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Oral Efavirenz Loaded Lactoferrin Nano Formulation

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ABSTRACT

Acquired immune deficiency syndrome (AIDS) is one of the global concerns in the present century. High active antiretroviral therapy (HAART), a combination of antiretroviral drugs proven successful for HIV-1 treatment. Efavirenz, a non-nucleotide/ nucleoside reverse transcriptase inhibitor often used as a component in HAART, has poor bioavailability and high toxicity. This review emphasized on lactoferrin based nano formulation of efavirenz and its advantages over soluble drug. Discussed preparation of nanoparticles and characterization using various techniques. In-vitro studies suggests reduction in cytotoxicity by 50% in case of nano formulation and also decrease in skin hypersensitivity. Pharmacokinetic profiling of efavirenz after oral administration in rats increases bioavailability of nano formulated drug and decreases hepatotoxicity and nephrotoxicity. Above observation manifested, lactoferrin nanoparticles as a potent vehicle for drug delivery.

Keywords: Acquired Immune Deficiency Syndrome, High Active Antiretroviral Therapy (HAART), Hepatotoxicity and Nephrotoxicity

INTRODUCTION

As per Global HIV and AIDS statistics, incidence of AIDS has declined by 16% in past eight years, till date there is no cure for HIV although it can be controlled if detected earlier. Food and Drug Administration, USA has recommended six classes of drugs for the treatment of AIDS: The nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors (FIs), CCR5 antagonists, and integrase inhibitors [1-2]. These antiretroviral classes of drugs wield for combination therapy in HIV infection, appellate as HAART (highly active antiretroviral therapy). Predominately concoction of two nucleotide/ nucleoside reverse transcriptase inhibitors (NRTIs) and a non-nucleotide/ nucleoside reverse transcriptase inhibitor (NNRTIs) availed for HAART to suppress Virus RNA levels [1-2].

Efavirenz is an FDA approved HIV-1 inhibitor, comes under non-nucleoside reverse transcriptase inhibitors (NNRTIs) [3] and endorsed component of initial treatment for AIDS globally [4]. It is eminently lipophilic having partition coefficient of 5.4 [5], bioavailability of efavirenz is sparse because of its poor solubility [6] and high affinity (>99%) for plasma proteins [7]. To overcome this limitation Kumar et al. developed a Lactoferrin protein-based nanoparticle delivery system to increase bioavailability of efavirenz. Lactoferrin, an iron binding glycoprotein displays anti-inflammation, anti-microbial and virucidal properties which makes it effective vehicle, moreover it is cost effective [8].

The intent of the study is to establish a substantial, lactoferrin based oral nano formulation to obtain prolonged drug release, reduce toxicity and enhance pharmacological properties along with anti-viral activity [8]. In this study, Lacto-EFV-nano (EFV loaded lactoferrin nanoparticles) is evaluated for improved bio distribution, prepared using Sol-oil chemistry as, this procedure is elementary and rapid and does not affect native protein structure, yields particles of approximately 45-60 nm with higher encapsulation of drugs ~ 59%. This method of preparation is advantageous over other prevailing methods excluding use of chemicals that maybe rather harmful; for example chitosan based nanoparticles has prepared using glutaraldehyde which affects chemical conformation of the components and have cytotoxic effects [9].EFV loaded lactoferrin nanoparticles were characterized using Field emission Scanning electron microscopy (FESEM) and Dynamic light scattering(DLS) to scrutinize particle size, polydispersity Index and stability of

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particles in colloidal state. Size of blank lactoferrin nanoparticles is around 19-35nm and EFV loaded lactoferrin nanoparticles are around 45-60nm in FE-SEM. Analysis of blank lactoferrin and EFV loaded lactoferrin nanoparticles using dynamic light scattering divulges particle size of 72 + 3.4 nm and 10 + 5.3 nm respectively. Dynamic light scattering (DLS) estimate size of particles present in colloidal form, which can be affected by Hydrogen bond interactions between nanoparticles surface charges and water molecules. Negative charge of -23 +1.2 mV on the surface of nanoparticles denoted stability in suspension. DLS also analyze polydispersity index (PDI) suggests homogenous nature and size distribution of particles. From DLS PDI value < 0.341 has obtained which indicates homogenous size distribution of nanoparticles population. As current quantum dot model system suggests that particle size smaller than 5.5 nm can be easily excreted [10], the significantly higher sized lactoferrin nanoparticles are better equipped to sustain in blood circulation for longer period, indicating prolonged release yielding beneficiary therapeutic effects. Lacto-EFV-nano were also characterized using FT-IR and Differential scanning calorimetry (DSC) thermogram. FT-IR data showed miniature version of observed peaks in Lacto-EFV-nano compared to soluble drug suggesting electrostatic interaction in nano formulation. Thermogram data suggested an improved stability at 138°C also protecting the encapsulated drug at 260°C that degrades soluble drug. Lacto-nano releases the maximum drug at pH -5 (i.e., at endosomal pH) due to conformational changes induced in protein but stable at gastric pH, making this a more potent delivery vehicle over Chitosan nanoparticles [11].

