

Original Article- Pharmaceuticals**HEMATOLOGICAL PARAMETERS AND BLOOD SMEAR EFFECTS OF TRAMADOL ON MALE RABBITS****Fayrouz. A. khaled^{*1}, AMAAL. A. Younus² and Rui. M. Sale³**¹ Chemistry Department, Faculty of Science, Omar Al-Mokhtar University, El -Beida-Libya² Judicial experience & research center, El -Beida-Libya³ Faculty of Dentistry, Omar Al-Mokhtar University, El -Beida-Libya**Corresponded Author: Fayrouz A. Khalid faylzobair@yahoo.com*

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ABSTRACT

Analgesics are a bunch of drugs that act totally different ways on the central apprehensive framework to absense of pain and alleviation from torment. It is in this manner imperative to ponder the impacts of organization these analgesics to decide the side impacts for them utilize. Hence we decided to study the hematological effects of tramadol on male rabbits. Tenth rabbits were arbitrarily partitioned into two break even with bunches (each bunch five rabbits). The primary gather was utilized as a control. The moment gather was utilized to consider the impact of tramadol (50 mg/kg body weight) for six weeks. Hemoglobin (Hb) substance, ruddy blood cells (RBCs) number and hematocrit (Hct) esteem diminished, whereas white blood cells (WBCs) and platelets tallies expanded after tramadol organization. Verbal organization of tramadol induced significant changes within the morphology of erythrocytes. In rabbit treated with tramadol the cells were appeared change in typical shape from star molded to sickle cells. The ponder appeared the destructive impacts of tramadol on the hematological parameters and blood spread on mail rabbits.

Keywords: Hematological Parameters, Tramadol, Rabbits**INTRODUCTION**

Opioids are the foremost capable painkillers. Their utilize is fitting for the treatment of moderate-to-severe persistent torment (5–10-point torment concentrated) with the objective to control this indication and to progress capacities and quality of life[1]. Tramadol may be a synthetic, centrally acting pain relieving, accessible in Europe since 1977 and within the Joined together States since 1995 for the treatment of torment disorders already amiable as it were to the sedative analogues[2]. Tramadol has been in clinical utilize for the alleviation of mellow to direct torment in human and veterinary medication [3]. Tramadol is additionally utilized perioperatively in veterinary anesthesia because it essentially decreases the prerequisites of unstable anesthetics and opioid agents[4]. Tramadol, a engineered racemic blend of the 4-phenyl-piperidine simple of codeine, has gotten broad acknowledgment in human medication since it was to begin with presented in 1977 in Germany[5]. These days, tramadol is broadly utilized as an pain relieving medicate in human medicine[6]. Its component of activity is based on the hindrance of climbing torment to the central anxious framework by its

official to μ - sedative receptors and hinder the reuptake of norepinephrine and serotonin[7]. Ceaseless tramadol organization leads to the appearance of its poisonous impacts on different organs of the body[8].

MATERIALS AND METHOD**Tested compounds**

In this study tramadol was used. tramadol was purchased from pharmacy alsalam hospital in El -Beida-Libya.

Animals and treatments

Develop male Unused Zealand White rabbits age of 6 - week and introductory weight of (1892 \square 50.79 Kg) were utilized. Creatures were exclusively housed in cages and weighed week by week all through 6-week test period. Feed and water were provided ad libitum. Rabbits fed pellets which consisted of 30 % berseem (*Trifolium alexandrinum*) hay, 25 % yellow corn, 26.2% wheat bran, 14 % soybean meal, 3 % molasses, 1 % CaCl₂, 0.4 % NaCl, 0.3 % mixture of minerals and vitamins, and 0.1 % methionine. The vitamin and mineral premix per kg contained the following IU/gm for vitamins or minerals: vit A-4000,000, vit D3-5000,

