Psoralea glandulosa L. as a Potential Source of Anticancer Agents for the Melanoma Treatment

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Cancer continues to be one of the major causes of death worldwide and only modest progress has been made in reducing the morbidity and mortality of this dreadful disease; in particular limited chemotherapeutic agents are available for melanoma treatment. Therefore, the research and development of more effective and less toxic drugs by the pharmaceutical industry has become necessary. Many substances present in plants are known to be effective and versatile chemopreventive and antitumoral agents in a number of experimental models of carcinogenesis.*Psoralea glandulosa* L. (Fabaceae) is a Chilean resinous shrub, characterized by producing resinous exudates from its glandular trichome that covers the surface of leaves and stems. It is known by the vernacular names 'culen', 'cule' and 'hualhua'. It is also known by the Aymara name of 'Wallikaya', which is commonly used in the Mapuche communities. *P. glandulosa* has long been used in folk medicine as vulnerary and for hemorrhoids. It acts as antiseptic in treatment of infections and skin diseases caused by bacteria and fungus (Madrid et al., 2012). Earlier research on the secondary metabolites of this plant led to the isolation of two furanocoumarins, angelicin and psoralen, together with drupanin methyl ester and the meroterpenoid bakuchiol. In addition, the isolation of a mixture of cyclobakuchiols A and B has been reported. Bakuchiol, present in high concentration in resinous exudates and earlier isolated from *P. corylifolia* L., a traditional Chinese medicinal plant used for the treatment of skin cancer, has been shown to exhibit interesting anticancer activities in preclinical studies (Mjeed et al., 2012). Therefore, based on the above rationales and observations, in an ongoing effort to identify new natural anticancer compounds for the treatment and/or prevention of melanoma cancer, the present study was undertaken to investigate the biological activity of the dichloromethane extract of resinous exudates from aerial parts of *P. glandulosa*, and its active components, against human melanoma cancer cells (A2058), testing several biochemical parameters, such as cell vitality (MTT assay), cell membrane integrity (lactate dehydrogenase release), genomic DNA fragmentation (COMET assay) and caspase-3 activity. In addition, the expression of Bcl-2 and Bax proteins was evaluated. The active components were analysed by ^{1}H and ^{13}C NMR, $[a]_D$. The results obtained show that the extract, after 48 h of treatment, inhibited the growth of cancer cells with IC_{50} value of 10.5 μg/ml, while the most active compounds were the meroterpenoids bakuchiol, 12-hydroxy-iso-bakuchiol, 3-hydroxy-bakuchiol and bakuchiol acetate. In fact, psoralen was less effective against A2058 cells. Our data also demonstrate that the extract induces apoptotic cell death that could be related to an overall action of the meroterpenoids present. In fact, these molecules were able to induce a high DNA fragmentation, correlated to a significant increase in caspase-3 enzyme activity and Bax protein levels, in conjunction with a decrease in Bcl-2. In summary, our study provides a further *in vitro* scientific support for the use of several *Psoralea* species for cancer-related diseases, and indicates that *P. glandulosa* may be considered a source of molecules for the prevention and treatment of neoplastic diseases, including melanoma.

Madrid et al. (2012). *J Ethnopharmacol*. 144, 809-811.
Majeed et al. (2012). *Eur J Med Chem.* 49, 55-67.