Research Article

SOHAG JOURNAL OF SCIENCES

https://doi.org/10.21608/sjsci.2025.363437.1259

Evaluating the effects of anticoagulant rodenticide bromadiolone in wild rats (*Rattus rattus frugivorous*) co-administered with aspirin on haemostatic, hematological and oxidative stress parameters.

Rana S. Sarhan[1], Mohamed F. El-Sayed[2,*], Magdy B. Wilson[1], Abd El-Aleem S. S. Desoky[3]

[1] *Agriculture Research center, Doki, Egypt*
[2] *Zoology Department, Faculty of Science, Sohag University, Sohag 82524, Egypt*
[3] *Plant Protection Department, Faculty of Agriculture, Sohag University, Sohag 82524, Egypt*
[*]*Email: mohamed_farag@science.sohag.edu.eg*

Received: 24th February 2025, **Revised:** 8th April 2025, **Accepted:** 16th May 2025
Published online: 28th June 2025

Abstract: The control of rodents which have a negative effect on human health, domestic animals, economic crops and animal poisoning is primarily based on the use of anticoagulant rodenticides. Bromadiolone is a wide-use long-acting anticoagulant rodenticide. Aspirin (acetylsalicylic acid, ASA) has its biological target, on cyclogenase enzymes drives various functions including haemostasis and inflammation. The aim of the present study was to investigate the beneficial effects of bromadiolone and aspirin as anticoagulants exposure for 4 days on hematological, haemostatic, and antioxidant parameters in wild rats. Twenty-four rats were collected from Shandaweel farm, agricultural research center, Sohag, Egypt were randomly divided into four groups. The first group acted as a control group, the second group was fed with bromadiolone (0.44 mg/kg b. wt) loaded with wheat grains, the third group was orally treated with ASA (60 mg/kg b. wt), whereas the fourth group was treated with bromadiolone along with aspirin. The main findings showed significant alterations in hematological, hemostatic parameters and the oxidative stress markers in rats treated with bromadiolone and aspirin compared to bromadiolone or aspirin alone. The results indicate that the combination of different anticoagulants may provide a successful tool for rodent control and a more environmentally friendly method of protection of non-target animals.
Keywords: Aspirin, Bromadiolone, anticoagulants, *Rattus rattus frugivorous.*

1. Introduction

Rodents are known as the most destructive mammalian pests [1]. They are one of the major pests causing damage to standing crops, stored food products, poultry, and animal farms [2,3,4]. Rodents are considered a big problem to the environment due to the chemicals used for their control and due to their diversity, feeding habits, high reproductive rates, and public health as carriers of zoonoses [5,6,7]. The wild rat, Rattus rattus, a frugivorous species, is one of the most commonly encountered and economically important rodents. It not only causes major damage to standing crops and stored crop products but also acts as a disease carrier and vector [8]. Anticoagulant rodenticides have been used for about five decades [9]. They are the most effective method to control undesired rodent species. Bromadiolone (Br) is a second-generation anticoagulant rodenticide having a single-dose effect [10]. It has a beneficial effect against rodents that have resistance to first-generation anticoagulants [11].

Bromadiolone, a hydroxy-coumarin, has been used for about fifty years and is widely available as superwarfarin. It is a member of coumarins and a vitamin K1 antagonist. Chemically, anticoagulant rodenticides are derivatives of coumarin. Coumarin derivatives induced serious vascular injuries, leading to massive bleeding and rapid death, making them suitable for the control of rodents [12]. They act as antagonists of vitamin K. Also, they act as non-competitive inhibitors of vitamin K epoxide reductase, more specifically. Inhibition of the enzyme vitamin K epoxide reductase causes a decrease in the concentration of active coagulation factors, which depend on vitamin K, leading to a longer coagulation time, which primarily leads to death [13]. The toxicity of Br in different organs in rodents has been studied. Br induces histopathological alterations in the liver of the black rat (*Rattus rattus*), indicated by hemorrhage in the central vein and blood vessels, necrosis in some hepatic regions, and pyknotic nuclei [14]. Also, black rats treated with Br caused pathological changes in the architecture of the kidney manifested by atrophy in the glomerular capsule with rupture in Bowman's space, disappearance of glomeruli, necrosis in the proximal and distal convoluted tubules, and severe hemorrhage in the glomeruli and tubules. Bromadiolone-treated rats with different doses showed severe congestion in the central vein, blood sinusoids, vascular degeneration, inflammatory cells infiltration, fatty infiltration, and pyknotic nuclei in hepatocytes [15]. In male *Banicota bengalensis* rats which fed with 100 mg/kg b. wt of Br for times ranging between 24 and 120 hrs. caused a significant increase in the levels of serum hepatic biomarkers (AST, ALT, ALP, LDH and bilirubin). In parallel with the alterations in the hepatic biomarkers, Br exhibited several histological changes in the hepatocytes indicated by degeneration of hepatocytes with focal

