INTRODUCTION

Resveratrol is a natural polyphenolic compound that is widely present in red wines and other dietary components such as peanuts, grapes and mulberries. It has been demonstrated to have various biological activities including free radical scavenging, anti-inflammation, vasorelaxation, induction of endothelial nitric oxide synthase, and anti-cancer activity (Zbikowska and Olas, 2000). The anti-platelet effect of resveratrol has also been extensively studied, which serves as one of the major activities related with cardiovascular protective effect (Olas and Wachowicz, 2005). Indeed, resveratrol is effective against platelet adhesion to collagen or fibrinogen and granular secretion, as well as the whole procedures of aggregation (Zbikowska et al., 1999; Olas et al., 2001b). Diverse biochemical functions have been suggested as mechanisms underlying the anti-aggregatory effect of resveratrol including the inhibition of eicosanoid synthesis and phosphoinositide hydrolysis (Zbikowska et al., 1999; Olas et al., 2005; Crescente et al., 2009), the suppression of reactive oxygen species (ROS) production (Olas et al., 1999; Olas et al., 2001a), the blocking of calcium signaling (Dobrydneva et al., 1999), the stimulation of nitric oxide generation (Gresele et al., 2008), and the modulation of signaling molecules such as protein kinase C (Yang et al., 2008b), phospholipase C (Yang et al., 2008a), and p38 MAPK (Shen et al., 2007). Resveratrol exists as either the trans-isomer [(E)-resveratrol, 5-{(E)-2-(4-hydroxyphenyl)ethenyl}benzene-1,3-diol; CAS Number 501-36-0] or cis-isomer [(Z)-resveratrol, 5-{(Z)-2-(4-hydroxyphenyl)ethenyl}benzene-1,3-diol; CAS Number 61434-67-1] (Orallo, 2006) (Fig. 1). The term resveratrol has, however, generally referred to only the trans-isomer and little attention has been paid to cis-resveratrol. As a necessary consequence, most studies were done with trans-resveratrol or with an undefined mixture of both isomers, and little is known regarding the biological activities of cis-resveratrol (Orallo, 2006). Now, however, a few chemical companies have started to produce cis-isomer. There are only a limited number of reports that have examined the biological effects of cis- versus trans-resveratrol. For instance, cis-resveratrol exhibited slightly weaker effects in...
anti-cancer activity (Pettit et al., 2002) and elevated cytosolic calcium in vascular myocytes more potently (Campos-Toimil et al., 2005; Campos-Toimil et al., 2007). Recently, Rius et al. (2010) tested the inhibitory effect of cis- and trans-resveratrol against angiotensin II (AngII)-mediated vascular inflammation and found only the trans-isomer to be effective, although it is not clear whether such a result is caused by a difference in potency or is due to different mechanisms (Rius et al., 2010). Taken together, they allow us to hypothesize that the effect on platelet activity may also be different between cis- and trans-resveratrol. Hence, this study was designed and performed to investigate the effect of cis-resveratrol on platelet aggregation and to compare it with the effect of the trans-isomer.

**MATERIALS AND METHODS**

**Materials**

Both cis- and trans-resveratrol were purchased from Cayman Chemical Co. (Ann Arbor, MI, USA). Collagen and ADP were from Chrono-log Co. (Havertown, PA, USA) and thrombin was obtained from Sigma-Aldrich Co. (St. Louis, MO, USA). All other chemicals used were of the highest purity available and purchased from standard suppliers.

**Animals**

All animal experiments were conducted in accordance with protocols approved by the Ethics Committee of the Animal Service Center at Chonnam National University. Male Sprague-Dawley rats weighing 150-250 g were purchased from Daehan Biolink (Eumseong, Korea). Prior to experiments, animals were acclimated for 1 week in the laboratory animal facility and maintained at constant temperature and humidity with a 12-hr light/dark cycle. Food and water were provided ad libitum.

**Preparation of platelets and measurement of platelet aggregation**

A platelet aggregation study was performed using a 4-channel aggregometer (Chrono-log, Havertown, PA, USA) as de-