**Supporting Information**

**Table S1**

The experiment data for the yield of SDSP using Box-Behnken design.

| Run | Independent variables | | | Responses |
|---|---|---|---|---|
| | A: Enzyme concentration (U/g) | B: Solid-liquid ratio | C: Reaction time (h) | Y: yield of SDSP (%) |
| 1 | 4000 | 1:16 | 5 | 24.33 |
| 2 | 4000 | 1:16 | 5 | 24.74 |
| 3 | 4000 | 1:16 | 5 | 24.34 |
| 4 | 3000 | 1:16 | 6 | 25.15 |
| 5 | 4000 | 1:16 | 5 | 24.28 |
| 6 | 4000 | 1:14 | 6 | 24.71 |
| 7 | 3000 | 1:18 | 5 | 23.29 |
| 8 | 3000 | 1:16 | 4 | 22.84 |
| 9 | 4000 | 1:18 | 6 | 25.26 |
| 10 | 5000 | 1:16 | 4 | 23.42 |
| 11 | 4000 | 1:14 | 4 | 20.92 |
| 12 | 4000 | 1:16 | 5 | 24.59 |
| 13 | 3000 | 1:14 | 5 | 20.04 |
| 14 | 5000 | 1:18 | 5 | 23.10 |
| 15 | 5000 | 1:14 | 5 | 22.87 |
| 16 | 4000 | 1:18 | 4 | 23.20 |
| 17 | 5000 | 1:16 | 6 | 25.57 |

**Table S2**

Primer sequences for qRT-PCR.

| Gene | Primer |
|---|---|
| *daf-2* | 5′-CGGTGCGAAGAGAGGATATT-3′ |
| | 5′-TACAGAGGTCGCCGTTACTG-3′ |
| *age-1* | 5′-AGTGGATTCGGAAACAATGC-3′ |
| | 5′-GGAATCGATGCACTTTCA-3′ |
| *akt-1* | 5′-TCACCGATGCGATTGTCT-3′ |
| | 5′-AACTCCCCACCAATCAACAC-3′ |
| *sir-2.1* | 5′-TTCTTGTGTTGACTGGCGCT-3′ |
| | 5′-GTCCTGGGAAGATTTCTCTCG-3′ |
| *daf-16* | 5′-CCAGACGGAAGGCTTAAACT-3′ |
| | 5′-ATTCGCATGAAACGAGAATG-3′ |
| *skn-1* | 5′-AGTGTCGGCGTTCCAGATTTC-3′ |
| | 5′-GTCGACGAATTGCGAATCA-3′ |
| *hsf-1* | 5′-TTGACGACGACAAGCTTCCAGT-3′ |
| | 5′-AAAGCTTGCACCAGAATCATCCC-3′ |
| *act-1* | 5′-CCAGGAATTGCTGATCGTATGCAGAA-3′ |
| | 5′-TGGAGAGGAAGCGAGGATAGA -3′ |
| *sod-3* | 5′-CCAACCAGCGCTGAAATTCAATGG-3′ |
| | 5′-GGAACCGAAGTCGCGCTTAATAGT-3′ |
| *gsh-px* | 5′- ATGGCACTTTGGCAGCTCA-3′ |
| | 5′- ACGCGCAAAAAGTAGCAACGC-3′ |
| *hsp-16.1* | 5′-GCAGAGGCTCTCCATCTGAA-3′ |
| | 5′-GCTTGAACTGCGAGACATTG-3′ |
| *hsp-16.2* | 5′-TATGGCTCTGATGGAACG-3′ |
| | 5′-GATTGATAGCGTACGACC-3′ |
| *hsp-12.6* | 5′-ATGATGAGCGTTCCAGTGATGGCTGACG-3′ |
| | 5′-TTAATGCATTTTTCTTGCTTCAATGTGAAGAATTCC -3′ |
| *gst-4* | 5′- ATGCTCGTGCTCTTGCTGAG-3′ |
| | 5′- GACTGACCGAATTGTTCTCCAT-3′ |
| *gcs-1* | 5′- GTCGATGAAGCCAGATGGTTGT-3′ |
| | 5′- CGATCGTCGACACTTGCACTAA-3′ |

**Table S3**

Statistical summary of the surface response analysis.

| Source | Sum of Squares | Mean square | F value | p value | Significance |
|---|---|---|---|---|---|
| Model | 34.64 | 4.33 | 42.84 | < 0.0001 | *** |
| A | 1.66 | 1.66 | 16.43 | 0.0037 | ** |
| B | 4.96 | 4.96 | 49.10 | 0.0001 | ** |
| C | 13.27 | 13.27 | 131.29 | < 0.0001 | *** |
| AB | 2.28 | 2.28 | 22.59 | 0.0014 | ** |
| BC | 0.75 | 0.75 | 7.41 | 0.0261 | * |
| $A^2$ | 2.09 | 2.09 | 20.70 | 0.0019 | ** |
| $B^2$ | 8.55 | 8.55 | 84.59 | < 0.0001 | *** |
| $C^2$ | 1.02 | 1.02 | 10.13 | 0.0129 | * |
| Residual | 0.81 | 0.10 | | | |
| Lack of fit | 0.65 | 0.16 | 4.08 | 0.101 | |
| Pure error | 0.16 | 0.04 | | | |
| Cor total | 35.45 | | | | |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

