

## Phytoestrogenic activity in *Cyclopia genistoides*

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The genus *Cyclopia* is part of the rich fynbos plant kingdom of the Western Cape. Fermented *Cyclopia* is traditionally consumed as the fragrant, caffeine-free honeybush tea. *Cyclopia intermedia*, *C. subternata*, *C. sessiliflora*, and *C. genistoides* are most commonly used for commercial honeybush tea production. It has been shown that numerous flavonoids are present in *C. intermedia*(1)and *C.subternata*(2). Some of these flavonoids, like formononetin and naringenin, are known for mediating a weak estrogenic effect via estrogen receptors (ERs)(3). Such compounds are commonly referred to as phytoestrogens. Phytoestrogens are becoming increasingly popular as an alternative to standard hormone replacement therapy (HRT) as some are reported to be selective estrogen receptor modulators (SERMs), which may have fewer side-effects than traditional HRT. In addition, epidemiological studies show that Asian women who generally follow a diet rich in phytoestrogens have fewer hot flushes (4)and that the incidence of breast cancer (5)in this population is also remarkably less.

Preliminary screening of the four *Cyclopia* species for binding ability to both ER isoforms (ER-alpha and ER-beta) identified *C. genistoides* as the most promising species for further investigation of estrogenic potential. Specifically the current study concentrates on methanol extracts of *C. genistoides*. In addition, four phenolic compounds, namely luteolin, formononetin, naringenin, and mangiferin found to be present in the *Cyclopia* species are examined.

Our experimental strategy to assess the estrogenic activities of these phenolic compounds and methanol extracts included investigation of (i) binding to the hER-alpha and hER-beta in a whole cell binding assay, (ii) transactivation of a promoter reporter construct containing a estrogen response element via hER-alpha or hER-beta, (iii) proliferative or anti-proliferative effect on breast cancer cells (MCF-7 and MDA-MB-231), and (iv) binding to sex hormone binding globulin a plasma protein that regulates the availability and metabolic clearance of steroids binding to it.

<sup>1</sup> Ferreira, D., Kamara, B.I., Brandt, E.V., and Joubert, E. (1998) Phenolic compounds from *Cyclopia intermedia* (Honeybush tea) *J. Agric Food Chem.* 46, 3406-3410 <sup>2</sup> Kamara, B.I., Brand. D.J., Brandt, E.V., and Joubert, E. (2004) Phenolic metabolites from honeybush tea (*Cyclopia subternata*) *J. Agric Food Chem.* 52, 5391-5395 <sup>3</sup> Kuiper, G.G., Lemmen, J.G., and Carlsson, B. (1998) Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. *Endocrinology* 139(10), 4252-4263 <sup>4</sup> Boulet, M.J., Oddens, B.J., Lehert, P., Vemer, H.M., and Visser, A. (1994) Climateric and menopause in seven Southeast Asian countries. *Maturitas* 19, 157-176 <sup>5</sup> Adlercreutz, H. (2002) Phytoestrogens and cancer. *Lancet Oncol.* 3(6), 364-373