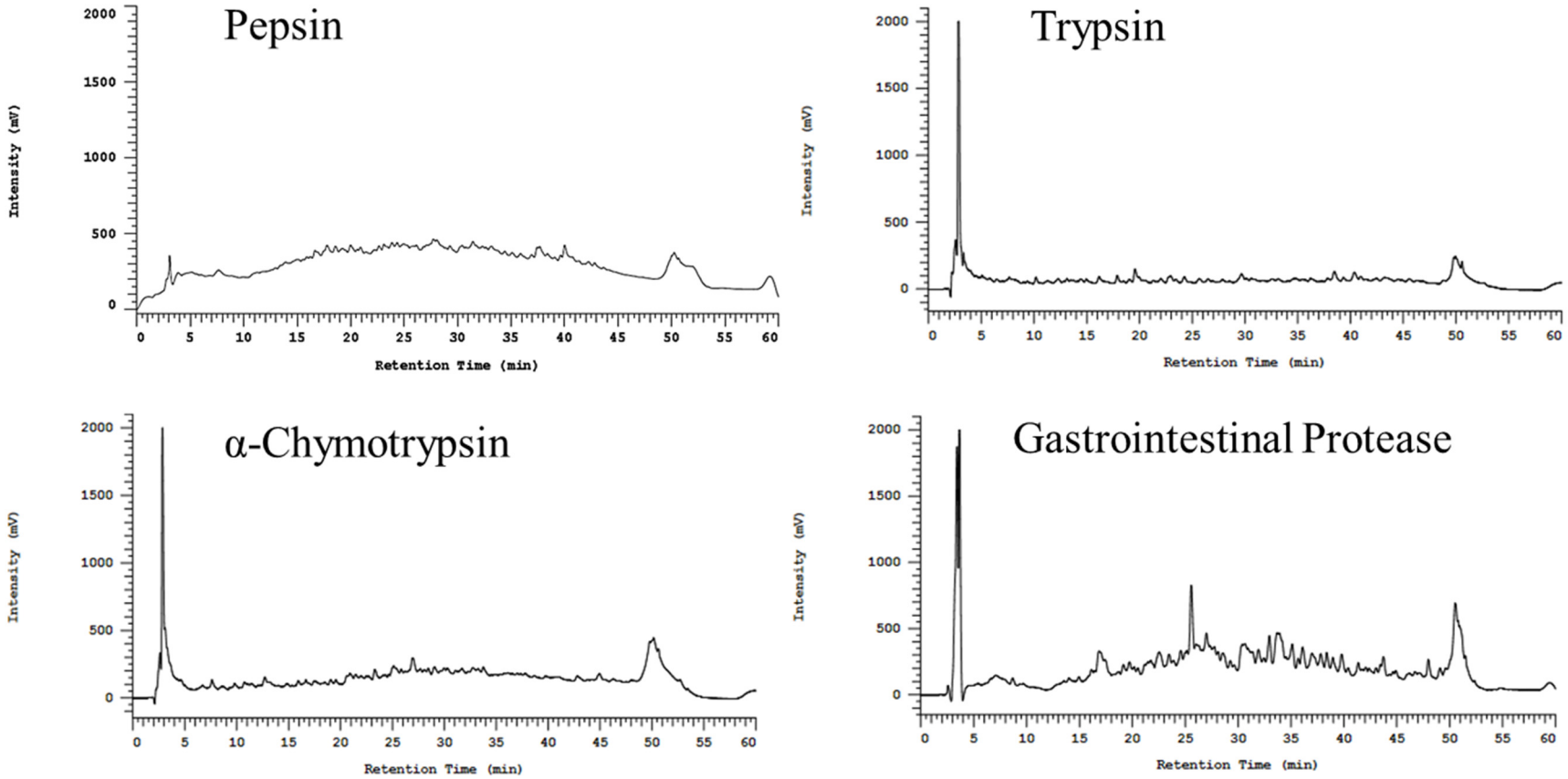


**Figure S1.** RP-HPLC chromatogram of 50 μg/μL BGSP hydrolysate generated from pepsin, trypsin, α-chymotrypsin, and gastrointestinal protease

