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Luteolin supplementation ameliorates cobalt-induced oxidative stress and inflammation by suppressing NF-κB/Kim-1 signaling in the heart and kidney of rats

Ademola Adetokunbo Oyagbemi [a], Akinleye Stephen Akinrinde [a,*], Olamide Elizabeth Adebiyi [a], Theophilus Aghogho Jarikre [b], Temidayo Olutayo Omobowale [c], Olufunke Eunice Ola-Davies [a], Adebowale Benard Saba [d], Benjamin Obukowho Emikpe [c], Adeolu Alex Adedapo [d]

[a] Department of Veterinary Physiology and Biochemistry, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[b] Department of Veterinary Pathology, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[c] Department of Veterinary Medicine, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[d] Department of Veterinary Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Ibadan, Nigeria

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ABSTRACT

Cobalt-induced cardiomyopathy and renal toxicity have been reported in workers in processing plants, hard metal industries, diamond polishing and manufacture of ceramics. This study was designed to investigate the influence of Luteolin supplementation on cobalt-induced cardiac and renal toxicity in rats. Exposure of rats to cobalt chloride ($CoCl_2$) alone caused significant ($p < 0.05$) increases in cardiac and renal H_2O_2, malondialdehyde (MDA) and nitric oxide (NO), along with increased serum myeloperoxidase (MPO) activity. In addition, there were significant ($p < 0.05$) reductions in cardiac and renal glutathione peroxidase (GPx), glutathione S-transferase (GST) and reduced glutathione (GSH). $CoCl_2$ induced higher immuno-staining of nuclear factor kappa beta (NF-κB) in the heart and kidneys, and the kidney injury molecule (Kim-1) in the kidneys. Treatment with Luteolin or Gallic acid produced significant reversal of the oxidative stress parameters with reductions in NF-κB and Kim-1 expressions, leading to suppression of histopathological lesions observed in the tissues.

1. Introduction

Environmental exposure to cobalt is common because of its use in industrial processes, nutritional supplements, recreational or medicinal products or implanted medical devices made of high-performance, wear-resistant cobalt alloys (Unice et al., 2012; Packer, 2016). Previous reports indicated that the production of refined cobalt has increased steadily the world over (IARC, 2006), with production figures at about 123,000 tons of world cobalt mine production and 91,300 tons of cobalt refinery production in 2014 (Shedd, 2014), thus, increasing the risk of environmental and industrial exposures. Because of its ability to stimulate red blood cell production, cobalt has been used historically to treat refractory anaemia and is now increasingly used by athletes to increase red cell mass and boost exercise performance (Lippi et al., 2006). Exposure to high concentrations of cobalt has been reported to cause cardiomyopathies in workers involved in processing plants, hard-metal, diamond polishing and ceramic industries (Sauni et al., 2017), and in patients undergoing hip arthroplasty with cobalt implants (Umar et al., 2019).

Similar to cardiomyopathies that were documented in heavy-beer drinkers, reported cases of industrial cobalt exposure are characterized by a sub-acute onset of heart failure, sinus tachycardia, pericardial effusions, polycythaemia, cyanosis, and hypotension (Packer, 2016). Additionally, nephrotoxic effects have also been observed in excessive exposure to cobalt (Garoui et al., 2012). The kidney is an important target of heavy metal toxicity because of its ability to reabsorb and accumulate divalent metal ions. Studies in orthopaedic metal toxicity identified that metal ions such as cobalt and chromium emanating from implanted devices are excreted by the kidneys and have the potential to induce tubular necrosis (Keegan et al., 2007).

Management of cobalt toxicity in exposed individuals have included chelation therapy with agents that bind metals and aid its renal excretion, thus, reducing the metal ion load in the body, while the removal of causative implant remains the recommended treatment in patients

* Corresponding author.
E-mail addresses: as.akinrinde@mail.ui.edu.ng, leyesteve2000@yahoo.com (A.S. Akinrinde).

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