Call for Applications: PhD Fellowship

Structure-activity relationships of novel anti-diabetic ruthenium compounds: synthesis, characterization, mechanistic, *in vitro* and *in vivo* studies

Abstract:

Diabetes is a global epidemic, which has caused over 1.6 million deaths in 2016 (World Health Organization, URL link: *https://www.who.int/news-room/fact-sheets/detail/diabetes*, accessed on 25/03/2019). The consequences of chronic Type II diabetes is normally alleviated by intravenous insulin injections in combination with dietary interventions. However, this conventional therapy poses major health risks (*viz.* cardiovascular diseases, blindness, kidney failures and amputations) due to the development of insulin-resistance. In addition, insulin injections can be regarded as primitive, tedious and uncomfortable in comparison to oral-administration and transdermal patches, which offer more facile administration of drugs.

Transition metal complexes are widely utilized in medicine for various diagnostic and therapeutic applications [**1**]. Their diverse medicinal diversity stems from their variable redox, electronic, photochemical and stereo-electronic properties. In particular, organoruthenium complexes have been investigated for their anti-diabetic properties [**2**]. Our preliminary studies indicate that our novel candidate anti-diabetic metallo-drugs, $[Ru^{II}(H_3ucp)Cl(PPh_3)]$ (H_4ucp = 2,6-*bis*-((6-amino-1,3-dimethyluracilimino)methylene)pyridine), illustrated optimal activities accompanied with negligible cytotoxicity levels in diet-induced pre-diabetic rats [**3 – 5**].

In this research project, we envisage investigating the mechanisms of activities of these leading anti-diabetic metal-based drugs. Furthermore, new derivatives of the aforementioned metal complexes will be synthesized and characterized and the structure-activity relationships of the analogues will be explored. Biodegradable electro-spun nanofibers will be utilized as drug carriers during the anti-diabetic studies and the dissolution rates will be examined *via* various physicochemical techniques.

References:

[1] C.-N. Ko, G. Li, C.-H. Leung, D.-L. Ma, *Dual function luminescent transition metal complexes for cancer theranostics: The combination of diagnosis and therapy*, Coordination Chemistry Reviews, 2019, **381**, 79.

[2] L. Ma, Y. Fu, L. Yu, X. Li, W. Zheng, T. Chen, *Ruthenium complexes as inhibitors of human islet amyloid polypeptide aggregation, an effect that prevents beta cell apoptosis*, RSC Adv., 2015, **5**, 17405.

[3] L.P. Mabuza, M.W. Gamede, S. Maikoo, I.N. Booysen, P.S. Ngubane, A. Khathi, *Effects of a Ruthenium Schiff Base Complex on Glucose Homeostasis in Diet-Induced Pre-Diabetic Rats*, Molecules 2018, **23**, 1721.

[4] I.N. Booysen, S. Maikoo, M.P. Akerman, B. Xulu, *Novel ruthenium(II) and (III) compounds with multidentate Schiff base chelates bearing biologically significant moieties*, Polyhedron, 2014, **79**, 250.

[5] L.P. Mabuza, M.W. Gamede, S. Maikoo, I.N. Booysen, P.S. Ngubane, A. Khathi, *Cardioprotective effects of a ruthenium(II) Schiff base complex in diet-induced prediabetic rats*, Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2019, **12**, 217.

Core character attributes:

The ideal candidate must be meticulous, self-motivated and dedicated. In addition, the candidate must show a high level of integrity as confidentiality is of utmost importance. Furthermore, the candidate must be a dynamic individual who can work effectively in team-orientated environment.

Core skills:

The candidate must be competent in common Microsoft software packages as well as have good communication and writing skills. Also, theoretical or experimental experience in electron microscopy, computational, bioinorganic and/ or analytical chemistry will be beneficial.

Value of PhD studentship:

PhD studentship will be R 120 000 for the first year and will be renewable subjected to satisfactory progress by all stakeholders.

How to apply?

Candidates must forward their detailed CVs to Prof. I Booysen (Booyseni@ukzn.ac.za) by 31/01/2020. Three contactable references must be included in the CV and certified copies of degree certificates must be attached. No late applications will be considered. If you are not contacted by the 05/02/2020 for an interview, please consider your application unsuccessful.