necrosis, inflammation, vacuolization, and inflammatory cell infiltration [16]. In *Mus musculus,* Br caused hepatomegaly and nephrotoxicity revealed by necrosis and accumulation of toxic metabolite debris in the renal glomerular and tubular cortex regions [17]. However, there is little data on the toxic effects of Br on the hematological and haemostasis parameters in rodents. It has been reported that Br led to a significant reduction in the values of RBCs, hemoglobin concentration, HCT% %, MCH, MCHC, and MCV in Wistar albino rats. But it caused a significant increase in WBCs, lymphocytes, and segmented granulocytes. On the other hand, it caused a significant decrease in monocytes, eosinophils, and basophils [18]. In *Mus musculus*, Br caused a significant decrease in RBC count, hemoglobin concentration, WBCs, and platelets [15].

ASA is one of the most used drugs as an analgesic, anti-inflammatory, antipyretic, and antithrombotic [19, 20]. ASA is a highly reactive molecule that can acetylate various macromolecules in biological systems, such as proteins, nucleotides, and lipids [21]. Antithrombotic activity of ASA through acetylation of proteins of the blood coagulation, including fibrinolysis [22] and prevents thrombin formation that is catalyzed by a calcium-ion-dependent complex of tissue factor and activated factor VII [23]. The inhibition of this complex through ASA promotes the inhibition of factors IX and X, then the formation of the prothrombin complex and thrombin is subsequently inhibited [24]. The current study was carried out to evaluate the potential toxicity of Br as a rodenticide on hematological and haemostasis parameters and antioxidant enzyme activities in wild rats (*Rattus rattus frugivorous*) for four days. Also, this study was extended to explore the antithrombotic property of ASA in combination with Br as an anticoagulant.

2. Materials and methods

2.1. Chemicals

Bromadiolone (4-hydroxycoumarin) super caid KZ 0.005% bait wheat grains were purchased from Kafr El-Zayat Pesticides and Chemicals (KZD). Aspirin (Acetylsalicylic acid) was purchased as powder with a purity 95% from Labo Chem (India), dissolved in distilled water, and administered as an aqueous suspension orally.

2.2. Animals

Twenty-four rats (wild rat*, Rattus rattus frugivorous*) were hunted from Shandaweel farm, Agricultural Research Center, Sohag, Egypt. The rats were housed in a well-ventilated experimental house and rat cages. By the guidelines for laboratory animal care (Ethical Committee No. CSRE-8-24). The rats were fed with crushed corn and allowed free access to tap water *ad libitum.*

2.3. Experimental procedure

Before experimentation, rats were given two weeks to acclimatize. Four groups of six rats were created by random selection. Water and food were given to the first group, which served as the control. Bromadiolone was administered at a dose of 0.44 mg/kg body weight [25]. to the second group. 60 mg/kg body weight of ASA was administered to the third group [26]. The fourth group was treated with bromadiolone along with aspirin. All the treatments were administered orally once a day for four days using a stomach tube. Every day, the rats were observed for clinical symptoms in their cages.

2.4. Blood collection

Upon the end of the experimental period, the rats were sacrificed by cervical dislocation under light diethyl ether after fasting overnight. The blood sample was collected from each rat and transferred directly into sterilized anticoagulant tubes and analyzed immediately for hematological indices. At the same time, a drop of blood from the punctured tail of each rat was taken on a microscope glass slide to evaluate the haemostatic parameters.

