Effects of the Dietary Flavonoid Chrysin in Isolated Rat Mesenteric Vascular Bed

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Chrysin · Flavonoids · Mesenteric resistance vascular bed · NO · cGMP · Endothelium-derived hyperpolarizing factor

Abstract
In the present study, the effects of the bioflavonoid chrysin (5,7-dihydroxyflavone) were analyzed on the perfusion pressure of isolated mesenteric vascular bed. The vasorelaxant effects of chrysin were more potent on intact endothelium than on denuded vessels. This endothelium-dependent response induced by chrysin was inhibited in the presence of NG-nitro-L-arginine methyl ester (L-NAME), KCl, tetraethylammonium (TEA), BaCl2, TEA plus L-NAME, and ouabain plus BaCl2, while incubations with indomethacin and glibenclamide did not modify the response induced by this bioflavonoid. Neither gap junction inhibition with carbenoxolone nor epoxyeicosatrienoic acid synthesis inhibition with sulfaphenzazole (selective CYP 2C/3A inhibitor) or 7-ethoxyresorufin (selective CYP 1A inhibitor) inhibited the chrysin-induced relaxation. Moreover, chrysin increased L-NAME-sensitive cGMP accumulation in intact vascular mesenteric preparation. In conclusion, chrysin shows vasodilator effects on resistance vessels, which depend partially on the functional endothelium and appear to be related to the NO/cGMP pathway and, possibly to the release of endothelium-derived hyperpolarizing factor.

Introduction
Flavonoids comprise a large group of polyphenolic compounds [1]. The flavone chrysin (5,7-dihydroxyflavone) (fig. 1) is present in honey and propolis [2] and in low concentrations in fruits, vegetables and beverages [3]. Most flavonoids have been reported to modulate the vascular tone [4–9]. In vitro experiments in isolated rat aorta have revealed that chrysin was able to induce endothelium and NO-dependent vasorelaxation, mediated by the prevention of superoxide anion (O\textsuperscript{2-})-induced inactivation of endothelium derived NO and also by the potentiation of guanosine 3’,5’-cyclic monophosphate (cGMP)-induced vasodilatation [10]. In addition, it has been recently reported that chrysin exerts antihypertensive effects, reduces left ventricular hypertrophy and endothelial dysfunction in spontaneously hypertensive rats [11]. Further-
more, to our knowledge there is no information about the effects of chrysin in resistance arteries. Therefore, in the present study we have analyzed the vasodilator effects of this flavone in rat resistance vascular bed tone and further characterized the mechanism of its vascular smooth muscle-relaxant effect.

**Methods**

**Isolated Perfused Mesenteric Bed**

The isolated perfused mesentery of the rat was prepared by the method of McGregor [12]. Briefly, male Wistar rats (250–300 g), were killed by a blow on the head and then exsanguinated. The superior mesenteric artery was rapidly cannulated and the mesenteric vascular bed perfused via the artery for 5 min (2 ml/min) with warm (37 °C) and gassed (95% O2-5% CO2) Krebs buffer of the following composition (in mM): NaCl 118, KCl 5, NaHCO3 25, MgSO4 1.2, CaCl2 2, KH2PO4 1.2 and glucose 11 at pH 7.4, containing heparin (100 U/ml). The ileocolic and colic branches of the superior mesenteric artery were ligated. The intestine was separated from the mesentery and the preparation was supported on a Petri dish and the arteries perfused at a constant flow of 2 ml/min with Krebs buffer without heparin [13]. Changes in the perfusion pressure were measured with a pressure transducer placed approximately 15 cm from the tip of the cannula. The preparation was allowed to equilibrate for 30–45 min and its viability was checked by a bolus injection of 60 μmol KCL. Then, the preparation was perfused with phenylephrine (50 μM), which induced a sustained increase in perfusion pressure and a concentration-response curve was constructed by perfusing with increasing concentrations (0.1–100 μM) of the flavonoid. In some experiments, mesenteric beds were preincubated with the NO synthase inhibitor L-NAME (100 μM), the cyclooxygenase inhibitor indomethacin (10 μM), or a mixture of both drugs, prior to the addition of chrysin. In other mesenteric bed preparations, the potassium channel blockers tetraethylammonium (TEA, 3 mM, alone or with L-NAME), KCl (30 mM, with isotonic replacement by NaCl), BaCl2 (1 mM), glibenclamide (1 μM), BaCl2 (100 μM) or the mixture BaCl2 (100 μM) plus ouabain (10 μM), were added to the phenylephrine solution. We also analyzed the effect of the gap junction inhibitor carbenoxolone (100 μM), and the epoxyeicosatrienoic acid (EET) synthesis inhibitors, sulfaphenazole (10 μM) and 7-ethoxyresorufin (3 μM), selective blockers of cytochrome P450 (CYP) 2C/3A and CYP 1A, respectively, on chrysin-mediated relaxation. In another group of preparations, endothelium removal was attained by perfusing with sodium deoxycholate (0.3% in distilled water) for 30 s [14] and then the preparation was allowed to equilibrate for another 30 min. Cumulative addition of vehicle (DMSO) did not have significant effect (4 ± 6% relaxation at the highest concentration of DMSO tested, n = 3). The functional endothelium removal procedure was verified in all preparations by the lack of relaxant effect of a bolus of ACh (10 nmol).

