



**Schematic diagram of Fuzi's active compound DA in treating vascular senescence.** Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) identified the top 10 compounds as possible active anti-senescence compounds. Subsequently, experiments proved that DA decreased aging biomarkers, such as p16, p21, p53, and  $\gamma$  H2A.X in mRNA or protein levels. To elucidate the possible targets that DA binding to, the network pharmacology method was employed to get 119 targets, and these targets were further filtered by the cytohub in Cytoscape 3.8.0 to simplify to 8 targets. Molecular docking and BLI results foretold that HDAC1 was the presumed target. The following CRISPR-Cas9-base technology ulteriorly confirmed that DA's anti-senescence capacity depended on HDAC1. **DA binds to HDAC1 and inhibits its degradation by ubiquitination.** The enhancement of HDAC1 by DA stimulation caused the condensed of chromosomes and which lowered the expression of H3K4me3, and eventually decreased the expression of p21.