2.5. Determination of hematological indices

A Celltac hematological analyzer (Celltac, Japan) was used to assess the complete blood count (CBC), red blood corpuscles (RBCs), hemoglobin concentration (Hb) (g/dl), hematocrit value (HCT%), mean corpuscular volume (MCV) (fl), mean cell hemoglobin (MCH) (pg), mean corpuscular hemoglobin concentration values (MCHC) (g/dl) and red cell distribution width (RDW) (%), total leucocytic count (WBC) (x 10^3/ml), platelet count (PLT) (x 10^3/ml), mean platelet volume (MPV) (fl), platelet distribution width (PDW) (%), plateletcrit value (PCT) (%), neutrophils count (NeuL) (x 10^3), lymphocytes (Lymph) count (x 10^3), monocytes (Mon.) count (x 10^3), eosinophils (EOS) count (x 10^3) and basophils (BAS) count (x 10^3).

2.6. Determination of haemostatic parameters

For determination of haemostatic parameters, a microscope glass slides, and Coa Data 504 (Top check 2) was used to assess bleeding time (BT) (min./sec.), clotting time (CT) (min./sec.), prothrombin time (PT) (sec.), calcium (Ca+2) (mmol/L), factor VII (FVII) (%), and factor IX (FIX) (%).

2.7. Estimation of oxidative stress markers

Serum was used to evaluate oxidative stress markers, including the level of malondialdehyde (MDA) as an indicator of lipid peroxidation (LPO), and the activites of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase using Bio Diagnostic kits from Diagnostic Research and Reagents Company, Giza, Egypt.

2.8. Statistical analysis

The aggregated data were presented as the mean ± standard deviation (SD). Using SPSS version 29.0.10 software, one-way analysis of variance (ANOVA) and Duncan's multiple range test were used to determine statistical significance. P values less than 0.05 were regarded as significant, P< 0.01 was very significant, and P< 0.001 was extremely significant.

3. Results

3.1. Hematological indices

It should be noted that significant differences were found between the groups for all examined parameters. Highly significant (P<0.0003) decreases in all erythrocytic indices

(RBCs, Hb concentration, HCT%, MCV, MCH, MCHC and PDW, RDW-SD) in the ASA-treated group, but a highly significant (P≤0.004) increase in RDW-CV was noticed in respect to control. Also, Br induced a highly significant (P≤0.0002) decrease in all erythrocytic indices in respect to control. However, it induced a significant (P≤0.0075) increase in RBC count, MCHC and RDW-CV. (Table S1).

Aspirin and Br induced a significant (P≤0.0005) increase in platelet count and PCT, whereas it induced a significant (P≤0.006) decrease in MPV and PDW in comparison with control (Table S1).

Total WBCs, Lymph, Mon, Eos and Bas counts were highly significantly (P≤0.0001) decreased in ASA and Br-treated groups compared with the control, while a significant (P≤0.00001) increase was observed in Neutrophils in both groups (Table S1).

A significant (P≤0.0001) increase in RBCs and Hb concentration in Br-treated group were observed, comparing with the aspirin-treated group, whereas a non-significant decrease and significant (P≤0.04) increase in RBCs and Hb concentration in ASA along with Br, in respect to Br-treated group was documented. Also, the same result was obtained with MCV, MCH, MCHC and RDW-SD. On the other hand, a significant (P≤0.002) decrease in RDW-CV and HCT% was observed in Br and ASA along with Br-treated groups, in respect to ASA and Br-treated group (Table S1).

A significant (P≤0.01) increase and non-significant decrease in platelets and PCT% and PDW was observed in Br and Br-treated groups, comparing with the ASA-treated group (Table S1). However, a non-significant decrease in the same parameters was observed in respect to the Br-treated group. In contrast, a significant (P≤0.3) decrease in MPV was noticed in Br and ASA along with Br-treated groups, comparing with the ASA-treated group, while a non-significant decrease was observed in the same parameter in ASA along with Br, in respect to Br-treated group (Table S1). Administration of Br and ASA with Br resulted in a significant (P<0.03) decrease in WBC count, in respect to the ASA-treated group, while ASA with Br resulted in a non-significant increase in the same parameter, compared with the Br-treated group. Treatment with ASA and ASA along with Br induced a significant (P<0.004) increase in Neutrophil's count, in respect to the aspirin-treated group. Also, treatment with ASA along with Br resulted in a significant (P<0.02) increase in the Neutrophils count, compared with the Br-treated group. Administration of Br induced a non-significant decrease in Lymphocytes, but ASA along with Br resulted in a significant (P<0.04) decrease in the same parameter, comparing with the Br-treated group. Treatment with ASA along with Br caused a non-significant decrease in the same parameter, in respect to the Br-treated group. The same result was documented for Eos. Administration of Br and ASA with Br resulted in a non-significant increase in Mon relative to the ASA-treated group (Table **S1**).

