

Supplementary Material

Table S1. RMSD value between EGFR and native ligand of IIVO after molecular docking using CDOCKER, LibDock and LigandFit docking algorithm

No.	CDOCKER			LibDock			LigandFit		
	Pose	Reference	RMSD value (Å)	Pose	Reference	RMSD value (Å)	Pose	Reference	RMSD value (Å)
1	IIVO-1	IIVO-1	0.0000	IIVO-1	IIVO-1	0.0000	IIVO-1	IIVO-1	0.0000
2	IIVO-2	IIVO-1	3.2411	IIVO-2	IIVO-1	13.4153	IIVO-2	IIVO-1	1.6592
3	IIVO-3	IIVO-1	1.9480	IIVO-3	IIVO-1	17.4821	IIVO-3	IIVO-1	7.2496
4	IIVO-4	IIVO-1	17.1064				IIVO-4	IIVO-1	9.8477
5	IIVO-5	IIVO-1	7.7512						
6	IIVO-6	IIVO-1	2.9591						
7	IIVO-7	IIVO-1	13.3061						
8	IIVO-8	IIVO-1	22.5397						
9	IIVO-9	IIVO-1	21.1556						
10	IIVO-10	IIVO-1	11.4168						
11	IIVO-11	IIVO-1	15.5136						

Table S2. The Box-Behnken experimental design and the response for the SCP

Run order	Independent variable				Soluble peptides content (mg/mL)	
	Time (h)	Temperature (°C)	E/S (U/g)	pH	Experimental	Predicted
1	3.5	45	6000	7.5	0.3985	0.3895
2	3.5	45	6500	7.0	0.3083	0.3200
3	3.5	50	6000	7.0	0.4879	0.4900
4	3.5	50	6000	7.0	0.4898	0.4900
5	4.5	50	6500	7.0	0.3825	0.3806
6	4.0	50	5500	7.5	0.4351	0.4345
7	3.5	50	6000	7.5	0.4326	0.4260
8	4.5	55	6000	7.0	0.4531	0.4466
9	4.5	50	6000	6.5	0.4263	0.4200
10	4.0	55	6000	7.5	0.4569	0.4575
11	4.0	45	5500	7.0	0.3993	0.3780
12	4.0	50	5500	6.5	0.4737	0.4695
13	4.0	45	6000	6.5	0.3741	0.3665
14	3.5	55	6000	7.0	0.4931	0.4874
15	4.0	55	6000	6.5	0.5034	0.5065
16	3.5	45	6000	7.0	0.3622	0.3614
17	4.0	50	6500	6.5	0.3980	0.3895
18	3.5	50	6000	6.5	0.4725	0.4669
19	3.5	50	5500	7.0	0.4608	0.4574
20	4.5	50	6000	7.5	0.4435	0.4351
21	4.0	50	6000	7.0	0.4995	0.4900
22	4.5	50	5500	7.0	0.4163	0.4166
23	4.0	55	6500	7.0	0.4432	0.4240
24	3.5	50	6500	7.0	0.3815	0.3774
25	4.0	50	6000	7.0	0.5037	0.4900
26	4.0	50	6500	7.5	0.4037	0.3985
27	4.0	50	6000	7.0	0.4913	0.4900
28	4.5	45	6000	7.0	0.3677	0.3646
29	4.0	55	5500	7.0	0.4840	0.4820

