Supporting Information

Figure S1

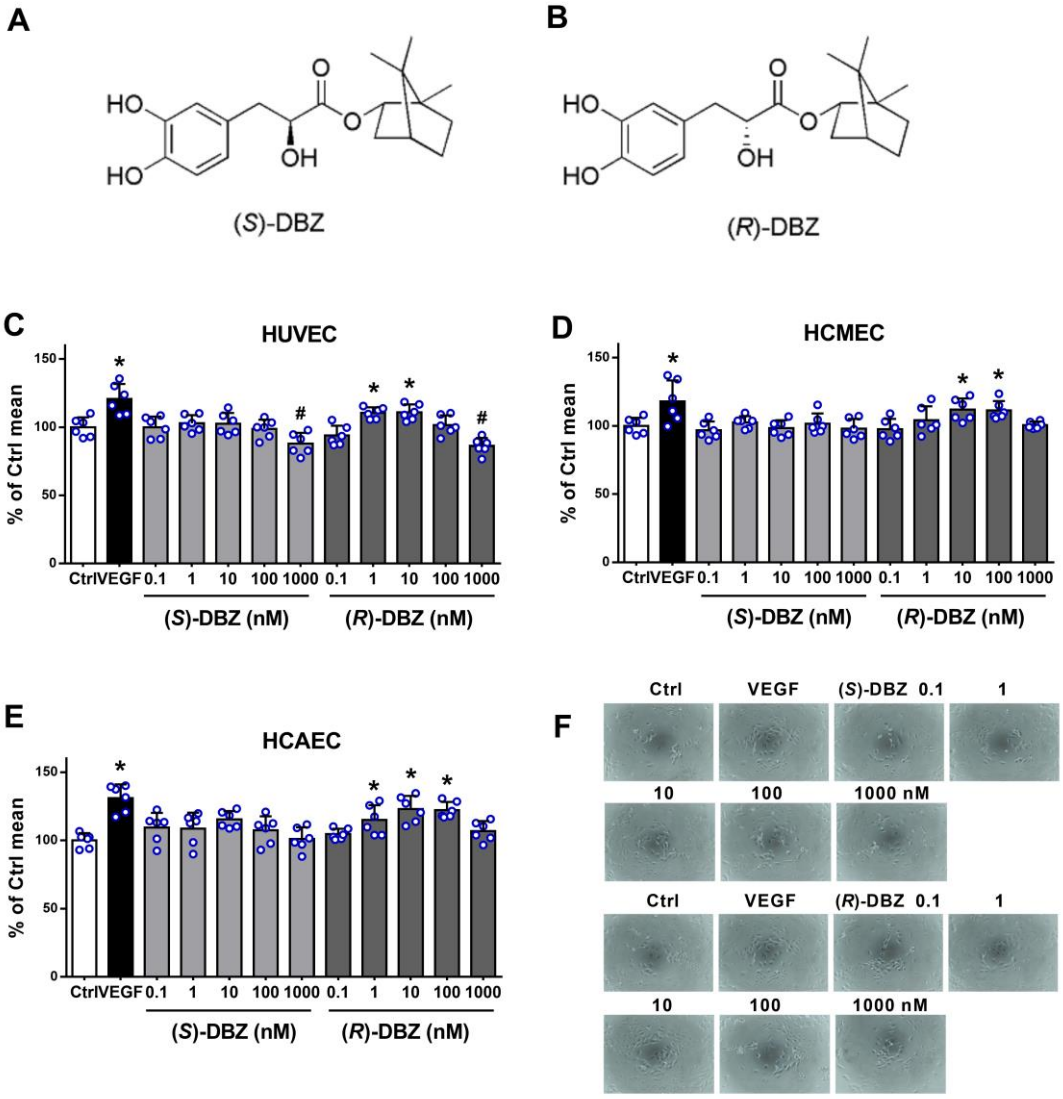

Figure S1

Chemical structure of (**A**) (*S*)-DBZ and (**B**) (*R*)-DBZ and their effects on endothelial cell proliferation. (**C**) HUVEC, (**D**) HCMEC, and (**E, F**) HCAEC were treated with increasing concentrations of (S)-DBZ or (R)-DBZ for 48 h respectively, and cell proliferation was measured by the CCK-8 assays. Cells treated with VEGF-A (20 ng ml^{-1}) served as positive controls. Data are presented as the means ± SD (n = 6 independent experiments performed in

triplicate). Statistical analyses were performed by one-way ANOVA followed by Dunnett's *post hoc* test or unpaired Student's two-tailed *t*-test. *P<0.05 *vs.* control group. HUVEC, human umbilical vein endothelial cells; HCMEC, human coronary artery endothelial cells; HCAEC, human cardiac microvascular endothelial cells.

