

**Supplementary Table S1. Molecular docking parameters for key protein targets of diosmin.**

Protein	Coordinates	Box
PI3K	X: -28.144, Y: -20.159, Z: 16.353	30 Å × 30 Å × 30 Å
Akt1	X: -19.676, Y: 0.475, Z: 13.895	30 Å × 30 Å × 30 Å
NF-κB p65	X: 59.161, Y: -42.741, Z: -50.225	30 Å × 30 Å × 30 Å
TNF-α	X: -13.745, Y: -3.110, Z: 18.859	30 Å × 30 Å × 30 Å

**Supplementary Table S2. Sources and dilution ratios of antibodies used in this study.**

<b>Antibody</b>	<b>Supplier</b>	<b>Application/Type</b>	<b>Dilution ratio</b>
anti-ZO-1	Proteintech	Primary antibody	1: 500
anti-Occludin	Proteintech	Primary antibody	1: 5000
anti-E-cadherin	Proteintech	Primary antibody	1: 1000
anti-GAPDH	Proteintech	Primary antibody	1: 5000
anti-PI3K p85 $\alpha$	Abmart	Primary antibody	1: 1000
anti-AKT	Abmart	Primary antibody	1: 1000
anti-p-AKT (Ser473)	Abmart	Primary antibody	1: 1000
anti-mTOR	Abmart	Primary antibody	1: 700
anti-p-mTOR (Ser2448)	Abmart	Primary antibody	1: 700
anti-NF- $\kappa$ B p65	Abmart	Primary antibody	1: 2000
anti-p-NF- $\kappa$ B p65 (Ser536)	Abmart	Primary antibody	1: 2000
anti-I $\kappa$ B $\alpha$	Abmart	Primary antibody	1: 2000
anti-p-I $\kappa$ B $\alpha$ (Ser32/Ser36)	Abmart	Primary antibody	1: 2000
anti- $\beta$ -Tubulin	Proteintech	Primary antibody	1: 10000
anti-BCL2	Abmart	Primary antibody	1: 1000
anti-BAX	Proteintech	Primary antibody	1: 5000
anti-TNF- $\alpha$	Wanleibio	Primary antibody	1: 2000
HRP goat anti-mouse IgG (H+L)	ABclonal	Secondary antibody	1: 5000
HRP goat anti-rabbit IgG (H+L)	ABclonal	Secondary antibody	1: 5000

**Supplementary Table S3. Primer sequences, amplification efficiencies, and R<sup>2</sup> values for qRT-PCR analysis.**

Gene	Forward Primer (5'→3')	Reverse Primer (5'→3')	Efficiency (%)	R <sup>2</sup>
IL-1 $\beta$	CAGGCAGGCAGTATCACTCATTG	GGCTTTTTTGTTGTTTCATCTCGG	102.8	0.981
IL-6	GGCTTTTTTGTTGTTTCATCTCGG	GGACTCTGGCTTTGTCTTTCTTGT	95.72	0.986
IL-10	GCTGGACAACATACTGCTAACCGAC	ATCATTCCGATAAGGCTTGGCA	109.52	0.977
TNF- $\alpha$	CAGGCGGTGCCTATGTCTC	CGATCACCCGAAGTTCAGTAG	91.36	0.980
GADPH	AGGTCGGTGTGAACGGATTG	TGTAGACCATGTAGTTGAGGTCA	99.46	0.992

**Supplementary Table S4. Top 20 core targets ranked by degree, betweenness centrality, and closeness centrality in the PPI network.**

Rank	Degree	betweenness centrality	closeness centrality
1	TNF	TP53	TP53
2	TP53	TNF	TNF
3	AKT1	AKT1	AKT1
4	NFKB1	NFKB1	NFKB1
5	HIF1A	SRC	MMP9
6	MMP9	EGFR	HIF1A
7	CASP3	TLR4	EGFR
8	EGFR	MMP9	CASP3
9	TLR4	HIF1A	SRC
10	ESR1	PTGS2	TLR4
11	SRC	ESR1	PTGS2
12	PTGS2	CASP3	ESR1
13	PPARG	PPARG	PPARG
14	IGF1	MMP2	MMP2
15	JAK2	PARP1	IGF1
16	MMP2	SERPINE1	JAK2
17	IL2	IGF1	IL2
18	KIT	JAK2	KIT
19	SERPINE1	TERT	SERPINE1
20	BCL2L1	ABCG2	BCL2L1