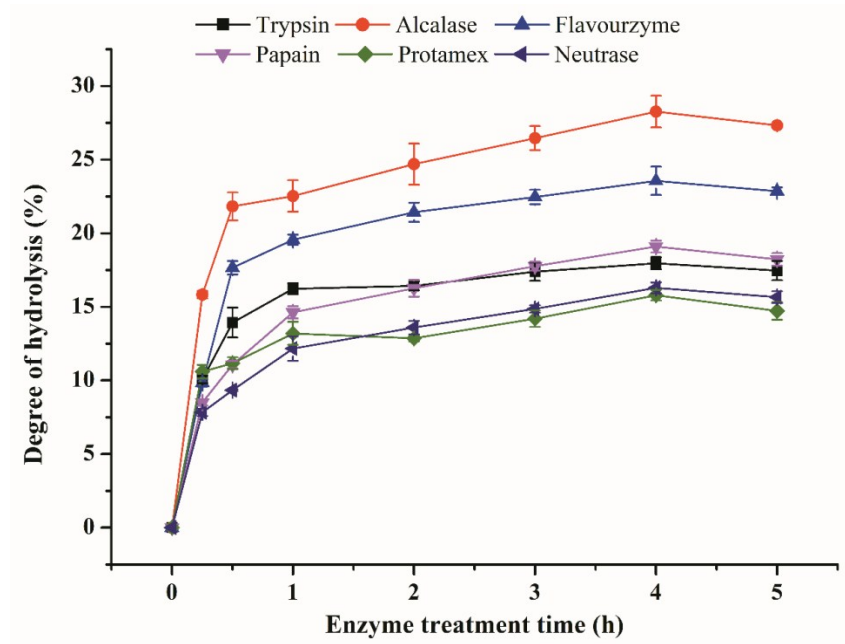


Fig. S1 Degree of hydrolysis of yak bone collagen by the six different enzymes during 5 hours

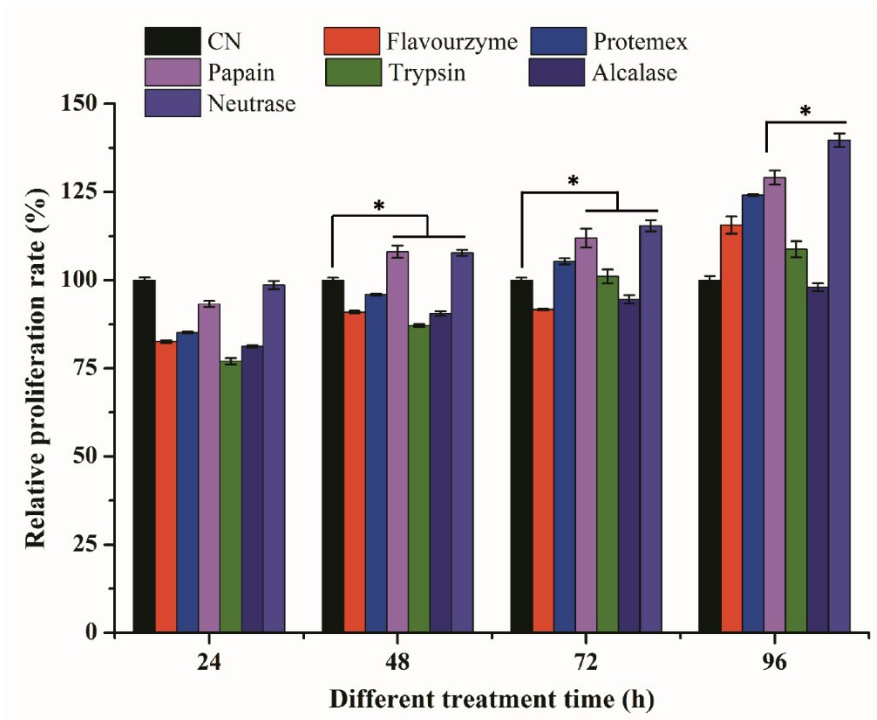


Fig. S2 Comparison the effect of six different enzymes hydrolysates on OPPA (asterisks indicate significant differences compared with control group at $P < 0.05$)

