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Analysis of the HIV-1 Tat exon 2 gene motifs as a potent candidate for therapeutics against HIV infection

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HIV-1 tat gene is a regulatory gene responsible for initiation and elongation of viral transcription through the LTR transactivation, composed of two coding exons yielding a protein of 101 amino acids. Exon 1 (1–72aa) is important for viral transcription and Exon 2 (73–101 aa) is believed to have major role in cell adhesion and cellular uptake of the exogenous Tat and facilitates apoptosis. The aim of our study was to analyse HIV-1 tat exon 2 and to assess its potential for therapeutics against HIV infection. Comparative analysis of nucleotide sequences of HIV-1 patients with Indian reference isolate (HIV-1C-IN) showed that samples had ~75% similarity with HIV-1C-IN and phylogenetic analysis showed them falling in close cluster of HIV-1 clade C. The tat exon 2 sequences displayed the presence of conserved RGD motif and ESKKKVE motif. Presence of RNA binding domains was reported, which if undergoes any mutation may alter the binding of the Tat with TAR element, essential for the Tat-mediated trans-activation. Hence making the domain a potential drug target. Further sequence analysis of the samples suggest that in CCMB121 lysine residue was not seen to be conserved at position number 90 which may be hypothesized in downregulating the HIV-1 replication. Even though Tat plays an important role in viral transcription, till date there is no Tat based drugs designed, for this the novel CTL epitope (DPSGSEESK) observed by us can be analysed for posing as drug target.

Development of controlled porosity osmotic pump tablet for oral administration of Metformin and Glipizide

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Osmotically controlled oral drug delivery systems (OCODDS) utilize osmotic pressure as the energy source for the controlled delivery of drugs. Drug release from these systems is independent of pH and hydrodynamic conditions of the gastro-intestinal tract (GIT) to a large extent, and release characteristics can be easily adjusted by optimizing the parameters of the delivery system. A system that can deliver multi- drug at prolonged rate is very important for the treatment of various chronic diseases such as diabetes, asthama and heart diseases. Type 2 diabetes mellitus emerges as a result of multiple pathophysiologic changes. If the pharmacotherapy of type 2 diabetes should be tailored to the underlying pathophysiology, it would be necessary to use a combination of agents with complementary mechanisms of action. The two principal defects in type 2 diabetes are insulin deficiency and insulin resistance. Therefore, combining an insulin-providing agent with an insulin-sensitizing agent will augment the efficacy of current antihyperglycemic agents. The objective of present study is to develop controlled porosity osmotic pump (CPOP) that can deliver drugs having complementary mechanism of action i.e. insulin providing agent (glipizide) with insulin sensitizing agent (metformin) in controlled manner upto 12 hrs. It was prepared by incorporating drugs in the core and coated with various types (PVP, PEG 400, HPMC) and levels (30, 40, 50 % w/w of polymer) of pore former at weight gain of 8, 12 and 15%.