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THE INVESTIGATION OF EFFICACY AND POTENTIAL ANTI-HIV PROPERTIES OF LOPINAVIR, LOPINAVIR/RITONAVIR, RITONAVIR, UPON LOADED MESOPOROUS SILICA NANOPARTICLES (MSNPS), BASED DRUG DELIVERY SYSTEM

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Abstract

The human immunodeficiency virus (HIV), which causes AIDS, is one of the mostdeadly diseases. Worldwide, HIV/AIDS continues to be a severe threat to people's health. The study's objective is to determine Lopinavir, Lopinavir/Ritonavir, and Ritonavir work against HIV after being loaded with mesoporous silica nanoparticles (MSNPs). The weight ratio of RTV in LPV/r in Methodology was 1:4. For drug loading, DMSO was mixed with LPV/r, LPV, RTV, and MSNPs at a weight ratio of 1:2. The loading capacities were determined and the LPV/r-MSNP, LPV-MSNP, and RTV-MSNP produced for usage were freeze-dried. The surface interaction of produced nanoparticles with other pharmacological compounds employed in the manufacture of nano-anti retrovial therapy ART/s was investigated using the FT-IR. After each experiment is conducted in pairs, residuals-based methods will be calculated. To evaluate the analytical importance of value differences, a one-way ANOVA was performed. Data are provided as the mean using the software, with a 95 percent overall coefficient of determination, and differences were considered substantial when p 0.05. Results revealed that a higher release of all medications was seen at pH 6.8. However, compared to LPV, LPV/r and RTV had a less pronounced drug release pattern. The aqueous property of LPV, RTV, and LPV/r as they get more complex. The LPV, RTV, and LPV/r are the more complex causes of the aforementioned phenomena. Furthermore, only a small number of aromatic rings rich in electrons are present in the molecules of LPV, RTV, and LPV/r. A new era in medication delivery based on nanotechnology will begin with the development of such a sophisticated nano-therapeutic system, particularly in the prevention and treatment of HIV/AIDS.

Keywords*:Lopinavir, Lopinavir/Ritonavir, Ritonavir, Nanoparticles, HIV.*

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Introduction

HIV eventually leads to AIDS, or associated immune deficiency epidemic, in which the immune system steadily deteriorates, promoting the development of pathological disorders that might be lethal. HIV is often a highly contagious virus that may be transmitted by contact with or movement of serum, pre-ejaculate, body fluids, or cervical mucus. A research found that as long as one person's immunogenicity is consistently lowered, condom-free sexual intercourse cannot spread the virus (Rodger et al., 2019). With the identification of the macrophages and lymphocytes that promote HIV-1 production, significant progress has been made in our knowledge of the process (Thorley and others, 2010).

The International System of Units (SI) has a length unit called the nanometer (nm) (SI). The size range that continues to hold such fascination is often between 100 nm and the atomic level, or about 0.2 nm, even though materials may exhibit different and enhanced features in this range compared to the same material at a greater scale. Nanomaterials are an outstanding aspect of technological progress since they provide created particles a large potential to make things with superior seasons (Bayda et al., 2019).

In order to maintain therapeutic blood levels for longer periods of time, controlled-release delivery methods may lengthen their half-lives. The degree to which patients adhere to their antiretroviral medication may be significantly affected by this (ARTs). For the purpose of making sure that medications reach latent reserves, ARTs may be delivered to CD4+ T cells, macrophages, the brain, and other distant organs. The distribution of hydrophobic and hydrophilic medicines into and across various tissues may also be improved by DDSs because to the NPs' tiny size. For HIV/AIDS therapy and prevention in clinical settings, this DDSs component looks to have the greatest potential (Sagar et al., 2014).

Aside from that, drugs for retroviruses mostly affect pathogens that live within cells with minimal impact. Even after the early human immunodeficiency virus (HIV) outbreak, drug is still exceedingly difficult to get from these HIV repositories (Kim et al., 2022). The effectiveness and possible anti-HIV qualities of Lopinavir, Lopinavir/Ritonavir, and Ritonavir following loading Mesoporous Silica Nanoparticles (MSNPs) were examined in this study.