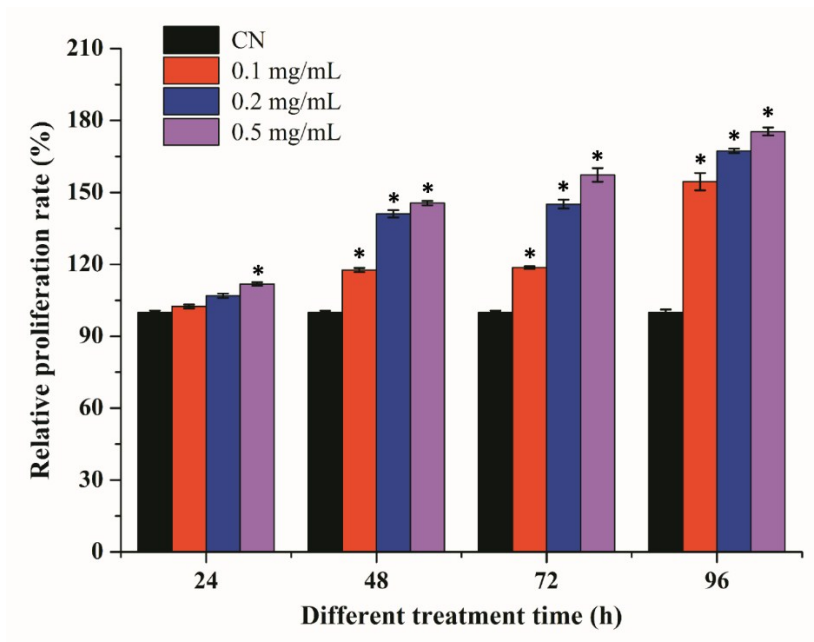


Fig. S3 The OPPA of peptides (0.1, 0.2 and 0.5 mg/mL) at different culture time (asterisks indicate significant differences compared with control group at $P < 0.05$)

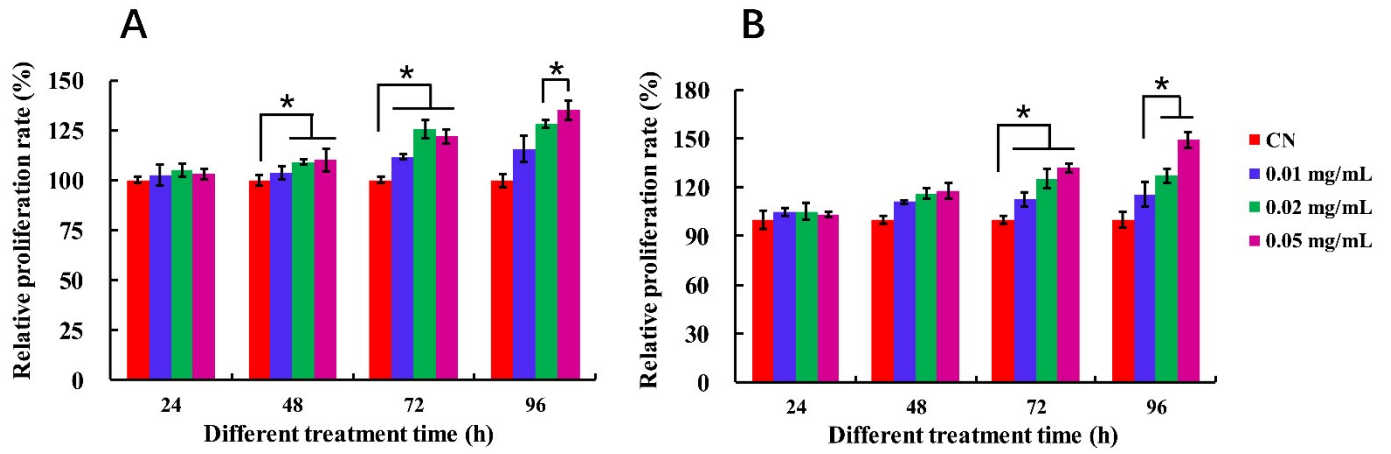


Fig. S4 The OPPA of the synthetic peptides (GP-16 and GD-18) (0.01, 0.02 and 0.05 mg/mL) at different culture time. (A) Synthetic peptide GP-16; (B) Synthetic peptide GD-18 (asterisks indicate significant differences compared with control group at $P < 0.05$)