Acute toxicity via oral administration of naproxen in body mass gain and organs mass of female albino rats (Rattus rattus)

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ABSTRACT

Naproxen, 4,2-(6′-methoxy-2′-naphthyl)-propionic acid is a nonsteroidal anti-inflammatory drug (NSAID); as in recent toxicity research, the determination of danger has been demonstrated in rats with a curative dose compared to the human dose. Actually, it is used in both rheumatic and non-rheumatic inflammatory pain. In this study, repeated oral doses of naproxen were administered once daily. The research model consisted of 20 white rats. The four groups, each consisting of five individuals, received the drug for 28 days at the following doses: 500, 750, and 1000 mg/kg/day. Group 1 was the control group, receiving saline as a daily dose. Group 2 received 500 mg/kg each day, Group 3 received 750 mg/kg each day, and Group 4 received 1000 mg/kg each day. The rats were slaughtered after 28 days of treatment. After receiving treatment for 28 days, the rats were slaughtered, and the animals were weighed before and after the end of the period, as well as the vital organs (liver, kidney, and testicle), followed by statistical studies of the recorded weights. As a result of the drug's effect, weight was affected in a decreasing manner from the lowest dose to the highest according to the study program, and statistically significant differences were observed. Cases of hematuria were recorded, which led to damage and a sharp drop in weight. The harmful effects of naproxen are notable in the short term. Thus, this assay was conducted to certify the effect of naproxen on body weight gain as a primary criterion for harm in female rats.

Keywords: *Body weight, Hematuria, Naproxen, Non rheumatic, Rat, Rheumatic.*

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Highlights of this paper

- This study examines the prevalence of uncontrolled and unsupervised sedative abuse.
- The results indicate that harm is evident if high doses are continued.
- The main risk factors identified include drug use at certain doses, concentrations, and duration of treatment.

1. INTRODUCTION

The Naproxen has been nonsteroidal antiinflammatory drug (NSAID) already advocated for use in aching and inflammatory rheumatic and certain nonrheumatic cases [1]. It may be administered through the mouth or rectally using a convenient once or twice daily regimen. Dosage adjustments are not usually required in the elderly or those with mild renal or hepatic impairment although it is probably prudent to start treatment at a low dosage and titrate upwards in such categories of patients [2].

Naproxen's effectiveness as an painkiller, antipyretic, antiinflammatory cure, compared to NSAIDs, has been confirmed in clinical trials. This compound has potential for controlling rheumatic diseases, particularly those of intrinsic origin, ankylosing spondylitis, and psychologically triggered pain, such as migraines, postpartum pain, and menstrual pain[3].

Pharmacodynamics in animal studies, in which the adrenal glands were removed, indicated its non-steroidal properties. The chain of effects begins with a reduction in prostaglandin levels and thus suppression of the overall activity of cyclooxygenase in body fluids. As a result of its direct effect on body fluids, it causes intestinal bleeding in the form of micro-necrosis, compared to its counterparts in the non-steroidal family [4].

The most obvious effect is the effective suppression of platelet aggregation, which shows its direct effect on bleeding time in mammals and consequently the physiological damage to kidney function, especially in those who have kidney failure as a result of physiological damage or due to age [5].

Pharmacokinetics: In the case of sodium salt, the absorption rate is more rapid in gastric juice, resulting in higher and faster plasma concentrations. It takes an hour between peak concentrations in body fluids and plasma, making it an ideal choice for the treatment of acute pain. However, it has been found in twice forms but the post-absorption pharmacokinetics of the sodium salt and its parent acid are identical [6].

2. EXPERIMENTAL ANIMALS

The research model is twenty female albino rats (Rattus rattus) that were conducted to determine the side effects and toxicity of naproxen and its effect on weights before and after the end of the experiment for twenty-eight days, weights ranging between 210 and 240 grams, were incubated in a laboratory environment with ideal humidity and temperature and in cages with dimensions as shown (plastic cages with dimensions of 44 cm length, 27 cm width, 20 cm height) covered with special metal covers [7].

2.1. Drug Used

The main groups deal with Naproxen 500, 750 and 1000 mg kg for each day by employing therapeutic doses and done on purpose for the relative mass of the rats. The physic titer has been fitted within normal saline (N.S) for getting ready the distinct concentrations of the physic on the report of to the groups mentioned in the design of this study [8]. The selection of N. S as diluting liquid depending on. The aspirin doses that are supposed to be given when doubling the volume of the initially prepared solution [9] as follow.

1. G. one has been administrated 1 ml of normal saline per day as control group.

2. G. two has been administrated 500 mg/kg that taking 1 ml from bulk solution
3. G. three has been administrated 750 mg/kg that taking 1ml from bulk solution.
4. G. four has been administrated 1000 mg/kg that taking 1ml from bulk solution.

3. RESALTS

3.1. Body Mass

The changing possibility out coming of the Oral Control in Different Doses of Naproxen on either Body mass (g) and proportion of mass Gain (%) in Female Rats at closing program.