Material and method:

Preparation and development of Keletra® (Lopinavir/Ritonavir), Lopinavair® (LPV) and Ritonavir® (RTV) loaded MSNPs

The ratio of RTV weight to LPV/r weight was 1:4. DMSO was mixed with LPV/r, LPV, RTV, and MSNPs in a 1:2 weight ratio for drug loading. Steroid Indicate that consumers were aliquoted by spinning the material for 25 minutes at a rate of 14,000 revolutions per minute after it had been mixed for 24 hours. The pellet was washed three times in order to remove any remaining free medication. The amount of drugs in the leftovers was estimated by absorbing light in the UV-vis range between 200 and 400 nm. For later usage, the produced LPV/r-MSNP, LPV-MSNP, and RTV-MSNP were freeze-dried, and the loading capacities were determined.

Fourier Transform Infrared Spectroscopy (FT-IR)

The FT-IR was used to search at how the surfaces of synthesised nanoparticles interact with other drug molecules that are part of the process of making nano-ART/s.

Data analysis

Methods with residuals will be calculated for each experiment after it is executed in pairs. To evaluate the analytical importance of value differences, a one-way ANOVA was performed. Data are provided as the mean using the software, with a 95 percent overall coefficient of determination, and differences were considered substantial when $p< 0.05$.

Result and Discussion

Permeation was achieved by encapsulating LPV and/or RTV solely inside the pores of Populated. Visible spectrophotometry was used to determine the trapping efficacy, which was determined to be about 43% (wt%) for all formulations based on UV readings.

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Only a few more peaks from the FT-IR analysis of the Pharmaco, Automatic generation, LPV/r-MSNP, and 4pm were found to correctly indicate LPV, LPV/r, and RTV inside the MSNPs. The research also allowed for the in situ characterization of functional group adsorption on nanoparticle surfaces and showed the composition of a silica matrix formation.

It was anticipated that the disintegration rate would be at these levels since the ph of the lymph nodes' pits has been proven to be 6.8. (Wu et al., 2019). The outcomes demonstrated that each medication—LPV, RTV, and LPV/r—continuously released at both pH levels throughout the study. All medications released more readily as the pH reached 6.8. However, compared to LPV, LPV/r and RTV had a less pronounced drug release pattern. The watery characteristic of LPV/r, RTV, and more complex LPV.

