

Prevalence and prevention of sexually transmitted viral infections in the Bolivian Amazonas

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Mikrobiologens föreläsningssal, våning 3, Guldhedsgatan 10A, Göteborg, torsdag den 26 mars 2020, klockan 09.00

av **Marianela Patzi Churqui**

Fakultetsopponent:

Docent Marianne Jansson

Avdelningen för medicinsk mikrobiologi

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Avhandlingen baseras på följande delarbeten

- I. **Marianela Patzi-Churqui**, Katty Terrazas-Aranda, Jan-Åke Liljeqvist, Magnus Lindh, Kristina Eriksson. Prevalence of viral sexually transmitted infections and HPV high-risk genotypes in women in rural communities in the department of La Paz, Bolivia. Manuscript in-press. *BMC Infectious Diseases*, 2020.
- II. **Marianela Patzi-Churqui**, Liza Lind, Karolina Thörn, Alexandra Svensson, Otto Savolainen, Katty Terrazas-Aranda, Kristina Eriksson. Extracts of *Equisetum giganteum L* and *Copaifera reticulata Ducke* show strong antiviral activity against the sexually transmitted pathogen herpes simplex virus type 2. *J Ethnopharmacology*. 2017;210:192-7.
- III. **Marianela Patzi-Churqui**, Alexandra Svensson, Karolina Thörn, Otto Savolainen, Roger Carvajal-Saravia, Katty Terrazas-Aranda, Kristina Eriksson. Antiviral and immunomodulatory potentials of medicinal plants *Tipuana cf tipu (Benth) Kuntze*, *Erythroxylum coca Lam* and *Mangifera indica L*. Manuscript.

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Abstract

This thesis investigates the prevalence of sexually transmitted viral infections in women living in the Amazonas region of Bolivia and explores whether Bolivian medical plants can affect the immune system and prevent or treat infections with Herpes simplex virus type 2 (HSV-2) and inflammation. Universidad Mayor de San Andrés in La Paz together with international and local organizations work in a cooperative program that aims to improve the health of women, especially in poor rural areas of the Amazonas that are inhabited mainly by indigenous tribes. Part of this thesis work was carried out in Bolivia as fieldwork during the dry seasons. This involved the collection and preparation of human biological samples and medical plants that were later used in clinical laboratory assessments and experimental studies at the University of Gothenburg, Sweden. In the cross-sectional study of 394 indigenous participants in **Paper I**, 64% were found to be positive for at least one viral sexually transmitted infection. The seroprevalence of HSV-2 was 53% and that of hepatitis B virus (HBV) was 10.3%. Of the women with antibodies to HBV, 16% also had HBV antigen in their blood, indicating ongoing infection. The frequency of high-risk human papillomavirus (HPV) infection was 27%, with the most prevalent high-risk HPV types being HPV 56, 39 and 31, followed by HPV 16 and 18. None of the participants were seropositive for HIV. For **Papers II** and **III**, plants used in traditional Tacana medicine as anti-infectious and anti-inflammatory remedies were collected with the help of a local guide. Hydro-ethanolic extracts of *Equisetum giganteum*, *Croton lechleri*, *Uncaria tomentosa*, *Copaifera reticulata*, *Tipuana cf tipu*, *Mangifera indica* and *Erythroxylum coca* efficiently blocked HSV-2 infection of cell cultures without any significant cytopathic effects. In **Paper II**, we show that *E. giganteum*, *C. lechleri*, *U. tomentosa*, and *C. reticulata* can prevent HSV-2 infection in a mouse model genital herpes, and we also demonstrate that extracts of these plant efficiently block viral attachment and entry but not viral replication post-entry. In **Paper III**, we show that extracts of *T. tipu* and *M. indica* not only block viral infectivity, but are also efficient antiviral agents when administered after viral entry in Vero cells. *T. tipu* also promotes anti-viral immunity by inducing the production of type III interferons, and it primes for both inflammatory (IL-1 β) and chemotactic (CXCL10) chemokines in human peripheral blood mononuclear cells. In **Paper III**, we show that several of these plants have anti-inflammatory properties, as they block LPS-induced inflammasome activation and subsequent release of IL-1 β . These studies reveal that infections with HPV, HBV and, in particular, HSV-2 are common in women in the Bolivian Amazonas, and that the pattern of high-risk HPV types differs from that covered by the HPV vaccine Gardasil. Several medicinal plant extracts are identified as promising anti-HSV-2 microbicides, and some of these plants can also modify anti-viral and inflammatory responses.

Keywords: Sexually transmitted infections, indigenous women, Bolivian Amazonas, HSV-2, HBV, HPV, medical plants, microbicides, cytokines