

## Effect of Extra Panadol on Blood and Behavior of Rats

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### Abstract

**Aim:** To study the effect of Panadol extra on blood and behavior of rats.

**Methods:** Locally bred male albino Wister rats weighing about 145 to 155 g on arrival purchased from animal house, research institute of Agha Khan University Karachi Pakistan were used throughout the experiments. Total of 24 rats were grouped into two: 12 rats called control and 12 test group. Normal saline was given to control while, 500 mg/tablet (extra Panadol) into 30 mg/kg body weight was dissolved in water and was given to rats. Behavioral study was observed. After 3 weeks of treatment rats were decapitated. Automated Hematology Analyzer SYSMEX XP 100 and Biochemical analyzer the Roche/Hitachi 902 was used for liver enzymes and hematological analysis.

**Results:** Panadol extra has no effect on locomotor activity and the effect of stimulatory activity of rats increases. Depression and anxiety of rats decreases and at the same time it is useful to enhance memory. Hematological parameters and liver enzymes were also non-significantly decreased in test group of rats as compare to control group. Panadol extra is considered a good choice of drug and its side effects are very rare if it is used properly but by frequent and prolonged or excessive use of Panadol extra rats become unable to Fight against diseases and it also highly significantly decreases the PLT count by which their blood clotting mechanism is highly disturbed.

**Conclusion:** Present study concludes that this drug may be used to enhance memory and decrease anxiety and depression for good performance.

**Keywords:** Panadol extra; Depression; Anxiety; Memory

### Introduction

Plant-derived compounds have mostly significant anti-inflammatory and anti-nociceptive effects [1]. It was estimated that about 40% of all medicines have been derived directly or indirectly from natural sources in the market today, 25% being from plants, 13% from micro-organisms and 3% from animals [2]. Some relevant examples of drugs derived from natural sources are also found in the market [3]. Analgesic drugs act in various ways on the peripheral and central nervous systems [4]. These include paracetamol, the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) such as the salicylates, and opioid drugs such as morphine and oxycodone [5]. The opioid analgesics can be used for either short-term or long-term relief of severe pain [6]. The evidence is described for the probability of the activity exhibited by analgesics and their antagonists being due to their association with a specific receptor surface.

Previously, clinical results of paracetamol with phenacetin were also reported, another aniline derivative. It was claimed that, unlike phenacetin, paracetamol had a slight tendency to produce methemoglobinemia [7]. Paracetamol was then quickly discarded in favor of phenacetin. In another study, it was also reported that large doses of paracetamol given to albino rats did not cause methemoglobinemia [8]. It was suggested that methemoglobinemia is produced in humans mainly by another metabolite, phenyl hydroxylamine [9]. Since then as an analgesic agent with few side-effects and little interaction with other pharmaceutical agents, Paracetamol was then added to the British Pharmacopoeia and has gained popularity. Caffeine acts as a natural pesticide and commonly consumed by humans in infusions. Caffeine in humans acts as a central nervous system stimulant, temporarily warding off drowsiness and restoring alertness [10].

Panadol extra which is also an analgesic drug. Panadol extra soluble tablets contain two active ingredients, paracetamol and caffeine [11].

Paracetamol as known is a simple painkilling medicine used to relieve mild to moderate pain and fever. Despite its widespread use for over 100 years, it was not fully understood that how paracetamol works to relieve pain and reduce fever [12]. However, it is now thought that it works by reducing the production of prostaglandins in the brain and spinal cord. The caffeine in Panadol Extra can cause anxiety and sleeplessness, but this is very rare when Panadol Extra is used correctly. However, it is more likely to get these side effects if subject consume caffeine-containing food and drinks when taking Panadol Extra. Panadol Extra is taken to help to relieve pain. It can be used to relieve pain that is short-term, for instance, after having a tooth removed. Other types of short-term pain that Panadol Extra can be used to treat include: headache and migraine, cold and flu symptoms (paracetamol also reduces fever), muscle aches, sore throat, period pain, joint pain caused by arthritis [13]. The purpose of the present study was to determine the effect of Panadol extra on blood and behavior of rats.

