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A polyphenol-enriched fraction of *Cyclopia intermedia* decreases lipid content in 3T3-L1 adipocytes and reduces body weight gain of obese db/db mice

B.U. Jack [a,c], C.J. Malherbe [b], B. Huisamen [a,c], K. Gabuza [a], S. Mazibuko-Mbeje [a,1], A.E. Schulze [b,2], E. Joubert [b,d], C.J.F. Muller [a], J. Louw [a], C. Pheiffer [a,*]

[a] *Biomedical Research and Innovation Platform, South African Medical Research Council, P.O. Box 19070, Tygerberg 7505, South Africa*
[b] *Post-Harvest and Wine Technology Division, Agricultural Research Council (ARC), Infruitec-Nietvoorbij, Private Bag X5026, Stellenbosch 7599, South Africa*
[c] *Division of Medical Physiology, Faculty of Medicine and Health Sciences, University of Stellenbosch, PO Box 19063, Tygerberg 7505, South Africa*
[d] *Department of Food Science, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa*

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ABSTRACT

Extracts of *Cyclopia* species, indigenous South African fynbos plants used for the production of honeybush tea, have potential as anti-obesity nutraceutical ingredients. Previously, we demonstrated that aqueous extracts of *C. maculata* and *C. subternata* exhibited anti-obesity effects in 3T3-L1 adipocytes. In this study, we further explored these anti-obesity effects of *C. maculata* and *C. subternata* as well as *C. intermedia* for the first time. Extracts were prepared using a 40% methanol–water mixture (40% MeOH) in order to enhance the polyphenolic content of the extracts. Moreover, these extracts were separated into aqueous and organic fractions using liquid–liquid partitioning with *n*-butanol and water to further enrich the polyphenol content of the organic fractions. Extracts of all three *Cyclopia* species decreased the lipid content in 3T3-L1 adipocytes, although differences in bioactivity of their aqueous and organic fractions were observed. The organic fraction of *C. intermedia* was further investigated. This fraction dose-dependently decreased the lipid content in 3T3-L1 adipocytes without affecting cell viability, while increasing mRNA expression of *HSL* (1.57-fold, $P < 0.05$), *SIRT1* (1.5-fold, $P = 0.07$), *UCP3* (1.5-fold, $P < 0.05$) and *PPARγ* (1.29-fold, $P < 0.05$). Daily treatment of obese db/db mice with 351.5 mg/kg bodyweight of the organic *C. intermedia* fraction for 28 days decreased bodyweight gain by 21% ($P < 0.05$) without any effect on food or water consumption. The organic fraction was enriched in phenolic content relative to the extract with neoponcirin, a flavanone not previously identified in *Cyclopia* species, mangiferin, isomangiferin and hesperidin comprising 17.37% of the organic fraction of *C. intermedia* compared to 4.96% of its "large scale" prepared 40% MeOH extract. Their specific roles as anti-obesity agents in these models needs to be studied to guide product development.

1. Introduction

Obesity, a multifactorial metabolic disorder, has been described as a global pandemic that is rapidly spreading in several parts of the world. The number of overweight and obese individuals has increased from 857 million in 1980 to 2.1 billion in 2013, translating to nearly 30% of the world's population being either overweight or obese (Ng et al., 2014). The disorder, characterised by the excessive accumulation of fat (Caballero, 2007), occurs mainly due to an imbalance between energy intake and energy expenditure (Jung and Choi, 2014). Obesity increases the risk of non-communicable diseases including type 2 diabetes (T2D), cardiovascular diseases and certain types of cancers (Pi-Sunyer, 2009), creating an urgent need for effective anti-obesity interventions.

Lifestyle modifications, such as diet and exercise, are the preferred interventions for the prevention and treatment of obesity. However, the adherence to healthy diets and exercise routines is poor, with an increased reliance on pharmacotherapy to treat obesity (Hunter et al., 2008; Lagerros and Rössner, 2013). Anti-obesity drugs are plagued by several adverse effects, and many have been withdrawn from the market (Adan, 2013). Globally, increased research efforts are being directed

* Corresponding author.
E-mail address: carmen.pheiffer@mrc.ac.za (C. Pheiffer).
[1] Current address: Institute for Diabetes and Obesity, Helmholtz-Zentrum München, German Research Center for Environmental Health (GmbH), Parkring 13, 85748 Garching, Germany.
[2] Current address: Department of Viticulture and Oenology, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa.

