in the parenthesis denotes Number of animals used in the experiment. **Lower:** The representative tracing of the intravenous β-eudesmol-induced depressor response in the thiopental-anesthetized rat. At arrow mark, the indicated doses (30, 100 and 300 μg/kg) of β-eudesmol were administered into a femoral vein at 20-30 min interval. The chart speed was 20 mm/min.

blood pressure. Then, nicorandil injected intravenously to the normotensive thiopental-anesthetized rat produced a dose-dependent decrease in arterial blood pressure.

In 8 rats, as shown in Fig. 1, intravenous 30 μg/kg of nicorandil produced a fall in arterial blood pressure to −16±0.8 mmHg ($P < 0.01$) from the original baseline of 122±9 mmHg. Increasing intravenous doses of nicorandil to 100 and 300 μg/kg caused the dose-related reduction in arterial pressure responses to −33±2 mmHg ($P < 0.01$) and −42±3 mmHg ($P < 0.01$) from the original baseline, respectively.

Influence of chlorisondamine and phentolamine on β-eudesmol-induced hypotensive responses in the anesthetized rats – In 6 experimental animals, the effect of chlorisandamine on the cardiovascular reponses to intravenous injection of β-eudesmol was studied. Chlorisandamine (1.0 mg/kg), an autonomic ganglionic blocking agent was given into a femoral vein of the rat. Following the administration of chlorisondamine, the baseline of blood pressure was reduced from 122±10 mmHg to 75±6 mmHg. The responses of arterial blood pressure by β-eudesmol, when given intravenously at 30, 100 and 300 μg/kg, were −12±2 mmHg, −21±1 mmHg and −35±2 mmHg from the pre-injection level, respectively. However, after pretreatment with chlorisondamine they were markedly inhibited by − 4±0.4 mmHg ($P < 0.01$), −6±0.3 mmHg ($P < 0.01$) and −14 ± 1.5 mmHg ($P < 0.01$) from the original baseline, respectively as shown in Fig. 2.

In order to investigate whether β-eudesmol-induced hypotensive response is mediated by the blockade of

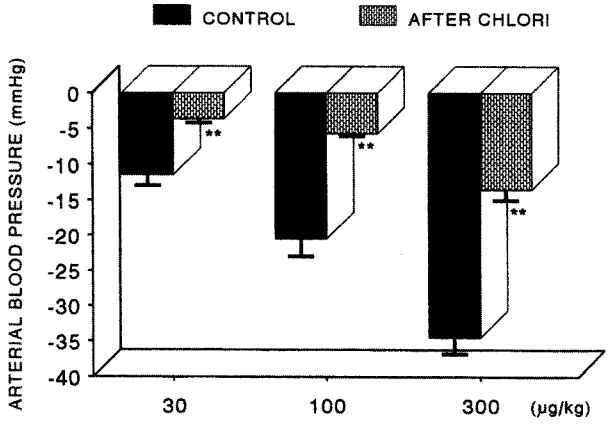

Fig. 2. Influence of chlorisondamine (CHLORI) on intravenous β-eudesmol-evoked hypotensive responses. Chlorisondamine (1.0 mg/kg) was given intravenously after completion of the corresponding control responses of β-eudesmol. "CONTROL" and "AFTER" represent changes of arterial pressure induced by β-eudesmol before (CONTROL) and after pretreatment with chlorisondamine. Statistical significance was obtained by comparing the changes between groups of "CONTROL" and "AFTER". Other legends are the same as in Fig.1. **: $P < 0.01$.

adrenergic α-receptors, it was of interest to test the influence of phentolamine, an antagonist of adrenergic α-receptors, on β-eudesmol-induced hypotensive responses. In 6 rats, in order to examine the relationship between adrenergic α-receptors and β-eudesmol-induced depressor action, phentolamine (2.0 mg/kg) was given intravenously after obtaining the control responses of intravenous β-eudesmol. In the presence of phentolamine, depressor responses induced by intravenous β-eudesmol at doses of 30, 100 and 300 μg/kg were inhibited to 4±0.4 mmHg ($P < 0.01$), −10±2 mmHg ($P < 0.01$) and 16±2 mmHg ($P < 0.01$), respectively in comparison with their corresponding control responses of −24±2 mmHg, −36±3 mmHg and −46±3 mmHg, as shown in Fig. 3.

