The hemolymph and purified proteins of oyster *Crassostrea belcheri* exhibited significant antibacterial activity against *Vibrio spp*. The inhibitory effects of hemolymph (protein concentration of 6.363±0.923 mg/ml) against *V. harveyi*, *V. vulnificus* and *V. cholerae* were 29.51±1.66, 22.31±1.68 and 33.38±0.42 respectively. Purified P3 protein (80 µg/ml) had strong inhibitory effects on *V. Parahaemolyticus* (95.03±0.47), *V. vulnificus* (91.13±0.85), *V. Alginolyticus* (86.06±1.13), *V. Harveyi* (62.31±0.46) and slight effect on *V. cholerae* (87.7±3.82). The antibacterial activity against *V. parahaemolyticus* of the P3 protein was fully effective at 30°C, pH 6-8 with 10 mM of calcium ion. Molecular weight of the protein P3 was determined by SDS-PAGE and two-dimensional electrophoresis. The protein P3 consisted of two subunits, 25.0 kDa (pI~3) and 30.5 kDa (pI~5). Amino acid sequencing of the two protein subunits were analyzed by LC-MS/MS. Comparison with nrFasta database revealed that the 25.0 kDa protein was homologous to Sarcoplasmic calcium-binding protein (SCP). The 30.5 kDa protein showed highest homology to hemocyte extracellular superoxide dismutase from Pacific oyster, *C. gigas*. 