

# The Administration of Nano Suspensions Containing Antiviral Agents from the Nose to the Brain is One Method of Treating Neuro-AIDS Patients

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### Abstract

Intranasal drug delivery is one in all the battle areas of the analysis in targeting drug to the brain. Nose to brain drug delivery follows the exteroception pathway and supposedly proverbial to be a lot of economical to deliver neuro-therapeutics to the brain by circumventing the BBB and thereby increasing bioavailability of medicine within the brain. The advantage of this technique is non-invasiveness, speedy onset of action and helps to realize web site specific delivery. During this analysis work Nano suspension were ready victimization combination of antiretroviral agents for Neuro-AIDS treatment. Nano suspensions were ready by high-speed homogenization, wet edge and aggressive homogenization techniques. Formulations were analyzed by SEM, FTIR, and DSC. Morphology and stability analysis was done by analysing letter of the alphabet potential, particle size, and PDI. Ex-vivo diffusion study and histopathological analysis was performed victimization goat nasal tissue layer. air mass homogenization was found to be best technique for formulation of nanosuspension. Antiviral medicine may well be delivered with success by optimizing nasal dose type.

# Introduction

Human immunological disorder infection (HIV) affects over thirty six.7 million individuals worldwide, in step with the UNAIDS report 2017, and 1.8 million individuals were recently infected with HIV in 2016. Since the emergence of the epidemic AIDS-related sicknesses has killed over thirty five million individuals globally [1]. it's well undeniable fact that HIV includes a wrecking impact on the human system which ends in AIDS and furthers varied opportunist diseases that cause the death of the patient[2]. The initial symptoms of HIV infection embrace immune suppression; however it additionally has peculiar medical specialty manifestations targeting the Central system nervosum (CNS). Once HIV enters the brain, it remains there for Associate in Nursing extended amount of your time, presumptively till the individual dies. HIV-associated dementedness (HAD) is characterised by medical specialty, motor, and psychological feature abnormalities once the virus enters the brain directly. Survival of HIV-positive persons has been improved because of the appliance of more and more powerful and extremely active antiretroviral agents (HAART). Combination therapies (cART) have endeavoured for quick and efficacious treatment. Varied drug delivery approaches ar fictitious to beat the disadvantage related to antiretroviral medical aid [3]. Although the utilization of more and more intense and dynamic antiretroviral agents like HIV proteolytic enzyme inhibitors (PIs), nucleoside/nucleotide polymerase inhibitors (NRTIs), non-nucleoside polymerase substance (NNRTIs), and infective agent entry inhibitors has improved the survival of HIV-infected people, symptoms of neuroaids act 30-50 p.c of the HIV population. Antiretroviral medical aid (ART) medicine wills which may} cross the barrier (BBB) can facilitate cut back infective agent load, limit the virus's development within the brain parenchyma, and improve neurocognitive impairment. Infected cells, on the opposite hand, are unaffected by HIV-1 transcription and translation from infective agent genomes [4]. All of the patients World Health Organization are treated and have complete infective agent suppression have low-level pathology. To cut back HIV-1 transcription and residual viruses, new treatment medicine are needed. Several Nano particulate preparations are developed today to directly reach the central nervous system. Nano emulsion, Nano suspension, micellar carriers, nanoparticles, liposomes, and alternative formulation boosts brain porousness, thence lowering virus load. A BCS category IV medicine Norvir (RTV) and Lopinavir (LPV) is created into Nano suspension for the nose to brain delivery to boost solubility and porousness with the appliance of surfactants. A mixture dispersion of drug particles in Associate in nursing binary compound section with particle sizes smaller than one metric linear unit is thought as Nano suspension [5]. The drug's solubility is improved in each the binary compound and macromolecule phases. The first goal of this study is to form Nano suspensions of the antiretroviral agents Norvir and Lopinavir victimization applicable ways like wet edge, high-speed homogenization, and aggressive homogenization. RTV and LPV are used as double-boosted PIs during this study. Together medical aid with 2 PIs, a small dose of RTV is run as a booster. A mixture of RTV and LPV formulation was created by combining the 2 suspensions [6].