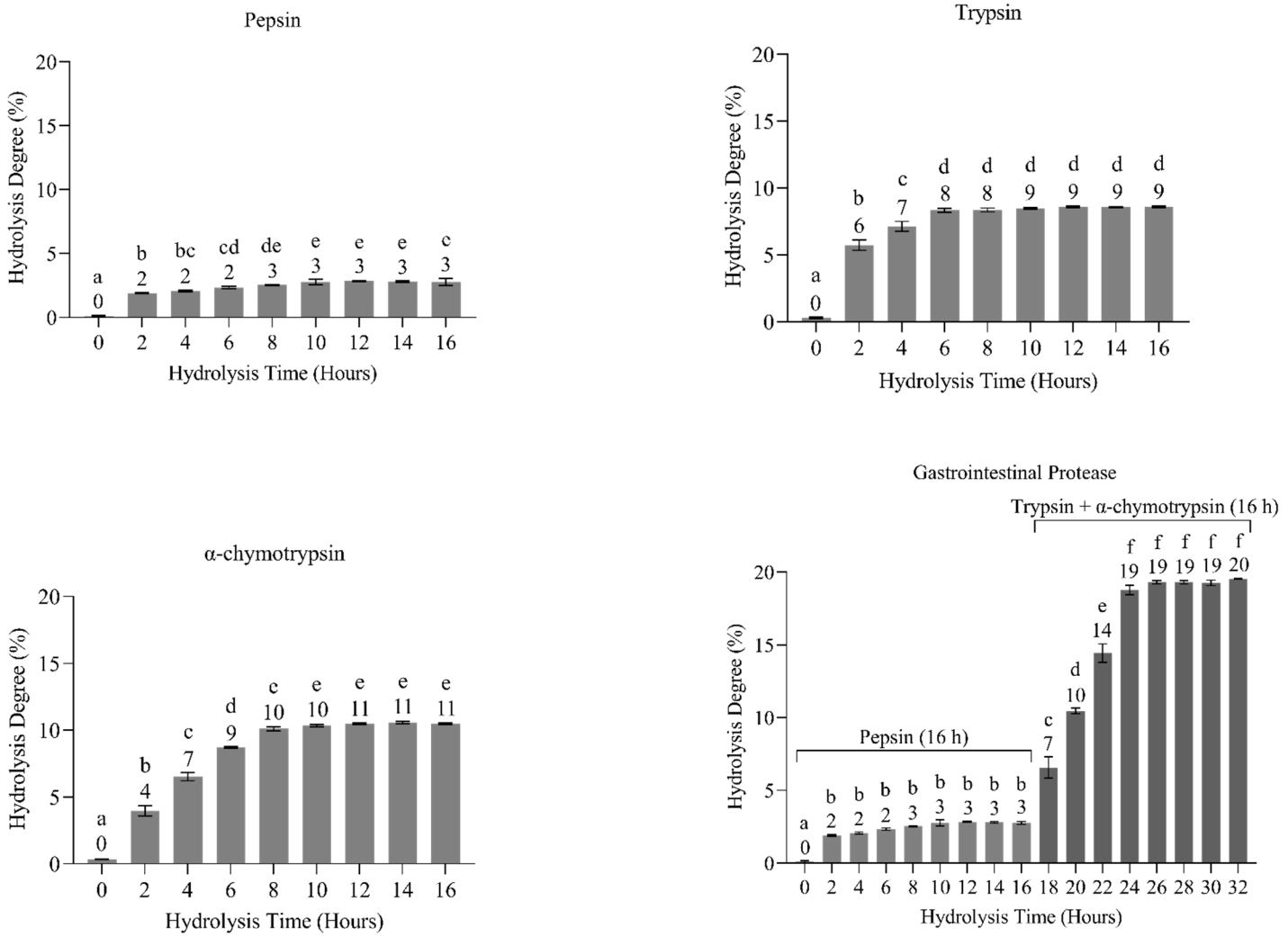


**Figure S2.** Hydrolysis Degree of BGSP hydrolysate generated from pepsin, trypsin, α-chymotrypsin, and gastrointestinal protease. Different letters mean significantly different ($p<0.05$) of liberated amino acids at certain hydrolysis times compared to the control (0 hours).

