Pharmacological evaluation of Natural Sea Salt against doxorubicin induced cardiac toxicity via Gut Microbiome

Turky Omar Asar
Jeddah University: University of Jeddah
Muhammad Shahid Nadeem
King Abdulaziz University Faculty of Sciences
Fahad A. Al Abbasi
King Abdulaziz University Faculty of Sciences
Ryan Adnan Sheikh
King Abdulaziz University Faculty of Sciences
Salma Naqvi
Gulf Medical College: Gulf Medical University
Salman Bakr I. Hosawi
King Abdulaziz University Faculty of Sciences
Naif Abdullah R. Almalki
King Abdulaziz University Faculty of Sciences
Sultan Alhayyani
King Abdulaziz University College of Sciences and Arts in Rabigh
Vikas Kumar
SHIATS: Sam Higginbottom University of Agriculture Technology and Sciences
Sheikh Rizwanuddin
Graphic Era Deemed to be University
Mohammed Kaleem
Dadasaheb Balpande College of Pharmacy
Firoz Anwar (fanwar1@kau.edu.sa)
King Abdulaziz University Faculty of Sciences https://orcid.org/0000-0003-3553-3512

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Abstract

Cardiovascular complications including cardiac toxicity pose a major health threat worldwide. These complications can be handled by reducing the associated risk factors including diet. Gut microbiome is prominently associated with cardiovascular diseases. The present study demonstrates how the gut microbiota, under the effect of table salt and natural sea salt, modulates doxorubicin-induced cardiac toxicity. Experimental animals were divided into six groups (n = 6) as: Group I. Normal control (NC); Group II: table salt (0.3%) (NTS); Group III: natural sea salt (0.3%) (NSS.); Group IV: Doxorubicin-induced cardiac toxicity control (2mg/kg) (DC); Group V:DC + Table salt (0.3%) (DTS.); and Group VI: DC + Natural sea salt (0.3%) (DSS). CKMB, CRP, lipid profile was assayed in serum, GUT microbiota in stool, and histopathological variations in heart tissues were studied. Significant alterations were observed in the analytical values of blood parameters in the doxorubicin versus the normal control group. Also, a significant variation was observed in DTS and DSS groups for CKMB ($p < 0.001$), CRP ($p < 0.01$; $p < 0.05$), TC, TG, LDL ($p < 0.0001$) and HDL ($p < 0.05$, $p < 0.01$) respectively, when compared with DC group. Presence of gut microbes were identified in the stool samples. The population of Proteobacteria and Spirochetes were significantly lowered the DC group as compared to all other groups. However, the treatment with the sea salt increased the richness of this phylum to 36-fold, while table salt increased only by 9-fold. The change in microbial population is a direct marker for cardiac toxicity, which was highly prevented by sea salt as compared to table salt. Histopathological alterations in cellular architecture of the heart reflect a marked effect of the salts on it. Our observations suggest that a diet with natural sea salt demonstrated a significant protection to cardiac toxicity that may have initiated via inflammation after doxorubicin injury compared to the table salt.

Introduction

Cardiovascular diseases comprise 10% of global health burden and contribute to 30% of worldwide mortality(S. &M. 2018). Excessive salt intake has always been a considerable factor in manifestation of cardiac complications inclusive of cardiac failure. It is attributed to 4.1 million deaths annually(Collaborators 2016). An acute myocardial infarction (AMI) gives rise to complex interactions between myocardial intra and extracellular components, and effects various epigenetic as well as neurohumoral regulations. It may lead to geometrical and morphological deviations in a normal cardiac architecture, resulting in cardiac toxicity (Ky et al. 2013). These changes are also associated with hypertension (Maceira &Mohiaddin 2012) and raised body mass index (Rider et al. 2013).Cardiac toxicity influenced via inflammation through Inflammasome activation, interleukin 6 along with CRP are associated with cardiac injury (Fonseca &Izar 2022)

Studies emphasizing reduction of sodium intake largely focus on the management of hypertension with decreased cardiovascular risk(Naqvi et al. 2021, Tang et al. 2017). Some researchers have also evidenced that excessive salt intake may mark severe cardiac complications by increasing left ventricular mass, independent of its effect on blood pressure (Ferrara et al. 1984, Harsha et al. 2004). Few studies on the other hand, highlight the deleterious consequences of low sodium intake on CVS owing to the