## Materials and Methods

Ritonavir, Lopinavir, HPMC 3CPS (Methocel E3), Poloxamer 407 (Pluronic F127) were received as gift samples from Glen mark Pharmaceuticals Ltd R & D Centre. Sodium Lauryl sulphate purchased from Thomas Baker Chemicals Pvt. Limited.

## High speed homogenization

A high-speed homogenizer (IKAT25 Ultra Turrax) was used to make the nan suspension [8]. HPMC, Poloxamer 407, and Sodium

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lauryl sulphate were accurately weighed and dissolved in water on a magnetic stirrer [9]. This solution was then subjected to high-speed homogenization. The drugs (RTV and LPV) were disseminated gently into the solution and homogenized for 90 min at 20,000 rpm.

## Wet milling technique

Nano suspension was produced by using Dyna mill<sup>\*</sup> (Glenmark Pharmaceuticals Ltd R & D Centre, Nashik). Coarse pre-suspension of drug and excipients (HPMC 3 CPS, Pluronic F127, Sodium lauryl sulfate) was prepared using high-speed homogenization [7,8]. Further, this suspension of a drug was fed into the Dyna mill containing small beads of zirconium oxide with a size of 2.3 mm. The grinding chamber and the beads rotate at high shearing speed. The drug particles bombard over the sides of the grinding chamber. The force of friction and impaction of particles in the chamber results in particle size reduction [9].

## High pressure homogenization

To begin, the micronized drug particles were pre-suspended in a surfactant and polymer solution using a high-speed homogenization technique. Then the coarse micronized pre-suspension had been subjected to high-pressure homogenization at different pressure/cycles (each cycle 90 s/min). For particle size reduction, many cycles were used [10].

## Particle size and zeta potential determination

The particle size of the developed formulations was measured to asses if any difference in particle size depending on the method used to make the Nano suspension [11]. The formulation was diluted in water at 1:100 ratios and particle size was measured. Using a Zeta size ZS 90 (Malvern Instrument Ltd., UK) at a 90° angle, fluctuations in light scattering (due to Brownian motion) are identified in photon correlation spectroscopy [12]. The batches with lower particle sizes were selected for further characterization like zeta potential determination. The Nano suspension was deposited in a folded capillary cell and then into the analysing chamber of a Zetasizer ZS 90 which uses the Electrophoretic Light Scattering (ELS) technique to detect zeta potential [13].

## **Results and discussion**

## Solubility study

From the experimental work, the solubility was noticed to be  $0.0080 \pm 0.36$  mg/mL for RTV and  $0.0166 \pm 0.21$  mg/mL for LPV which are close to the reference values. Nano sizing has resulted in a 10-fold increase in solubility of APIs. The results show that particle size reduction increases the drug's solubility and can also boost its bioavailability. Reduced particle size increases the surface area of the drug particle, which improves solubilityThe surfactants employed in the formulation help to lower the drug's hydrophobicity, which aids in its solubilization.

## **FTIR** analysis

The principle peaks for drug and excipients are retained, indicating

that no chemical changes have occurred in the drug. As a result, drug excipients are discovered to be appropriate for one another.

## Conclusion

Nano suspension of combination of antiviral agents Ritonavir and Lopinavir was prepared using stabilizers. The increase in pressure leads to decrease in particle size and finally the drug release is increased. The study demonstrates that the developed Nano suspension A3 (Ritonavir) and B2 (Lopinavir) formulation have particle size 125.5 nm and 82.79 nm and zeta potential – 22.7 mV and – 19.1 mV respectively. The cumulative release of Ritonavir and Lopinavir was found to be 70.185  $\pm$  0.196% and 84.457  $\pm$  1.020% respectively. From the above results we conclude that High pressure homogenizer is an effective instrument to reduce the particle size than the Wet milling technique and High speed homogenizer. The low the particle size the more is the bioavailability the brain targeting then becomes possible as the drug will pass efficiently through the Trans cellular route.

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