

Study of medicinal plants and quality control of preparations used for the treatment of tuberculosis in Senegal

Summary

Pulmonary tuberculosis (TB) has reappeared in recent years with the occurrence of many cases of resistance and multi-resistance (MDR) encountered against basic antibiotics namely rifampicin and isoniazid. Most of the new TB cases are found in sub-Saharan Africa because of the progression of HIV infection. This disease affects about 10 million people worldwide, 10% of whom are HIV patients. A treatment is available in developing countries with the "End-TB" strategy. There are however more and more treatment failures due to non-compliance, antibiotic resistance and the occurrence of major adverse effects. It is urgent to find new therapeutic opportunities to counter the expansion of the disease. TB is described as a consumptive disease that causes wasting when it reaches people with weakened immune systems or living in conditions of promiscuity and malnutrition. In the African context, the population often uses traditional medicine to treat common ailments including cough and fever, classic symptoms of tuberculosis.

The aim of the present work was to identify the plants traditionally used in the management of TB. This approach combined an ethnopharmacological survey in patients and traditional healers, followed by an evaluation of the antimycobacterial activity of these preparations and the identification of major active principles with an anti-infective effect.

This led to the identification of two aqueous extracts of *Combretum aculeatum* and *Guiera senegalensis*, two combretaceae widely used in Senegal in traditional medicine. Bioassay guided isolation using a novel stringent *in vitro* model, has identified the most active compounds in these extracts as well as some of their metabolites. By extrapolating the possible bioavailability of the active ingredients, we have been shown a possible rationale for the use of these plants in Tb treatment. Analytical quality control approaches of drug preparations using capillary electrophoresis were applied for the determination of one active ellagitannin punicalagin in *C. aculeatum* extracts. In addition this analytical technique was also used to monitor the quality of first-line anti-TB drugs in a fixed dose combination. This part should finally permit a practical implementation of validated control quality procedures at the local level for an improved treatment of the patients.

This thesis, in 'cotutelle', is the result of a collaborative project between the University Cheikh Anta Diop of Dakar (UCAD-Department of Plant Biology) and the University of Geneva (School of Pharmacy Geneva-Lausanne-EPGL). Thus, the surveys and collections of plants were carried out in Senegal; pharmacognostic investigations at the laboratory of phytochemistry and bioactive natural products and quality control approaches in the laboratory of biomedical and metabolomic analyses (analytical sciences) at the EPGL.

Disciplines: Life, Health and Environmental Sciences / Pharmaceutical Sciences

Key words: Tuberculosis - medicinal plants - *Mycobacterium marinum* - Host-pathogen assay - *Combretum aculeatum* - *Guiera senegalensis* - quality control - Capillary electrophoresis