3.2. Haemostatic parameters

A highly significant (P<0.000002) increase in the bleeding time (BT), clotting time (CT), prothrombin time (PT), Factor VII % (FVII) and Factor IX (FVI) in the groups treated with ASA, Br and ASA along with Br was observed, in respect to the control group. However, a highly significant (P<0.0005) decrease in Ca^{2+} was observed in all treated groups, in respect to control group (Table **S2**).

Comparing with ASA-treated group, administration of Br and ASA along with Br resulted in a highly significant (P≤0.001) decrease and a non-significant decrease in BT, respectively. But a highly significant (P≤0.00002) increase in CT was observed in Br and ASA along with Br-treated groups. Treatment with Br and ASA with Br resulted in a non-significant decrease and a significant (P≤0.001) increase in PT. A highly significant (P≤0.0007) increase and a significant (P≤0.0001) decrease in Ca^{2+} was observed in Br and ASA along with Br-treated groups. A highly significant (P≤0.000009) decrease and a highly significant (P≤0.000003) increase in FVII and FIX in Br and ASA along with Br were documented (Table S2).

The administration of ASA along with Br resulted in a highly significant (P≤0.0002) increase in BT, CT, PT, FVII, and FIX%, but a highly significant (P≤0.00009) decrease was documented in Ca^{2+} in respect to Br-treated group (Table S2).

3.3. Oxidative stress markers in serum

The administration of ASA and ASA with Br resulted in a highly significant (P≤0.0002) decrease in MDA, while a highly significant (P≤0.00003) increase in the same parameter was observed in ASA-treated group, comparing with the control group. Also, the same results for SOD activity. For CAT acivity, a non-significant increase and decrease was observed in ASA and ASA along with Br, respectively, while a highly significant (P≤0.0001) decrease was documented in Br-treated group. Comparing with the control group, administration of ASA and Br resulted in a highly significant (P≤0.00001) increase and a highly significant (P≤0.00001) decrease in GST activity, while a non-significant decrease in the same parameter on administration of ASA in respect to the control group was observed (Table S3). In respect to ASA-treated group, administration of Br resulted in a highly significant (P<0.0001) increase in MDA level, and SOD and GST activities, while it caused a significant (P<0.00008) decrease in CAT activity. Administration of ASA along with Br resulted in a highly significant (P<0.00007) increase in SOD and GST activites, but it caused a significant (P<0.00003) decrease in MDA level and CAT activity (Table S3). Treatment with ASA along with Br induced a significant (P<0.00006) increase in MDA level, and SOD, CAT and GT activities, compared with Br-treated group (Table S3).

4. Discussion

Anticoagulant rodenticides have been used worldwide to control commensal rodents. Bromadiolone is a second-generation anticoagulant rodenticide. Generally, hematological parameters are used as health and physiological indicators for human and experimental animals. In this respect, it has been reported that the hematological variations are associated with the effects of Br on blood coagulation [18]. The current study showed that short-term (4 days) exposure to Br induced significant variations in the hematological parameters which