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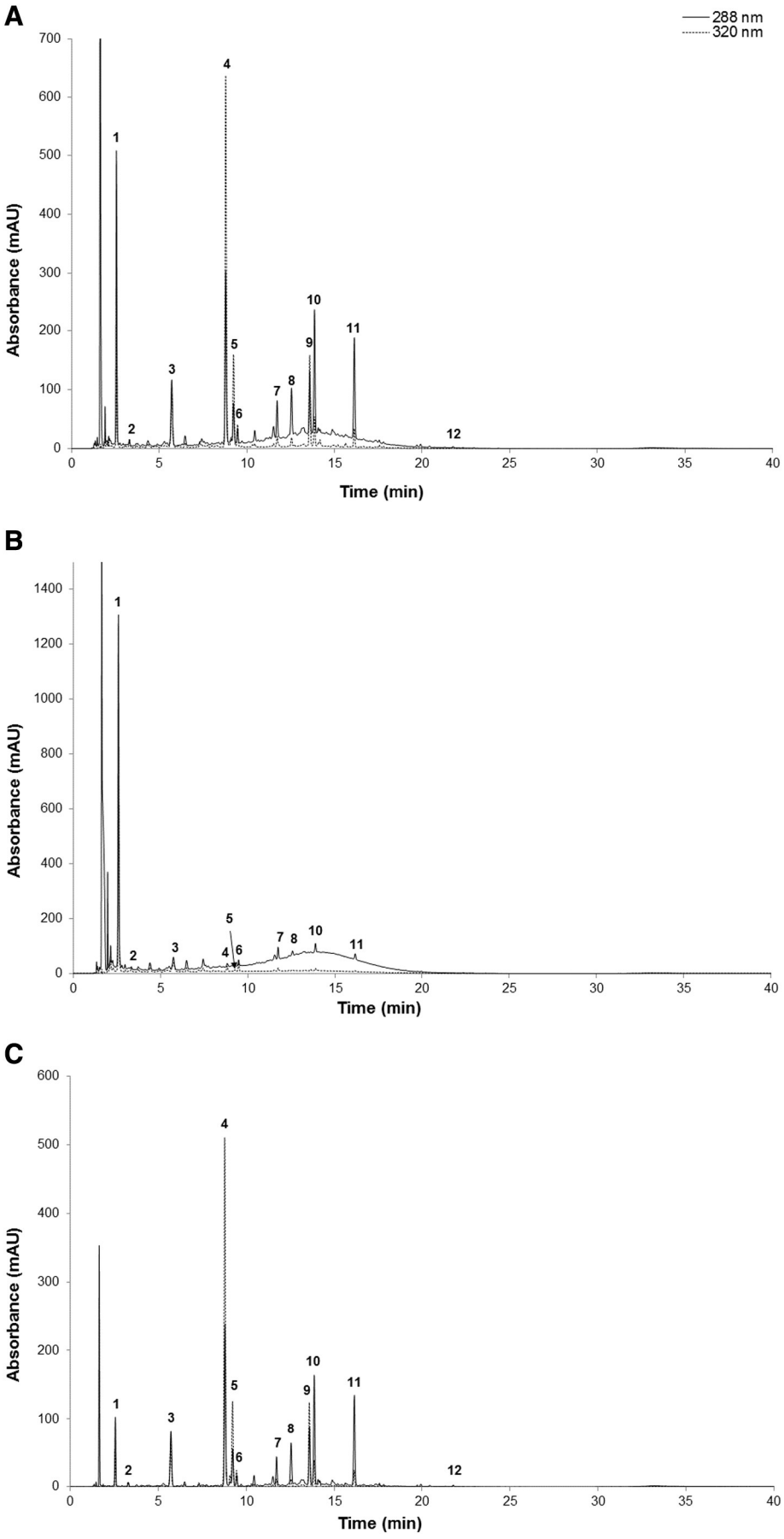

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