

Peptides - inhibitors of collagenase

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Currently synthetic non-protein amino acids and peptides based thereon are widely used in biotechnology and pharmacy. The influence of non-protein amino acids and peptides synthesized at the SPC "Armbiotechnology" NAS RA on the activity of serine proteases was studied earlier and the novel inhibitors of these enzymes were described [1].

Matrix metalloproteinases (MMPs) are a major group of enzymes that regulates cell-matrix composition. The collagenase from *Clostridium histolyticum* (EC 3.4.24.3) investigated in the present work is a member of this group of enzymes. Ample evidence exists on the role of MMPs in normal and pathogenic processes including embryogenesis, wound healing inflammation and cancer. The association of MMPs with cancer metastasis makes them an attractive target for development of novel antimetastatic drugs aimed at inhibiting MMP activity [2].

About 40 non-protein amino acids and peptides have been screened. The docking analysis was used for selection of compounds which are able to interact with collagenase. Then the influence of selected non-protein amino acids and peptides on the activity of collagenase was studied. Collagenase activated by CaCl_2 was mixed with investigated compound. The mixture was dropped on the surface of 0.6% agarose gel mixed with gelatin (5 mg/ml) and incubated at 37°C. The diameter of cleared spots was measured after 2-3 hours. According to obtained data (S)- β -[4-phenyl-3-propyl-5-thioxo-1,2,4-triazol-1-yl]- α -alanine (calculated $K_i = 25.86 \text{ uM}$), (S)- β -[4-allyl-3-(pyridin-3'-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine (calculated $K_i = 156.18 \text{ nM}$) and tripeptide allyl-glycyl-(S)- β -[4-allyl-3-(pyridin-3'-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine (calculated $K_i = 2.47 \text{ uM}$) have demonstrated the ability to inhibit collagenase activity.

1. N. Hovhannisyan, Sh. Harutyunyan, A. Hovhannisyan, A. Hambardzumyan, M. Chitchyan, M. Melkumyan, G. Oganezova, N. Avetisyan. *Amino Acids*. 37, 531-536, **2009**.
2. Ricardo A. García, Dennis P. Pantazatos, Christopher R. Gessner, Katrina V. Go, Virgil L. Woods, Jr., and Francisco J. Villarreal. *Mol Pharmacol*. **67**, 1128-1136, **2005**.