CONTENTS

SUMMARY

Laboratory studies were applied to investigate the effieieney of three antieoagulant rodentieides, Brodifaeoum, Chlorophaeinone and Warfarin on the both sexes of albino Norway rats, *R. norvegicus* and house mouse *Mus musculus* which were fed on either maize and wheat or vegetables the obtained results could be summarized in the following:

1-The toxicological effects of the three rodenticides acute oral toxicity Determinations, LD_{30}, LD_{50} and LD_{90}:-

1-A- Brodifacoum treatments on albino Norway rat *R. norvegicus*:-

The LD_{30}, LD_{50} and LD_{90} in males which were fed on maize and wheat were 0.11, 0.23 and 1.64 mg/ kg b.w. while in females were 0.260, 0.354 and 2.70 mg/ kg b.w. while the LD_{30}, LD_{50} and LD_{90} in males which were fed on vegetables were 0.13, 0.225 and 0.95 mg/ kg but they were 0.12, 0.231 and 1.25 mg/ kg b.w., respectively.

1-B-Brodifacoum treatmeuts on albino house mouse *Mus musculus* :-

The LD_{30}, LD_{50} and LD_{90} in males which were fed on maize and wheat were 0.235, 0.46 and 2.385 mg/ kg b.w. in females were 0.284, 0.556 and 2.872 but they were 0.175, 0.407 and 3.018 mg/ kg b.w in males which were fed on vegetables while they were 0.184, 0.417 and 3.273 mg/ kg b.w. in females.

2-A-Chlorophacinone treatments on albino Norway rat *R. norvegicus*:-

The LD_{30}, LD_{50} and LD_{90} were 7.18, 16.043 and 114.84 in females which were fed on maize and wheat in males 58.61, 12.8 and 6.87 mg/ kg b.w. while they were 13.33, 24.532 and 108.88 mg/ kg b.w. but they were 14.56, 26.523 and 113.72 mg/kg b.w. in females which they fed on vegetables.

2-B-Chlorophacinone treatments on albino house mouse *Mus musculus* :-

The LD_{30}, LD_{50} and LD_{90} were 7.932, 22.39 and 178.823 mg/kg b.w. in males which were fed on maize and wheat. But they were 8.155, 22.677 and 26.142 mg/kg b.w. in females while in case of vegetables, they were 8.401, 20.312 and 175.111 in males, but they were 8.796, 21.538 and 215.299 mg/kg b.w. in females.

3-A- Warfarin treatments on albino Norway rat *R. norvegicus*:-

The LD_{30}, LD_{50} and LD_{90} were 48.14, 151.194 and 633.1 mg/kg b.w. in males. But they were 85.29, 196.75 and 1517.28 mg/kg b.w. in females that were fed on maize and wheat. While those were 146.87, 333.025 and 2483.63 mg/kg b.w. in females were fed on vegetables in males which were 210.59, 435.945 and 2583.63 .

3-B- Warfarin treatments albino house mouse *Mus musculus* :-

The LD_{30}, LD_{50} and LD_{90} were 257.811, 480.56 and 2217.223 in males, but they were 266.207, 489.575 and 2170.123 mg/kg b.w. in females, which were fed on maize wheat respectively, whilc in vegetables they were 133.832, 380.419 and 4887.439 mg/kg b.w. in males while they were 175.50, 407.894 and 5203.665 in females.

2-Biological effect :-

2-A- The effect of the 3 sublethal doses ($^1/_{10}$ LD_{90}, $^1/_{10}$ LD_{50} and $^1/_{10}$ LD_{30}) from the 3 rodenticides on the pregnant females of albino Norway rat:

On the implantation sites and embryos resorption. All the 3 rodenticides induced a considerable reduction in numbers of implantation sites in both left and right horn uterus. Obtained results showed that Brodifacoum, Chlorophacinone and Warfarin at $^1/_{10}$ LD_{90} in the two cases of feeding were more effective than the other sublethal doses, all implantation sites formed fetuses without any resorbed oncs. A significant reduces in the mean of implantation when fcmales were treated with Brodifacoum and Chlorophacinone at $^1/_{10}$ LD_{90} in both cases of fed. A significant reduce in the mean of implantation when females were fed on maizc and wheat treated with Brodifacoum at $^1/_{10}$ LD_{50}, whilc,

there was non-significant in the mean of implantation in the other rodenticides.

The maximum reduction reached 100% when females were treated with Brodifacoum and Chlorophacinone at $^{1}/_{10}$ LD_{90}, while, the minimum reduction was 12.5% when females were fed on Maize and Wheat treated with Warfarin at $^{1}/_{10}$ LD_{30}.

