

GREEN ROOIBOS EXTRACT AND ASPALATHIN

Aspalathin-rich green rooibos extract (GRT Extract) and synthetic aspalathin as novel therapeutic preparations for the treatment and management of metabolic disease

BACKGROUND

Non-communicable diseases (NCDs) are the world's leading cause of death, leading to more deaths each year than all other diseases combined. Contrary to popular belief, the majority of deaths related to NCDs occur in low- and middle-income countries (LMIC), with over 80% of cardiovascular and type 2 diabetes (T2D) deaths occurring in these countries. In view of the limited access, long-term inefficacy, side effects and cost of modern oral anti-diabetic agents in Africa, plant-based therapies for the treatment and prevention of NCDs are gaining considerable prominence. One of the most utilized indigenous plants in South Africa is Rooibos, *Aspalathus linearis*, which is commonly used as a herbal tea. The major biologically active phenolic compound of Rooibos, aspalathin, has been shown to possess a number of health beneficial effects relevant to the management of Type 2 Diabetes and Cardiovascular disease. The aspalathin content of the rooibos plant varies depending on a number of factors, and its level in the plant material drops even further during the oxidation process used to produce fermented rooibos, the product commonly prepared as a herbal tea. However, in order to use Rooibos as a plant-based medicine for the management of certain NCDs, it would be important to produce a product that ensures a consistent content of aspalathin.

TECHNOLOGY DESCRIPTION

The SAMRC and the Agricultural Research Council (ARC) have developed a method for the production of aspalathin-rich unfermented green rooibos extract (GRT Extract), containing a minimum of 12% aspalathin, and having a number of beneficial effects in the management of conditions linked to glucose and lipid metabolism. These include a glucose lowering effect, ameliorated insulin resistance in vitro, protection of pancreatic beta cells against oxidative stress, protection of heart cells and lowering of cardiovascular risk factors. In addition, the SAMRC has also developed and patented a 5-step method for the synthesis of aspalathin, to be developed into an active pharmaceutical, as well as for use as a nutritional supplement.

VALUE PROPOSITION

Synthetic aspalathin and aspalathin-rich green rooibos extract (GRT Extract) can be utilized in novel therapeutic preparations for the treatment and management of metabolic dysfunction, including the modulation of glucose and cholesterol and thereby lowering cardiovascular risk. The products have application in the complementary medicine, nutritional supplement and veterinary markets.

CURRENT STATUS

The SAMRC has generated in vitro and in vivo data on the beneficial effects of GRT Extract and synthetic aspalathin in glucose and lipid metabolism. A Phase I clinical trial is planned

for 2019 with the GRT Extract. The production method for GRT Extract has been licensed to a South African manufacturer of wellness product solutions and active pharmaceutical ingredients. Small-scale synthesis of aspalathin (15-20g) has been optimized by an external service provider and more preclinical studies are planned for 2019.

INTELLECTUAL PROPERTY STATUS & PUBLICATIONS

A patent for the synthesis of aspalathin has been granted in the USA and South Africa.

Publications:

- Muller et al., 2012. Acute assessment of an aspalathin-enriched green rooibos extract (*Aspalathus linearis*) extract with hypoglycemic potential. *Phytomedicine* 20: 32-39.
- Mazibuko et al., 2013. Amelioration of palmitate-induced insulin resistance in C2C12 muscle cells by rooibos (*Aspalathus linearis*). *Phytomedicine* 20: 813-819.
- Mazibuko et al., 2015. Aspalathin improves glucose and lipid metabolism in 3T3-L1 adipocytes exposed to palmitate. *Mol Nutr Food Res* 59: 2199-2208.
- Johnson et al., 2016. Aspalathin, a dihydrochalcone C-glucoside, protects H9c2 cardiomyocytes against high glucose induced shifts in substrate preference and apoptosis. *Mol Nutr Food Res* 60: 922-934.
- Patel et al., 2016. Inhibitory Interactions of *Aspalathus linearis* (Rooibos) Extracts and Compounds, Aspalathin and Z-2-(-D-Glucopyranosyloxy)-3-phenylpropenoic Acid, on Cytochromes Metabolizing Hypoglycemic and Hypolipidemic Drugs. *Molecules* 21: 129.
- Dlodla et al., 2017. Aspalathin protects the heart against hyperglycemia-induced oxidative damage by up-regulating Nrf2 expression. *Molecules* 22: 129.
- Johnson et al., 2017. The transcription profile unveils the cardioprotective effect of aspalathin against lipid toxicity in an in vitro H9c2 model. *Molecules* 22: 219.
- Johnson et al., 2017. Aspalathin Reverts Doxorubicin-Induced Cardiotoxicity through Increased Autophagy and Decreased Expression of p53/mTOR/p62 Signalling. *Molecules* 22: 1589
- Dlodla et al., 2017. Hyperglycemia-induced oxidative stress and heart disease-cardioprotective effects of rooibos flavonoids and phenylpyruvic acid-2-O-β-D-glucoside. *Nutr Metab* 14:45.
- Muller et al., 2018. Potential of rooibos, its major C-glucosyl flavonoids, and Z-2-(-D-glucopyranosyloxy)-3-phenylpropenoic acid in prevention of metabolic syndrome. *Crit Rev Food Sci Nutr*. 58:227-246.
- Johnson et al., 2018. Aspalathin from Rooibos (*Aspalathus linearis*): A Bioactive C-glucosyl Dihydrochalcone with Potential to Target the Metabolic Syndrome. *Planta Med* 84:568-583.

GREEN ROOIBOS EXTRACT AND ASPALATHIN (CONTINUED)

Aspalathin-rich green rooibos extract (GRT Extract) and synthetic aspalathin as novel therapeutic preparations for the treatment and management of metabolic disease

- Smit et al., 2018. Myocardial Glucose Clearance by Aspalathin Treatment in Young, Mature, and Obese Insulin-Resistant Rats. *Planta Med* 84:75-82.
- Dlodla et al., 2018. Aspalathin, a C-glucosyl dihydrochalcone from rooibos improves the hypoglycemic potential of metformin in type 2 diabetic (db/db) mice. *Physiological Research*.
- Mazibuko-Mbeje et al., 2019. Aspalathin-Enriched Green Rooibos Extract Reduces Hepatic Insulin Resistance by Modulating PI3K/AKT and AMPK Pathways. *Int. J. Mol. Sci.* 20(3): 633; doi:10.3390/ijms20030633
- Mazibuko-Mbeje et al., 2019. Aspalathin, a natural product with the potential to reverse hepatic insulin resistance by improving energy metabolism and mitochondrial respiration. *PLOS ONE* 14(5): e0216172. <https://doi.org/10.1371/journal.pone.0216172>.
- Orlando et al., 2019. Aspalathin-Rich Green Rooibos Extract Lowers LDL-Cholesterol and Oxidative Status in High-Fat Diet-Induced Diabetic Vervet Monkeys. *Molecules* 24: 1713; doi:10.3390/molecules24091713.

OPPORTUNITIES

The SAMRC is seeking international partners for the formulation and sale of GRT Extract and partners for the development of synthetic aspalathin as a pharmaceutical.



FOR MORE INFORMATION PLEASE CONTACT:
info.ship@mrc.ac.za
+27 (0)21 938 0991
www.samrc.ac.za/content/innovation-samrc