Figure S2

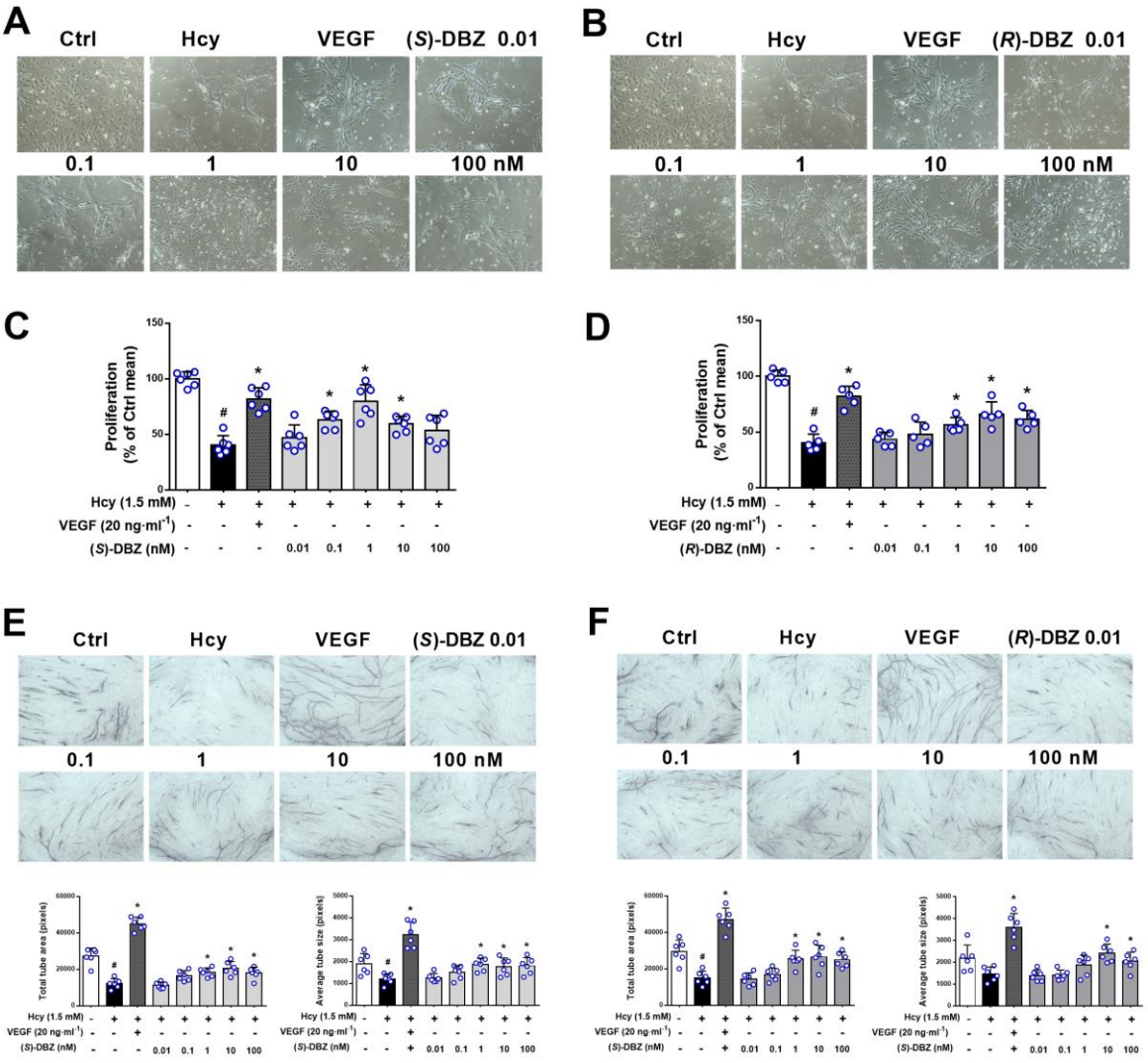

Figure S2

Effects of (*S*)-DBZ and (*R*)-DBZ on HUVEC viability and tube formation in homocysteine (Hcy)-injured model. (**A**-**D**) HUVEC were pre-treated with various concentrations of DBZ

