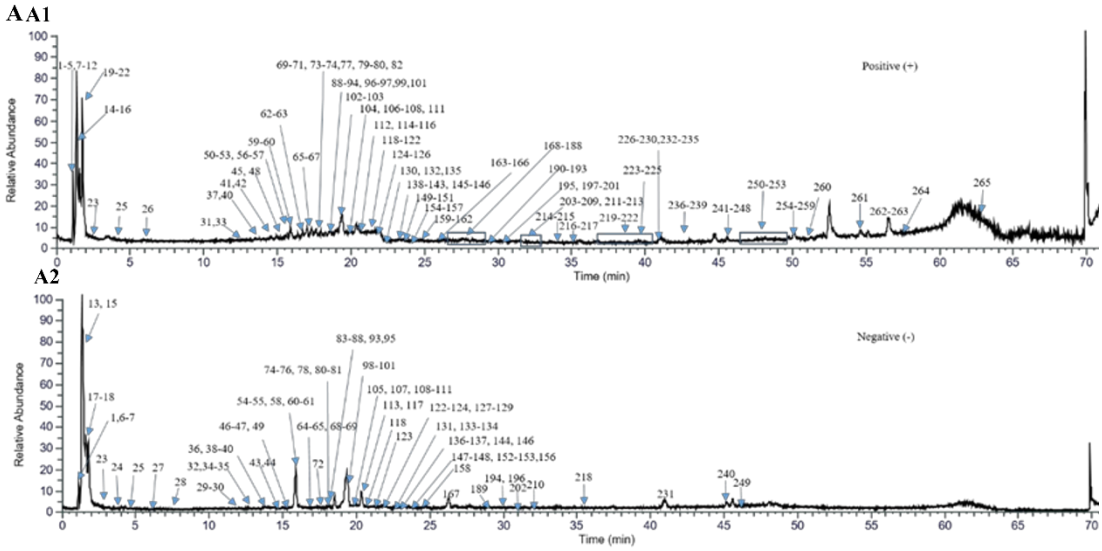
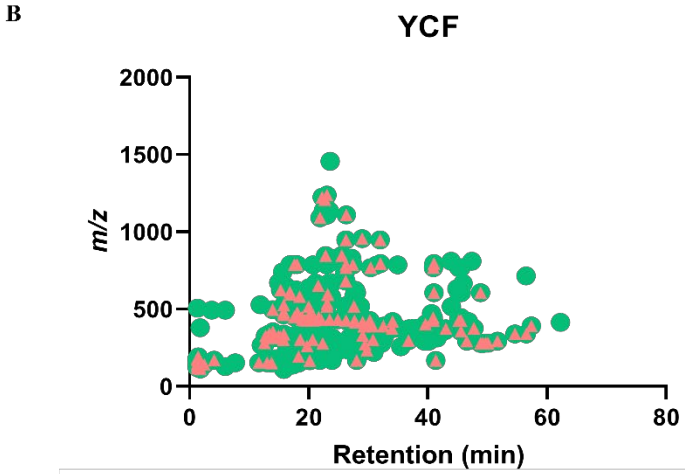