000, vit E-16,7 g, K-0.67 g, vit B1-0.67 g, vit B2-2 g, B6-0.67 g, B12-0.004 g, B5-16.7 g, Pantothenic acid-6.67 g, Biotein-0.07 g, Folic acid-1.67 g, Choline chloride-400 g, Zn-23.3 g, Mn-10 g, Fe-25 g, Cu-1.67 g, I-0.25 g, Se-0.033 g, and Mg-133.4 g (Rabbit premix produced by Holland Feed Inter. Co.). The chemical analysis of the pellets[9] showed that they contained 15.8 % crude protein, 11.3 % crude fibre, 3.7 % ether extract, 7.2 % ash, 92.9 % organic matter and 62.4 % nitrogen free extract % as DM basis. The first group was used as control, while, groups 2 was treated with tramadol by gavage at a dose of 50 mg/kg B.W/day (1/50 of tramadol) lethal dose[10], for 6 successive weeks.

Hematological Parameters

Blood tests were collected from the ear vein of all creatures each week all through the 6-week exploratory period. Blood tests were gotten within the morning some time recently gets to to bolster and water. Values determined from total blood check (CBC). All CBC tests were performed by programmed blood cell analyzer (XP-300 Mechanized Hematology Analyzer, Sysmex American, Inc [11]. CBC were performed on EDTA as anti-coagulated tests. Differential cell tallies were performed physically utilizing Dif-Quik-stained blood smears. Information were recorded agreeing to the taking after categories: white blood cell (WBC); ruddy blood cell (RBC); hemoglobin (HB); cruel corpuscular volume (MCV); mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC).

Preparation of blood smears

Lean movies, 3-5 cm in length, of the suctioned a drop of blood were made employing a smooth-edged glass spreader of not more than 2 cm in width. The blood parts are dragged behind the spreader and take off a path of cells behind them. After drying, films were dried within the discuss, and after that settled by drenching in a jolt of methanol for 15-20 min. Slides were exchanged to a recoloring bump containing Giemsa’s recolor (1 volume of recolor with two volumes of refined water). After recoloring for 15-30 min, the slides were exchanged to a jostle containing buffered water, pH 7, quickly washed in three or four changes of water and at long last permitted to standing undisturbed in water for a brief time (as a rule 2-5 min) for separation to require put. . Slides were exchanged to a recoloring jolt containing Giemsa’s recolor (1 volume of recolor with two volumes of refined water). After recoloring for 15-30 min, the slides were exchanged to a jolt containing buffered water, pH 7, quickly washed in three or four changes of water and at long last permitted to standing undisturbed in water for a brief time (more often than not 2-5 min) for separation to require put.

RESULT

Effect of tramadol on morphological pattern observed in blood smear

Oral administration of tramadol induced profound alterations in the morphology of erythrocytes. In rabbit treated with tramadol the cells were showed alteration in normal shape from star shaped to sickle cells. (Figure 1).

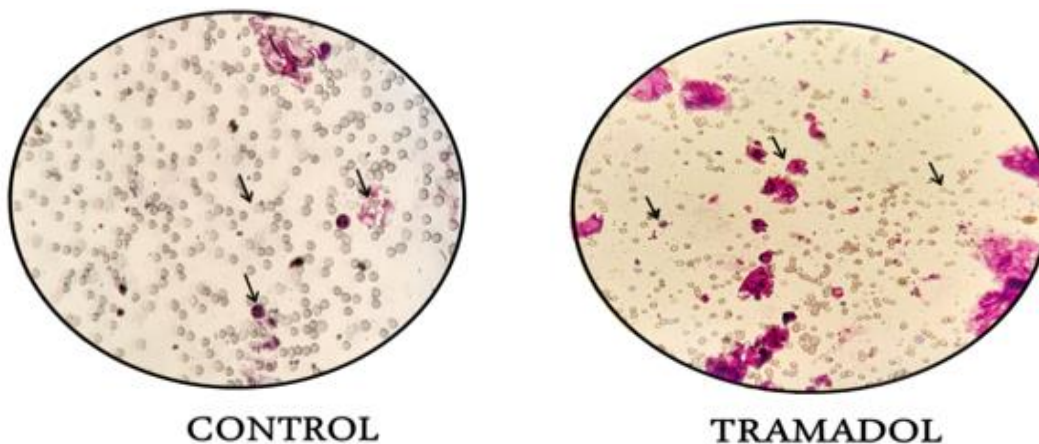


Figure 1. Photomicrographs showing peripheral blood smears of rabbits in two groups.