Analysis of cellular release kinetics of drug suggests prolong and controlled release of drug from Lacto-EFV-nano as compare to other burst releasing Solid lipid nanoparticles (100% of drug in <5 min) [12]. In-vitro studies suggested the same, indicating 50% less cytotoxicity in cell lines. The nano formulation also decreases skin hypersensitivity by 1.5 folds rather apparent in soluble EFV treatments [13]. The antiviral activity of drug was also improved in terms of its $IC_{50}$from 2.56 nM to 1.1 nM in nano formulation, where antiviral property of Lactoferrin nano formulation (IC50 <4μM) seemed to act in additive manner.

Pharmacokinetic (PK) analysis for soluble drug and nano formulation for oral administration in rats was performed (and parameters were calculated using KINETICA version 5.0 software) where [3-4] fold increase in AUC (area under the plasma concentration time curve) along with [6-7] fold increase in AUMC (area under the first moment curve) were observed in animals treated with nano formulation compared to soluble EFV; conveying improved PK profile along with increased bioavailability. 30% increment of peak plasma concentration (C_{max}) of EFV and 100% increment in time to reach C_{max} (T_{max}) has been observed. In animals a gender biased observation for higher peak plasma concentration and drug exposure time (AUC) was made for female rats. The nano formulation showed lower Hepatotoxicity and Nephrotoxicity compared to soluble drug while lipid profiles were unaltered.

The essence of the study suggests a more stable directed and sustained vehicle for EFV that can counter the negative impacts of the drug while increasing bio availability and bio distribution with improved PK profile. This nano formulation shows a bright opportunity for novel drug deliveries eliminating the side effects.

REFERENCES

1. Gulick RM, Ribaudo HJ, Shikuma CM (2006) Three- vs four-drug antiretroviral regimens for the initial treatment of HIV-1 infection: A randomized controlled trial. JAMA 296: 769-781.
2. Riddler SA, Haubrich R, DiRienzo AG (2008) Class-sparing regimens for initial treatment of HIV-1 infection. N Engl J Med 358: 2095-2106.
3. Department of Health and Human Services (2008) Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Accessed on: March 27, 2008. 1: 128
4. Antiretroviral therapy for HIV infection in adults and adolescents (2006) Recommendations for a public health approach RW. Accessed on: March 27, 2008.
5. Joly V, Yeni P (2000) Non-nucleoside reverse transcriptase inhibitors. Ann Med Intern 151: 260-267.
6. Avachat AM, Parpani SS (2015) Formulation and development of bicontinuous nanostructured liquid crystalline particles of efavirenz. Colloids Surf B Biointerfaces 126: 87-97.
7. Boffito M, Back DJ, Blaschke TF (2003) Protein binding in antiretroviral therapies. AIDS Res Hum Retroviruses 19: 825-835.
8. Suzuki YA, Kelleher SL, Yalda D (2003) Expression, characterization and biologic activity of recombinant human lactoferrin in rice. J Pediatr Gastroenterol Nutr 36: 190-199.
9. Qi LF, Xu ZR, Li Y, Jiang X, Han XY, et al. (2005) *In vitro* effects of chitosan nanoparticles on proliferation of human gastric carcinoma cell line MGC803 cells. World J Gastroenterol 11: 5136-5141.
10. Choi HS, Liu W, Misra P (2007) Renal clearance of quantum dots. Nat Biotechnol 25: 1165-1170.
11. Chaudhury A, Das S (2011) Recent advancement of chitosan-based nanoparticles for oral controlled delivery of insulin and other therapeutic agents. AAPS Pharm SciTech 12: 10-20.

12. Uner M, Yener G (2007) Importance of solid lipid nanoparticles (SLN) in various administration routes and future perspectives. Int J Nanomed 2: 289-300.

13. Phillips EJ, Kuriakose B, Knowles SR (2002) Efavirenz-induced skin eruption and successful desensitization. Ann Pharmacother 36: 430-432.