showed that Br caused a significant increase in RBCs count, in comparison with the control. This result did not agree with the study which revealed that Br caused a significant decrease in RBCs count [18]. The increase in RBCs may be due to a bone marrow dysfunction induced by Br that caused overproduction of RBCs, a case known as erythrocytosis. The present study revealed that Br caused a significant increase in MCH, MCHC and RDW-CV. These findings were in consistent with the study of Suljević et al. [18] which revealed that Br induced a significant increase in these parameters. The increase in RBCs can affect the hematological indices such as MCH and MCHC which may lead to an increase in such indices as confirmed in this study, since Br induced an increase in MCH and MCHC. The increase in MCH referred to anemia caused by Br which renders the absorption of B-vitamins as a crucial factor required for synthesis of RBCs. In support of this suggestion, the increased value of MCHC means that Br induced spherocytosis and decreased MCV and rised MCHC and increased osmotic fragility of erythrocytes [27]. This seems to be the case in this study. The previous studies [28,29] revealed that Br induced low levels of Hb and Hct %, which is in accordance with our findings. Also, measurement of hematological indices in the blood of rats exposed to bromadiolone showed a decrease in Hb and Hct % values [30]. So, we assume that Br has stronger toxicological impact inducing numerous pathological changes in erythrocytic indices leading to hemolysis which is a case of anemia. Platelets are a vitally important part of the blood that helps bleeding through forming clot. The decrease in the platelets is a sign of dangerous internal bleeding. In the present study, Br induced a significant decrease in the platelets count. So, we suggest that Br as rodenticides has severe toxic effect on platelets causing a case known as thrombocytopenia which may lead to the death of rat by stopping formation clot. Platelet indices (MPV, PCT and PDW) are useful markers for determination causes of thrombocytopenia as hypo-productive or hyper-destructive like immune thrombocytopenia purpura. The rise in MPV and PDW was suggested to be due to impaired production of platelets which lead to aplastic anemia and inflammation. So, the increase in MPV and PWD because of Br exposure may lead to a severe anemia via impairing the production of platelets in the hematopoietic organs and/or increasing clotting time and activated partial thromboplastin time, which is a sing of toxication causing severe bleeding and death of rats [31]. The decrease in PCT is a sign of preventing blood clot due to the toxic effect of Br on bone marrow. So, the alterations in erythrocytic indices, platelets, and platelet indices are indications of the severe toxicological effect of Br on the hematopoietic organs like bone marrow. Furthermore, the assumption of findings of anemia and hemolysis can be caused by a short-term exposure to superwarfarins, as determined in this study.

White blood cells (WBCs) and the differential leukocytic indices (Neut., Lymph., Mon., Eos., and Bas.) are generally used as markers of body health since these cells are produced in bone marrow and act as the natural immunity that defends the body against toxins and xenobiotics. The results of the present study demonstrated that Br caused a highly significant decrease in WBCs and all the differential leukocytic indices except Neut., which showed a marked significant increase in relative to the control. The decreased WBCs may be due to the suppression of the immunological defense system because of the toxic effect of Br on bone marrow. Also, the decreased differential leukocytic indices support the suggestion that Br has a severe toxic effect on bone marrow, since all these indices are produced in bone marrow, and they are part of the immune system. While the increased Neut. may be due to stress-induced inflammatory alterations in the bone marrow, leading to dysfunction of the hematopoietic organs, especially bone marrow. Bleeding time (BT) and clotting time (CT) are frequently used as tests for platelet function. In this study, Br induced a significant increase in BT and CT. These findings are in accordance with the results which indicated that anticoagulant rodenticide caused an increase in the BT [31]. The prolonged BT and CT are associated with a decrease in the platelets [32,33]. This seems to be the case in the present study since Br induced a significant decrease in the platelet count. So, it can be concluded that the altered in BT and CT occurs after the fall in platelet count.

The inactivation of platelets, BT, and CT caused blood to flow freely through the vascular system. The increased BT and CT and fall in platelets may lead to severe bleeding and death of rodents, because of intoxication of anticoagulant rodenticides, bromadiolone. In the present study, Br induced a marked increase in the prothrombin time, factor VII, and factor IX. This finding is in an accordance with the studies which revealed that rodenticides (superwarfarin) caused a significant increase in the coagulation profile [35].

Vitamin K is an essential co-factor for activation of clotting factors II, VII, IX, and X via carboxylation. In absence of Vit. K, these coagulation proteins will remain non-functional, a precursor state [36]. It is reported that Br interferes with Vit. K epoxide reductase leading to a marked decrease in the levels of this vitamin [16]. Vit. K is consumed by carboxylation of proteins and is present as vitamin K epoxide, which impairs the biosynthesis of clotting proteins [37]. The body converts Vit. K epoxide back to Vit. K by the enzyme Vit. K epoxide reductase. Anticoagulant rodenticides inhibit this enzyme, leading to a lack of active vitamin K [38]. As a result, concentration of the clotting factors reduces, since more precursor proteins can be found in an inactive form. This seems to be the case in the current study.

