The cytotoxicity and the antivirus activity of native hemocyanin, \textit{RtH}, derived from the Bulgarian marine mollusk \textit{Rapana thomasiana} and its structural isoform, \textit{RtH2}, against HSV replication was evaluated on three HSV strains – two \textit{wt} strains, TM (HSV 1) and Bja (HSV 2), and one ACV\textsuperscript{R} mutant with \textit{tk} gene mutation, DD (HSV 2). The experiments were performed on continuous RD 64 cells and three HSV 1 and HSV 2 strains were used, two mutants sensitive to acyclovir and one resistant mutant.

Both compounds were found to be effective inhibitors of \textit{wt} HSV replication. Both compounds did not exhibit any effect on the infectious virus yield on ACV\textsuperscript{R} mutant. The most promising, active and selective, anti-HSV agent, especially to genital herpes virus, was found to be the functional unit of native hemocyanin – \textit{RtH2}. \textit{RtH2} did not induce apoptosis/necrosis 8 h after virus infection and the target of its action, was found to be the viral but not the host cell DNA.

\textbf{Key words:} Herpes Simplex Virus, \textit{Rapana thomasiana}, Hemocyanin, Resistance