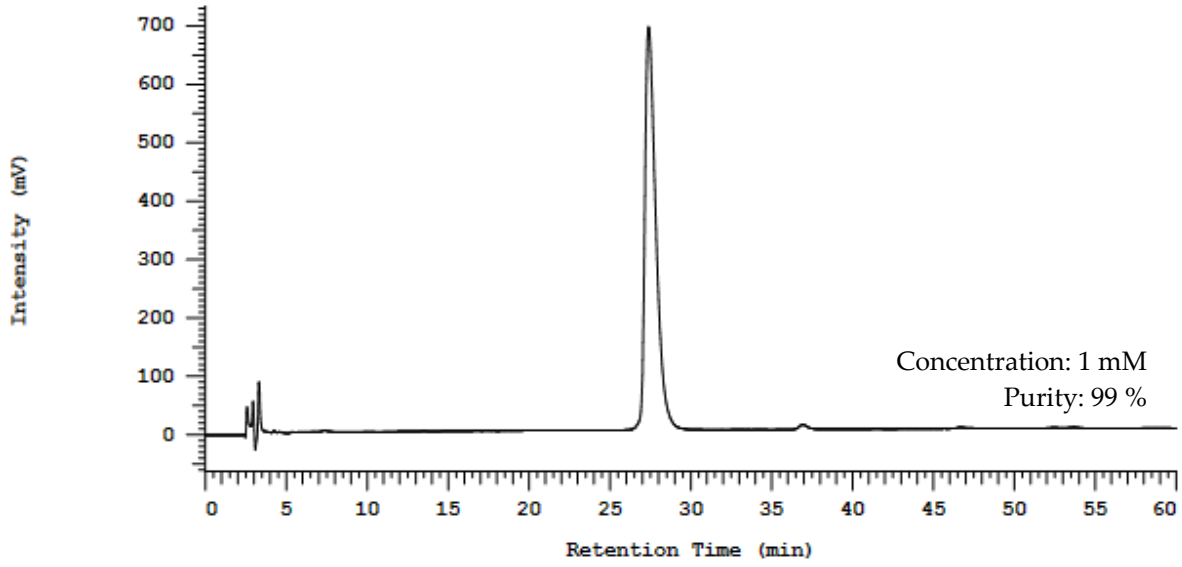


**Figure S3.** RP-HPLC chromatogram of synthetic AW6

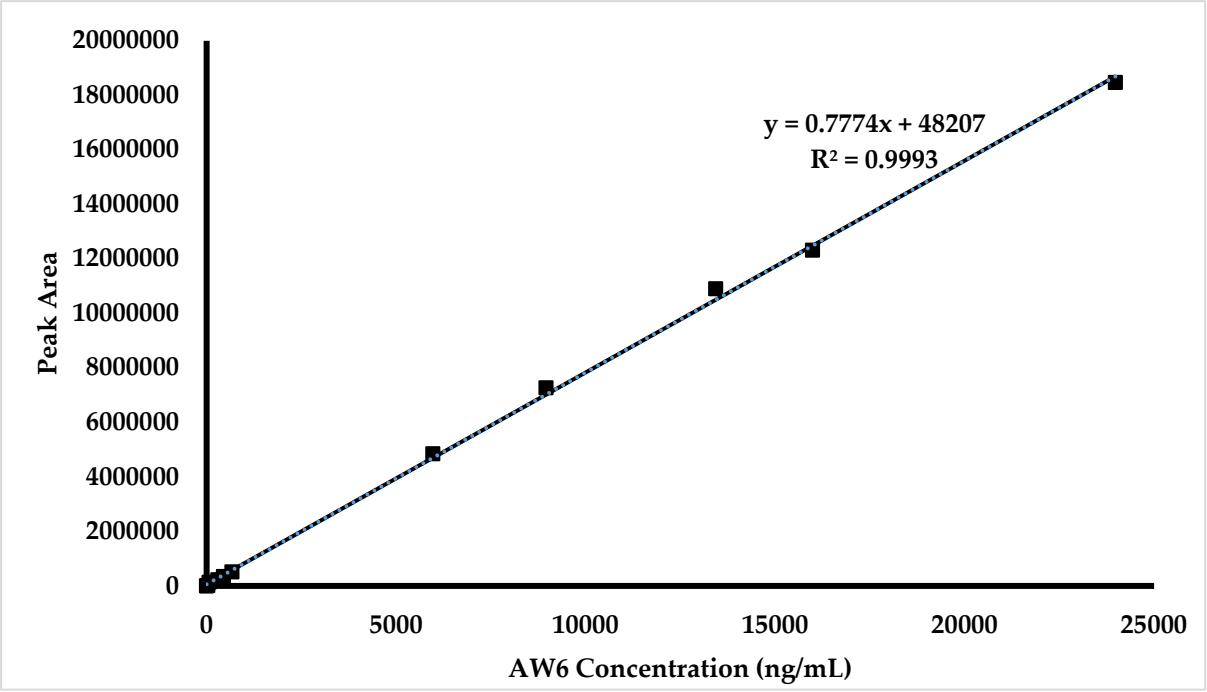


**Figure S4.** The standard calibration curve of AW6

**Table S1.** Identified peptides from GP BGSP hydrolysate fraction F5 from RP-HPLC fractionation

| Identified Protein | Peptide Sequence | m/z (Observed) | Mass | Peptide Length |
|---|---|---|---|---|
| (gi\|157829880) chain A, alpha-momocharin (sequence coverage 28%) | PALDSAISTL | 494.2716 | 986.5284 | 10 |
| | DEVPSLATI | 944.4933 | 943.4862 | 9 |
| | ATISLENSW | 1020.5003 | 1019.4924 | 9 |
| | TISLENSW | 949.4633 | 948.4553 | 8 |
| | VVTSNIQLL | 493.7979 | 985.5808 | 9 |
| | IQLAQGNNGIF | 587.8142 | 1173.6143 | 11 |
| | EKIPIGL | 385.2444 | 768.4745 | 7 |
| | IPIGL | 512.3445 | 511.3370 | 5 |
| | DSAISTLL | 819.4460 | 818.4385 | 8 |
| | ISLENSW | 848.4136 | 847.4076 | 7 |
| | ITLPY | 606.3495 | 605.3425 | 5 |
| | VYNIPL | 718.4134 | 717.4061 | 6 |
| | AAAGAL | 473.2718 | 472.2645 | 6 |
| (gi\|1229803397) legumin A-like [Momordica charantia] (sequence coverage 18%) | IQVVDDRGQTIF | 695.8691 | 1389.7252 | 12 |
| | NIIKVEGPL | 982.5919 | 981.5858 | 9 |
| | YIIEPNGL | 918.4926 | 917.4858 | 8 |
| | AAEEGLEW | 904.4037 | 903.3974 | 8 |
| | IIEPNGLL | 868.5144 | 867.5065 | 8 |
| | ALPVQVI | 739.4713 | 738.4639 | 7 |
