Haematological and Pathophysiological Alterations Induced by Rodenticides in Rats

A THESIS

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CONTENTS

List of Tables

List of Figures

Summary

Rodents pose a serious practical problem to crop fields not only by causing damage to various growth stages of plant but also by causing contamination in transportation and storage, the control of rodents is an urgent necessity.

Superwarfarins are very potent, long-lasting anticoagulant rodenticides inhibit the enzyme vitamin K epoxide reductase, thus reducing the recycling of Vit K, which is necessary for activation of several clotting factors. Amongst the superwarfarins typically incorporated into rodent bait, brodifacoum is the most widely used. The biologic potency of BDF is thought to be attributable to their high lipid solubility and increased affinity for hepatic tissue and enzymes. However, its inhibitory effect on blood clotting activity and Vitamin K cycle in the liver of rats seems to be transient.

Dicumarol counteracts the haemostatic mechanism through inhibition of Vit K epoxide reductase. This suppresses the recycling of Vit K and prevents the γ-carboxylation of glutamate residues in the clotting factors. DIC induced haemorrhage in cattle and calves accompanied by prolonged prothrombin and activated partial thromboplastin times.

An emerging genetic resistance against rodenticide represents one of the most challenges to eradication programs. Previous studies tried to overcome this practical issue using combination baits which have low cost and ecotoxicological concern but from humanness viewpoint have long days-to-death. Therefore, development of interventions that take another step wide jump on the road to enhance efficacy of anticoagulant rodenticide is highly recommended. The antithrombotic effect of Acetylsalicylic acid is well established and it

is mediated *via* acetylation of blood clotting factors and suppression of its synthesis, inhibition of platelets, prevention of thrombin formation, and acceleration of fibrinolysis.

This thesis was undertaken to identify the possible synergistic effect of BDF or DIC in combination with ASA as a new formulation of rodenticide with respect to the potential changes in haemostatic, haematological, liver and kidney function and oxidative stress parameters in addition to the histopathology of some target organs in a hope to translate the findings to the practical field.

The results of this study revealed that:

1. Rats exposed to combination of either BDF or DIC with ASA were characterized by a significant prolongation in CT and PT, and decrease in factors VII and IX while increase ionized Ca levels versus those exposed only to BDF or DIC. The addition of ASA to BDF caused more increase in BT, while addition of ASA to DIC caused more decrease in factor VII level.
2. Administration of ASA with BDF resulted in induction of oxidative stress as manifested by increase in plasma LPO level and decrease of CAT activity in lung and heart and kidney SOD compared to administration of BDF alone. There was increase in brain LPO , NO and GSH levels in kidney, and decrease in liver and heart SOD , liver CAT and Lung NO activities.
3. Anticoagulant effect of BDF or DIC was highly potentiated evident by a marked reduction in PLT count. The obvious decrease in EOS, LYM and MON count indicate the immunosuppressive effect of DIC when combined with ASA.
4. The combination of ASA with BDF or DIC exaggerate the histopathological changes in the studied targeted organs.

In conclusion : Co-admistration of ASA with any of BDF or DIC improves their efficacy as rodenticides.

Future recommendations

Further studies are needed to:

1. Explore in depth the molecular mechanisms by which ASA synergistically enhances the anticoagulant effects of BDF and DIC.