SUMMARY AND CONCLUSIONS
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Glutathione S-transferases (GSTs, EC 2.5.1.18) constitute a complex family of enzymes with multiple functions that are mostly associated with the biotransformation/detoxification of a wide spectrum of xenobiotics. They exist in complicated but distinct isozyme forms in different mammalian tissues. They are distinguishable by catalytic and immunological properties and by primary structure as well. Though their role in detoxification of xenobiotics is well known, their involvement in antioxidant defenses especially during oxidative stress is not well defined. In the present study structural and functional characterization was undertaken for GSTs from liver and lung tissues of animals subjected to oxidative stress. Female albino rats at weanling stage were fed on diets deficient and/or supplemented with vit.E and/or Se for a period of 13 weeks to induce oxidative stress by impairing vit.E and Se-GSH Px antioxidant activities.

1. Feeding of female albino rats with vit.E and/or Se deficient diets for a period of 13 weeks reduced vit.E and Se levels in hepatic and lung tissues to almost negligible levels.

2. Vitamin E and Se deficiency resulted in the stimulation of enzymes involved in GSH metabolism.

3. Vitamin E and/or Se deficiency in female albino rats resulted in oxidative stress in liver and lung tissues as evidenced by increased levels of lipid peroxides and decreased Se-GSH Px levels. Of these two, lung tissue is relatively more susceptible to oxidative damage.

4. Oxidative stress by Se deficiency resulted in the induction of GSTs both in liver and lung tissues as evidenced by increased specific activity of GSTs in cytosolic fractions, increased total affinity purified GST protein and decreased purification fold of Se deficient groups.
5. Western blot analysis of crude cytosol fractions, **SDS-PAGE** and RP-HPLC analysis of affinity purified proteins of vit.E and/or Se deficient animals revealed induction of \( \text{Ya}_2 \) and Yc subunits in liver tissue compared to that of +E+Se animals.

6. In the lung tissue, which lacked Ya subunits, only GSTs with Yc subunits were induced in response to vit.E and/or Se deficiency.

7. Substrate specificity studies have revealed that GSTs with Ya subunits exhibit maximum activity with fatty acid endoperoxides such as PGH2, whereas Yc containing subunits showed maximum activity with organic hydroperoxides.

8. Substrate specificity of cytosol fractions and affinity purified GSTs from liver and lung tissues of vit.E and Se deficient animals showed increased activity with CHP, the organic hydroperoxides including 15-HPETE and 13-HPODE.

9. The increase of GSTs with peroxidase activity of GSTs towards organic peroxides like CHP, 15-HPETE and 13-HPODE observed in vit.E and/or Se deficient animals is consistent with an adaptive mechanism to enhance antioxidant defenses under oxidative stress.

10. Liver GSTs from vit.E and/or Se deficient animals had significantly higher \( \text{PGF}_{2\alpha} \) synthase activity in comparison to vit.E and Se supplemented animals. This observation coincides well with the increased GST Ya subunit in vit.E and/or Se deficient animals, which exhibits endoperoxidase activity. No significant differences, however, were observed in PG formation in the lung tissue of vit.E and/or Se deficient animals.

11. \( \text{LTC}_4 \) synthase activity of GSTs when measured in liver and lung tissues showed higher activity in the lung compared to liver tissue. This was attributed to high concentration of Yb subunits present in lung tissue, which exhibits higher \( \text{LTC}_4 \) synthase activity.
From these studies it is concluded that, GSTs in addition to their role in detoxification of xenobiotics, play a predominant role in antioxidant defense and are selectively induced during oxidative stress.