Effect of β-eudesmol on norepinephrine-induced

hypertensive responses in the anesthetized rats – Since β-eudesmol-induced depressor responses were greatly inhibited by pretreatment with chlorsondamine or phentolamine as shown in Fig. 2 and 3. It was suggested that β-eudesmol could cause hypotension through the blockade of peripheral adrenergic α-receptors. It was of interest to examine the effect of intravenous β-eudesmol on norepinephrine-evoked pressor responses. In 12 rats, norepinephrine at doses of 1, 3 and 10 μg/kg caused dose-dependent pressor responses of 18±1 mmHg, 29±2

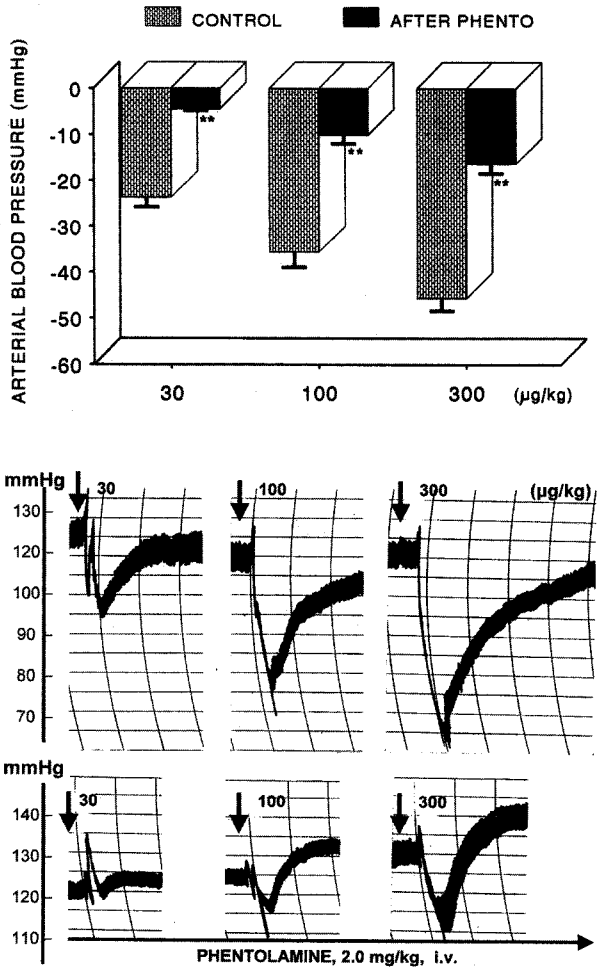

Fig. 3. Upper: Influence of phentolamine (PHENTO) on intravenous β-eudesmol-evoked hypotensive responses. Phentolamine (2.0 mg/kg) was given into a femoral vein after obtaining the corresponding control responses of intravenous β-eudesmol. Other legends are the same as in Fig. 1 and 2. **: $P < 0.01$. **Lower:** The representative tracing of phentolamine effect on intravenous β-eudesmol-induced depressor responses in the anesthetized rat. At arrow marks, the indicated doses (30, 100 and 300 μg/kg) of β-eudesmol were administered into a femoral vein. Upper panel: β-Eudesmol-induced hypotensive responses in a non-treated rat. Lower panel: β-Eudesmol-induced hypotensive responses in a phentolamine-pretreated rat. Phentolamine was given into a femoral vein with a dose of 2.0 mg/kg. The chart speed was 20 mm/min.

