Prodrug approaches for long-acting antiretroviral drugs

Long-acting antiretroviral injectables (LAIs) are employed to reduce toxicity, extend drug half-life, reduce dosing frequencies, improve patient adherence and improve disease outcomes. Those that have reached patient care include injectable drug crystal nanosuspensions, liposomes, polymeric microspheres, gels, oil-based emulsions, and implants, amongst others. Due to the increasing prevalence of many chronic diseases that include schizophrenia, diabetes, atherosclerosis, cancer and infectious diseases that include the human immunodeficiency virus (HIV), the demand for long acting regimen that show simplicity in usage have led to increased demand. For HIV care, antiretroviral drugs (ARVs) that are parenterally administered as prodrugs revolve around inherent poor lipid solubility and reduced membrane permeation to tissue reservoir sites that include the lymph node, gut, spleen and brain. Such limitations coupled with rapid body elimination of drugs lead to high drug clearance and toxicities. These concerns have buoyed research in our laboratories towards developing prodrug strategies that serve to improve parenteral delivery of poorly soluble drugs with limited shelf lives. Such factors have created a new need for any or all effective ARV LAIs. Our laboratories pioneered the use of long-acting antiretroviral therapy creating formulations characterized by slow drug dissolution, poor water-solubility, excellent bioavailability and limited off-target toxicities. By design the formulations need affect regimen adherence. High ARV payloads serve to improve the pharmacokinetic and pharmacodynamic drug profiles. We share each of the newer chemical and polymer drug modifications that allow the production of slow-release drug carriers enabling drugs to reach viral reservoir sites and accelerate viral suppression. Each and all of the listed references represent the growing number of strategies being applied to increase the effectiveness of current ARV regimens[1-35].

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