**Determination of cGMP Production in Mesenteric Bed**

Intact vascular mesenteric beds were dissected and incubated for 20 min in the absence or presence of chrysin (50 μM). Incubations were performed either alone or with L-NAME (100 μM) in Krebs solution bubbled with 95% O2-5% CO2 gas mixture and kept at 37 °C. When used, L-NAME was added 15 min before the exposure to chrysin. In parallel, the same protocol was performed on some mesenteric beds without endothelium. The reaction was stopped by the addition of ice-cold HCl (0.1 N), and in any case, the tissue was homogenized in 0.3 ml of 6% trichloroacetic acid and the homogenate centrifuged at 2000 g for 15 min. The pellet was used to determine the protein content of the tissue, following the method of Bradford [15]. The supernatant was extracted four times with 5 volumes of diethyl ether, and then desiccated in N2 atmosphere at 60 °C. cGMP content was determined using an enzyme immunoassay kit (Amersham Pharmacia Biotech, Buckinghamshire, UK). Results are expressed as fmol cGMP/mg of protein of the vascular mesenteric tissue.

**O2− Measurement in Mesenteric Arteries**

O2− release in intact main mesenteric artery segments was quantified by lucigenin chemiluminescence, as previously described by O’Hara et al. [16]. Rat isolated mesenteric vascular bed was immediately removed and placed in ice-cold Krebs buffer. The main mesenteric artery was then cleaned of adherent adventitial adipose tissue and cut into rings 2–3 mm in length. Rinsed rings were incubated for 30–60 min at 37 °C in HEPES-containing physiological salt solution (pH 7.4) of the following composition (in mM): 119 NaCl, 20 HEPES, 4.6 KCl, 1 MgSO4, 0.15 Na2HPO4, 0.4 KH2PO4, 5 NaHCO3, 1.2 CaCl2, and 5.5 glucose. The vascular O2− production was stimulated by addition of NADPH (100 μM). Incubations were performed in the presence of chrysin (50 μM) or vehicle (DMSO). Rings were then placed in tubes containing physiological salt solution in the presence of chrysin or DMSO, and with or without NADPH. Lucigenin was injected automatically at a final concentration of 5 μM. Changes in O2− release were determined by measuring luminescence over 200 s in a scintillation counter (Lumat LB 9507, Berthold, Germany) in 5-second intervals. O2− release is expressed as relative luminescence units/min/mg of wet weight vascular tissue.

**Drugs**

All drugs used were of analytical grade and were purchased from Sigma Chemical (Alcobendas, Madrid, Spain). Stock solutions of chrysin and glibenclamide were prepared in DMSO, and indomethacin was dissolved in a sodium carbonate (2 mM) solution. All other drugs were prepared in distilled deionized water, and further dilutions were made in Krebs solution.