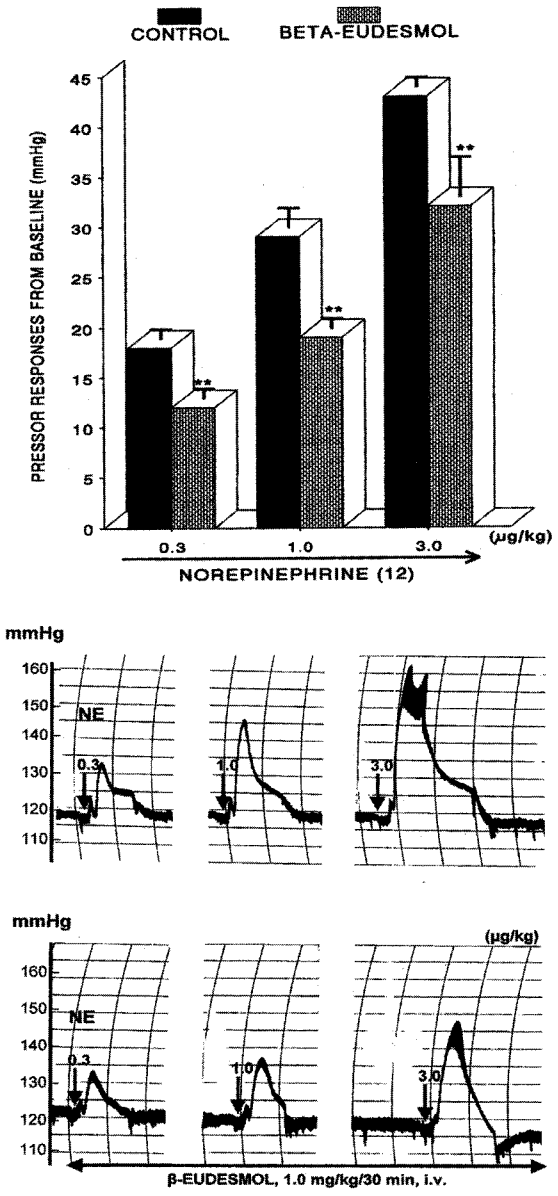

Fig. 4. Upper: Influence of intravenous β-eudesmol on norepinephrine-evoked pressor responses. Ordinate: Changes of blood pressure from baseline level in mmHg. Abscissa: Intravenous doses of norepinephrine in μg/kg. Vertical bar on the top of each column indicates standard error of mean. There was statistically significant difference in changes of norepinephrine-evoked pressor responses between before and after pretreatment with β-eudesmol. β-Eudesmol was infused into a femoral vein with a rate of 1.0 mg/kg/30 min after obtaining the corresponding control responses of intravenous norepinephrine. The original base-line of arterial blood pressure was 118±12 mmHg. **: $P < 0.01$. **Lower**: The representative tracing of β-eudesmol effect on intravenous norepinephrine (NE)-induced pressor responses in the anesthetized rat. At arrow marks, the indicated doses (0.3, 1.0 and 3.0 μg/kg) of NE were administered into a femoral vein. Upper panel: NE-induced hypertensive responses in a non-treated rat. Lower panel: NE-induced hypertensive responses in a β-eudesmol-pretreated rat. β-Eudesmol was infused into a femoral vein with a rate of 1.0 mg/kg/30 min. ABP: Arterial blood pressure in mmHg. The chart speed was 20 mm/min.

mmHg and 43±1 mmHg from the original baseline (125±14 mmHg), respectively. However, after infusion of β-eudesmol with a rate of 1 mg/kg/30min, they were significantly depressed to 12±1 mmHg ($P < 0.01$), 19±1 mmHg ($P < 0.01$) and 32±4 mmHg ($P < 0.01$) at the above same doses, respectively (Fig. 4). Fig. 4 (lower) shows that norepinephrine-evoked pressor responses are greatly attenuated after pretreatment with intravenous β-eudesmol.

Effects of β-eudesmol on contractile responses induced by phenylephrine and high K^+ in the rat aortic strips – The resting (basal) tension from the isolated rat aortic strips reaches a steady state after the perfusion with oxygenated Krebs-bicarbonate solution for 90 min before the experimental protocol is initiated. The resting tension was adjusted to 0.5 g. The effect of β-eudesmol on phenylephrine- as well as high potassium chloride-mediated contractile responses in the rat aorta was examined. In the present study, β-eudesmol itself did not produce any effect on the resting tension in the aortic strips isolated from the rat (data not shown).

