

Design, In Silico, and In vitro Evaluation of Polymer-Based Drug Conjugates Incorporated with Derivative of Cinnamic Acid, Zidovudine, and 4-Aminosalicylic Acid against Pseudo-HIV-1

Naki, T; Matshe, William M; Obisesan, O; Balogun, Mohammed O; Oselusi ,O; Ray, Suprakas S; Aderibigbe, BA

Abstract

Background: The incorporation of anti-HIV drugs into polymer to form polymer-drug conjugates has been reported to result in improved therapeutic activity. Zidovudine, an anti-HIV drug, was explored alone and in combination with known drug molecules using polyamidoaminebased carriers. Objective: Polymer-drug conjugates incorporated with zidovudine, cinnamic acid, and 4-aminosalicylic acid were prepared and evaluated for their potential efficacy in vitro against pseudo- HIV-1. Methods: Aqueous Michael addition polymerization reaction was employed to prepare the conjugates. The conjugates were incorporated with zidovudine, cinnamic acid, and 4-aminosalicylic acid. They were characterized by SEM/EDX, XRD, FTIR, NMR, LC-MS, particle size analysis, in vitro analysis, computational studies, and in silico toxicity predictions. Results: The conjugates displayed spherically shaped morphology. The in vitro findings showed that polymer-drug conjugates, T15 and T16, with a single drug were effective against pseudo- HIV-1 at high concentrations of 111.11 and 333.33 µg/mL, respectively. Molecular docking studies supported the in vitro results. Additionally, SwissADME, ProTox-II, and GUSAR (General Unrestricted Structure-Activity Relationships) analyses revealed that these compounds have promising antiviral potential. Conclusion: The prepared polymer-drug conjugates with a single drug showed promising effects against the Pseudo-HIV-1, and the conjugates displayed features that make them potential anti- HIV therapeutics that require further studies.