**Analysis of Results**

Results are expressed as means ± SEM of measurements in n preparations from different animals. The −logIC50 drug concentration that inhibited 50% of the contractile response, was calculated in...
Table 1. Vasorelaxing effect of chrysin (0.1–100 μM) in different experimental conditions in rat vascular mesenteric bed precontracted by phenylephrine (50 μM)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>n</th>
<th>Perfusion pressure mmHg</th>
<th>Chrysin –log IC_{50}</th>
<th>E_{max}, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (+E)</td>
<td>12</td>
<td>46.2 ± 4.5</td>
<td>5.91 ± 0.12</td>
<td>100 ± 1.0</td>
</tr>
<tr>
<td>Control (-E)</td>
<td>8</td>
<td>42.5 ± 5.9</td>
<td>4.98 ± 0.09**</td>
<td>88.5 ± 5.3**</td>
</tr>
<tr>
<td>L-NAME (+E)</td>
<td>10</td>
<td>82.1 ± 4.7</td>
<td>5.53 ± 0.12*</td>
<td>92.8 ± 6.0</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>5</td>
<td>33.7 ± 5.2</td>
<td>5.87 ± 0.18</td>
<td>95.7 ± 2.8</td>
</tr>
<tr>
<td>Indomethacin + L-NAME</td>
<td>5</td>
<td>78.1 ± 10.5</td>
<td>5.27 ± 0.06**</td>
<td>95.0 ± 4.0</td>
</tr>
<tr>
<td>KCl (+E)</td>
<td>6</td>
<td>65.1 ± 11.6</td>
<td>5.12 ± 0.09**</td>
<td>89.5 ± 2.5**</td>
</tr>
<tr>
<td>KCl (-E)</td>
<td>5</td>
<td>49.3 ± 10.8</td>
<td>4.76 ± 0.03**</td>
<td>91.8 ± 4.0*</td>
</tr>
<tr>
<td>TEA</td>
<td>5</td>
<td>51.0 ± 9.9</td>
<td>5.46 ± 0.05*</td>
<td>98.4 ± 1.7</td>
</tr>
<tr>
<td>TEA + L-NAME</td>
<td>8</td>
<td>97.7 ± 11.6</td>
<td>5.29 ± 0.21**</td>
<td>96.0 ± 2.0</td>
</tr>
<tr>
<td>BaCl₂ (1 mM)</td>
<td>4</td>
<td>62.7 ± 1.9</td>
<td>5.15 ± 0.15**</td>
<td>90.0 ± 2.0*</td>
</tr>
<tr>
<td>BaCl₂ (100 μM)</td>
<td>5</td>
<td>51.4 ± 6.4</td>
<td>5.47 ± 0.12*</td>
<td>91.0 ± 3.0*</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>6</td>
<td>35.9 ± 7.0</td>
<td>5.89 ± 0.18</td>
<td>100 ± 1.0</td>
</tr>
<tr>
<td>BaCl₂ (100 μM) + ouabain</td>
<td>8</td>
<td>42.0 ± 6.1</td>
<td>5.44 ± 0.12*</td>
<td>95.5 ± 0.1</td>
</tr>
<tr>
<td>Carbenoxolone</td>
<td>6</td>
<td>34.6 ± 2.4</td>
<td>6.29 ± 0.12*</td>
<td>100 ± 2.0</td>
</tr>
<tr>
<td>Carbenoxolone + indomethacin</td>
<td>6</td>
<td>76.2 ± 7.5</td>
<td>5.97 ± 0.19</td>
<td>100 ± 1.0</td>
</tr>
<tr>
<td>+ L-NAME</td>
<td>7</td>
<td>39.1 ± 4.4</td>
<td>5.58 ± 0.17</td>
<td>100 ± 0.9</td>
</tr>
<tr>
<td>Sulfaphenazole</td>
<td>7</td>
<td>80.9 ± 9.8</td>
<td>5.50 ± 0.12**</td>
<td>92.0 ± 6.1</td>
</tr>
</tbody>
</table>

+E = with endothelium; –E = without endothelium. When not indicated, experiments were performed with endothelium. L-NAME: NG-nitro-L-arginine methyl ester; TEA = tetraethylammonium. –log IC_{50} = concentration (–log molar) that inhibits 50% of the contractile response; E_{max} = maximal relaxation. Concentrations of the different drugs used are described in the Methods section. Results are expressed as means ± SEM of n experiments.

* p < 0.05, ** p < 0.01 vs. control with endothelium, + p < 0.05 vs. L-NAME (+ E).

**Results**

**Flavonoid-Induced Vasodilatation in Rat Resistance Arteries**

Phenylephrine (50 μM) induced a sustained vasoconstriction increasing pressure perfusion in vascular mesenteric bed (table 1). Chrysin induced a concentration-dependent relaxation in precontracted vessels (the –logIC_{50} values are shown in table 1). Addition of chrysin concentration, up to 50 μM, had no effect on baseline perfusion pressure in the mesenteric bed (n = 3–4).