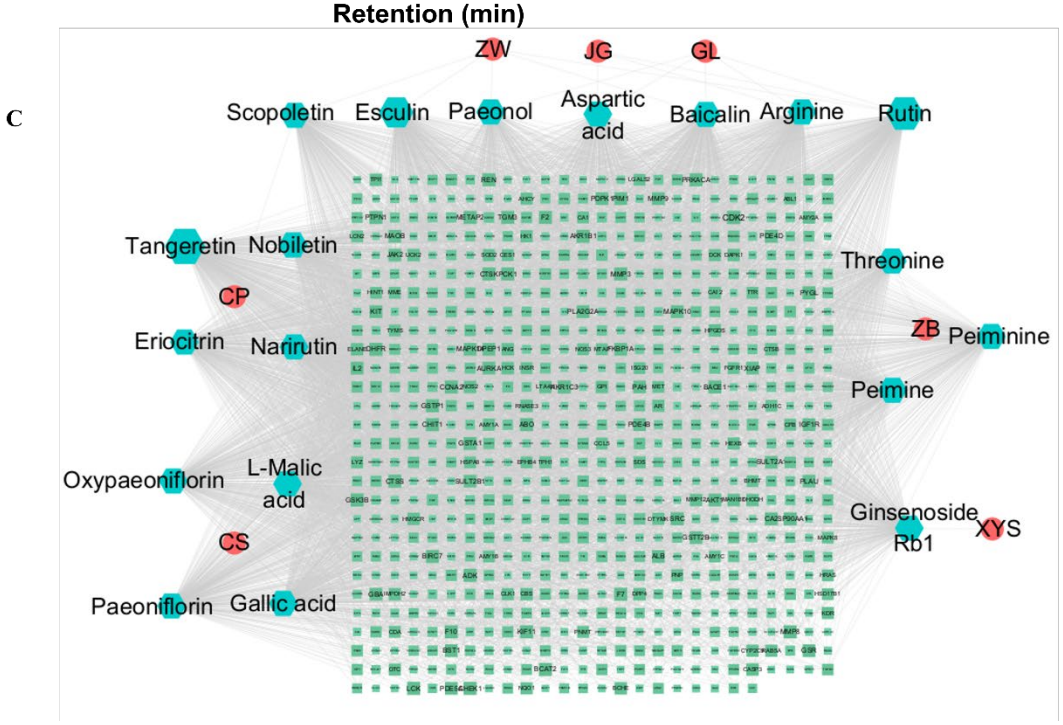
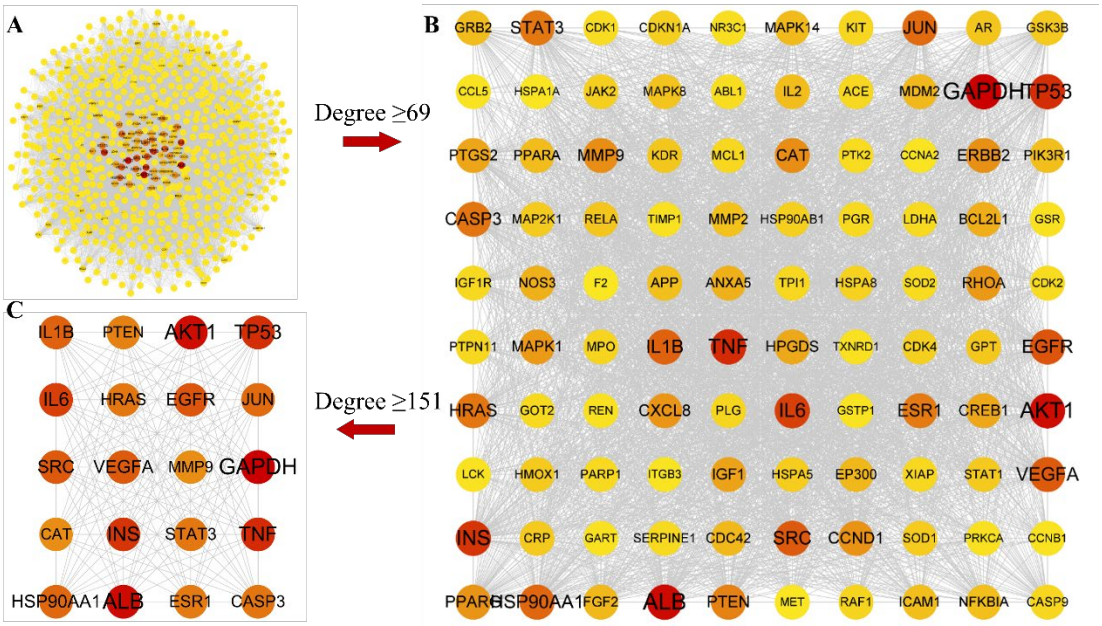