**Fig. S1**

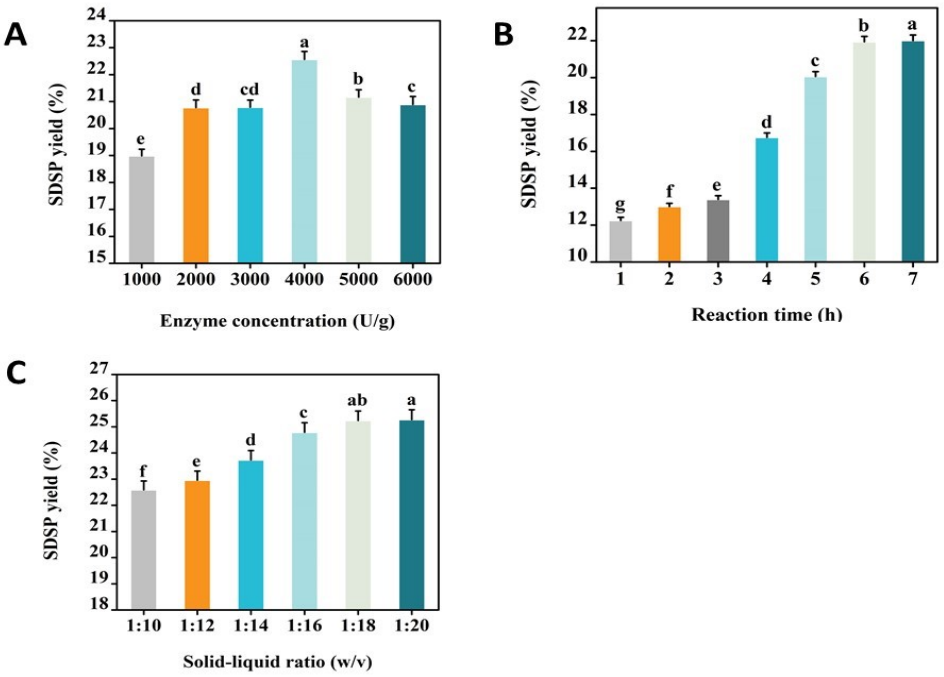


**Fig. S1.** Production of SDSP. **(A)** The effect of protease Sea-B-Zyme L200 concentrations on the yield of SDSP. Hydrolysis condition: 50 °C, reaction time 4 h, solid-liquid ratio 1:20. **(B)** The effect of reaction time on the yield of SDSP. Hydrolysis condition: 50 °C, protease concentration 4000 U/g, solid-liquid ratio 1:20. **(C)** The effect of solid-liquid ratio on the yield of SDSP. Hydrolysis condition: 50 °C, protease concentration 4000 U/g, reaction time 4 h. Relative values are depicted, and values are given as mean ± SD. Plots are representative of three independent experiments. Different letters (a-g) means significant difference ($p < 0.05$).

