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**Title of Thesis** : **Ameliorative Potential of Some Natural Compounds on  
Lead and Cadmium Altered Aortic and Tracheal  
Contractility**

### **Abstract**

Chronic as well as acute exposure of lead and cadmium are known factor for pathogenesis of chronic obstructive pulmonary disease, cardiovascular disorders, hypertension, endothelial damage and many respiratory dysfunctions. Both lead and cadmium are involved in alteration of smooth muscle contractions. Various natural compounds are known to possess antioxidant, anti-inflammatory and smooth muscle relaxation properties acting via pathways either dependent on or independent of NO and cause smooth muscle relaxations. They are also good scavengers of ROS and inflammatory mediators. However exact pathways, or relative contribution of various pathways, in causing these natural compounds induced relaxations is not known. If strategically employed, these molecules can be used as efficient ameliorators of altered contractions of smooth muscles exposed to lead and cadmium, restoring their normal functioning.

In this study, we investigate the effect of lead and cadmium on two smooth muscle systems: vascular smooth muscle (in aorta) and airway smooth muscle (in trachea) and elucidate the pathways contributing to this effect by employing specific donors/inhibitors of mediators involved in smooth muscle contraction, namely, sodium nitroprusside, apocynin and

indomethacin. Relative contribution of pathways mediating the contractile response of lead and cadmium on aorta and trachea is also explored. Five natural compounds, *viz.* curcumin, carvacrol, carvone, eugenol and linalool are investigated as smooth muscle relaxants along with pathways contributing to this effect. Ameliorative potential of these natural compounds is investigated on lead and cadmium caused altered contraction of aorta and trachea. Alignment of pathways of hypercontraction induced by lead and cadmium with pathways of relaxation by natural compounds is discussed for the identification of potential ameliorators of lead and cadmium hypercontracted aorta and trachea. Activities of key enzymes associated with alteration of smooth muscle *viz:* superoxide dismutase, glutathione peroxidase and nitric oxide synthase has been assessed in presence/absence of lead, cadmium and various potential ameliorators to trace the possible origin of ameliorative potential.

Results obtained show that Pb(II) and Cd(II) cause hyper-contraction of aortic as well as tracheal smooth muscle. This hypercontraction is mediated by ROS and NO- dependent pathways in case of Pb(II) and only ROS pathway in case of Cd(II). All five tested natural molecules: curcumin (-)carvone, carvacrol, eugenol and (+)linalool are found to be efficient relaxant of both smooth muscle system, relaxant effect of curcumin, carvacrol and eugenol appears to come from quenching of ROS and elevation of NO. Linalool causes this relaxation by elevating NO and inhibiting COX-mediated signaling whereas carvone only through COX-mediated signaling. In validation of their elucidated mechanism of action curcumin, carvacrol and eugenol are found to be efficient ameliorators of lead and cadmium altered contractility in both aortal and tracheal systems. Result of biochemical assays indicate that this amelioration does not originates from alteration in activities of SOD, GPx or NOS.