MINI-REVIEW

QADIRVIRTIDE

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ABSTRACT

Qadirvirtide is a fusion inhibitor that may be used as prophylaxis or for the treatment of AIDS. It is a synthetic peptide that is composed of 36 amino acids. Qadirvirtide blocks the entry of HIV genome into human CD4 cells by binding to HR1 as the virus can not come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited.

Keywords: Qadirvirtide, HIV fusion inhibitor, AIDS.

Qadirvirtide is a fusion inhibitor that may be used as prophylaxis or for the treatment of AIDS. It may be effective for enfuvirtide (the first fusion inhibitor) resistant AIDS patients, especially Pakistani's patients. It is a synthetic peptide that is composed of 36 amino acids (Qadir and Malik, 2010; Qadir and Malik, 2011):

YTSLIHSLIEEAQNQQEKNEQELLELDKWASLWNWF

The life cycle Human immunodeficiency virus (HIV) is started by fusion of the HIV envelope with human cell membrane (Luciw, 1996). The *env* gene encodes a polyprotein gp160 (envelop). The envelope is cleaved post-translationally by a cellular protease to yield gp120 and gp41 (McCune *et al.*, 1988; Leonard *et al.*, 1990). gp120 and gp41 are non-covalently joined together on the viral membrane (Lu *et al.*, 1995). The surface subunit gp120 determines viral tropism through interaction with the primary cellular receptor CD4 and particular chemokine receptors (Leonard *et al.*, 1990; Hoxie 1991). gp41 contains two lucine zipper like amino acid sequences: HR1 (heptad repeat 1) and HR2 (heptad repeat 2) (Chamber *et al.* 1990; O'Shea *et al.*, 1991; Landschulz *et al.*, 1998). HR1 is a heptad repeat region present on the amino-terminus (N-HR) of gp41, while HR2 is a heptad repeat region present on the carboxy-terminus (C-HR) of gp41 (Rasmussen *et al.*, 1991; Lu *et al.*, 1995; Delwart *et al.*, 1990; Wild *et al.*, 1992).

The entry process consists of receptor binding (Olshevsky, 1990; Kwong, 1998; Sullivan *et al.*, 1998) followed by coreceptor binding (Clapham, 2002; Deng, 1996), and ultimately membrane fusion allowing the viral core to enter the cell (Markosyan *et al.*, 2003). First, the viral gp120 binds specifically to CD4, a protein receptor on the target cell (Farzan *et al.*, 1998; Markosyan *et al.*, 2003).

Dimerization is an essential component of fusion of HIV envelope with human cell membrane (Earl *et al.*, 1990; Pinter *et al.*, 1989; Einfeld *et al.*, 1988) and the HR regions play the role in this associative process (Delwart *et al.*, 1990; Gallaher *et al.*, 1989; Buckland and Wild, 1989). After the attachment of gp120 with CD4 protein, gp120 is released from the virus envelope allowing exposing gp41. Then end of the gp41 is inserted into human cell membrane. Next step is the dimerization of the heptad repeats (HR1 and HR2). This dimerization causes the closeness of the two membranes, viral envelope and human cell membrane, resulting in the fusion of the membranes (Chan *et al.*, 1997; Weissenhorn *et al*,. 1997). Fusion of the membranes leads to form a pore for HIV material to enter into human cell (Weissenhorn *et al.*, 1997; Kliger *et al.*, 2001).

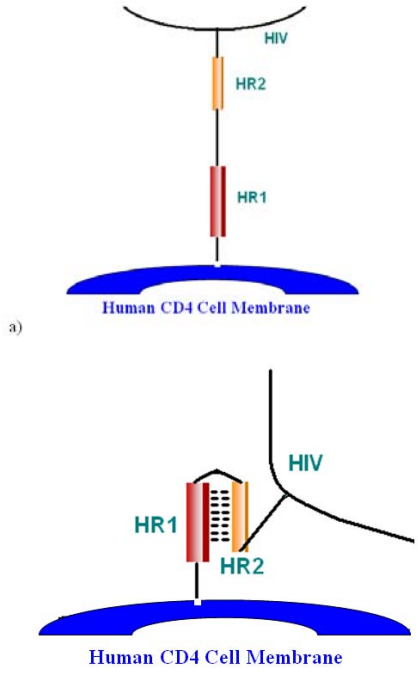

Fig. 1: Fusion of HIV envelope with human cell membrane. a) Attachment of the fusion peptide with human CD4 cell showing the two important regions of gp41 of HIV. b) Dimerization causes the closeness of the two membranes, viral envelope and human cell membrane, resulting in the fusion of the membranes.

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Qadirvirtide blocks the entry of HIV genome into human CD4 cells. It binds to HR1 of envelope protein on the virus and inhibits the joining of HR2 with HR1. So the virus can not come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited (Qadir and Malik, 2010; Qadir and Malik, 2011).

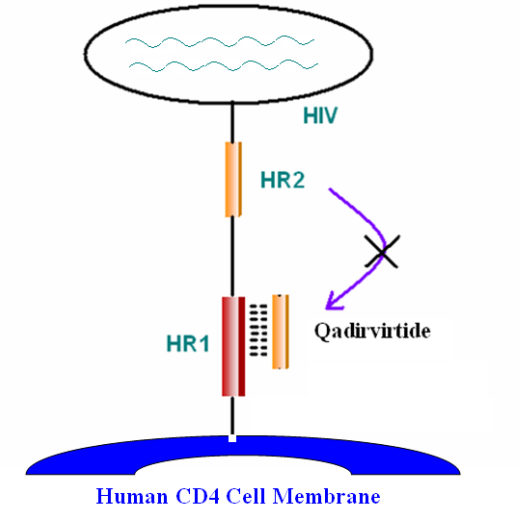

Fig. 2: Qadirvirtide blocks the entry of HIV genome into human CD4 cells by binding to HR1 as the virus can not come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited

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