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and

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Ph.D. in Chemistry

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Thesis on

**PHARMACOLOGICAL POTENTIAL
AND PHYTOCHEMICAL PROFILE
OF THREE UNEXPLORED
MEDICINAL PLANTS**

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ABSTRACT

Nature is a wide source of biologically active compounds investigated with the purpose to be used as drugs due to their biological activity and also useful in pharmaceutical discovery and drug design. Nowadays, medicinal plants play a major role in primary health care as therapeutic remedies in many developing countries.

The aim of my PhD project was the phytochemical and biological investigation of three plant species, used in Bolivian traditional medicine, but few scientific studies were reported, such as: *Azorella glabra* Wedd., *Minthostachys diffusa* Epl. and *Senecio clivicolus* Wedd.

On the basis of ethnobotanical uses, the samples were firstly analysed for their total content of polyphenols, flavonoids and terpenoids and for their *in vitro* antioxidant activity using different complementary assays. In particular, radical scavenging activity was tested against biological radicals such as nitric oxide (NO) and superoxide (SO) together with neutral or cationic (DPPH and ABTS) radicals; ferric reducing power and lipid peroxidation inhibitory capacity (FRAP and *Beta*-Carotene Bleaching tests) were also determined.

Oxidative stress is involved in different diseases, such as diabetes and neurodegenerative diseases. Then, the inhibitory ability of samples was investigated against α -amylase and α -glucosidase enzymes involved in diabetes and against acetylcholinesterase and butyrylcholinesterase enzymes considered as strategy for the treatment of Parkinson's or Alzheimer's diseases.

Moreover, cytotoxicity studies on cancer and non-cancer cell lines were carried out.

The antioxidant, antidiabetic, anticholinesterase and cytotoxic activities and the phytochemical profile were performed on aerial parts of *A. glabra*, *M. diffusa* and *S. clivicolus* for the first time.

Among all samples, the ethyl acetate fraction of *S. clivicolus* showed the highest antioxidant activity; instead, *M. diffusa* samples showed the highest antidiabetic potential and anti-cholinesterase activities. To confirm the inhibitory cholinesterase effects of the terpenes identified from *M. diffusa*, *in silico* docking analysis were also carried out.

Moreover, the *A. glabra* samples were tested for the first time on Multiple Myeloma (MM) cell lines using several assays. The chloroform fraction of *A. glabra* reduced the cell viability, and arrested the cell cycle on MM cells in G0/G1 phase, characteristic feature of apoptosis.

Instead, the ethyl acetate fraction of *S. clivicolus* was tested on hepatocellular carcinoma HepG2 cell line showed the ability to induct cell death via the mitochondrial apoptotic pathway.

In conclusion, this first report on *A. glabra*, *M. diffusa* and *S. clivicolus* phytochemical characterization and biological activity evaluation, demonstrates as these Bolivian plant species could be considered a source of health promoting compounds.

Some of the results obtained during this study might partially explain their ethnobotanical use, evidencing a potential economic added value for extract future use in the field of biotechnology applied to environmental, agricultural, health, pharmaceutical and cosmeceutical development.