Supplementary material

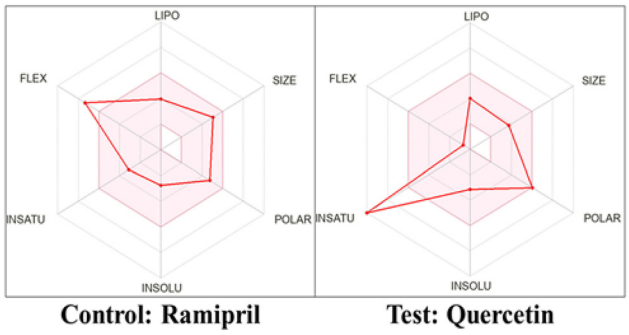

Figure S1: Bioavailability radar of ramipril and quercetin.

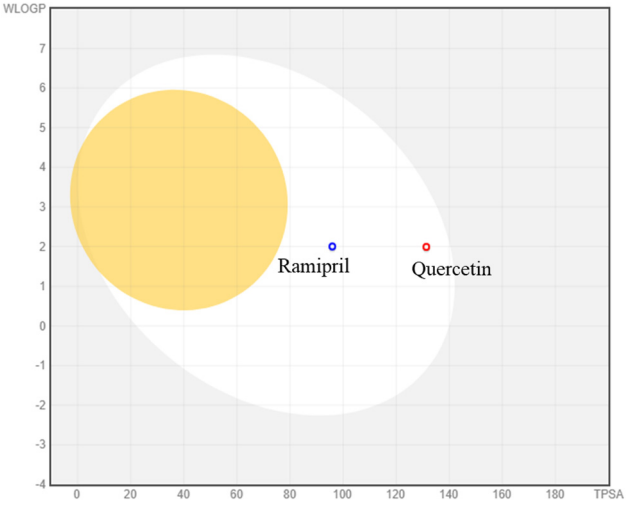

Figure S2: The boiled-egg plot of ramipril and quercetin.

Table S1: ADME classification from admetSAR

ADMET Predicted Profile	Ramipril (Control Compound)		Quercetin Test Compound	
	Value	Probability	Value	Probability
Absorption				
Human Intestinal Absorption	+	0.9761	+	0.9071
Caco-2 Permeability	−	0.8790	−	0.6417
Human Oral Bioavailability	−	0.8286	−	0.5429
Distribution				
Blood Brain Barrier	−	0.7250	−	0.7750
P-glycoprotein Substrate	+	0.6054	−	0.8360
P-glycoprotein Inhibitor	−	0.4852	−	0.9191
Subcellular Localization	Mitochondria	0.7325	Mitochondria	0.5829
Metabolism				
OATP2B1 Inhibitor	−	1	+	1
OATP1B1 Inhibitor	+	0.9338	+	0.8827
OATP1B3 Inhibitor	+	0.9434	+	0.9480
MATE1 Inhibitor	−	0.9800	+	0.6600
OCT2 Inhibitor	−	0.9500	−	0.9750
BSEP Inhibitor	+	0.8485	−	0.7052
CYP3A4 Substrate	+	0.6819	−	0.5564
CYP2C9 Substrate	−	1	−	1
CYP2D6 Substrate	−	0.7739	−	0.8553
CYP3A4 Inhibition	−	0.8309	+	0.6951
CYP2C9 Inhibition	−	0.9070	−	0.5823
CYP2C19 Inhibition	−	0.9025	−	0.9025
CYP2D6 Inhibition	−	0.9304	−	0.9287
CYP1A2 Inhibition	−	0.9045	+	0.9106
CYP2C8 Inhibition	−	0.9882	+	0.9818
CYP Inhibitory Promiscuity	−	0.5691	+	0.5822
UGT Catalyzed	−	0.000	+	0.700
Toxicity				
Organ Toxicity				
Hepatotoxicity	+	0.9188	+	0.7375
Eye Corrosion	−	0.9922	−	0.9905
Eye Irritation	−	0.9909	+	0.9505
Human Ether-a-go-go-Related Gene inhibition	−	0.6476	−	0.8410
Acute Oral Toxicity (c)	IV	0.6265	II	0.7348
Respiratory Toxicity	+	0.9556	+	0.8889
Skin Sensitization	−	0.9181	−	0.8771
Reproductive Toxicity	+	0.9556	+	0.7667
Nephrotoxicity	+	0.8034	−	0.8165
Genome Toxicity				

(*Continued*)

Table S1: *Continued*

ADMET Predicted Profile	Ramipril (Control Compound)		Quercetin Test Compound	
	Value	Probability	Value	Probability
Carcinogenicity (binary)	–	0.8700	–	1
Carcinogenicity (trinary)	Non-required	0.7037	Non-required	0.6750
Ames Mutagenesis	+	0.9400	+	0.8500
Micronuclear	+	0.6500	+	0.9300
Mitochondrial Toxicity	+	0.9625	+	0.5875
Estrogen Receptor Binding	–	0.5112	+	0.8301
Androgen Receptor Binding	–	0.8513	+	0.8785
Thyroid Receptor Binding	–	0.7040	+	0.5543
Glucocorticoid Receptor Binding	–	0.6554	+	0.8851
Aromatase Binding	–	0.7204	+	0.8070
PPAR Gamma	–	0.6198	+	0.9001
Eco-Toxicity				
Honey Bee Toxicity	–	0.8407	–	0.8728
Biodegradation	–	0.8500	–	0.8250
Crustacea Aquatic Toxicity	–	0.5100	–	0.5300
Fish Aquatic Toxicity	+	0.9540	+	0.9124

Table S2: ADME Predicted Profiles (regressions) classification from admetSAR

ADMET Predicted Profiles – Regressions	Ramipril; Control Compound		Quercetin; Test Compound	
	Unit	Value	Unit	Value
Water solubility	LogS	−3.299	LogS	−2.999
Plasma protein binding	100%	0.733	100%	1.164
Acute Oral Toxicity	log(1/(mol/kg))	1.639	log(1/(mol/kg))	2.526
Tetrahymena pyriformis	pIGC50 (ug/L)	0.577	pIGC50 (ug/L)	1.69

Table S3: Docking scores of various targets involved in the RAS Pathway with Quercetin and Ramipril

S No.	Protein Name	Drug Name	Affinity Score (KCAL/MOL)
1	Angiotensin-converting enzyme (ACE)	Quercetin	−7.42
		Ramipril	−6.52
2	Renin	Quercetin	−8.1
		Ramipril	−5.74
3	Angiotensin II type 1 receptor (AT1R)	Quercetin	−6.2
		Ramipril	−6.43
4	Angiotensin II type 2 receptor (AT2R)	Quercetin	−6.87
		Ramipril	−7.32
5	Angiotensin-Converting Enzyme 2 (ACE-2)	Quercetin	−5.77
		Ramipril	−6.1