A A1
Positive (+)
Relative Abundance
Time (min)
A2
Negative (-)
Relative Abundance
Time (min)


B
YCF
m/z
Retention (min)


C
ZW
JG
GL
Scopoletin
Esculin
Paeonol
Aspartic acid
Baicalin
Arginine
Rutin
Tangeretin
Nobiletin
Threonine
CP
Eriocitrin
Narirutin
ZB
Peiminine
Peimine
Oxypaeoniflorin
L-Malic acid
Ginsenoside Rb1
XYS
CS
Paeoniflorin
Gallic acid

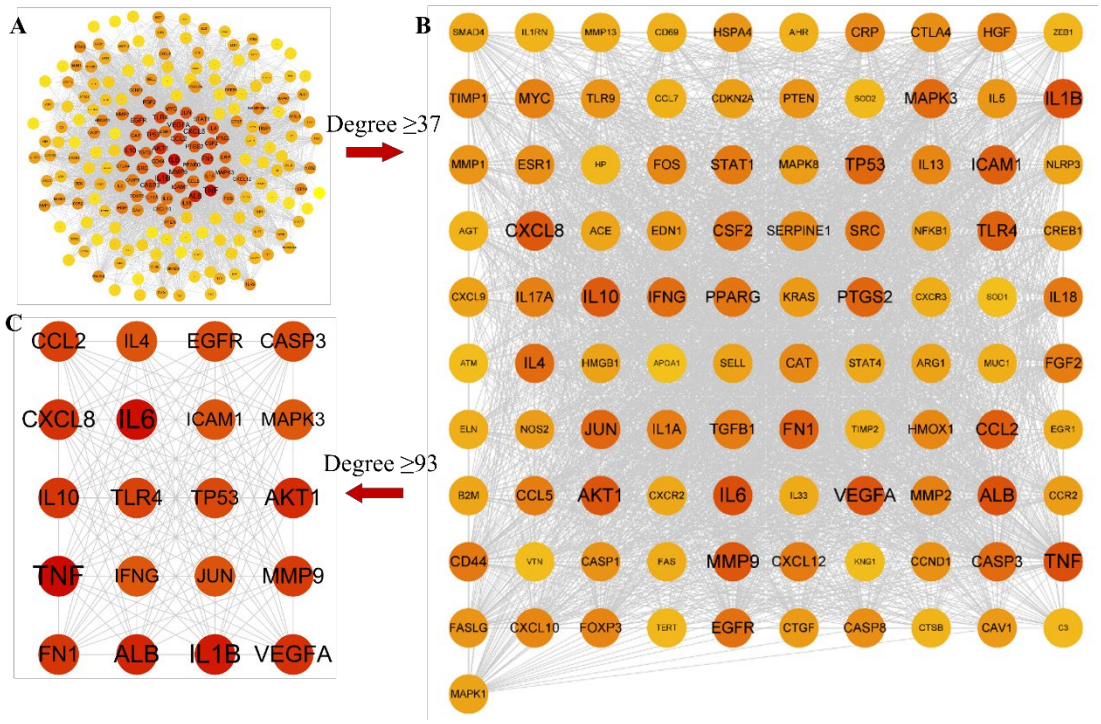
Supplementary Figure 1 Identification and analysis of chemical profiling of YCF

A: total ion current of YCF in positive (A1) and negative (A2) modes; B: identified compounds in medicated serum (red triangle) and extract (green round) of YCF; C: herb-component-target network of YCF. The size of the node is proportional to its degree. Round represents herb, hexagon represents active component, square represents target. YCF: Yangqing Chenfei formula; ZW: Ziwan (Radix Asteris Tatarici); JG: Jiegeng (Radix Platycodi); GL: Gualou (Fructus et Semen Trichosanthis); ZB: Zhebeimu (Bulbus Fritillariae Thunbergii); XYS: Xiyangshen (Radix Panacis Quinquefolii); CS: Chishao (Radix Paeoniae Rubra); CP: Chenpi (Pericarpium Citri Reticulatae).



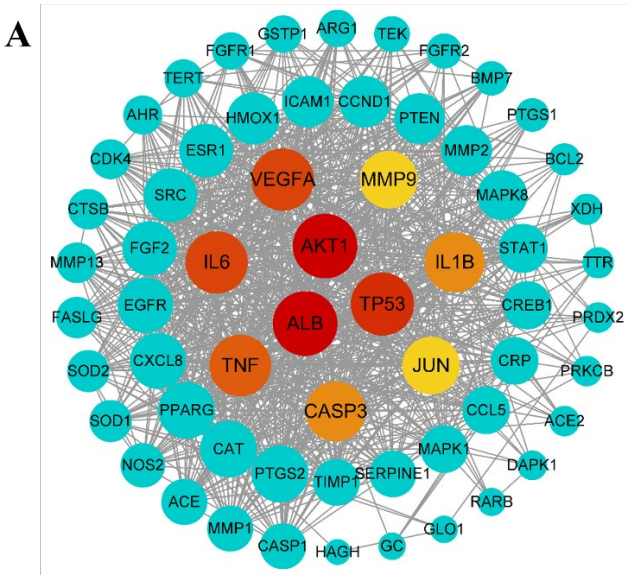
Supplementary Figure 2 PPI network of YCF-medicated serum active component targets

PPI: protein–protein interaction; YCF: Yangqing Chenfei formula.