When 10^{-5} M concentration of phenylephrine was administered into the aortic bath, its active tension amounted to 2.1±0.2 g from the resting tension level. In the presence of β-eudesmol at low concentrations of 2.5~5.0 μg/ml, 10^{-5} M-phenylephrine-induced tension amounted to 100~96.5% of the control contractile responses (Data not shown). However, in the presence of high concentration of β-eudesmol (10~40 μg/ml), 10^{-5} M-phenylephrine-induced contractile responses were also dose-dependently inhibited to 78~42% of the control responses (Fig. 5).

High potassium exerts two distinct effects on cells: (1) depolarization of cell membrane, and (2) depolarization-induced influx of calcium via voltage-dependent calcium channels (Wada *et al.*, 1985). When added through the bath, high potassium at the concentration of 5.6×10^{-2} M, which is a membrane-depolarizing agent, caused an increased aortic contraction (1.5±0.1 g). As shown in Fig. 6, high potassium (5.6×10^{-2} M)-induced contractile responses after pre-loading with 10~40 μg/ml of β-eudesmol were inhibited by 71~27% of their corresponding control

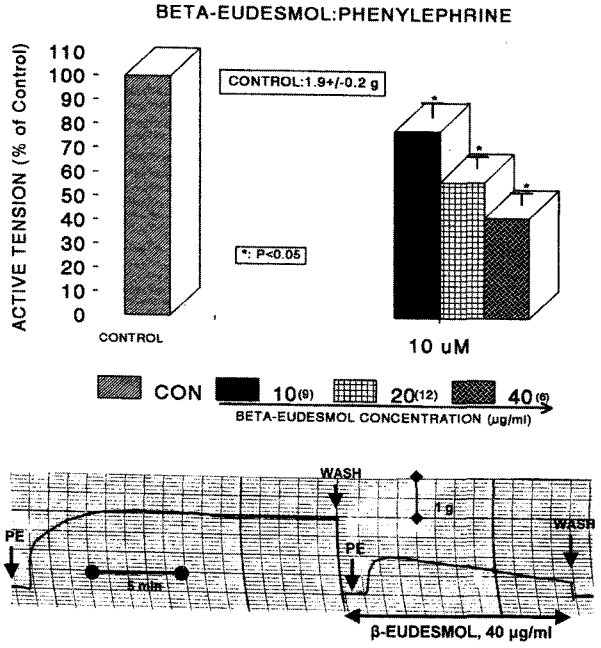

Fig. 5. Upper: Influence of β-eudesmol on phenylephrine (PE)-induced contractile response in the isolated rat aortic strips. The contractile response was induced by adding 10 M of PE after adaptation with normal Krebs solution for two hours prior to initiation of the experimental protocol. "CONTROL" denotes active tension induced evoked by PE before adding β-eudesmol (100%). Ordinate: the active tension (% of control). Abscissa: concentration of PE (μM). Statistical difference was obtained by comparing the control with the β-eudesmol-pretreated groups (10, 20 and 40 μg/ml). **Lower:** The typical tracing showing the effect of β-eudesmol on phenylephrine (PE)-induced contractile responses in the rat aortic strip. Left panel: PE-induced contractile response (Control). Right panel: PE-induced contractile response in the presence of 40 μg/ml of β-eudesmol. At arrow mark, the indicated dose (10 M) of PE was added to the bath. The chart speed was 5 mm/min.

