ABSTRACT

In order to achieve sustainable development of human societies the use of pesticide, insecticide and such other chemicals is inevitable. Throughout the world, the highest levels of pesticide exposure are found in pesticide manufactures and agricultural workers. Because of the extensive use of agricultural pesticides in food production, public are chronically exposed to low levels of pesticide residues through their diets (vegetables and fruits).

According to WHO (2004), unintentional poisonings kill an estimated 355,000 people globally each year. Self poisoning with pesticides accounts for about a third of all suicides worldwide. According to National Crime Records Bureau Ministry of Affairs, India (2010) suggest that 18.8% (n = 25,288) of India's 1,34,599 officially recorded suicides were self-poisonings with insecticides.

In this context, exploring the role of xenobiotic metabolizing enzymes in protection from day to day xenobiotic exposure acquires importance. Among these enzymes, role of paraoxonase1 (PON1) is outstanding. PON1 detoxifies organophosphate pesticides (OP) and nerve agents. Its role in protection against OP exposure is well documented. Besides its detoxification role, PON1 is well known for its antioxidant and antiatherogenic property. PON1 level is inversely correlated with the risk of cardiovascular disorders, neurological disorders, diabetes and cancer.

The role of PON1 as a xenobiotic metabolizing enzyme on the one hand, and as an antioxidant molecule on the other, have placed it is an unique position in the overall health and well being of humans. However, PON1 activity may vary about 40 fold among the population. This variation might be caused by due to genetic polymorphisms or by exogenous factors.

In this study, the xenobiotic metabolizing activity and detoxification activities of PON1 and effect of diverse environmental toxicants as well as endogenous potential metabolites on the activity of PON1 has been studied.
Our result shown that grapes and cauliflower were contaminated with pesticide residues. Pesticides such as chlorpyrifos and chlorothalonil inhibited the PON1 activity in vitro. However, chlorothalonil stimulated the HDL synthesis in vitro. Domestic pesticide such as mosquito repellent smoke slightly inhibited the PON1 activity initially, but the enzyme activity recovered probably by overcoming the inhibitory effect of mosquito coil smoke. Case series on pesticide poisoned subjects shown higher PON1 activity have better chance of detoxifying the lethal effect of acute organophosphate poisoning.

Physiologically occurring potentially toxic molecules such as nitrotyrosine and dityrosine did not inhibit PON1 activity, whereas, chlorotyrosine inhibited PON1 competitively. Glycated lysine and glycated histidine did not inhibit PON1, but glycated albumin increased PON1 activity in vitro. This may be a nonspecific effect on providing a hydrophobic environment to the PON1.

The role of HDL on lipoprotein oxidation was investigated. Addition of HDL did not protect LDL from oxidation. This is because, HDL among Indians itself susceptible for oxidation. Finally, ability of ketone bodies to inhibit PON1 was tested. At 25mM concentration, sodium acetoacetate did not inhibit PON1. Hydroxybutyrate was slightly decreased the PON1 activity, whereas, acetone and ethyl acetoacetate inhibited PON1 up to 30%.

Thus, several environmental toxicants, endogenously produced toxic metabolites and certain pathological conditions can influence the overall activity of PON1. Hence these variables can confound the role of PON1 as a diagnostic and prognostic marker of oxidative stress, risk of cardiovascular diseases and even pesticide exposure.