

1. CSE concentration pilot study

After starvation, PBS, 2.5% CSE, 5% CSE, 10% and 20% CSE were used to incubate the HUVECs 12 hours. The result showed that The CSE induced HUVECs apoptosis was concentration dependent. However, the cell necrosis also depended on concentration. 5% CSE induced the higher apoptosis cells than 2.5% CSE ($25.73 \pm 5.07\%$ vs. $11.50 \pm 2.01\%$), and less dead or necrosis cells than 10% CSE ($7.2 \pm 2.54\%$ vs. $13.9 \pm 9.78\%$) (S. table 1). Furthermore, 5% CSE did not lead significant more dead or necrosis cells than 2.5% CSE. Because of the above pilot study results, we choose the 5% CSE to treat cells.

Supplement Table 1 Apoptosis and necrosis in different CSE concentration group.

CSE concentration	Apoptosis cells (%)	Dead or Necrosis cells (%)
PBS	1.57 ± 0.54	0.97 ± 0.47
2.5%	$11.50 \pm 2.0251^*$	$5.93 \pm 1.74^*$
5.0%	$25.73 \pm 5.07^{*#}$	$7.2 \pm 2.54^*$
10.0%	$46.13 \pm 5.07^{*#}$	$13.9 \pm 9.78^{*#}$
20.0%	$21.60 \pm 1.55^{*#}$	$45 \pm 12.91^{*#}$

* indicates a statistically significant difference compared with PBS group ($P < 0.01$ by the ANOVA test). # indicates a statistically significant difference compared with 2.5% CSE group ($P < 0.01$ by the ANOVA test).