Ca^{2+} is an indispensable prerequisite for many steps in the coagulation cascade, since it is essential for the conversion of fibrinogen to fibrin and prothrombin to thrombin; as a cofactor for factors V, VII, VIII, IX, and XIII [39] and a stimulator for platelet aggregation. In the current study, the decrease in the Ca^{2+} may be revealed that the failure to utilize it in the pathway of hemostasis and activation of blood platelets.

Aspirin, which is considered as a gold standard anticoagulant drug, is used to overcome the health and economic threatening global problem of rodents. Aspirin action takes place via acetylation of proteins of blood coagulation including fibrinogen, promotes fibrinolysis [22], preventing thrombin formation via catalyzing Ca^{2+}. Activating factor VII and inhibition of factors IX and X to form prothrombin complex [24].

The bleeding time is used to evaluate the capacity of platelets

to form a hemostatic plug [40]. In this study, aspirin induced a marked increase in the bleeding time, which gives insight into its antiplatelet activity via irreversible inhibition of cyclooxygenase activity and suppression of platelets-associated substances secretion [23]. Also, the marked prolongation in the clotting and prothrombin times following treatment with ASA may be due to the reduction in the blood clotting factors. Acetylation of blood clotting proteins, inhibition of platelets-associated substances secretion, inactivation of factors VII, IX, X, and XIII, acceleration of the rate of fibrinolysis, and reduction of coagulation factors in the liver are the potential mechanistic events underlying the antithrombotic effects of aspirin [22]. This seems to be the case in the present study. The combination of aspirin with bromadiolone resulted in the same findings as that of each aspirin and Br on the clotting factors (prolonged bleeding, clotting, and prothrombin times; factors VII and IX, and decreased ionized Ca^{2+}). However, it should be stated that the prolongation in the clotting factors was more pronounced on the combination of both anticoagulants than that of each ASA or Br alone. This finding indicates that the combination of both anticoagulants can be used effectively in controlling rodents rather than using each ASA or Br alone.

Lipid peroxidation (LPO), superoxide dismutase (SOD), catalase (CAT), and glutathione S-transferase are important markers of oxidative stress, which mainly involves the scavenging of reactive oxygen species (ROS) to prevent the cell dysfunction [42]. Many studies have been aimed at evaluating the effects of different pesticides on the activity of antioxidant enzymes in different organs [43]. However, this is the first study on Br and ASA treated LPO on rodents. Aspirin induced a marked increase in the serum LPO, but Br and combination of ASA with Br resulted in a highly significant decrease in the serum LPO. These findings indicate that both anticoagulants may inactivate LPO efficiency as a defense system for protecting the animal against the production of free radicals.

SOD and CAT function equally as principal enzymes in the reduction of ROS. SOD removes superoxide radicals via forming H_2O_2, whereupon CAT and GPx can act to neutralize H_2O_2 [44]. The marked decrease in SOD and CAT activities in serum following Br treatment is consistent with the ability of Br to increase the superoxide radical anions and inhibit CAT activity [16,45]. For removing excess free radicals from the system, GST and GPx use GSH during course of their reactions. The marked decline in GST serum level in Br-treated group may be due to toxicity of Br which led simultaneously to decrease GST activity.

The marked significant increase in the serum levels of SOD, CAT and GST following ASA treatment revealed that ASA may cause over-production of superoxide radical anions and prevent the CAT and GST to neutralize H_2O_2, subsequently blocking of Vit K epoxide cycles in the liver by ASA which led to increase the hemorrhage causing the death of animal. The marked rise of LPO, the marked decline of SOD, CAT and GST serum levels following Br treatment may affect hematopoietic organs and thereby its conjugation with the oxidative enzymes may cause damage of these organs leading to inactivate them, hence increase of hemorrhage and finally the animal died. The marked rise in LPO, SOD, GST serum levels and the non-significant decrease in ASA treated group supports the above suggestion. Moreover, in the present study, the combination of ASA with Br causes a slight decrease in LPO, CAT and GST serum levels and marked increase in SOD. This may reflect the interruption of redox homeostasis under Br and ASA treatment.