**Endothelial Dependence**

The vasodilator effects of chrysin were analyzed in deoxycholate-denuded mesenteric beds compared with intact vessels. Endothelial removal did not affect the maximal contractile response to phenylephrine (table 1). Anyway, the relaxant response to ACh (10 nmol) was almost abolished (69.3 ± 5.3% and 9.0 ± 3.6% before and after deoxycholate treatment, respectively, n = 9; p < 0.01). In precontracted mesenteric bed, chrysin induced a concentration-dependent relaxant response, which was inhibited (7- to 8-fold shift of the curve to the right) by removal of the endothelium (fig. 2, table 1).

L-NAME (100 μM) partially inhibited the endothelial component of the chrysin-induced relaxation in mesenteric bed (fig. 2, table 1). Pretreatment of endothelium-intact mesenteric bed with indomethacin (10 μM) did not change the vasorelaxant effect of chrysin (table 1). Moreover, pretreatment with L-NAME plus indomethacin evoked similar inhibitory effect in the relaxation induced by chrysin than L-NAME alone. When the mesenteric
Fig. 2. Concentration-response curves of chrysin in phenylephrine (50 μM)-precontracted mesenteric beds without (●) or with functional endothelium (○) and in the presence of Nω-nitro-L-arginine methyl ester (L-NAME) (100 μM) (□). Histograms represent the vasodilator response induced by a bolus of acetylcholine (ACh, 10 nmol). +E = with endothelium; –E = without endothelium. Results represent means ± SEM of 8–12 experiments. *p < 0.05, ** p < 0.01 vs. control with endothelium.

Fig. 3. Concentration-response curves of chrysin in phenylephrine (50 μM)-precontracted mesenteric beds without functional endothelium (dashed line) and with (●) or without endothelium (■) in the presence of 30 mM KCl. Histograms represent the vasodilator response induced by a bolus of acetylcholine (ACh) (10 nmol). –E: without endothelium; +E: with endothelium. Data represent means ± SEM of 5–12 experiments. ** p < 0.01 vs. preparations with endothelium.

beds were stimulated by phenylephrine in Krebs solution containing 30 mM KCl, the concentration-response curve to chrysin was shifted to the right (table 1, fig. 3), abolishing its endothelium-dependent vasodilatation. In preparations without endothelium, membrane depolarizations with 30 mM KCl, partially inhibited the chrysin-induced relaxation (fig. 3).

Effect of K⁺ Channel Blockers in the Vasorelaxant Effect of Chrysin

Pretreatment of endothelium intact preparations with 3 mM TEA and 1 mM of BaCl₂, two non-selective K⁺ channels blockers, and 100 μM of BaCl₂, which blocks selectively the Kᵢₑ channel, produced a rightward shift of the concentration-response curve to chrysin. Previous incubation with L-NAME plus TEA abolished the endo-
Vascular Effects of Chrysin

Role of Gap Junction and EETs in the Vasorelaxant Effect of Chrysin

Inhibition of myoendothelial gap junctional communication by mesenteric bed perfusion with carbenoxolone significantly reduced the vasoconstrictor effect of phenylephrine and potentiated the vasorelaxant response induced by chrysin, even in the presence of L-NAME plus indomethacin. In contrast, carbenoxolone had no effect on ACh-induced vasodilation either in the presence or absence of L-NAME plus indomethacin (table 1).

Inhibition of endothelial EET synthesis by incubation with the CYP 2C/3A inhibitor sulfaphenazole did not modify chrysin-induced vascular mesenteric relaxation. Mesenteric bed perfusion with the CYP 1A inhibitor 7-ethoxysresorufin did not increase the inhibitory effects of L-NAME plus indomethacin on ACh- or chrysin-induced relaxation (table 1).

Effect of Chrysin in cGMP Content

In mesenteric vascular beds with a functional endothelium, chrysin (50 µM) produced an increase in the cGMP content, which was abolished by L-NAME (100 µM). However, no significant differences in the cGMP content were observed in endothelium-denuded preparations incubated with and without chrysin (fig. 5).