for 2 h, and then treated with 5 mM Hcy. After 48 h of incubation, cell viability was determined by Trypan blue assays. (**E, F**) HUVEC-HDF co-culture systems were pre-treated with various concentrations of DBZ for 2 h, then treated with 1.5 mM Hcy. After 12 days of incubation, tube formation was determined by vWF immunostaining, and total tube area and average tube size was quantified by the ImageJ software. Magnification: 40×. Data are presented as the means ± SD (n = 6 independent experiments performed in triplicate for both Trypan blue assays and co-culture assays). Statistical analyses were performed by one-way ANOVA followed by Dunnett's *post hoc* test or unpaired Student's two-tailed *t*-test. $^{*}P < 0.05$ *versus* Hcy group, $^{\#}P < 0.05$ *versus* control group.

Figure S3

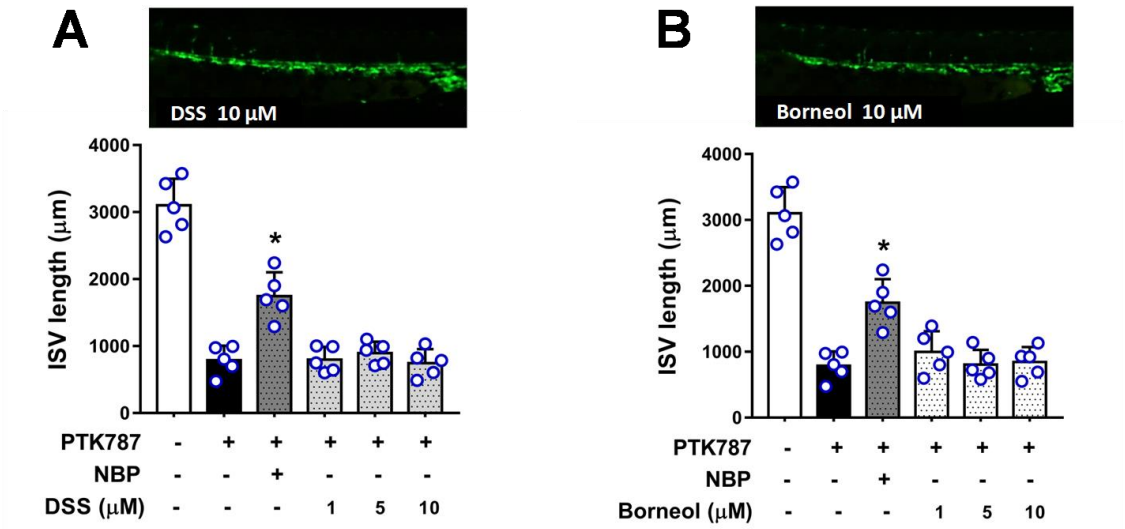

Figure S3

DSS (**A**) and borneol (**B**) have no significant effect on PTK787-induced ISV angiogenesis impairment in zebrafish embryos. Embryos were treated with PTK787, PTK787 with NBP,

PTK787 with DSS (1, 5, 10 μM) or PTK787 with borneol (1, 5, 10 μM) for 24 hs. Data were analyzed by using the ImageJ software package. Quantitative analysis indicated the total length of ISV for each group. Data are presented as the means ± SD (10 fish embryos per well from 5 time-independent experiments; n = 5). Statistical analyses were performed by one-way ANOVA followed by Dunnett's *post hoc* test. *P<0.05 *vs.* PTK787 treated group. DSS, tanshinol; NBP, butylphthalide.

Table S1: Enriched KEGG pathways of DBZ, DSS or Borneol

Term	adjusted P-value
DBZ	
hsa04068: FoxO signaling pathway	2.73E-04
hsa04066: HIF-1 signaling pathway	9.02E-04
hsa04611: Platelet activation	9.09E-04
hsa04210: Apoptosis	0.00362
hsa04530: Tight junction	0.00474
hsa04510: Focal adhesion	0.0108
hsa04015: Rap1 signaling pathway	0.0116
hsa04370: VEGF signaling pathway	0.0187
DSS	
hsa04066: HIF-1 signaling pathway	4.47E-05
hsa04068: FoxO signaling pathway	3.01E-04
hsa04210: Apoptosis	0.0211
hsa04510: Focal adhesion	0.0290
hsa04611: Platelet activation	0.0493
Borneol	
hsa04066: HIF-1 signaling pathway	1.89E-04
hsa04068: FoxO signaling pathway	8.60E-04
hsa04210: Apoptosis	0.0211