2-B- Effect of $^{1}/_{10}$ LD_{30} of the 3 rodenticides on females and fetuses of albino Norway rat :-

a- On gestation period and (number and weight of fetuses. The obtained results showed that the sublethal doses $^{1}/_{10}$ LD_{30} of all rodenticides used has non-significant effect on both gestation period and weight of fetuses in the two groups but they have a highly significant effeet on the mean number of fetuses when females were fed on maize and wheat with Brodifaeoum and Chlorophacinone, also, the same results were obtained when females were on vegetables treated with Brodifaeoum, while, the other treated ments gave a significant effect on the number of fetuses in the two groups of feeding.

b- On the weaning time and opening eyes the obtained results showed that the sublethal dose $^{1}/_{10}$ LD_{30} from Brodifacoum in the 2 cases of feeding has a signifieant increase in the mean time of weaning per days, while, there were non-signifieant increase on the mean time of weaning per days of other treatments in the 2 cases of fed, also, there were non-significant increase on the mean of

opening eyes in all treatments with the 3 rodentieides in the two groups of feeding .

All the 3 rodentieides were very aetive and causing inerease in the pereentages of absorbed fetuses in all the sublethal doses.

3-Clinical symptoms:-

The obtained results revealed that the three rodentieides induced a decrease in body weight of treated albino Norway rat when treated with the sublethal doses ($^1/_{10}$ LD_{90}, $^1/_{10}$ LD_{50} and $^1/_{10}$ LD_{30}). There was a significant decrease in the body weight when both sexes were treated with Brodifacoum at $^1/_{10}$ LD_{90} when were fed on maize and wheat or on vegetables, also, the same results were obtained when both sexes were treated with Chlorophacinone at the same dose which fed on maize and wheat or vegetables. There was a significant decrease in body weight in males and non-significant decrease in females.

The effect at $^1/_{10}$ LD_{50} of the three rodenticides used was a significant decrease in males and non-significant decrease in females in the two experiments, the same trend was observed at $^1/_{10}$ LD_{30} of the three rodenticides used. The maximum decrease was observed when males and females were fed on maize and wheat with difference at 7.2% and 6.4%, respectively, at $^1/_{10}$ LD_{90} of Brodifacoum, while, the minimum decrease was noticed at $^1/_{10}$ LD_{30} when females fed on maize and wheat with difference 0.79%, while it was 0.96% when females were fed on vegetables, at $^1/_{10}$ LD_{30} of Warfarin. The obtained results showed

that the losses in body weight of males albino rats were more than females after treated with the three rodenticides used.

The present results indicated that the effect of the three rodenticides used induced an increase in organs weight of treated albino Norway rat *R. norvegicus*, there was a significant increase in the liver and kidney weight. The effect of $^{1}/_{10}$ LD_{90} of Brodifacoum on both sexes gave a significant increase in liver and kidney weight in the two experiments of food, the same trend was occurred with Chlorophaeinone, but, there was non-significant increase in liver weight when both sexes of rats were fed on vegetables at $^{1}/_{10}$ LD_{90} of Warfarin, while a significant inerease in liver in both sexes when the rats were fed on maize and wheat.

The effect of $^{1}/_{10}$ LD_{90} of Chlorophacinone on kidney weight, a significant increase were detected in both sexes in the two experiments while, non-significant increase in kidney weight was detected at $^{1}/_{10}$ LD_{90} of Warfarin in females when fed on maize and wheat, but a significant increase was detected in males at the same dose and feeding.

There was a signifieant increase in liver weight when both sexes of albino Norway rats were fed on maize and wheat with either Brodifaeoum and Chlorophacinonc at $^{1}/_{10}$ LD_{50}, while non-significant inerease in liver weight when rats treated with Warfarin at the same dose. Non-significant increase in liver weight occurred when both sexes of albino rats were fed on vegetables with the three rodenticides used at $^{1}/_{10}$ LD_{50} except males when treated with Brodifacoum. Also, the obtained results

induced a significant inerease in kidney weight of males which were fed on maize and wheat at $^{1}/_{10}$ LD_{50} of either Brodifacoum on Chlorophacinone, while females showed non-signifieant inerease in kidney weight. The same results were observed with Warfarin at the same dose, but when albino rats were fed on vegetables, the results gave non-signifieant increase in kidney weight in both sexes when treated with the three rodenticides except with males, where there was a signifieant increase in kidney weight, while, the reproduetive system, spleen, lung, heart and brain showed non-signifieant increase in weights in the three rodenticides used in the two experiments at $^{1}/_{10}$ LD_{90} and $^{1}/_{10}$ LD_{50}, in the same time, all the organs were given a slightly increase in weights in the two experiments.

The maximum increase in liver and kidney weights were observed when males were fed on maize and wheat with differences of 21.8% and 22.7%, respectively, when treated with Brodifacoum at $^{1}/_{10}$ LD_{90}. The same results were observed when males treated with Chlorophacinone at the dose with differences 18.06% and 22.7% respectively.

When males were fed on vegetables, the percent of differences were 18.9% and 21.7% in liver and kidney weight, respectively when treated with Brodifacoum and 17.9% and 22.8% when treated with Chlorophacinone at $^{1}/_{10}$ LD_{90}.

The minimum increase in liver and kidney weights were noticed at $^{1}/_{10}$ LD_{30} in the two experiments.

The resultant effects mentioned that between the sublethal doses of the three rodentieides testes, the higher dose showed higher effect on the various organs of both sexes.