### Methods

Total of 24 rats used in this study, in which 12 rats are control and 12 test group. Locally bred male albino Wister rats weighing about 145 to 155 g on arrival purchased from animal house, research institute

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of Agha Khan University Karachi Pakistan was used throughout the experiments. The rats were housed individually in specially designed cages with saw dust cover floor in a quiet room, with free access to cubes of standard rat's food and water for at least, four days before starting the experiment. So that the rats could adapted them, to the new environment.

### Oral administration of drug

Control rats were given saline while 500 mg/tablet extra Panadol was dissolved in water and 30 mg/kg body weight was given to test rats. For the preparation of saline 4.5 g NaCl was dissolved in 500 ml water and then, it was freeze to get chilled saline. After 1st, 2nd and 3rd weeks of treatment different behavioral experiments were performed.

### Behavioral activity

The light-dark apparatus consists of two-compartment chamber (40 × 60 × 20 cm) comprising of a brightly illuminated area (40 × 40 cm) and a dark area (40 × 20 cm) separated by a wall with a round hole (7 cm diameter). Mice were placed individually in the illuminated part of the cage and following parameters were recorded during the test session of 5 min, total no. of crossing between the light and dark area, total time spent in the illuminated part of the cage. Drug-induced increases in behaviors in the white part of a two-compartment box are suggested as an index of anxiolytic activity. Home cage (26 × 26 × 26 cm) with saw dust covered floor was used for grooming and gnawing activity. The open field apparatus with 72 × 72 cm used for the novel object recognition task, for measuring anxiety and for exploration as well as locomotion. An animal taken out from the specialized cage and placed in the center square of the open field apparatus, rats move from the center square, crossing with all four paws, corner, sittings, grooming, gnawing, these all activities scored for 5 min.

The Morris Water Maze (MWM) was used in order to test hippocampal-dependent learning, including acquisition of spatial memory and long term spatial memory. During the Morris water maze test, the rat or mouse learns to escape from the water by locating a hidden platform with the help of visual cues. Optionally, the platform is removed in a second phase of the experiment, or placed in another quadrant, to investigate the animal's response to this new situation or to measure extinction. The forced swim test apparatus consists of a glass cylinder (20 cm diameter, 40 cm tall) filled with water to a depth of 20 cm and maintained at a room temperature.

At the start of the session, animals are removed from their own home cage and are gently lowered into the apparatus for a 10 min swim session. Testing may be conducted for a single stress session or repeated over 5 single daily test sessions to determine the anxiety of rats.

### Decapitation of rats

After 3 weeks of injections, rats were decapitated, by a specialized design apparatus, (guillotine). Blood and liver were collected quickly within 30 s of decapitation stored at low temperature (-70 °C) until analyzed for hematological and biochemical analysis.

### Laboratory analysis

Automated Hematology Analyzer SYSMEX XP 100 and Biochemical analyzer the Roche/Hitachi 902 was used for biochemical and hematological analysis.

### Statistical analysis

Results were represented as mean ± SD (n=12) significant difference by student t-test  $p < 0.01$  level from TG and CG following one-way ANOVA.

### Results

Figure 1a and 1b Panadol extra effects on TG and CG treated rats, in novel environment and home cage activity. Statistical analysis by student t-test (df2,12) (t=1.5526) ( $p > 0.01$ ) and (df2,12) (T=8.8117) (\*\* $p < 0.01$ ) individual difference by student t-test respectively shows that after administration of Panadol extra in TG the Novel Environment behavior decrease as compared to CG while, home cage activity increases as compared to CG.

Figure 1c and 1d shows Panadol extra effects on TG and CG treated rats, in light and dark activity. Statistical analysis by student t-test (df2,12) (T=1.9336) ( $p > 0.01$ ) and (df2,12) (T=10.9) (\*\* $p < 0.01$ ) individual difference by student T-test shows that after administration of Panadol extra in TG the entries in light portion was increased and rats spend their more time in light portion as compared to CG respectively.

Figure 1e-1g Panadol extra effects on TG and CG treated rats. Statistical analysis by student t-test (df2,12) (T=56.666) (\*\* $p < 0.01$ ), (df2,12) (T=18.1666) (++ $p < 0.01$ ) and (df2,12) (T=6.2333) (+ $p < 0.01$ ) individual difference by student T-test shows that after administration of Panadol extra in TG the forced swimming test behavior increases and the water maize activity behavior for short term and long-term memory decreases in TG as compared to CG.

