

**Short Communication****QADIR-C34****MUHAMMAD IMRAN QADIR\***

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**Email:** [mrirranqadir@hotmail.com](mailto:mrirranqadir@hotmail.com)(Received on Date: 7<sup>th</sup> February 2013Date of Acceptance: 25<sup>th</sup> June 2013)**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*

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

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## 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.<sup>1-5</sup> Qadir-C34 is a fusion inhibitor that may be effective for enfuvirtide resistant AIDS patients.<sup>6,7</sup> It differs from Qadirvirtide<sup>8</sup> in such a way that it is composed of the amino acids which have different binding sites.

**Table 1:** Classification of Fusion Inhibitors

*Peptides Binding to HR1:* Enfuvirtide, Qadirvirtide, Qadir-C34

*Peptide Binding to HR2:* N36, 5-Helix

*Non-peptide Fusion Inhibitors:* XTT formazan, NB-64

Qadir-C34 is a synthetic peptide which consists of thirty four amino acids. The amino acids along with their positions are given here<sup>6,7</sup>:

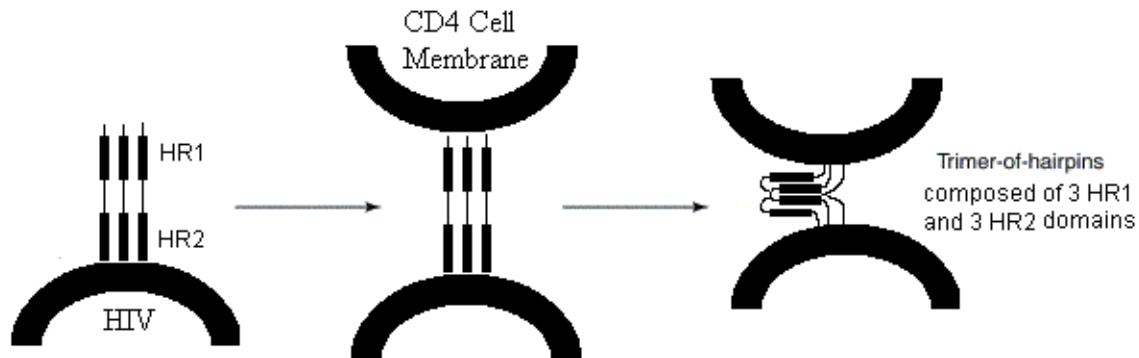
WMEWDREINNYTSLIHSLIEEAQNQQEKNEQELL

The HIV life cycle is begun by fusion of the HIV envelope with human cell membrane.<sup>9</sup> 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)<sup>10</sup>, and a fusion peptide (FP) which is inserted in the human CD4 cell membrane during the fusion process (Figure1).<sup>12-13</sup>



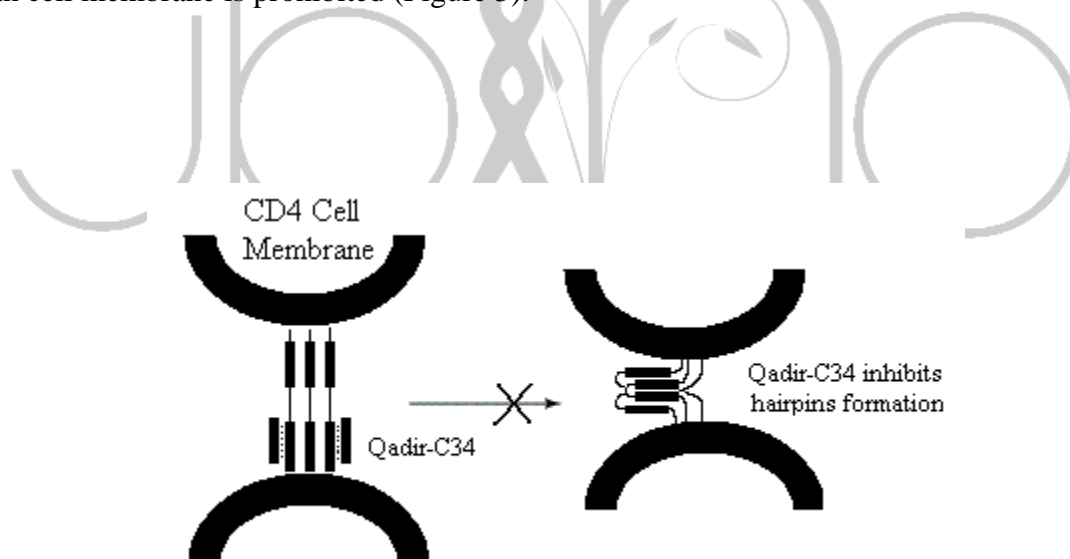
**Figure 1:** Regions of gp41 of HIV envelope: transmembrane region (TR), Heptad Repeats (HR1 and HR2), and fusion peptide (FP).