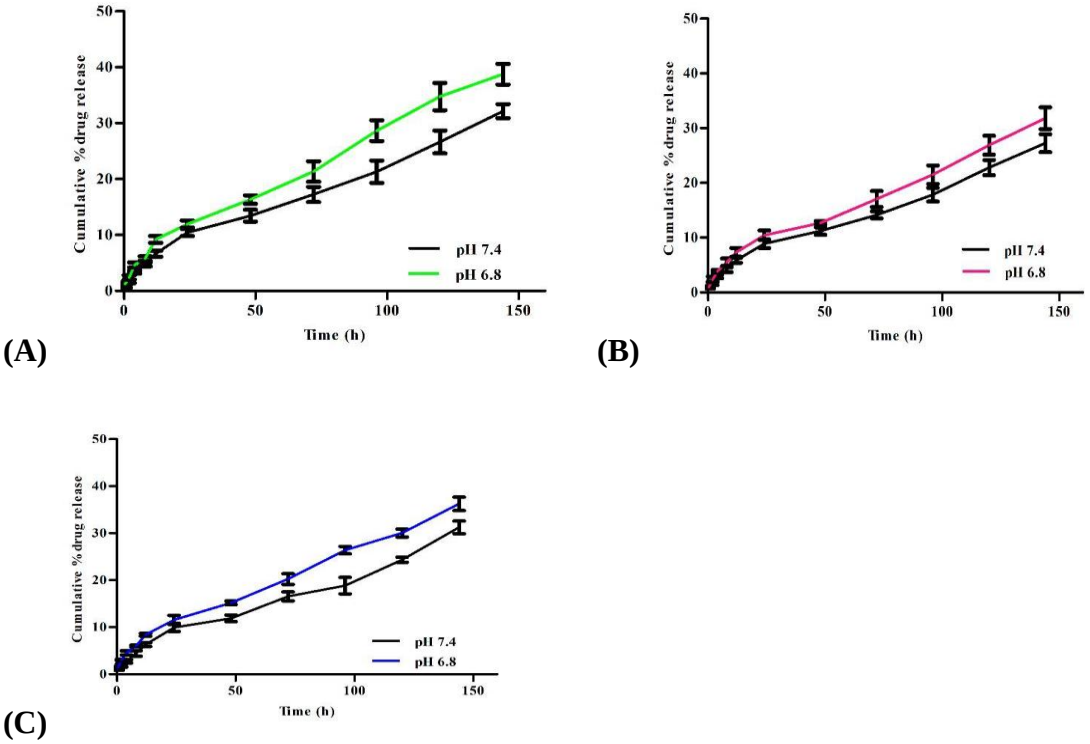

Figure 1: Release profiles of, **(A)**LPV, **(B)** RTV, **(C)** LPV/r **(D)**, loaded MSNPs at physiological pH (7.4) and acidic pH (6.8) for 144 h.

The LPV, RTV, and LPV/r are the more complex causes of the aforementioned phenomena. Furthermore, only a small number of aromatic rings rich in electrons are present in the molecules of LPV, RTV, and LPV/r. Additionally, the complexation of MSNPs' amine group, which causes cumulative releases of less than 20% over the course of 48 hours and more than 35% before 144 hours on LPV, RTV, and LPV/r, may have contributed to the increased release of LPV, RTV, and LPV/r in comparison to other Craft at acidic medium (Figure 1 A B, and C) By interfering with RTase activity, the released LPV, RTV, and LPV/r from MSNPs will suppress the virus by halting transcription (Abadi et al., 2020)

Table 1: Anti HIV assay of of free LPV, RTV, LPV/r and dually or individually loaded ART inside the MSNPs in infected TZM-bl cells and PBMCs with different strains of HIV-1

		Anti–HIV1 Assay TZM-bl Cells				***Anti–HIV1 Assay PBMCS***			
Sr. No	***Compound Name***	***IC50 HIV1 VB28 (R5) (µg/mL)***	***TI HIV1 VB28 (R5)***	***IC50 HIV1 UG070 (X4) (µg/mL)***	***TI HIV1 UG070 (X4)***	***IC50 HIV1 VB28 (R5) (µg/mL)***	**TI HIV1 VB28 (R5)**	**IC50 HIV1 UG070 (X4) (µg/mL)**	**TI HIV1 UG070 (X4)**
1	***LPV***	0.13±0.01	1160.515	0.11±0.12	1384.073	0.12±0.02	274.52	0.11±0.12	198.16
2	***RTV***	1.08±0.29	104.22	1.61 ±0.12	69.91	0.41±0.29	1369.3	0.57±0.12	1384.07
3	***LPV/r***	.10±0.01	1462.17	0.13±0.025	1139.06	0.10±0.01	1462.2	0.12±0.025	1343.94
4	***MSNP***	2.02±0.71	137.51	18.11±1.21	15.35	1.87±0.71	148.6	14.13±1.21	26.312

The IC50 values for all other ARTs (LPV and RTV) loaded MSNPs were found to be less for all cases in infected TZM-bl cells and PBMCs, indicating higher efficacy of drug-loaded-MSNP in virus suppression. Moreover, the HIV-1 p24 Gag antigen level (pg/mL) in infected MΦ subjected to the compounds were revealed the efficiency of LPV/r-MSNP and LPV-MSNP in suppressing HIV-1 after 3 and 5 days post-infection (Table 1). The lesser IC50 values for LPV/r-MSNP and LPV-MSNP resulted in the achieving of higher TI in comparison to free LPV/r and LPV for almost ≈23 and ≈36 folds, respectively.

Conclusion

The loading/conjugation of an HIV-1 medication (LPV/r,LPV, and RTV) results in the synthesis of different inorganic NPs as new cocktail-like nanoparticle DDSs. This strategy tackles the present constraints of HIV-1 therapy, including toxicity, inadequate cellular uptake of medicines, short half-life in vivo, their biodistribution in vivo through intravenous injection, administration for increased drug delivery, and a description of the DDS hurdles.

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