Figure 2a and 2b Panadol extra effects on blood samples on TG and CG treated rats in Hb% and RBC. Statistical analysis by student t-test (df2,12) (T=3.029) ( $p > 0.01$ ) and (df2,12) (T=3.490) ( $p > 0.01$ ) individual difference by student T-test shows after administration of Panadol extra the HB% and RBC non-significantly decreases in TG as compare to CG of male rats.

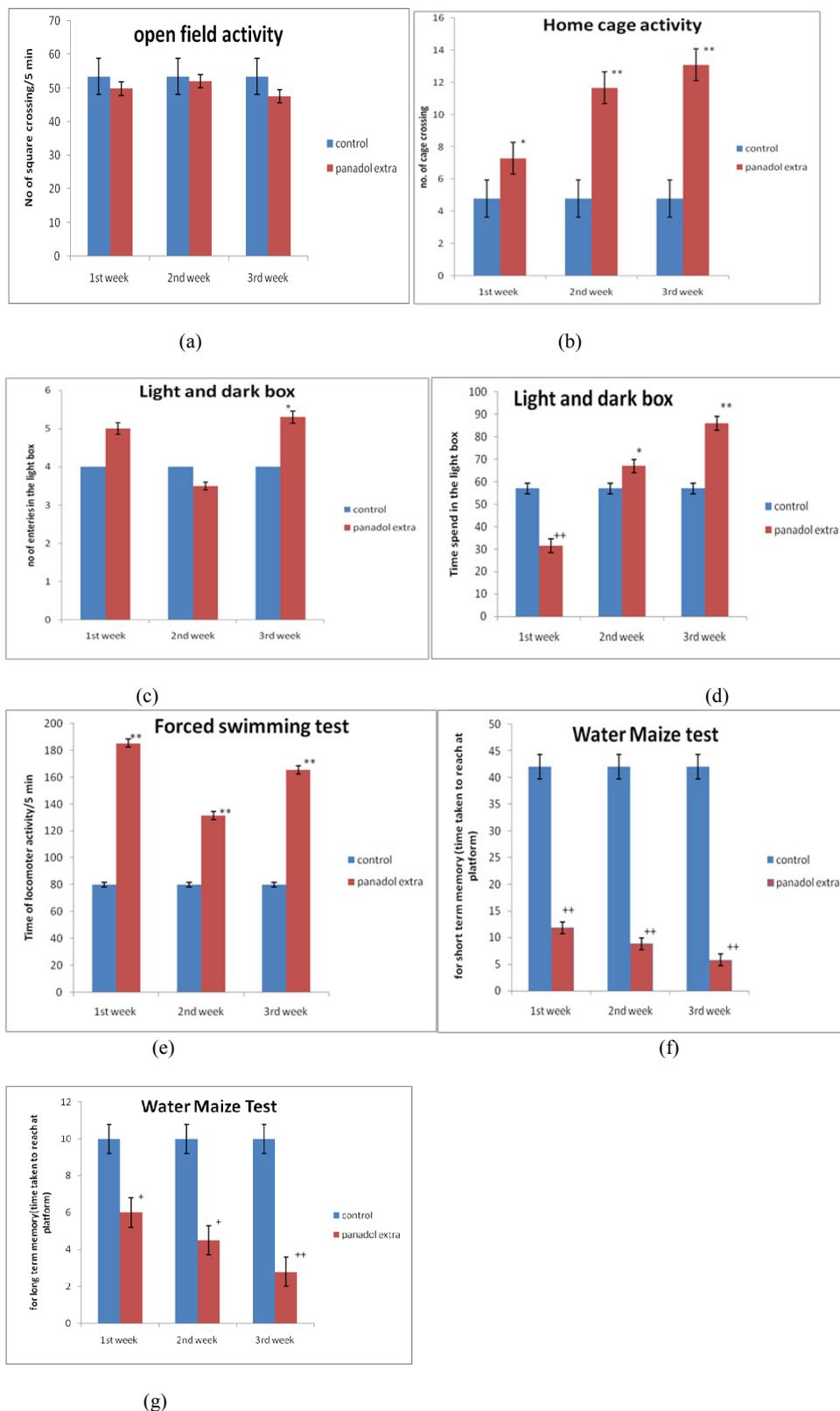
Figure 2c-2e statistical analysis by student t-test (df2,12) (T=2.890) ( $p > 0.01$ ), (df2,12) (T=10.985) (++ $p < 0.01$ ) and (df2,12) (T=41.40) (++ $p < 0.01$ ) shows that after administration of Panadol extra, the PCV, MCV and MCH are non-significantly decreased in TG as compare to CG respectively.