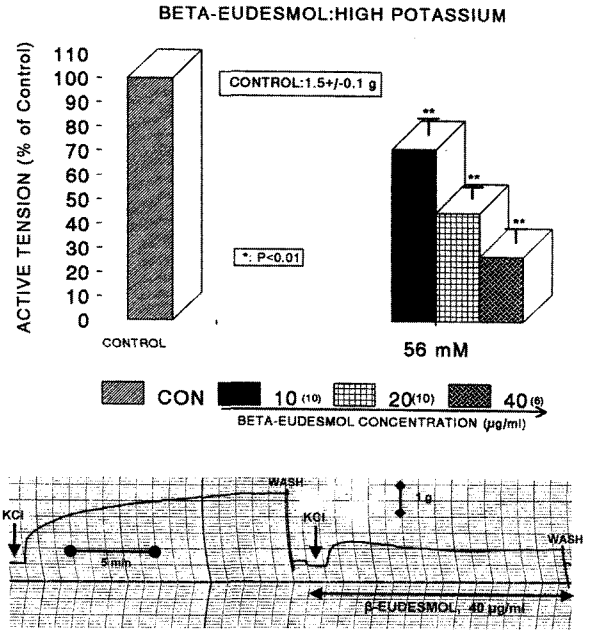

Fig. 6. Upper: Influence of β-eudesmol on high potassium-induced contractile responses in the isolated rat aorta. High potassium (56 mM) was added into the bath before and after pretreatment with 10, 20 and 40 μg/ml of β-eudesmol, respectively. Other legends are the same as in Fig. 5. **Lower:** The typical tracing showing the effect of β-eudesmol on high potassium (KCl)-induced contractile responses in the rat aortic strip. Left panel: KCl-induced contractile response (Control). Right panel: KCl-induced contractile response in the presence of 40 μg/ml of β-eudesmol. At arrow mark, the indicated dose of KCl (56 mM) was added to the bath. The chart speed was 5 mm/min.

responses in a dose-dependent fashion, respectively.

Discussion

The present experimental results demonstrate that intravenous β-eudesmol causes a dose-dependent depressor action in the anesthetized rat. It seems that β-eudesmol also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic α_1-receptors, in addition to the unknown mechanism of the direct vasorelaxation. Taken together with previous result, it seems that there is no difference in mode of action between bornyl acetate and β-eudesmol.

In support of this idea, one of active ingredients contained in *Magnolia obovata* Thunberg, terpenoid, bornyl acetate, greatly inhibited ACh-evoked secretion, but it only slightly suppressed high K^+-induced secretion in the cultured bovine adrenal chromaffin cells (Tachikawa *et al.*, 2000). This is the first report showing the effect of β-eudesmol on nervous systems. Accordingly, honokiol and bornyl acetate are probably at least active ingredients responsible for the inhibition of ACh-evoked catecholamine secretion by the extract of magnolia bark. However, amounts of β-eudesmol (above 13 μM) and magnolol (above 84 μM) sufficient to inhibit secretion are contained in the magnolia bark extract used in this study (above 400 μg/ml). In terms of these findings, the results obtained from the present study seem likely that β-eudesmol can cause the depressor effect. Moreover, The bark of *M. obovata* Thunberg is prescribed in many Chinese traditional medicines against anxiety. Actually, the extract of magnolia bark with ester has been reported to show depressant actions on the central nervous system, i.e. sedation, loss of righting reflex, and depression of drug-induced convulsions (Watanabe *et al.*, 1973). It has been demonstrated that the crude extract obtained by hot water treatment of magnolia bark, which contains both hydrophilic and hydrophobic substances, inhibited the secretion of catecholamines from bovine adrenal chromaffin cells stimulated by ACh (Tachikawa *et al.*, 2000). This suggests that magnolia bark contains some effective ingredients inhibiting the activity of the sympathetic nervous system in addition to suppressing that of the central nervous system. This inhibition seems likely to be relevant to vasorelaxant effect of β-eudesmol.

In general, among drugs that interfere with peripheral sympathetic function, adrenergic α-receptor blocking agents alone cause reversal of the epinephrine pressor response (Constantine *et al.*, 1973). When epinephrine is administered to untreated animals, its α-agonist properties predominate, resulting in a rise in mean arterial pressure. However, in the presence of adrenergic α-receptor blockade, the peripheral β_2-agonist properties of epinephrine predominate and a fall in arterial pressure or reversal of the pressor response is observed. In contrast, the pressor responses to norepinephrine are impaired by adrenergic α-receptor blockade, but are not reversed (Freis *et al.*, 1951) as this agent processes little β_2-agonist activity (Ablad *et al.*, 1975). In terms of the fact that phenylephrine-evoked contractile response is greatly depressed by β-eudesmol and also β-eudesmol-induced depressor responses were blocked by the pretreatment with phentolamine, an adrenergic α_1-blocker , it is thought that β-eudesmol has vascular dilatatory activity through the adrenergic α-receptor blockade. Moreover, in the present work, the finding that β-eudesmol attenuated the norepinephrine-induced pressor responses demonstrates that β-eudesmol possesses the antagonistic activity of adrenergic α_1-receptors.

