Short Communication

QADIR-C34

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ABSTRACT

Qadir-C34 is a synthetic peptide which consists of thirty four amino acids. It is a fusion inhibitor that may be effective for enfuvirtide resistant AIDS patients. Qadir-C34 blocks the entry of HIV genome into human CD4 cells by binding to HR1 of gp41 of HIV envelope.

Keywords: Qadir-C34, HIV fusion inhibitor

Number of Tables : 1        Number of Figures: 3        Number of References:21
INTRODUCTION

HIV Fusion inhibitors may be classified according to their binding sites (Figure 1). T20 or enfuvirtide is the only FDA approved Fusion inhibitor for the use of AIDS patients. The other fusion inhibitors are under research. Resistance to existing antimicrobial drugs led to the search for the new drugs, or alternative techniques to increase the efficacy of the drugs.\textsuperscript{1-5} Qadir-C34 is a fusion inhibitor that may be effective for enfuvirtide resistant AIDS patients.\textsuperscript{6,7} It differs from Qadirvirtide\textsuperscript{8} in such a way that it is composed of the amino acids which have different binding sites.

Table 1: Classification of Fusion Inhibitors

<table>
<thead>
<tr>
<th>Peptides Binding to HR1:</th>
<th>Enfuvirtide, Qadirvirtide, Qadir-C34</th>
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<tbody>
<tr>
<td>Peptide Binding to HR2:</td>
<td>N36, 5-Helix</td>
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<tr>
<td>Non-peptide Fusion Inhibitors:</td>
<td>XTT formazan, NB-64</td>
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</tbody>
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Qadir-C34 is a synthetic peptide which consists of thirty four amino acids. The amino acids along with their positions are given here:\textsuperscript{6,7}:

\texttt{WMEWDREINNYTSLHSLIEAQNQQEKNEQELL}

The HIV life cycle is begun by fusion of the HIV envelope with human cell membrane.\textsuperscript{9} gp41 of HIV envelope is composed of four regions; transmembrane region (TR) which is embedded in the viral envelop, two hydrophobic Heptad Repeats (HR1 and HR2)\textsuperscript{10}, and a fusion peptide (FP) which is inserted in the human CD4 cell membrane during the fusion process (Figure 1).\textsuperscript{11-13}

\texttt{Figure 1: Regions of gp41 of HIV envelope: transmembrane region (TR), Heptad Repeats (HR1 and HR2), and fusion peptide (FP).}

Bending of HR regions of gp41 of HIV envelope is very important in the fusion of HIV and CD4 cell membrane.\textsuperscript{14-19} Three HR1 helices form an interior, parallel-coiled-coil trimer, while three HR2 helices pack in the reverse direction.\textsuperscript{20} The formation of this 6-helix bundle causes closeness of the HIV envelop and human CD4 cell membrane so that the fusion of the two membranes occurs leading to form a pore for HIV material to enter into human cell (Figure 2).\textsuperscript{21}
Qadir-C34 inhibits the entrance of HIV genetic material into human CD4 cells. It binds to HR1 of envelope protein on the virus and avoids the attachment of HR2 with HR1. So the virus cannot come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited (Figure 3).6,7

Figure 2: Fusion of HIV envelope with human cell membrane. Trimer-of-hairpins formation causes the closeness of the two membranes, viral envelope and human cell membrane, resulting in the fusion of the membranes

Figure 3: Qadir-C34 blocks the entry of HIV genome into human CD4 cells by binding to HR1 as the virus cannot come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited
REFERENCES


