

Research Article



Evaluation of Haematological and Reproductive Effect of Paracetamol (Acetaminophen) in Female Albino Rats

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ABSTRACT

The effect of oral administration of 7.5 mg/kg BW on haematological and plasma biochemical parameters in albino rats were investigated. The paracetamol was administered by gavage on daily basis for haematological study; the paracetamol was administered orally for 21 days for estrous cycle study. Treatment of rats with 7.5 mg/kg BW of paracetamol caused insignificant ($p > 0.05$) changes in the RBC, PCV, HBTWBC, platelet, neutrophil, lymphocyte, eosinophil, monocyte and haematometric indices (MCV, MCHC, MCH) values relative to their respective controls. Treatment of rats with paracetamol (7.5 mg/kg BW) caused non-significant changes in the duration of all phases of estrous cycle relative to their relative to their respective controls. These findings probably indicates that paracetamol has no deleterious effect on the blood chemistry and fertility of female albino rats.

Keywords: Paracetamol, Red blood cell, Total white blood cell, Estrous cycle, Albino rats.

INTRODUCTION

Paracetamol is classified as a mild analgesic. It is commonly used for the relief of headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies. In combination with opioid analgesic, paracetamol can also be used as post-surgical pain and providing palliative care in advanced cancer patients¹.

Paracetamol toxicity has been reported to be the foremost cause of acute liver failure in the Western world, and accounts for most drug overdoses in the United States, United Kingdom, Australia and New Zealand². Its prolonged daily use has been reported to increase the risk of upper gastrointestinal complications such as stomach bleeding³ and may cause kidney or liver damage⁴. Its derivative, nitroparacetamol, has been reported to exhibit anti-inflammatory and anti-nociceptive activities in the rat⁵.

The genotoxicity of paracetamol in mice and rats has also been reported⁶.

This study aims at investigating the effect of paracetamol on haematological and reproductive parameters in female albino rats.

MATERIALS AND METHODS

Experimental Animals

Adult female albino rats weighing between 160 g and 180 g bred in the Animal House of Physiology Department, LAUTECH, Ogbomoso were used. They were housed under standard laboratory conditions with a 12 hours daylight cycle and had free access to feed and water; they were acclimatized to laboratory conditions for two weeks before the commencement of the experiments. All experiments were carried out in compliance with the

recommendations of Helsinki's declaration on guiding principles on care and use of animals.

Drug

Paracetamol tablets (Emzoe Pharm Ltd) were bought from Jeopat pharmacy, Ogbomoso, Nigeria.

1500 mg of paracetamol were dissolved in 2000 ml (2 litres) of distilled water to give a concentration of 0.75 mg/ml.

The dosages of paracetamol administered in these studies were in accordance with those reported previously⁷.

Experimental Design

Haematological and Histopathological Study

Ten animals were randomly divided into two groups with each group consisting of five rats. The two groups of rats were subjected to the following oral treatments once a day for 30 days:

Group I rats received 7.5 mg/kg BW of paracetamol.

Group II rats received 0.5 ml of distilled water as the control group.

Twenty-four hours (day 31) after the last dosing of the two groups, blood samples were collected and the animals were then euthenised by cervical dislocation. The ovaries and uteri were dissected out, cleaned of fat, blotted with filter papers, and then fixed in Bouin's fluid. The tissues were then processed histological as described below.

Estrous Cycle Study

Vaginal smears of female rats were examined microscopically every day at a constant interval of 9.00 – 10.00 a.m. for 21 days. The smears were stained using the



Papanicolaou's staining technique and the recognized cells were classified into different phases of estrous cycle based on their relative proportions. The durations of the different phases of the estrous were determined. Then, five rats showing at least three regular 4 – 5 day cycles were given 7.5 mg/kg BW of paracetamol for 21 days and their vaginal smears were evaluated similarly during this period. In this study, the experimental animals also served as the control vis-à-vis, the first 21 days served as the control days, while the last 21 days served as the treatment days.

Collection of Blood Samples

Blood samples were collected through the medical cantus into EDTA bottles for haematological analysis.

Determination of Haematological Parameters

The red blood cells (RBC) and total white blood cells (TWBC) counts were determined by the improved Neubauer haemocytometer method. The haemoglobin (Hb) concentration was determined according to previous reported method⁸, using the cyanomethaemoglobin method. The packed cell volume (PCV) was determined by the micro-haematocrit method according to previous reported method⁹. Schilling method of differential leucocyte count was used to determine the distribution of the various white blood cells¹⁰. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were computed according to previous reported method⁸.

Statistical Analysis

The mean and standard error of mean (S.E.M.) were calculated for all values. Comparisons between the control and the treated groups were done using the student's t-test. Differences were considered statistically significant at $p < 0.05$.

Table 1: Effect of 30 days treatment of rats with paracetamol (7.5 mg/kg BW) on haematological parameters (n = 5, *P<0.05).