Figure 2f-2h statistical analysis by student t-test (df2,12) (T=0.426) ( $p > 0.01$ ), (df2,12) (T=15.21) (++ $p < 0.01$ ) and (df2,12) (T=9.580) (+ $p = 0.01$ ) shows after administration of Panadol extra in TG the MCHC has no effect while, TLC and PLT were highly significantly decreased as compare to CG.

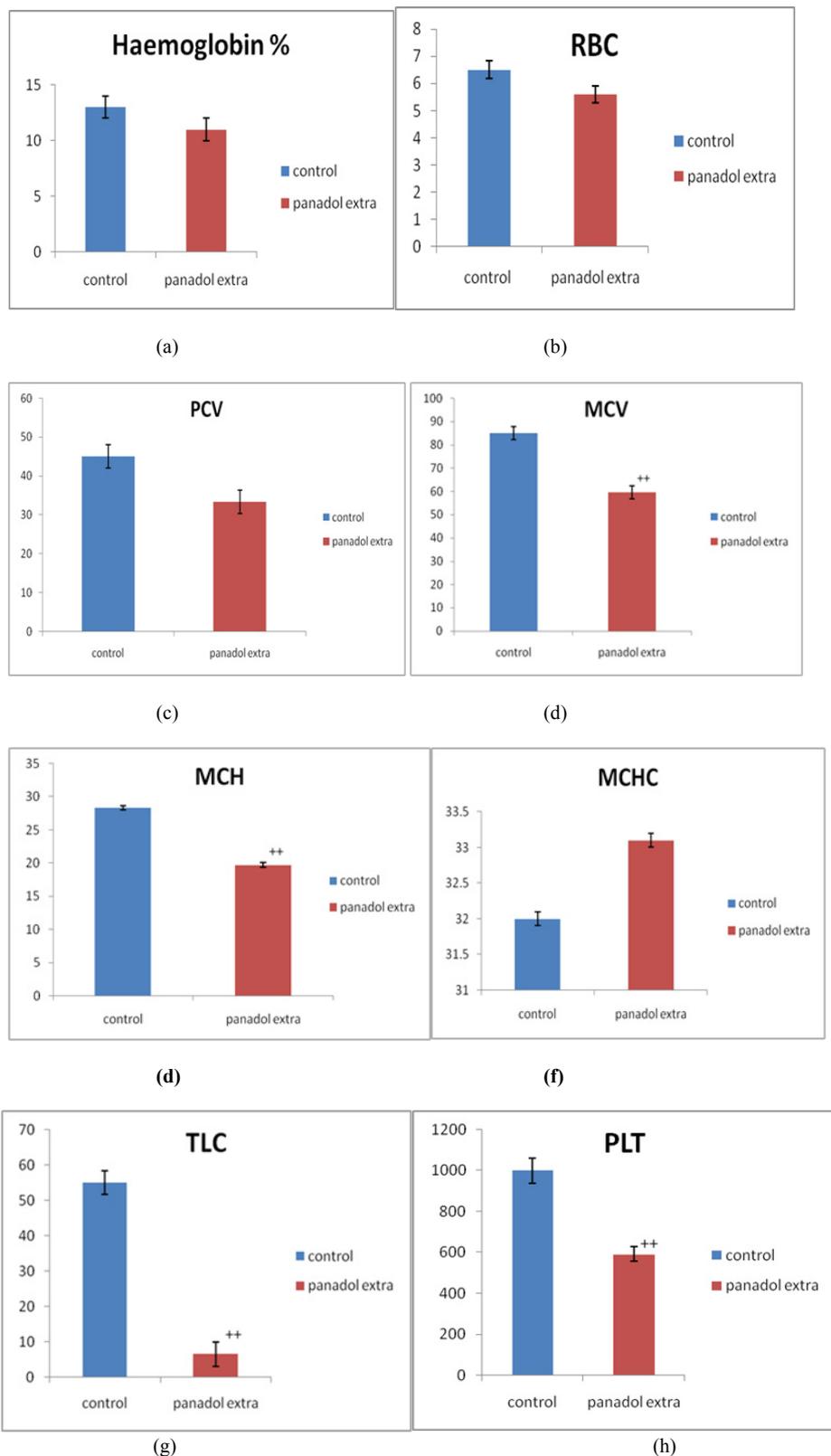
Figure 3a-3c statistical analysis by student t-test (df2,12) (T=848.14) ( $p < 0.01$ ), (df2,12) (T=829.14) ( $p < 0.01$ ) and (df2,12) (T=1972.9) ( $p < 0.01$ ) the enzyme AST, LDH and CPK were extremely significantly increases as compare to CG.