| | PAGATHW | 739.3508 | 738.3449 | 7 |
| | TLAQIL | 658.4133 | 657.4061 | 6 |
| | IIKVEGPL | 434.7789 | 867.5429 | 8 |
| | EGLEW | 633.2882 | 632.2806 | 5 |
| | HSIIF | 308.6762 | 615.3380 | 5 |
| (gi\|1229809665) superoxide dismutase [Cu-Zn] [Momordica | GASDVVSGTIF | 1052.5234 | 1051.5186 | 11 |
| | AVAVL | 472.2747 | 471.3057 | 5 |
| | DVVSGTIF | 837.4351 | 836.4280 | 8 |

| | | | | |
|---|---|---|---|---|
| charantia] (sequence coverage 11%) | | | | |
| | VVVAGEF | 720.3925 | 719.3854 | 7 |
| | NVANQLDPYL | 573.7944 | 1145.5718 | 10 |
| | EPTTSDVVVAGEFDQGSGSMR | 1084.9948 | 2167.9690 | 21 |
| | TLAQLL | 658.4130 | 657.4061 | 6 |
| | QLFPR | 330.6841 | 659.3755 | 5 |
| | LFGSL | 536.3083 | 535.3006 | 5 |
| | APLVSW | 672.3657 | 671.3643 | 6 |
| *_de novo_ sequencing (only) | QGLVSW | 689.3613 | 688.3544 | 6 |
| | NLDLGL | 644.3618 | 643.3541 | 6 |
| | LVVEL | 572.3657 | 571.3581 | 5 |
| | QGKK | 230.7098 | 459.2805 | 4 |
| | LPLGL | 512.3439 | 511.3370 | 5 |
| | APLLSDSF | 849.4352 | 848.4279 | 8 |
| | ALVNAF | 634.3193 | 633.3486 | 6 |
| | HSAGF | 518.2610 | 517.2285 | 5 |
| | SPVWVY | 375.6943 | 749.3748 | 6 |

*_de novo_ sequencing (only): PEAKS executed _de novo_ peptide sequencing based on LC-MS/MS raw data without being assigned to the protein database matching