Bending of HR regions of gp41 of HIV envelope is very important in the fusion of HIV and CD4 cell membrane.<sup>14-19</sup> Three HR1 helices form an interior, parallel-coiled- coil trimer, while three HR2 helices pack in the reverse direction.<sup>20</sup> 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).<sup>21</sup>



**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

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 can not come close to the human cell membrane and ultimately fusion of the viral envelope with human cell membrane is prohibited (Figure 3).<sup>6,7</sup>



**Figure 3:** Qadir-C34 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

**REFERENCES**

**Buckland R, Wild F.:** Leucine zipper motif extends. *Nature* **338**:547,1989.

**Chambers P, Pringle CR, Easton AJ:** Heptad repeat sequences are located adjacent to hydrophobic regions in several types of virus fusion glycoproteins. *J Gen Virol* **71**(12):3075-3080,1990.

**Chan DC, Fass D, Berger JM, Kim PS.:** Core structure of gp41 from the HIV envelope glycoprotein. *Cell* **89**:263-273,1997.

**Delwart EJ, Mosialos G, Gilmore T.** Retroviral envelope glycoproteins contain a leucine zipper like repeat. *AIDS Res Hum Retroviruses* **6**:703-706,1990

**Earl PL, Doms RW, Moss B.** Oligomeric structure of the human immunodeficiency virus type 1 envelope glycoprotein. *Proc Natl Acad Sci USA* **87**:648-652,1990

**Ehsan O, Qadir MI, Malik SA, Abbasi WS, Ahmad B.** . Efficacy of nanogold-insulin as a hypoglycemic agent. *J Chem Soc Pak*, **34**(2): 365-370,2012

**Einfeld D, Hunter E.** Oligomeric structure of a prototype retrovirus glycoprotein. *Proc Natl Acad Sci USA* **85**:8688-8692,1988

**Gallaher WR, Ball JM, Garry RF, Griffin MC, Montelaro RC.** A general model for

the transmembrane proteins of HIV and other retroviruses. *AIDS Res Hum Retrovir* **5**:431-440,1989.

**Hussain A, Khalid SH, Qadir MI, Massud A, Ali M, Khan IU, Saleem M, Iqbal MS, Asghar S, Gul H** Water Uptake and Drug Release Behaviour of Methyl Methacrylate-co-itaconic acid [P(MMA/IA)] Hydrogels Cross-linked with Methylene Bis-acrylamide. *J Drug Delvr Sci Tech*, **21**(3): 249-255,2011

**Javed F, Qadir MI, Janbaz KH, Ali M.** . Development of novel drugs from marine microorganisms. *Critical Rev Micro*, **37**(3): 245–249,2011

**Lu M, Blacklow SC, Kim PS** (1995). A trimeric structural domain of the HIV-1 transmembrane glycoprotein. *Nat Struct Biol* **2**:1075–1082,1995

**Luciw PA.** Human immunodeficiency virus and their replication. In: *Field virology* (Fields BN, Knippe DM, Howley PM, eds). Philadelphia (PA): *Lippincott-Raven*. Pp. 1881-952,1996

**Masood MI, Qadir MI, Shirazi JH, Khan IU** Beneficial effects of lactic acid bacteria on human beings. *Critical Rev Micro*, **37**(1): 91–98,2011

**Naz S, Qadir MI, Ali M, Janbaz KH.** Nanotechnology for imaging and drug delivery in cancer. *J Chem Soc Pak*, **34**(1), 107-111,2012

**Nisar L, Qadir MI, Malik SA, Tabassum N:** Characterization of the immunodominant regions within gp41 of env gene of HIV in Pakistan. *J Chem Soc Pak*, **33**(4): 545-548,2011

**Pinter A, Honnen WJ, Tilley SA, Bona C, Zaghoulani H, Gorny MK, Zolla-Pazner S.** Oligomeric structure of gp41, the transmembrane protein of human immunodeficiency virus type 1. *J Virol* **63**:2674-2679,1989

**Qadir MI** Qadirvirtide. *Pak J Pharm Sci*, **24**(4): 593-595,2011

**Qadir MI and Malik SA.** Genetic Variation in HR Region of env gene of HIV: A

Perspective for Resistance to HIV Fusion Inhibitors. *AIDS Res. Hum. Retrovir.*, **27**: 57-63,2011

**Qadir MI, Malik SA** HIV fusion inhibitors. *Rev Med Virol*, **20**:23-33,2010

**Qadir MI, Malik SA, Nisa TU, Tabassum N, Ali S, Nisar N** : Characterization of HR region of gp41 of HIV. *Int J Agric Biol*, **12**: 456-458,2010

**Weissenhorn W, Dessen A, Harrison SC, Skehel JJ, Wiley DC.** Atomic structure of the ectodomain from HIV-1 gp41. *Nature* **387**:426-430,1997