5. Conclusion

According to the data obtained in the current study, it can be concluded that both ASA and Br caused damage in the hematopoietic processes in the bone marrow through decreasing the erythrocytic indices. Also, both anticoagulants suppress the immune defense system by decreasing the WBCs and differential leukocyte counts, platelets and platelet indices. The prolonged time of clotting factors and thrombocytosis are results of severely impaired cascade coagulation. Moreover, the changes in the oxidative stress are indicators of the toxicity of both anticoagulants. So, the administration of each ASA and Br or their combination are means of effective control of rodent population in economic crop fields

CRediT authorship contribution statement:

Mohamed F. El-Sayed, Magdy B. Wilson Rana S. Sarhan, Mohamed F. El-Sayed, Magdy B. Wilson, Abd El-Aleem S.S. Desoky methodology, Rana S. Sarhan, Mohamed F. El-Sayed; validation, Mohamed F. El-Sayed, Magdy B. Wilson, Abd El-Aleem S.S. Desoky; formal analysis, Rana S. Sarhan; investigation, Rana S. Sarhan, Mohamed F. El-Sayed, Magdy B. Wilson, Abd El-Aleem S.S. Desoky; resources, Mohamed F. El-Sayed, Magdy B. Wilson, Abd El-Aleem S.S. Desoky; data curation, , Rana S. Sarhan, writing—original draft preparation, Rana S. Sarhan; writing—review and editing, Mohamed F. El-Sayed, Magdy B. Wilson, Abd El-Aleem S.S. Desoky; visualization, Rana S. Sarhan, supervision, Mohamed F. El-Sayed, Magdy B. Wilson. All authors have read and agreed to the published version of the manuscript.

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] B. Sinha, *In Proc Indian Natn Sci Acad*, 82 (2014) 235-245.
[2] L. B. Santra, C. K. Manna, *J of Zoology*, 27 (2008) 85-90.
[3] N. S. Neena Singla, B. K. Babbar, *Indian J. APP. Agric. & Apicul. Res*, 10 (2010) 98-111.
[4] N. Singla, B. K. Babbar, *India. Sugar Tech*, 14 (2012) 76-82.
[5] G.R. Singleton, J. Redhead, *International Rice Institute, Los Baños, Philippines*, (1990) 75-82.
[6] L. H. Swanepoel, C. M. Swanepoel, P. R. Brown, S. J. Eiseb, S. M. Goodman, M. Keith, F. Kirsten, H. Leirs, T. A. A. Mahlaba, R. H. Makundi, *PLoS One* 12(3) (2017) 1-20.
[7] N. Singla., L. D. Singla, K. Gupta, N. K. Sood, *J. Parasitic Diseases*, 37 (2013)16-20.
[8] M. Chellappan, *Polyphagous Pests of Crops*, (2021) 457-532.

