

Herpes simplex virus (HSV) causes a contagious infection that affects approximately 60% to 80% of adults worldwide. HSV-1 is associated mainly with infections of the mouth, pharynx, face, eye, and central nervous system (CNS), while HSV-2 is associated with infections of the anogenital region, although both serotypes may infect both areas. HSV has the ability to invade the CNS, to produce encephalitis and keratitis. HSV-1 and -2 persist in the body by becoming latent in the cell bodies of nerves and after the initial or primary infection. People infected with HSV-1 or HSV-2 can expect to have several outbreaks (symptomatic recurrences) within a year. There are no vaccines and treatment strategies for primary herpes infections are limited to the antiviral agents blocking viral replication. Therefore, there is an urgent need to develop an effective anti-herpesviral microbicide, which can be applied locally by persons suspecting recurrent or primary HSV infection. Ideally, an antiviral microbicide should work by binding cell-free virus and thus blocking its further spread to neighbouring uninfected cells. Furthermore, it should also show some immune activity, helping to induce the innate and adaptive immune response.

Nanomaterials are a diverse class of small-scale (<100 nm) objects, formed by molecular-level engineering. The use of nanoparticles-based antiviral agents has several advantages. NPs have the characteristics of high surface-to-volume ratios, enabling the packaging of multiple antiviral agents onto the surface of nanoparticles. Based on its antimicrobial activity, silver particles (AgNPs) have become one of the most prominent nanomaterials. Furthermore, gold nanoparticles (AuNPs) facilitate delivery of antigens and adjuvants to the immune system, promote the therapeutic effect, and possess an adjuvant effect on their own. Nanocarriers provide an opportunity for the rational design of vaccines that can mediate targeted delivery of various antigens and adjuvants or immune regulatory agents in ways unachievable with classical vaccination approaches.

The aim of this project is to test the antiviral potential and the adjuvant properties of functionalised nanoparticles of noble metals (silver and gold). In particular, this project involves the use of selected tannins and/or alkylosulfonates to functionalise AgNPs and AuNPs to be further used in biological tests of toxicity as well as virucidal and adjuvant activities in herpes simplex type 1 and 2 infections. We hypothesize that conjugation of silver/gold nanoparticles with tannic acid and other substances mimicking heparin sulfate proteoglycans can consist an effective anti-viral microbicide to be applied upon the mucosal/skin tissues with additional adjuvant properties boosting anti-viral response not only during primary infection, but also later, upon recurrent infection. The antiviral and adjuvant properties will be tested using in vitro and in vivo models of HSV-1 and HSV-2 infections. The test results will help to define rules for construction of a safe, nanoparticle-based microbicide as well as to define the local immune response upon its application onto damaged, pathogen-inflicted skin and mucosa. This in turn should further lead to development of our knowledge about safety and biological interactions of nanoparticles.