UNIVERSITY OF KWAZULU-NATAL ™

INYUVESI YAKWAZULU-NATALI

THE EFFECTS OF *SYZYGIUM AROMATICUM*-DERIVED -OLEANOLIC ACID (OA) ON REACTIVE OXYGEN SPECIES IN THE HEART, LIVER AND THE KIDNEY OF STZ-INDUCED DIABETIC RATS

[1]Blessing N Mkhwanazi, Ntethelelo H Sibiya, Metse Serumula, Rene Myburg & [1]Cephas T Musabayane

School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu- Natal, Private Bag X54001, Durban, South Africa

INTRODUCTION

The onset of diabetic complications is attributed to sustained hyperglycaemia which triggers the generation of free radicals and oxidative-related micro- and macrovascular damages [1]. Recent studies report that intense glycaemic control by the subcutaneous administration of insulin cannot completely restore the balance between reactive oxygen species (ROS) and antioxidants [2].

Preliminary studies in our laboratory indicate that transdermally delivered *Syzygium aromaticum*-derived oleanolic acid (OA) has the ability to lower blood glucose in experimental diabetes mellitus due to the sustained release of the triterpene. Research has indicated that some plant derived bioactive compounds such as flavonoids and tannins have antioxidant properties [3]. However, no work has been done to determine the effects of OA on oxidative stress.

OBJECTIVES

The aim of the study was to evaluate the effects of *Syzygium aromaticum*-derived OA on some biomarkers of oxidative stress in the heart, liver and kidney of the STZ induced diabetic rats.

MATERIALS AND METHODS

Extraction of OA

- OA was extracted from *Syzygium aromaticum* [(Linnaeus) Merrill & Perry] [Myrtaceae] clove flower buds using a previously validated protocol [4].
- Cloves (500 g) were sequentially extracted twice at 24h interval with dichloromethane, and ethyl acetate (EA) yielding ethyl acetate solubles (EAS) containing MA /OA and methyl corosolate.
- OA was isolated using silica gel column and recrystallized from methanol/chloroform and its structure confirmed by ^{1}H and ^{13}C-NMR compared with literature data [5].

Animals

Male Sprague –Dawley rats (250-300 body weight) bred and maintained at Biomedical Research Unit (BRU), University of KwaZulu-Natal were used in this study.

Induction of diabetes mellitus

Diabetes mellitus was induced in rats with a single intraperitoneal injection of streptozotocin (STZ, 60mg/kg) dissolved in freshly prepared 0.1M citrate buffer (pH 6.3).

Effects of OA oxidative stress

The acute effects of OA on malondialdehyde (MDA), an indicator of lipid peroxidation and the antioxidant enzyme, glutathione (GSH) concentrations were evaluated in the heart, liver and kidney of STZ-induced diabetic rats following a glucose load after an 18-hour fast. Rats administered pectin-free OA or transdermally delivered insulin acted as untreated and treated positive controls, respectively. Heart, liver and kidney samples of liver and gastrocnemius muscle (1–1.5 g) were harvested after 6-h in separate groups of non-diabetic and STZ-induced diabetic rats for the determination of MDA and GSH.

RESULTS AND DISCUSSION

Effects of OA on oxidative stress

By comparison with non-diabetic rats, STZ-induced diabetic rats exhibited oxidative stress and impaired antioxidant defense mechanisms in the heart, liver and kidney tissues of as assessed by elevated MDA levels and reduced GSH concentration (Figures 1 and 2). Free radicals are extremely reactive and produce damage and modify cell functions. Under normal circumstances, there are antioxidant enzymes and macromolecules that remove and protect the cells from the damaging effects of free radicals.

OA like insulin significantly reduced the levels of MDA in the hearts and livers of STZ-induced diabetic rats (Figure 1).

OA significantly increased GSH concentration in the heart of STZ-induced diabetic rats although levels in the kidney and liver were not altered (Figure 2).

Interestingly, insulin treatment did not alter the GSH concentrations in the heart, liver and kidney tissues.

CONCLUSION

These results suggest that OA is a potential drug for diabetes mellitus that would not only lower blood glucose, but also can avert complications that arise due to oxidative stress.

REFERENCES

1. Niedowicz DM, Daleke DL. (2005). Cell Biochem Biophys. 43:289-330.
2. Goldstein BJ, Mahadev K, Wu X (2005). Diabetes.54:311-21.
3. Farkas O, Jakus J, Héberger K (2004). Molecules. 9, 1079-1088.
4. Madlala HP, Masola B, Singh M, Musabayane CT (2012). Renal Failure. 34: 767-769
5. Gohari AR, Saeidnia S, Hadjiakhoondi A, Abdoullahi M, Nezafati M (2009). Journal of Medicinal Plants. 8: Supplement 5

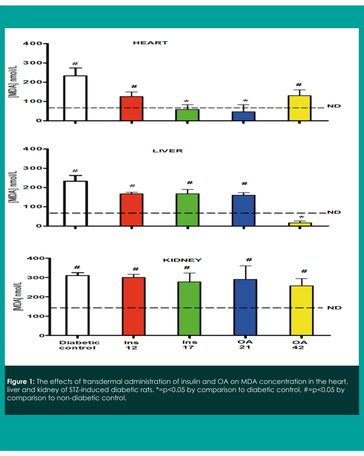

Figure 1: The effects of transdermal administration of insulin and OA on MDA concentration in the heart, liver and kidney of STZ-induced diabetic rats. *=p<0.05 by comparison to diabetic control, #=p<0.05 by comparison to non-diabetic control.

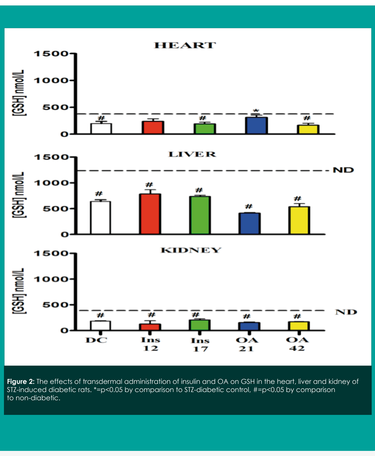

Figure 2: The effects of transdermal administration of insulin and OA on GSH in the heart, liver and kidney of STZ-induced diabetic rats. *=p<0.05 by comparison to STZ-diabetic control, #=p<0.05 by comparison to non-diabetic.