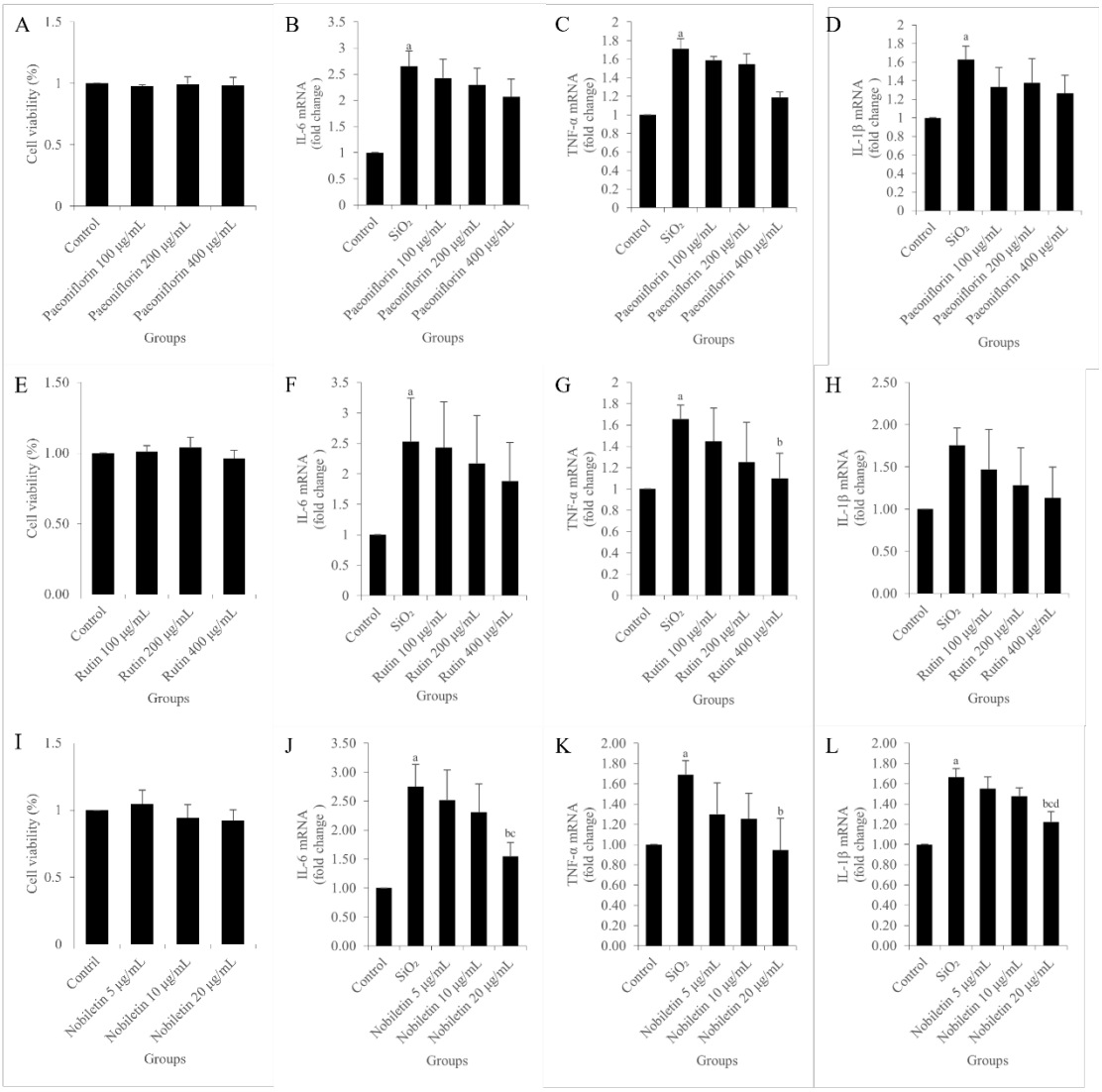
Supplementary Figure 3 PPI network of silicosis genes

PPI: protein–protein interaction.