Parameters	Control	Treated
PCV (%)	35.00±1.30	37.40±1.63
Hb (g/dl)	11.52±0.50	12.48±0.49
RBC ($\times 10^6/\mu\text{l}$)	6.11±0.33	6.50±0.41
MCV (fL)	57.54±1.32	57.86±1.13
MCHC (g/dl)	32.90±0.18	33.39±0.16
MCH (pg)	18.93±0.41	19.33±0.47
TWBC ($\times 10^3/\mu\text{l}$)	8.43±0.58	7.31±0.61
Platelets ($\times 10^5/\mu\text{l}$)	1.45±0.12	1.43±0.10
Neutrophils (%)	37.60±5.04	40.40±5.75
Lymphocytes (%)	60.80±4.87	57.80±5.49
Eosinophils (%)	0.40±0.24	1.20±0.37
Monocytes (%)	1.20±0.49	1.40±0.40

RESULTS

Effect on Haematological Parameters

Treatment of rats for 30 days with paracetamol (7.5 mg/kg BW) caused non-significant ($p > 0.05$) changes in PCV, Hb, RBC, MCV, MCHC, MCH, TWBC, platelet, neutrophil, lymphocyte, eosinophil and monocyte values relative to their controls.

Effect on Estrous Cycle

Treatment of rats for 21 days with paracetamol (7.5 mg/kg BW) caused non-significant ($p > 0.05$) changes in the duration of all the phases of estrous cycle relative to their controls.

Table 2: Effect of 21 days treatment of rats with paracetamol (7.5 mg/kg BW) on estrous cycle (n = 5, * $p < 0.05$)

Phase	Control	Treated
Proestrous	4.60±0.23	6.00±1.87
Estrous	6.70±0.80	5.80±1.46
Metestrous	3.40±0.51	3.00±0.63
Diestrous	6.20±0.74	6.20±1.32

DISCUSSION

The values obtained for RBC showed the non-significant effects of 30-day treatment of rats with MEVA on red blood cells (RBC) counts and indices relating to it (Hb, PCV, MCV, MCH and MCHC) when compared with the control. This is an indication that there was no destruction of red blood cells and no change in the rate of production of RBC (erythropoiesis). This also shows that MEVA does not have the potential to stimulate erythropoietin release from the kidneys, which is the humoral regulator of RBC production¹¹. The non-significant effects of the 30-day treatment with MEVA at all doses also indicate that there were no change in the oxygen-carrying capacity of the blood and the amount of oxygen delivered to the tissues since RBC and haemoglobin (Hb) are very important in transferring respiratory gases¹². It has been reported that values of RBC and associated parameters lower than normal ranges are indicative of anemic conditions while higher values are suggestive of polycythemia¹³, thus, the 30-day treatment with MEVA may not have the potential to induce anemia or polycythemia. Also, the 30-day treatment of rats with MEVA at all treatment doses may not have adverse effects on the bone marrow, kidney and haemoglobin metabolism, since it has been reported that only substances which significantly affect the values of red blood cells and associated parameters would have effects on the bone marrow, kidney and haemoglobin metabolism¹⁴.

The extract caused non – significant changes in the MCV and MCH values which could be an indication of absence of macrocytic anaemia since increased MCV and MCH values are known to be indicative of macrocytic anaemia.

Also, MEVA caused non-significant change in the MCHC value which suggest and absence of hereditary spherocytosis since MCHC values are known to be elevated in hereditary spherocytosis.

The insignificant change in neutrophil count caused by extract probably indicates that the ability of the body to attack and destroy invading bacteria, viruses and other injurious agents (Phagocytosis) has not been compromised. The non-significant change in lymphocyte count suggests that the acquired immune responses of the body has not been compromised by the extract; while the non-significant change in monocyte count probably indicates that the phagocytic function of the body has not been compromised by extract. The non-significant change in eosinophil count probably indicates that the anti-allergic and anti-parasitic injections response of the body have not been compromised by extract.

The insignificant change in TWBC count caused by MEVA suggests that the immune system has not been compromised. Contrary report was given by ¹⁵ in *Pelargonium reniforme* extract treated rats. Also, the insignificant change in the platelet count caused by extract could be an indication that it does not has the potential to stimulate thrombopoietin production ¹⁶ with the hemostatic capability of the blood maintaining the *status quo* since platelets mediate in the blood-clotting mechanism.

Treatment of rats for 21 days with paracetamol produced non-significant changes in the duration of all the phases of the estrous cycle compared to the control and this suggests that the drug did not cause an imbalance of the ovarian and extra-ovarian hormones, since it has been reported that imbalance in these hormones leads to irregularity in ovarian functions and duration of the estrous cycle ¹⁷. Similar results were given by ¹⁸ in *Portulaca oleracea* extracts treated rats.

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