Modeling of peptides based on heterocycle substituted non-protein amino acid, synthesis and in vitro study of their impact on collagenase activity

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More than 15 new peptides have been constructed on the basis of (S)-\(\beta\)-[4-allyl-3-propyl-5-thioxo-1,2,4-triazol-1-yl]-\(\alpha\)-alanine non-protein amino acid by ChemOffice software. The study of their possible interaction with collagenase enzyme was implemented by molecular docking program – AutoDockVina software. Analyzing the obtained results, 9-fluorenylemethoxycarbonylglucyl-(S)-\(\beta\)-[4-allyl-3-propyl-5-thioxo-1,2,4-triazol-1-yl]-\(\alpha\)-alanine dipeptide was identified by maximum values of Gibbs free energy (\(\Delta G\)) and minimum values of inhibition constant (\(K_I\)) of ligand-macromolecular interaction (Fig. 1). The synthesis of the mentioned dipeptide was implemented by the method of activated esters (Scheme 1) [1].

\textit{Scheme 1}

\begin{equation}
\Delta G \approx -8.1; \ K_I \approx 1.16
\end{equation}

\textit{Fig. 1.}

The impact of synthesized peptide on collagenase enzyme activity was studied \textit{in vitro} using various peptide concentrations, and the data were presented in the Table. Besides, IC\textsubscript{50} of peptide having an impact was determined, which was 0.982 μmol/l.

<table>
<thead>
<tr>
<th>Concentration, μmol/l</th>
<th>Inhibition %</th>
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<tbody>
<tr>
<td>0.6708</td>
<td>43.82</td>
</tr>
<tr>
<td>1.3417</td>
<td>58.33</td>
</tr>
<tr>
<td>2.6834</td>
<td>81.72</td>
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</tbody>
</table>

\textit{Fig. 2. Graphical curve of IC\textsubscript{50} value}

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