### Discussion

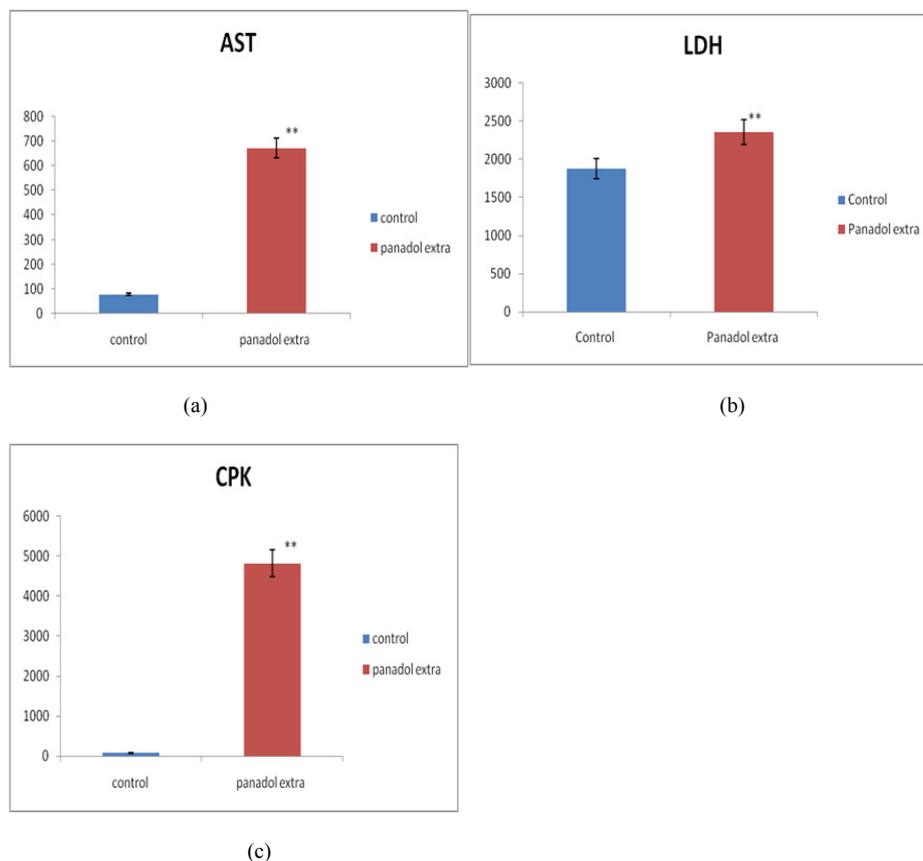
Present study shows that Panadol extra has no significant effects on locomotor activity. It has salicylic acid in it which causes subutilize of blood which may be alternatively increases the activeness of rats through which the stimulatory activity of rats also increases day by day. Caffeine in Panadol extra may increase the anxiety but due to the



**Figure 1:** Determination of behavioral activity. Values are mean  $\pm$  SD (n=12) significant difference by student t-test  $p < 0.01$  level from control and test. Behavioral studies including: (a) Open field activity (no. of square crossing); (b) Home cage activity (no. of cage crossing); (c) Light and dark activity (no. of entries in the light box); (d) Light and dark activity (time spend in the light box); (e) Forced swimming activity (time of locomotor activity); (f) Water maize test (for short term memory); and (g) Water maize test (for long term memory).



**Figure 2:** Laboratory analysis for hematological parameters. Values are mean ± SD (n=12) significant difference by student t-test p<0.01 level from control and test. Hematological parameters including: (a) Hemoglobin percentage (Hb) g/L; (b) red blood cells (RBC) 10<sup>12</sup> cells/L; (c) Packed Cell Volume (PCV) L/L; (d) Mean corpuscular volume (MCV) fL; (e) Mean cell hemoglobin (MCH) pg; (f) Mean corpuscular hemoglobin concentration (MCHC) g/L; (g) Total leucocytes count (TLC) 10<sup>9</sup>/L; and (h) Platelets (PLT) 10<sup>9</sup>/L.