4- Biochemical responses:-

4-A- ALT and AST enzymes :-

Effect of Brodifaeoum, Chlorophacinone and Warfarin on Alanine Aminotransferase (ALT) and (AST) Apartate aminotransferase this part of the present study is an attempt to measure the effect of sublethal doses ($^1/_{10}$ LD_{90}, $^1/_{10}$ LD_{50} and $^1/_{10}$ LD_{30}) of the rodenticides on (AST), (ALT) activity in sirm in both sexes of albino Norway rat *R. norvegicus*, which were fed on maize and wheat in the first experiment and vegetables in the second one obtained results showed that, the amount of ALT and AST enzymes recorded in check control was less than the amount in all treatments, while the amount of ALT and AST enzymes in plasma of the albino Norway rat *R. norvegicus*, increased after rodenticides treatments. Whereas a significant increase in the level of enzymes was found when females were treated with the three rodenticides at the sublethal dose $^1/_{10}$ LD_{90}. The same trend was observed when females were treated at $^1/_{10}$ LD_{50}, while non-significant different was observed, when females were treated with Warfarin at the same dose. Also, when females were treated with the three rodenticides at $^1/_{10}$ LD_{30}, non-significant different the level of enzyme was obtained. These results were recorded when albino Norway rat *R. norvegicus*, were fed on vegetables. The same results were observed when females were fed on maize and wheat. The

maximum differences were 46.2% and 45.0% when females fed on maize and wheat & vegetables at $^{1}/_{10}$ LD_{90}, respectively. While the minimum differences at $^{1}/_{10}$ LD_{30}, were 5.8% when females were fed on maize and wheat & 6% when females were fed on vegetables.

A significant differences in males when they were fed on the two kinds of food at $^{1}/_{10}$ LD_{90}, of Chlorophacinone the same results was detected with Warfarin. There was non-significant different in the level of enzyme at $^{1}/_{10}$ LD_{30}, with the 3 rodenticides. While the minimum differences were 14.3% when males were fed on vegetables and 21.3% in the eontrol.

4-B-Total protein:-

- The three rodenticides increase total plasma protein level in treated albino Norway rat *R. norvegicus* .
- There was a highly significant increase in the level of total protein when both sexes were treated with Brodifacoum at the sub-lethal dose $^{1}/_{10}$ LD_{90}.
- The effect of Brodifacoum at $^{1}/_{10}$ LD_{50} equals the effect of Chlorophaeinone at $^{1}/_{10}$ LD_{90} where there was a highly significant increase in the level of total protein in case of males and females fed on vegetables and males fed on maize and wheat but there was a significant increase in case of females fed on maize and wheat.
- There was a significant increase in the level total protein when both sexes were treated with Chlorophacinone at $^{1}/_{10}$ LD_{50} .

- There was a significant increase in females and highly significant increase in males when albino rats were treated with Warfarin at $^{1}/_{10}$ LD_{90} .
- There was non-significant increase in total protein level at $^{1}/_{10}$ LD_{30} when albino Norway rats *R. norvegicus* were treated with the three rodenticides.
- The maximum increase was noticed when males fed on maize and wheat were treated with Brodifacoum at $^{1}/_{10}$ LD_{90} females.

4-C-Cholesterol :-

- Plasma cholesterol level of albino Norway rat *R. norvegicus* was decreased when treated with the three rodenticides.
- There was a significant decrease in the level of Cholesterol when both sexes were treated with Brodifacoum and Chlorophacinone at the sub-lethal dose $^{1}/_{10}$ LD_{90} when albino Norway rat *R. norvegicus* were fed on vegetables.
- A highly significant decrease in the level of Cholesterol in males and females fed on maize and wheat when treated with Brodifacoum at $^{1}/_{10}$ LD_{90}.
- A non-significant decrease in the level of Cholesterol was observed when but sexes were treated with Brodifacoum and Chlorophacinone at $^{1}/_{10}$ LD_{50} and $^{1}/_{10}$ LD_{30}.
- The maximum decrease was observed when males and females fed on maize and wheat the minimum decrease

was noticed when males were treated with Warfarin at $^{1}/_{10}$ LD_{30} fed on vegetables.

4-D-Effect of Brodifacoum., Chlorophacinone and Warfarin rodenticides on bleeding time in both sexes of *R. norvegicus:*

The results in case of fed on maize and wheat showed a highly significant difference between rodenticides after 24, 48 and 72 h at $^{1}/_{10}$ LD_{90}, $^{1}/_{10}$ LD_{50} and 24 h at $^{1}/_{10}$ LD_{30}; while there was no significant difference after 48 and 72 h.

The effect of these rodenticides on bleeding time, could be arranged according to their effeetiveness in descending order as follows; Brodifacoum > ehlorophacinone > warfarin.

Also, results showed no significant difference between replicates and sexes at the three periods of bleeding time.

In the case of fed on vegetables, the results revealed a highly significant differenee between treatments at the dose $^{1}/_{10}$ LD_{90}.

Also, the results showed a highly significant differences between doses during three periods in the two cases of feeding except the Warfarin treatment after 72 h.