**Table S2.** Identified peptides from GP BGSP hydrolysate fraction S1 from SCX fractionation

| Identified Protein | Peptide Sequence | m/z (Observed) | Mass | Peptide Length |
|---|---|---|---|---|
| (gi\|157829880) chain A, alpha-momocharin (sequence coverage 6%) | ATISLENSW | 1020.4997 | 1019.4924 | 9 |
| | TPIVL | 542.3547 | 541.3475 | 5 |
| (gi\|1229803397) legumin A-like [Momordica charantia] (sequence coverage 4%) | ALPVQVIASAY | 566.3237 | 1130.6335 | 11 |
| | FAVPAGATHW | 528.7667 | 1055.5188 | 10 |
| (gi\|1229803542) 11S globulin seed storage protein 2-like [Momordica charantia] (sequence coverage 5%) | IVVAF | 548.3444 | 547.3370 | 5 |
| | IVAVSAGTVEW | 1131.6045 | 1130.5972 | 11 |
| | VIPQFY | 766.4132 | 765.4061 | 6 |
| (gi\|1229778196) aspartic proteinase-like [Momordica charantia] (sequence coverage 3%) | ILGDIF | 677.3859 | 676.3795 | 6 |
| *de novo sequencing (only) | VVVAGEF | 720.3921 | 719.3854 | 7 |
| | WLVPSVY | 862.9591 | 862.4589 | 7 |
| | NVANQLDPYL | 573.7931 | 1145.5718 | 10 |
| | WELTL | 661.3743 | 660.3483 | 5 |
| | LFLPPF | 733.4279 | 732.4210 | 6 |
| | EPTTSDVVVAGEFDQGSGSMR | 1084.9946 | 2167.9690 | 21 |
| | VFLPQF | 750.4175 | 749.4112 | 6 |
| | SLPDLVF | 790.9355 | 789.4272 | 7 |
| | NLPLLL | 682.4500 | 681.4425 | 6 |
| | APLVSW | 672.3745 | 671.3663 | 6 |

**de novo* sequencing (only): PEAKS executed *de novo* peptide sequencing based on LC-MS/MS raw data without being assigned to the protein database matching

**Table S3.** The comparison of molecular interaction between lisinopril and AW6 on ACE (PDB code = 1O86)

| ACE Catalytic Site | | Lisinopril | | APLVSW | |
|---|---|---|---|---|---|
| Pocket | Amino Acid Residues | Interaction | Distance (Å) | Interaction | Distance (Å) |
| S1 | Ala354 | H-Bond | 2.9 | - | - |
| | Glu384 | H-Bond | 2.7 | - | - |
| | Tyr523 | H-Bond | 2.8 | H-Bond (Ser5 side chain) | 1.9 |
| S1’ | Glu162 | H-Bond | 3.4 | - | - |
| S2’ | Gln281 | H-Bond | 2.2 | - | - |
| | His353 | H-Bond | 2.8 | H-Bond (Trp6 main chain) | 2.3 |
| | Lys511 | H-Bond | 2.9 | Ionic (Trp6 main chain)<br>π-π (Trp6 side chain) | 3.3<br>6.8 |
| | His513 | H-Bond | 3.1 | H-Bond (Ser5 side chain) | 2.2 |
| | Tyr520 | H-Bond | 2.6 | H-Bond (Trp6 main chain) | 2.3 |
| Non-Catalytic Site | Glu143 | - | - | H-Bond (Ala1 main chain)<br>H-Bond (Ala1 main chain)<br>Ionic (Ala1 main chain) | 2.4<br>2.3<br>2.8 |
| | Asn70 | - | - | H-Bond (Ala1 main chain) | 2.5 |

**Table S4.** The comparison of molecular interaction between diprotin A and AW6 toward DPP4 (PDB code = 1WCY)

| DPP4 Catalytic Site | | Diprotin A | | APLVSW (AW6) | |
|---|---|---|---|---|---|
| Pocket | Amino Acid Residues | Interaction | Distance (Å) Molecule B | Interaction | Distance (Å) |
| S2 | Glu205 | H-Bond | 2.73 | - | - |
| | Glu206 | H-Bond | 2.65 | - | - |
| | Tyr662 | H-Bond | 3.00 | - | - |
| S1 | Tyr547 | H-Bond | 2.68 | - | - |
| | Tyr631 | H-Bond | 2.98 | - | - |
| S1’ | Arg125 | H-Bond | 2.99 | - | - |
| Non-catalytic Site | Ser59 | - | - | H-Bond | 2.00 |
| | Ile407 | - | - | H-Bond | 1.80 |
| | Arg471 | - | - | H-Bond<br>Charge | 1.90<br>2.50 |
| | Glu408 | - | - | H-Bond<br>Charge | 1.80<br>2.80 |