Supplementary Figure 4 PPI network of interection of genes

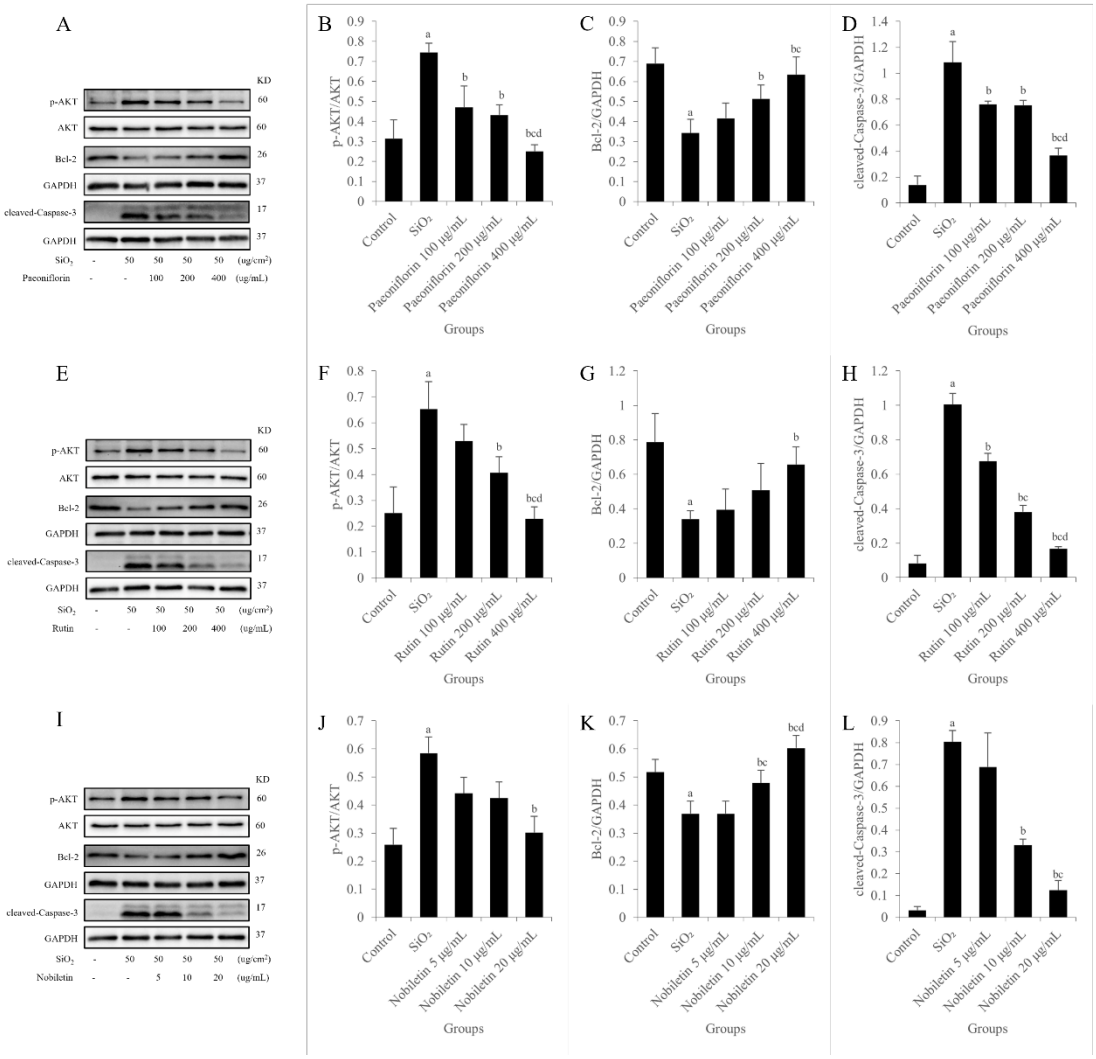
PPI: protein–protein interaction.