**Fig. S2**

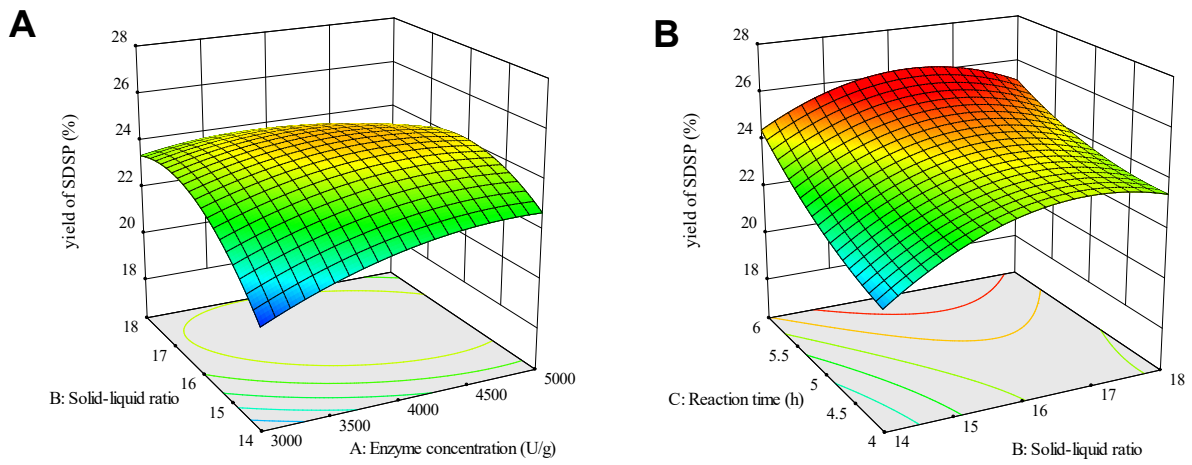


**Fig. S2.** Three-dimensional (3D) response surface plots. **(A)** Yield of SDSP (%) as a function of enzyme concentration (U/g) × solid-liquid ratio. **(B)** Yield of SDSP (%) as a function of solid-liquid ratio × reaction time (h).

**Fig. S3**

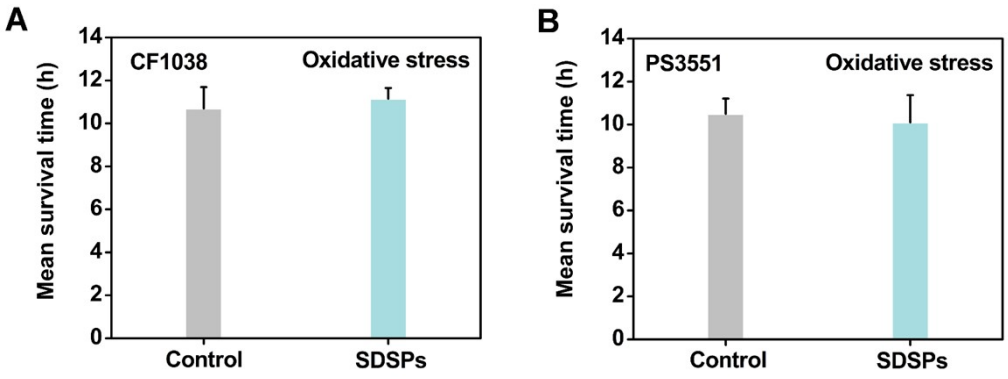


**Fig. S3.** Mean survival time (h) of *daf-16* and *hsf-1* mutants under oxidative stress. **(A)** Mean survival time of *daf-16* mutants under oxidative stress after $SDSP_{<2\ kDa}$ feeding for 48 h. **(B)** Mean survival time of *hsf-1* mutants under oxidative stress after $SDSP_{<2\ kDa}$ feeding for 48 h. (n = 60). Relative values are depicted, and values are given as mean ± SD. Plots are representative of three independent experiments. *p* value was calculated using Student's t-test.

Fig. S4

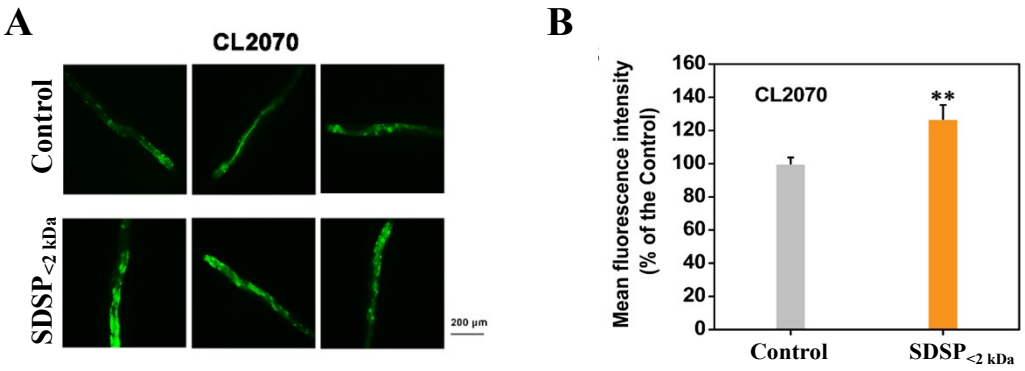


**Fig. S4. (A)** HSP-16.2 expression evaluated by fluorescence microscopy after $SDSP_{<2\ kDa}$ feeding for 48 h. (n = 30). **(B)** Quantification of HSP-16.2 fluorescence intensity by Image J software. (n = 30). Relative values are depicted, and values are given as mean ± SD. Plots are representative of three independent experiments. *p* value was calculated using Student's t-test. $p < 0.01$ (**) versus respective controls. Method: L2 stage CL2070 nematodes were transferred to 30 µg/mL $SDSP_{<2\ kDa}$-treated and untreated plates for 2 days, and then collected and washed with M9 buffer and anesthetized with tetramisole hydrochloride on a 2% agarose pad. GFP (green fluorescent protein) expression in the nematode was examined using a DeltaVision deconvolution microscope (GE, Boston, MA).