[9] P. Berny, A. Esther, J. Jacob; C. Prescott, *Anticoagulant rodenticides and wildlife*, 23(3) (2018) 259-286.
[10] R. Singh, Y. Saxena, *Pesticides*, (1989) 27-28.
[11] J. H. Greaves, A. P. Buckle, R. H. Smith, *CAB International, Wallingford, Oxon, UK,* pp. (1994) 197-217.
[12] Z. A. Radi, L. J. Thompson, *Veterinary and human toxicology*, 46(2) (2004) 83-84.
[13] S. Lefebvre, E. Benoit, V. Lattard, O. Basachan, H. Biteker, *Anticoagulation Therapy*, pp (2016) 1-30.
[14] M. A. Aly, M. A. Ayyad, *Egypt. J. Plant Protec. Res. Inst*, 5(4). (2022) 341-352.
[15] M. E. H. Zowail, R. Balshy, A. A. Asran, F. K. Khiry, M. H. M. Amer, *Egypt. J. Exp. Biol. (Zool.)*,15(2) (2019) 263-275.
[16] N. Sridhar, J. Baskaran, S. Thangapandiyan, S. Dhanasekaran, D. Vasantharaja, S. M. Bahu, Int. *J. Adv. Res*, 3(9) (2015) 1159-1170.
[17] K. Revadhi, M. Yogananda, *J. Environ. Biol*, 27(1) (2006) 135-140.
[18] D. Suljevic, S. Grabic, M. Mitatsilinovic-Bralic, M. *Foca. Cell. Biochem*, 113 (2022) 477-525-336.
[19] M.R. Montinari, S. Minelli, R. De Caterina, *Vascul. Pharmacol,* (2019) 1-8.
[20] M.E. Uvodich, M.P. Silfijander, M.G. Taunton, T.M. Mabry, K.R. Perry, M.P. Abdel, *J. Arthroplast*, 36 (2021) 2359-2363.
[21] M.N. Bortachina, L. Hermida-Nogueira, L.A. Maran, V. Casas, S.M. Hicks, *Vasc. Biol,* 41 (2021) 478-490.
[22] A. Undas, K.E. Brummel-Zeindins, K.G. Mann, *J. Thrombosis and Haemostasis*, 12 (2014) 1776-1787.
[23] Y.H. Mekaj, F.T. Daci, A.Y. Mekaj, *Clin. Risk Manag,* 11 (2015) 1449-1456.
[24] S. Buttnes, T. Orfeo, K.G. Mann, *Thromb. Vasc. Biol*, 29 (2009) 1989-1996.
[25] N. Garg, N. Singla, *CIB Tech J. Zool*, 3(2) (2014) 43-48.
[26] X. Liu, L.N. Xu, *Acta Pharmacol. Sinica*, 30 (1995) 662-667.
[27] S. Manciu, E. Matei, B. Trandafir, *Chirurgia (Bucur)*, 112(2) (2017) 110-116.
[28] D.J. Card, S. Francis, K. Deuchande, D.J. *Harrington, BMJ Case Rep*, (2014) 1-3.
[29] S. Altay, Y. Velibey, H. A. Cakmak, G. C. Boz, S. Koca, *Cardiovascular journal of Africa*, 23(9) (2012) 9-11.
[30] S. Kalinin, N. Marangoni, K. Knowl; A. Dey; K. Lis; S. Brodsky; R. Van Breemen; Z. Hauk, R. Ripper, I. Rubinstein, G. Weinberg, D.L. Feinstein, *Toxicol. Sci,* 159 (2017) 224–237.
[31] F.M. Bertolini, E. Borolo, R. Mast, S. De Arcangeli, T. Furlanello, V. Ongaro, C. Meneghini, S. del Pulgar, *J. Chromatogr. B,* 1232 (2024) 1–8.
[32] W. g. Kinra, P. Cdr, W. g. Tewari, V. Cdr, A.V.M. Raman, *J. Aerospace Med*, 53(1) (2009) 56–61.
[33] A. H. Kamal, A. Tefferi, R. K. Pruthi.July, *In Mayo Clinic Proceedings*, 82 (2007) 864-873.
[34] S.E. Kuhn, D.V.H. Hendrix, *Case Rep. Vet. Med,* (2013) 1–6.
[35] K. H. Webster, K. E. Harr, D. C. Bennett, T. D. Williams, K. M. Cheng, F. Maisonneuve, J. E. Elliott, *Ecotoxicology*, 24 (2015) 1087-1101.
[36] I. Valchev, R. Binev, V. Yordanova, Y. Nikolov, *Turkish Journal of Veterinary & Animal Sciences*, 32(4) (2008) 237-243.
[37] M.E. Mount, *Vet. Clin. North Am. Small Anim. Pract,* 18(1). (1988) 115–130.
[38] M.E. Mount, B.U. Kim, P.H. Kass, J. Am, *Vet. Med*, 222 (2003) 1070-1071.
[39] K.G. Mann, *Thrombosis and Haemostasis*,82 (1999) 165–174.
[40] R. Paniccia, R. Priora, A.A. Liotta, R. Abbate, *Vasc. Health Risk Manag*, 11 (2015) 133–148.
[41] M.S. Lord, W. Yu, B. Cheng, A. Simmons, L. Poole-Warren, J.M. Whitelock, *Biomaterials*, 30(28) (2009) 4898–4906.
[42] V. Thangapandiyan, S. Miltonprabu, *J. Physiol. Pharmacol*, 91 (2013) 528–537.
[43] S. Sodhi, R.S. Brar, H.S. Banga, *J. Vet. Sci. Tech,* 6 (2017) 340–345.
[44] M. Valko; D. Leibfritz; J. Moncol; M.T. Cronin; M. Mazur; J. Telser. J. Biochem. Cell Biol.: 39. (2007). 44–48.
[45] E. Akbel, D. Arsalan-Acoraz, H.H. Demirel, I. Kucukkurt, S. Ince, *Toxicol. Res. (Camb.)*, 7 (2018) 503–512.