Generally, it is well known that potassium chloride (KCl) opens voltage-dependent calcium channels by depolarizing the cell membrane of vascular smooth muscle, resulting in increased influx of extracellualr Ca^{2+} (Bolton, 1979; Schwartz & Taira, 1983; Dube *et al.*, 1985; 1988). Kim and his colleagues (1989) have shown that the contractile responses of vascular smooth muscle induced by $CaCl_2$ and KCl may result most likely from increased influx of extracellular Ca^{2+} through the voltage-dependent calcium channels. In terms of these results, the present findings that β-eudesmol inhibited the contraction of rat aortic smooth muscle evoked by not only phenylephrine (an α_1-adrenergic receptor agonist) but also by KCl (a membrane depolarizer) indicate that the vascular relaxation of β-eudesmol is mediated by the blockade of α_1-adrenergic receptors, in addition to the unknown mechanism of direct action.

In previous studies, three cellular mechanisms have been proposed to explain relaxant response of vascular smooth muscle: (i) blockade of extracellular Ca^{2+} entry into cells (Fleckenstein, 1977; Schwartz & Triggle, 1984), (ii) increase in binding or sequestration of intracellular Ca^{2+} (Watkins & Davidson, 1980; Imai & Kitagawa, 1981), and (iii) inhibiting the release of intracellular stored Ca^{2+} (Imai & Kitagawa, 1981; Ito *et al.*, 1980a; 1980b). In contrast, the contractions of vascular smooth muscles induced by neurohumoral agents have been composed of two components: Phasic contraction induced by the Ca^{2+} released from inside the cell and tonic tension related to the Ca^{2+} influx (Bevan, 1982; Dube *et al.*, 1988), both leading to increased intracellular calcium. In the light of these findings, it could not be ruled out

that β-eudesmol can dilate the contractile responses of vascular smooth muscle evoked by phenylephrin through the blockade of extracellular Ca^{2+} entry into the muscle cells. Furthermore, Tachikawa and his co-workers (2000) have found that β-eudesmol and honokiol (1-100 and 20-100 ìM), which are active components derived from *Magnolia obovata* Thunberg, inhibited the ACh-induced Na^+ influx in the cultured bovine adrenal chromaffin cells. Also, β-eudesmol (5-10 μM) diminished both ACh (at 50 μM)-induced and high K^+-induced $^{45}Ca^{2+}$ influxes.

On the other hand, a mixture of β-eudesmol and hinesol was shown to act as a sedative, to prolong sleep induced by hexobarbital, and to have anti-convulsive effects in mice exposed to electrical stimulation (Yamahara *et al.*, 1977). The mechanism by which β-eudesmol mediated these effects has been partially clarified. Thus, Satoh *et al.* (1992) showed that β-eudesmol inhibited Na^+, K^+-ATPase activity, whereas Kimura *et al.* (1991) demonstrated that it acted as a channel blocker for the nicotinic acetylcholine receptor in skeletal muscle cells. Furthermore, Tachikawa *et al.* (2000) showed that acetylcholine-induced catecholamine secretion from bovine adrenal chromaffin cells was suppressed by β-eudesmol through inhibition of Ca^{2+} influx. α-Eudesmol, a structural isomer of β-eudesmol, was also shown to be a P/Q-type Ca^{2+} channel blocker (Asakura *et al.*, 2000). Based on these reports, it seems that β-eudesmol has several pharmacological actions, which are relevant to Ca^{2+} channel blockade.

Collectively, these experimental results demonstrate that intravenous β-eudesmol causes a dose-dependent depressor action in the normotensive anesthetized rat at least partly through the blockade of adrenergic α-receptors. β-Eudesmol also causes vascular relaxation in the isolated aortic strips of the rat via the blockade of adrenergic α_1-receptors, in addition to the unknown direct vasorelaxation. Taken together with previous result, it seems that there is no difference in mode of action between bornyl acetate and β-eudesmol.

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