**Figure 3:** Laboratory analysis for Liver and Muscles enzymes. Values are mean  $\pm$  SD (n=12) significant difference by student t-test  $p < 0.01$  level from control and test. Liver and muscles enzymes including: (a) Aspartate transaminase (AST) U/L; (b) Lactate dehydrogenase (LDH) U/L; and (c) Creatine phosphokinase (CPK) U/L.

presence of paracetamol the anxiety decreases [14]. Low administration of drug increases anxiety but regular administration of drug decreases the anxiety. Caffeine intake and depression may be linked indirectly for people who are particularly sensitive to the effects of caffeine. Results of depression were observed significantly decreased, indicating that rats become undepressed. Laboratory studies show that paracetamol release serotonin, boosting its pain-relieving benefits have an indirect effect on memory by reducing feelings of depression. Previous study shows that paracetamol blocks the activity of an enzyme called cyclooxygenase-2, which stops production of these pain causing by prostaglandins and activate an area of the brain involved in learning, memory and problem-solving called the hippocampus [15].

Hematological parameters including Hemoglobin percentage, red blood cells, packed cell volume, mean corpuscular volume, mean cell hemoglobin, total leucocytes count and platelets were non-significantly decreased as compare to control rats. While, mean corpuscular hemoglobin concentration were highly significantly increased in test group. In response to injury and certain diseases one of the effects of prostaglandins is to sensitize nerve endings, causing pain [16]. As paracetamol reduces the production of these nerves sensitizing prostaglandins but pain threshold may increase. For relieving mild to moderate pain and fever, Paracetamol is known as effective as aspirin or ibuprofen but unlike aspirin and ibuprofen it has no anti-inflammatory effect. Caffeine is not only a mild stimulant that helps to reduce fatigue but also thought to enhance the painkilling effect of paracetamol [17].

As overdose of Panadol extra is dangerous and capable of causing serious damage to the liver and kidneys [18]. Thrombocytopenia (low platelet count) and leukopenia (low number of white blood cells) were also associated with Paracetamol. Mean corpuscular volume (MCV) is a measurement of the average size of RBCs. When the MCV is decreased, RBCs are smaller than normal (microcytic) [19]. MCH is used to help diagnose the type (cause) and severity of anaemia. The MCHC, a measure of the concentration of hemoglobin in a given volume of packed red blood cells. Aspartate aminotransferase was used to detect liver damage in conjunction with another liver enzyme, alanine aminotransferase [20]. Sometimes, AST may be used to monitor people who are taking medications that are potentially toxic to the liver. A lactate dehydrogenase test is a non-specific test for the evaluation of a number of diseases, released from cells into the fluid portion of blood when cells are damaged or destroyed. Thus, the blood level of LD is a general indicator of tissue and cellular damage. In blood, due to any muscle injury or damage Creatine phosphokinase increases. Inflammation in the muscles also raises the CPK level [21]. Present study shows that the values of CPK, AST and LDH enzymes were highly significantly increases in TG as compare to CG. The increase values of enzymes show that the Panadol extra have adverse effect on liver and tissues of rats. It results might be increases due to decapitation or may be increases due to daily administration of Panadol extra.

By daily administering of Panadol extra to test group rats is considered a useful drug and a good choice of drug because it has

salicylic acid in it which is blood thinner but it is useful for a limited period of time. If Panadol extra is used for a long time it has some adverse effects.

## Conclusion

It was concluded in the study that Panadol extra has no effect on locomotor activity and the effect of stimulatory activity of rats increases. Depression and anxiety of rats decreases and at the same time it is useful to enhance memory. Hematological parameters were non-significantly decreased in TG while, liver and muscles enzymes were highly significantly increased. In present study, it is considered a good choice of drug if, it is used properly but due to frequent and prolonged or excessive use of Panadol extra rats become unable to Fight against diseases and blood clotting mechanism is highly disturbed. So, the present study concludes that this drug may be used to enhance memory and to decrease anxiety and depression for good performance.

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