Supplementary Figure 5 Validation of the anti-inflammatory effects of paeoniflorin, rutin and nobiletin

A: effect of different concentrations of paeoniflorin on cell viability; B: effect of paeoniflorin on the IL-6 mRNA expression of silica-induced macrophages; C: effect of paeoniflorin on the TNF-α mRNA expression of silica-induced macrophages; D: effect of paeoniflorin on the IL-1β mRNA expression of silica-induced macrophages; E: effect of different concentrations of rutin on cell viability; F: effect of rutin on the IL-6 mRNA expression of silica-induced macrophages; G: effect of rutin on the TNF-α mRNA expression of silica-induced macrophages; H: effect of rutin on the IL-1β mRNA expression of silica-induced macrophages; I: effect of different concentrations of nobiletin on cell viability; J: effect of nobiletin on the IL-6 mRNA expression of silica-induced macrophages; K: effect of nobiletin on the TNF-α mRNA expression of silica-induced macrophages; L: effect of nobiletin on the IL-1β mRNA expression of silica-induced macrophages. The MHS cells were treated with 0, 100, 200, 400 μg/mL of paeoniflorin for 6 h respectively, then examined cell viability with cell counting kit-8 reagent. Control group was treated with an equal volume of phosphate buffered saline and dimethyl sulfoxide, SiO_2 group was treated with 50 μg/cm^2 SiO_2, paeoniflorin groups were treated with

100, 200, 400 μg/mL paeoniflorin for 6 h, rutin groups were treated with 100, 200, 400 μg/mL rutin for 6 h, nobiletin groups were treated with 5, 10, 20 μg/mL nobiletin for 6 h. TNF-α: tumor necrosis factor alpha; IL-1β: interleukin-1β; IL-6: interleukin-6. The experiment was repeated three times, and the data are presented as the mean ± standard deviation (n = 3). [a]$P < 0.05$ vs control; [b]$P < 0.05$ vs SiO_2; [c]$P < 0.05$ vs low concentration treatment; [d]$P < 0.05$ vs medium concentration treatment.



Supplementary Figure 6 Validation of the inhibitory effect of paeoniflorin, rutin and nobiletin on AKT/Bcl-2/Caspase-3 signaling pathways

A: western blot bands of p-AKT, AKT, Bcl-2, and cleaved-caspase-3 in MHS cells treated with SiO_2 and different concentration of paeoniflorin; B: effect of paeoniflorin on the p-AKT/AKT protein expression of silica-induced macrophages; C: effect of paeoniflorin on the Bcl-2/GAPDH protein expression of silica-induced macrophages; D: effect of paeoniflorin on the cleaved-caspase-3/GAPDH protein expression of silica-induced macrophages; E: western blot bands of p-AKT, AKT, Bcl-2, and cleaved-caspase-3 in MHS cells treated with SiO_2 and different concentration of rutin; F: effect of rutin on the p-AKT/AKT protein expression of silica-induced macrophages; G: effect of rutin on the Bcl-2/GAPDH protein expression of

silica-induced macrophages; H: effect of rutin on the cleaved-caspase-3/GAPDH protein expression of silica-induced macrophages; I: western blot bands of p-AKT, AKT, Bcl-2, and cleaved-caspase-3 in MHS cells treated with SiO_2 and different concentration of nobiletin; J: effect of nobiletin on the p-AKT/AKT protein expression of silica-induced macrophages; K: effect of nobiletin on the Bcl-2/GAPDH protein expression of silica-induced macrophages; L: effect of nobiletin on the cleaved-caspase-3/GAPDH protein expression of silica-induced macrophages. Control group was treated with an equal volume of phosphate buffered saline and dimethyl sulfoxide, SiO_2 group was treated with 50 μg/cm^2 SiO_2, paeoniflorin groups were treated with 100, 200, 400 μg/mL paeoniflorin for 6 h, rutin groups were treated with 100, 200, 400 μg/mL rutin for 6 h, nobiletin groups were treated with 5, 10, 20 μg/mL nobiletin for 6 h. AKT: protein kinase B; Bcl-2: B cell lymphoma-2; GAPDH: glyceraldehyde-3-phosphate dehydrogenase. GAPDH served as the loading control.. The experiment was repeated three times, and the data are presented as the mean ± standard deviation (n = 3). $^aP < 0.05$ vs control; $^bP < 0.05$ vs SiO_2; $^cP < 0.05$ vs low concentration treatment; $^dP < 0.05$ vs medium concentration treatment.