

Table S1: Primer set of each gene used for quantitative RT-PCR

<b>Gene Name</b>	<b>Primer</b>	<b>Sequence</b>
<i>ama-1</i>	forward	5'-CGG AGC AGC CAG GAA CTT C-3'
	reverse	5'-AAC GGG AAA AAT CTT ATG AAT-3'
<i>skn-1</i>	forward	5'-CTC TCT TCT GGC ATC CTC TAC CA-3'
	reverse	5'-TTC TTG GAT TCT TCT TCT TGT TCG T-3'
<i>ctl-1</i>	forward	5'-AAT GGA TAC GGA GCG CAT AC-3'
	reverse	5'-GCG TCA GTT GGA TCG AGA TT-3'
<i>sod-3</i>	forward	5'-TGG TGG TGG ACA CAT CAA TC-3'
	reverse	5'-ACC GAA GTC GCG CTT AAT AG-3'
<i>gst-4</i>	forward	5'-GCT GAA GCC AAC GAC TCC AT-3'
	reverse	5'-GAC CGA ATT GTT CTC CAT CGA-3'
<i>bec-1</i>	forward	5'-AGG AGC TGG AGC AAC AGT TGA AGA-3'
	reverse	5'-ATA TTG ACG TTC GGC TTC CAG CGA-3'
<i>lgg-1</i>	forward	5'-AAC AAC TTT GAG AAG CGT CGT GCC-3'
	reverse	5'-TCT TCT GGA CGA AGT TGG ATG CGT-3'

Table S2: Effect of phlorizin on lifespan in *C. elegans*

	<b>Phlorizin (<math>\mu\text{M}</math>)</b>	<b>Mean lifespan (d)</b>	<b><i>P</i> value<sup>1)</sup></b>	<b>% effect<sup>2)</sup></b>
1 <sup>st</sup> experiment	0	17.5		
	10	20.6	< 0.001	18.0
2 <sup>nd</sup> experiment	0	18.4		
	10	20.1	0.022	9.2
3 <sup>rd</sup> experiment	0	18.9		
	10	22.2	0.001	17.8

<sup>1)</sup> *P* value was calculated using the log-rank test by comparing the survival of the untreated control group (0  $\mu\text{M}$  phlorizin) to that of phlorizin-treated group (10  $\mu\text{M}$  phlorizin).

<sup>2)</sup> % effects were calculated by  $(C-P)/C*100$ , where *P* is the mean lifespan of phlorizin-treated group and *C* is the mean lifespan of the untreated control group.

Table S3: Effect of phlorizin and RNAi of *daf-16/skn-1* on A $\beta$ -induced toxicity in *C. elegans*

	Phlorizin ( $\mu$ M)	RNAi	Time when 50% of worms were paralyzed (h)	<i>P</i> value <sup>1)</sup>	% effect <sup>2)</sup>
1 <sup>st</sup> experiment	0	EV	4.9		
	10	EV	7.0	< 0.001	41.9
	0	<i>daf-16</i>	4.4		
	10	<i>daf-16</i>	4.8	0.453	7.9
	0	<i>skn-1</i>	4.5		
	10	<i>skn-1</i>	4.1	0.622	-7.1
2 <sup>nd</sup> experiment	0	EV	4.9		
	10	EV	6.4	0.001	29.8
	0	<i>daf-16</i>	5.3		
	10	<i>daf-16</i>	5.1	0.729	-3.8
	0	<i>skn-1</i>	5.5		
	10	<i>skn-1</i>	5.1	0.546	-7.9

<sup>1)</sup> *P* value was calculated using the log-rank test by comparing the rate of paralysis in the untreated control group (0  $\mu$ M phlorizin) to that of phlorizin-treated group (10  $\mu$ M phlorizin).

<sup>2)</sup> % effects were calculated by  $(C-P)/C*100$ , where *P* is the time when 50% of worms were paralyzed in phlorizin-treated group and *C* is the time when 50% of worms were paralyzed in the untreated control group.

