Journal of Infectious Diseases and Research
JIDR, 6(S4): 11
www.scitcentral.com
ISSN: 2688-6537

Abstract: Open Access

# An *In Vitro* Investigation of a Traditional Medicine Product with HIV-1 Therapeutic and Curative Potential

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*Published November 28, 2023*

## ABSTRACT

**Background:** Persistence of latent HIV-1 in resting CD4+ T cells is the principal barrier to cure development. One strategy currently being pursued to eliminate latently infected cells is to stimulate virus production from latency, which has shown limited success in clinical trials. Therefore, new, and improved latency reversing agents (LRAs) are necessary to reactivate latent viral reservoirs, facilitate HIV-1 eradication and cure development. In this study, we undertook to investigate the potential of a plant-based traditional medicine (Product Nkabinde) to reactivate latent HIV-1.

**Methods:** A half maximal inhibitory concentration (IC50) for a four-plant based mixture (Mixture) and single plant product (SDK-2) was determined using the ATP assay. *In vitro* antiviral activity of the Mixture and SDK-2 was assessed against HIV-1 subtype B (NL4.3 and YU2) and subtype C (CM070P.1 and CM019P.1.2) viruses in TZM-bl cells using the luciferase assay. Lastly, we evaluated the HIV-1 latency reversal potential of the Mixture and SDK-2 alone or in combination with LRAs using HIV-1 subtype B and C based latency model, JLAT-B and JLAT-C respectively.

**Results:** The IC50 concentration of 325µg/ml for the Mixture extract inhibited NL4.3 (88%), CM070P.1 (92%), CM019P.1.2 (80%) and YU2 (76%) while SDK-2 (106µg/ml) exhibited 64%, 89%, 34% and 37% inhibition of CM070P.1, CM019P.1.2, NL4.3 and YU2 replication, respectively. The Mixture exhibited less than 1% of the reactivation potential for both latency models. Interestingly, SDK-2 in combination with TNF-a exhibited a synergistic effect resulting in 65.4% reactivation of latent HIV-1 subtype C compared to 87.2% of subtype B.

**Conclusion:** Taken together, our data show that while both the Mixture and SDK-2 exhibit both inhibitory and stimulatory effect on HIV-1 infection, SDK-2 exhibit a pronounced reactivation potential in combination with TNF-a. Future experiments will assess the reactivation potential of SDK-2 in primary CD4+ T cells from people living with HIV-1 on suppressive antiretroviral therapy.

**Keywords:** HIV-1, ATP assay, TZM-bl

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**Citation:** Mngomezulu K, Madlala P, Gqaleni N & Ngcobo M. (2023) An *In Vitro* Investigation of a Traditional Medicine Product with HIV-1 Therapeutic and Curative Potential. J Infect Dis Res, 6(S4): 11.