Effect of tramadol on hematological parameters.

Table 1 represent the hematological parameters of male rabbits treated with tramadol (T). Results indicated that treatment with tramadol significant decrease in red blood cells (RBC), white blood cells (WBC), packed cell volume (PCV), platelet

count (PLT), hemoglobin (Hb), mean cell volume (MCV), mean cell hemoglobin (MCH) and mean cell hemoglobin concentration (MCHC).

Table 1. Changes Complete blood counts red blood cells RBCs, white blood cells WBCs, haemoglobin Hb, packed cell volume PCV, platelets, haemoglobin (Hb), and mean cell hemoglobin concentration (MCHC) and mean cell hemoglobin concentration (MCHC) of male rabbits treated with tramadol.

<i>Parameter</i>	<i>Experimental groups</i>	
	<i>Control</i>	<i>Tramadol</i>
<i>RBC ×106 (μl)</i>	5.62 ± 0.138 ^a	4.68 ± 0.158 ^a
<i>WBC ×103(μl)</i>	8.53 ± 0.18 ^a	7.41 ± 0.35 ^b
<i>HCT×103(μl)</i>	39.95 ± 0.280 ^a	35.68 ± 0.760 ^b
<i>PLAT ×103(μl)</i>	277.82 ± 8.740 ^a	243.05 ± 15.027 ^b
<i>Hb (g/dl)</i>	13.60 ± 0.16 ^a	11.97 ± 0.28 ^b
<i>MCV(fl)</i>	76.88 ± 2.26 ^a	77.98 ± 1.96 ^a
<i>MCH(pg)</i>	25.02 ± 0.84 ^a	28.98 ± 0.63 ^b
<i>MCHC(dl)</i>	32.69± 0.45 ^a	32.82 ± 0.57 ^b

Values are expressed as means ± SE; n = 5 for each treatment group. Mean values within a row not sharing a common superscript letters (a, b, c) were significantly different, p<0.05.

DISCUSSION

The show ponder appeared that tramadol caused diminish RBCS , Hb ,PCV and PLT (Tables 1) assention with[7], who found that organization of sildenafil (1.40 mg/kg/day) and tramadol (4 mg/kg/day) for 25 days to rabbits driven to significant diminishes in RBCs tally and Hb substance. The diminish within the RBCs tally may be due to the inhibitory impact of tramadol on erythropoiesis[13]. In expansion, the WBCs check expanded after organization of tramadol to rats. [13] clarified the height within the WBCs tally by the enactment of defense resistant framework. Whereas [7] detailed that tall lymphocyte rate in male rats infused by tramadol (100 mg/kg) for 30 days was the reason behind

the WBCs count elevation. The ruddy blood cells(RBCs) tally appeared a common diminish in reaction to tramadol organization. This finding may be clarified on the premise of inhibitory impact of tramadol on histogenesis. The diminished in RBC number and hemoglobin (Hb) brought down the oxygen supply to distinctive tissues hence coming about in moo vitality generation. Diminish in Hb contained MCH can be clarified due to diminished measure of RBC or impeded biosynthesis of heme in bone marrow. These discoveries are in assention with the detailed diminish in RBC check and Hb substance after treatment with tramadol [14].

CONCLUSION

The comes about of the display ponder convincingly illustrated that tramadol presentation come about in shifting degree of hematological parameters of rabbits. Tramadol harmful impacts ought to be maintained a strategic distance from amid long term treatment extraordinarily in huge measurements.

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