Effects of Metal Pollutants on Cardiovascular System

ABSTRACT
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ABSTRACT

Cardiovascular system is an integrated organ system consisting of heart and blood vessels. Any malfunction in cardiovascular system leads to cardiovascular diseases. Cardiovascular diseases are broadly classified in two groups that include diseases of heart and vascular diseases. Toxic metals target the vascular system tending towards both acute injury and disease promotion, contributing to a variety of disease conditions including atherosclerosis, edema, and hypertension.

Natural compounds are recognised to have cardiovascular health benefits and a lot of other health benefits too. Natural compounds cause relaxation of smooth muscles. Effect of dose dependent concentrations of nickel/cobalt on PE-induced contraction were investigated in isolated Wistar rat aortic rings using an organ bath system. Aortic rings were isolated from Wistar rats and suspended in the organ bath system. The tissue was then transferred and fixed in a chamber filled with Kreb's solution. The rings were mounted for measurement of isometric contractions in an organ bath chamber. Chamber was gassed with 95% O_2 and 5% CO_2. Tissue was suspended under the isometric tension of 2.0 g and allowed to equilibrate for 1 h with the change of fresh Kreb's buffer every 15 minutes. Contractile responses were tested with 1 µM phenylephrine.

We observed increased hypercontractile response on at varying concentrations of nickel/cobalt respectively. Nickel at 100 nM caused 80% increase in contraction in isolated aortic rings, and cobalt caused 32% increase in contraction with respect to control. We found that nickel mediated contraction is due to nickel mediated contraction is due to influx of extracellular calcium through T-type calcium channels in smooth muscle cells and increase in endothelium factors from endothelium.

Endothelium-intact aortic rings were incubated with 800 nM, 1 µM, 10 µM, 50 µM cobalt; we observed 20%, 22%, 32% and 27% increased contractions respectively, while no effect was seen in tension recording on cobalt exposure. Incubation of endothelium-intact aortic rings with 100 µM apocynin and 100 µM L-NAME suggested the role of NADPH oxidase in generation of reactive oxygen species (ROS) and decrease in bioavailability of nitric oxide (NO) from eNOS on exposure to cobalt. Aortic rings pre-incubated with 1 µM and 20 µM verapamil suggested role of both L-type and T-type calcium channels in efflux of extracellular calcium in

smooth muscle cells. We observed no role of store operated calcium channels (SOCC) in calcium efflux due to cobalt exposure and cyclooxygenase in generation of prostanoids in isolated aortic rings. Cobalt caused rise of PE-induced contractions as a result of the endothelial generation of ROS, by decreasing bioavailability of NO. Generation of ROS may be responsible for causing the influx of extracellular calcium through L-type and T-type Ca^{2+} channels in smooth muscle cells.

We investigated the effect of quercetin. resveratrol, carvacrol, eugenol, linalool on aortic rings in metal unexposed and nickel and cobalt exposed conditions. To gain insight of mechanism of action of relaxation, these natural compounds were employed with various modulators at their saturating concentration.

Resveratrol mediates relaxation by inhibiting NADPH oxidase enzyme and COX enzyme; it also causes inhibition of calcium channels and elevation of NO. Quercetin mediates relaxation by quenching ROS and by inhibiting calcium uptake and elevating NO. Quercetin play no role in blocking prostanoids generation. Carvacrol and eugenol mediate relaxation by quenching ROS and elevating NO in aorta. Linalool causes relaxation of aortic tissues by inhibition of Ca2+-influx, COX inhibition and NO-elevation. Quercetin, eugenol, carvacrol, linalool in addition to being good relaxants are found to be efficient ameliorators of hypercontraction in aortic tissues both, nickel & cobalt. Resveratrol proved to be efficient ameliorator of nickel caused hypercontraction but poor ameliorator of cobalt-mediated hypercontraction. This could be correlated with their relaxant activity pathways enhanced by nickel/cobalt. Ameliorative efficiency of all five natural compounds showed no significant difference in aortic system whether muscle is co-incubated with natural compounds and metal-ions or pre-incubated with natural compounds followed by metals. Nickel exposure causes minor but significant decrease in total nitrite level with respect to control. Cobalt exposure causes significant and considerable decrease in total nitrite level with respect to control, suggesting role of cobalt in endothelial dysfunction due to generation of reactive oxygen species. Increase in total nitrite level was observed in aortic rings incubated with natural compounds and metals, suggesting role of natural compounds in stabilising nitrite levels. Hence these natural compounds have a role in relaxation. Significant increase in total calcium level was observed in aortic rings incubated with nickel/cobalt. The natural compounds resveratrol, quercetin and linalool tested seem to be calcium channel blockers because they decreased total calcium level in aortic rings and scavenging of reactive oxygen species as validated by fluorescence microscopy using DHE dye.