Table S4: Effect of phlorizin and *skn-1* RNAi on increased mortality by HGD

	<b>Supplementation</b>	<b>RNAi</b>	<b>Mean lifespan (d)</b>	<b><i>P</i> value</b>
1 <sup>st</sup> experiment		EV	23.4	
	HGD	EV	19.4	< 0.001 <sup>1)</sup>
	HGD + PZ	EV	21.3	0.004 <sup>2)</sup>
		<i>skn-1</i>	20.1	
	HGD	<i>skn-1</i>	16.6	< 0.001 <sup>1)</sup>
	HGD + PZ	<i>skn-1</i>	17.6	0.346 <sup>2)</sup>
2 <sup>nd</sup> experiment		EV	18.8	
	HGD	EV	12.9	< 0.001 <sup>1)</sup>
	HGD + PZ	EV	21.0	< 0.001 <sup>2)</sup>
		<i>skn-1</i>	18.3	
	HGD	<i>skn-1</i>	13.1	< 0.001 <sup>1)</sup>
	HGD + PZ	<i>skn-1</i>	13.3	0.796 <sup>2)</sup>

<sup>1)</sup> *P* value was calculated using the log-rank test by comparing the survivals of no supplementation and HGD only with RNAi of the same gene.

<sup>2)</sup> *P* value was calculated using the log-rank test by comparing the survivals of HGD only and HGD + PZ with RNAi of the same gene.

HGD, high glucose diet (40 mM glucose); PZ, phlorizin (10 μM).

Table S5: Effect of phlorizin on degeneration of dopaminergic neurons

	<b>Supplementation</b>	<b>Relative fluorescence (%)</b>	<b><i>P</i> value</b>
1 <sup>st</sup> experiment		100.0 ± 5.76	
	6-OHDA	60.4 ± 5.28	< 0.001 <sup>1)</sup>
	6-OHDA + L-DOPA	113.9 ± 7.20	< 0.001 <sup>2)</sup>
	6-OHDA + PZ	102.9 ± 5.94	< 0.001 <sup>2)</sup>
2 <sup>nd</sup> experiment		100.0 ± 2.62	
	6-OHDA	73.6 ± 5.77	0.002 <sup>1)</sup>
	6-OHDA + L-DOPA	99.4 ± 3.19	0.002 <sup>2)</sup>
	6-OHDA + PZ	99.6 ± 4.72	0.004 <sup>2)</sup>
3 <sup>rd</sup> experiment		100.0 ± 3.70	
	6-OHDA	68.7 ± 3.27	< 0.001 <sup>1)</sup>
	6-OHDA + L-DOPA	100.4 ± 4.33	< 0.001 <sup>2)</sup>
	6-OHDA + PZ	107.1 ± 2.62	< 0.001 <sup>2)</sup>

<sup>1)</sup> *P* value was calculated using the Student's t test by comparing to the untreated control.

<sup>2)</sup> *P* value was calculated using the Student's t test by comparing to 6-OHDA-treated group.

6-OHDA, 6-hydroxydopamine; L-DOPA, L-3,4-dihydroxyphenylalanine; PZ, phlorizin (10 μM).

Table S6: Effect of *daf-16* or *bec-1* knockdown on lifespan extension by phlorizin

	RNAi	Mean lifespan (d)		<i>P</i> value <sup>1)</sup>
		Control	PZ	
1 <sup>st</sup> experiment	<i>daf-16</i>	12.9	12.8	0.941
	<i>bec-1</i>	18.9	18.5	0.724
2 <sup>nd</sup> experiment	<i>daf-16</i>	14.2	13.5	0.299
	<i>bec-1</i>	22.8	22.3	0.642
3 <sup>rd</sup> experiment	<i>daf-16</i>	14.0	13.6	0.459
	<i>bec-1</i>	23.0	22.6	0.359

<sup>1)</sup> *P* value was calculated using the log-rank test by comparing the survival of the untreated control group (0 μM phlorizin) to that of phlorizin-treated group (10 μM phlorizin).

PZ, phlorizin (10 μM).