Effects of Chrysin on NADPH Oxidase-Generated O₂⁻

Chrysin had no effect on basal mesenteric chemiluminescence generated by the reaction of O₂⁻ with lucigenin...
Fig. 6. Superoxide anion production measured with 5 μM lucigenin in main mesenteric artery incubated with DMSO or chrysin 50 μM in basal or NADPH 100 μM stimulated conditions. Each bar represents mean ± SEM of 6–15 experiments.* p < 0.05 vs. mesenteric rings incubated with DMSO.

Addition of NADPH (100 μM) increased mesenteric luminescence by about 3.2 fold, and under such conditions, chrysin (50 μM) prevented NADPH-induced rise in mesenteric luminescence by about 42% (p < 0.05).

Discussion

Previous reports have shown that chrysin exhibits endothelium- and NO-dependent vasodilator effects in isolated rat aorta [10]. In the present study we confirm this evidence in resistance arteries. Moreover, endothelium-mediated effects of chrysin in mesenteric vascular beds are related to endothelial NO production and L-NAME-sensitive increase on vascular smooth muscle cGMP levels, and the release of an endothelium-derived hyperpolarizing factor (EDHF) could also be involved in such effects.

Resistance arteries are responsible for the regulation of arterial pressure and local blood flow.

In a previous work, we demonstrated that a daily oral dose (20 mg/kg) of chrysin for 6 weeks reduced the elevated blood pressure in spontaneously hypertensive rats [11]. In the present study, chrysin concentrations of 0.1–1 μM produced significant vasodilator responses in isolated mesenteric beds. Taking into consideration the oral bioavailability of this flavonoid (0.003–0.02%) and its half-life of elimination (t_{1/2} = 4.6 h) [17], this range of concentrations could be reached in plasma after a long-term chrysin treatment. This vasodilator effect on resistance vessels might contribute to its antihypertensive effect.

The mechanisms involved in the endothelium-dependent vasorelaxant effect induced by chrysin were previously analyzed in the rat aorta [10]. This effect was mediated by the prevention of O_{2}^{-}-induced inactivation of endothelium derived NO under oxidative stress conditions (such as in the presence of hypoxanthine/xanthine oxidase or pyrogallol) and also by the potentiation of cGMP-induced vasodilation. However, changes in cGMP levels induced by chrysin when vessels are incubated in a normal medium have never been analyzed. NO induces most of its biological effects through the activation of soluble guanylate cyclase thus increasing cGMP [18]. In the present paper, we found that chrysin increased cGMP vascular mesenteric accumulation only in vessels with intact endothelium, an effect which was suppressed by nitric oxide synthase inhibition with L-NAME. Several studies have shown that flavonoids, such as chrysin, can inhibit cyclic nucleotide phosphodiesterases, a family of enzymes involved in the breakdown of the vasorelaxant cyclic nucleotides [19–20]. However, the increase in cGMP levels induced by chrysin seemed to be unrelated to the inhibition of cyclic nucleotide phosphodiesterases, since chrysin was unable to elevate cGMP levels in endothelium-denuded vascular mesenteric beds. These findings confirm that chrysin released NO from endothelial cells, leading to vascular cGMP accumulation and endothelium-dependent relaxation. We also found that chrysin reduced aortic O_{2}^{-} production only on NADPH-stimulated rings, suggesting no involvement of O_{2}^{-} in the endothelial NO increase evoked by chrysin under unstimulated conditions. The mechanisms by which chrysin stimulates NO production remains unknown.

Chrysin induced a relaxant response in precontracted mesenteric bed that was inhibited by the removal of endothelium, indicating the essential role of endothelium-derived factors for its vasodilator effect. The NO synthase inhibitor, L-NAME, inhibited this relaxation in the rat aorta to a similar extent as the removal of endothelium [10]. However, in the vascular mesenteric bed, L-NAME, at the concentration that abolished the rise of cGMP levels induced by chrysin, only partially inhibited the endothelial component of the chrysin-induced relaxation, suggesting the involvement of other endothelial factor/s in addition to NO.

Blockade of cyclooxygenase by indomethacin did not affect chrysin-induced relaxation, demonstrating that prostacyclins do not account for the vasorelaxant effect of chrysin in mesenteric arteries. It is well known that in this
type of vessels there is an additional component to endothelium-dependent relaxation that has been attributed to the EDHF [21]. Changing the bath from normal Krebs solution containing 5 mM KCl to 30 mM is known to blunt the vasorelaxant effect of EDHF [22]. When the vasorelaxant effect of chrysin was assessed in Krebs solution containing 30 mM KCl, a shift to the right of the concentration-response curve to chrysin was observed, suggesting the involvement of EDHF in the vasorelaxant effect of this flavonoid. However, the presence of 30 mM KCl in the Krebs solution also inhibited endothelium-independent relaxation induced by chrysin in vascular mesenteric bed, suggesting that the activation of K + channels, in an independent way to EDHF, might be involved in the effect of chrysin in vascular smooth muscle.

To analyze the role of K + channels, intact mesenteric beds were incubated with nonselective K + channel blockers, TEA and BaCl2 (1 mM). The endothelium-dependent vasorelaxant effect was inhibited in the presence of BaCl2 in a similar extent to the endothelium-independent one, while it was partially inhibited in the presence of TEA. Anyway, neither of the drugs managed to modify the ACh-relaxant response. The absence of TEA effect on the vasorelaxant effect induced by ACh is related to its low selectivity for KCa channels [23], which are involved in EDHF vasodilation.

When mesenteric beds were incubated with L-NAME and TEA to block the available endothelium-derived factors responsible for the relaxation induced by chrysin, we observed that its effects were the sum of the effects of the drugs in isolation, inhibiting the endothelium-dependent vasorelaxation. However this combination of inhibitors produced the same reduction than the incubation with only L-NAME in the ACh-induced relaxant response, confirming that TEA was unable to inhibit the EDHF effects in our experimental condition. These results suggest the participation of NO and, possibly, K + channels in the chrysin relaxant effect.

We have investigated the role of the different K + channels on the chrysin vasodilator effect. The incubation with glibenclamide did not modify the relaxation induced by either chrysin or ACh, showing that KATP channels are not involved in its effects. K + , EETs and gap junctions seem to be important for EDHF-mediated effects. Based on the hypothesis that EDHF is efflux of K + through the endothelial SKCa and IKCa channels that could elicit the hyperpolarization of the surrounding myocytes by activating Kir channels and/or the Na+-K+-pump [24], we incubated the mesenteric beds with the inhibitor of Kir channels, BaCl2 (100 µM). In such conditions, the curve shifted to the right, indicating Kir channels involvement in the chrysin vasorelaxant effect. However, this agent did not modify the ACh vasorelaxant response, suggesting that EDHF needs the combined stimulations of several K + channels, because activation of each type of channels separately was unable to produce the maximal hyperpolarization and relaxation. Therefore, the mixture of BaCl2 (100 µM) plus the inhibitor of the Na+-K+-pump ouabain (10 µM) induced an important inhibition in the endothelium-mediated relaxation to concentrations of chrysin below 1 µM, greater than the one induced by BaCl2. This mixture of drugs also produced a slight inhibition of the ACh relaxation, showing its effectiveness to block EDHF effects. These results suggest the participation of Kir channels and the Na+-K + pump in the endothelium-dependent vasodilator response induced by chrysin in vascular mesenteric bed. All pharmacological strategies which inhibit EDHF-mediated response to ACh in our experimental conditions (e.g. KCl 30 mM or BaCl2 100 µM plus ouabain) also inhibited endothelium-dependent relaxation to chrysin, suggesting that this agent might release EDHF. However, the mechanisms involved in EDHF release induced by chrysin remains to be elucidated.

Neither gap junction inhibition with carbenoxolone nor EETs synthesis inhibition with sulfaphenazole (selective CYP 2C/3A inhibitor) or 7-ethoxyresorufin (selective CYP 1A inhibitor) were able to inhibit both ACh- and chrysin-induced relaxation, suggesting no involvement of myoendothelial gap junction communication and EETs in EDHF-dependent relaxation induced by ACh or chrysin in this vascular bed in our experimental conditions.

In conclusion, the present findings indicate that chrysin exerts potent vasodilator effects in isolated resistance mesenteric vascular bed. These vasodilator effects are partially mediated by the integrity of the endothelium by stimulating the endothelial formation of NO. Kir channels and the Na+-K + pump activation, possibly by EDHF release, seemed to be involved in endothelium-dependent vasorelaxant effect induced by chrysin. Vasodilation induced by this flavonoid in resistance vessels may explain its antihypertensive effects and might contribute to explain the reduction of mortality due to ischemic heart disease attributed to this dietary group of compounds in epidemiological studies.
References