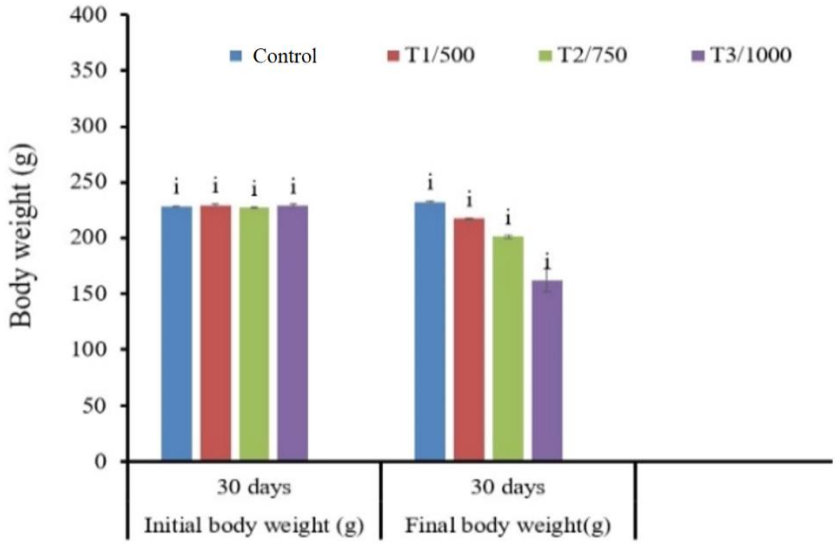
The closing observed a significant undergo exile ($p<0.05$) in final body mass of female rat after oral controlled with 500, 750, 1000 mg/kg/day of naproxen compared with control category as the following (239.8 ±1.2 ,217.2±1.3, 219.5±2.7 193.8±1.7)g respectively compared with the prime body mass as the following (232.4± 0.6, 227.4± 0.6, 232.4± 0.6 , 225.2 0.7 ±)g respectively.

Table 1. The changing possibility out coming of the oral control in different doses of naproxen on either final body mass (g) and proportion of mass Gain (%) in female rats.

Naproxen mg/kg/Day	prime body mass(g) (Mean± S.E)	Final body mass(g) (Mean± S.E)	Mass gain (%) (Mean± S.E)	Gaining (+) or lossing (-)
Control	232.4± 0.6 (A,b)	241.5 ±2.9 (A,a)	3.87 ±1.2 (A)	+
T1/500	227.4± 0.6 (B,a)	222.2±1.6 (B,b)	-2.28 ± 0.6 (B)	-
T2/750	232.4± 0.6 (C,a)	213.5±3.9 (C,b)	-8.3±1.5 (C)	-
T3/1000	225.2± 0.7 (D,a)	186.8±1.666(D,b)	-10.9± 2.3 (D)	-

Note: * The divers letters (Capital letters for degradation in column and small letters for row degradation in value) mention to significant differences ($P> 0.05$) between means while similar letters mention to non-significant differences between means.

The out come exhibited a significant decrease ($p<0.05$) in proportion of mass gaining of female rat after through mouth controlled with 500, 750, 1000 mg/kg/day of naproxen (-2.28 ± 0.6, -8.3±1.5, -10.9± 2.3)% respectively compared with control group (3.87 ±1.2) (Table 1, 2).



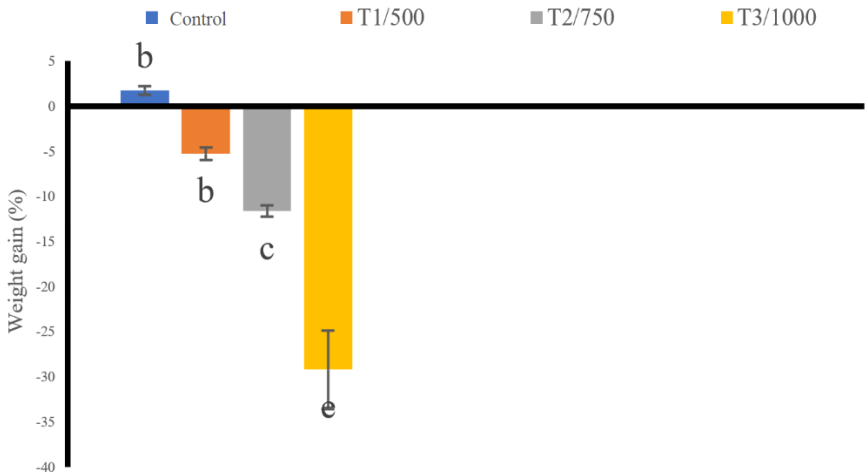


Figure 1. The changing possibility out coming of the oral control in different doses of naproxen on liver, kidney and bone relative mass (g/100g of Body mass) in female rats.

Figure 1 Illustrates the changing possibility out coming of the oral control in different doses of naproxen on liver, kidney and bone relative mass (g/100g of Body mass) in female rats.

3.2. Organs Weight

The outcome showed a significant decrease ($p<0.05$) in the relative masses of liver, kidney and bone (6.45±0.176, 6.1±0.158, 5.82± 0.163)g/100g, (1.53±0.042, 1.609±0.045, 1.735±0.046,) g/100g, (7.22±0.327, 7.056±0.282, 6.943±0.278) g/100g respectively after oral controlled with 500, 750,1000 mg/kg/day of Naproxen compared with control group (10.076±0.212)g/100g, (2.154±0.018) g/100g, (12.07±0.855) g/100g of body mass respectively, (Table 2).

Table 2. The changing possibility out coming of the oral control in different doses of naproxen on liver, kidney and bone relative mass (g/100g of Body Mass) in female rats.

Naproxen mg /kg/day	Relative organs mass (g/100g)		
	Liver (Mean± S.E)	Kidney (Mean± S.E)	Bone (Mean± S.E)
Control	10.076±0.21 (A)	2.154±0.01 (A)	12.07±0.85 (A)
T1/500	3.95±0.176 (B)	0.53±0.042(B)	8.22±0.327(B)
T2/750	3.71±0.158 (C)	0.609±0.045(C)	8.056±0.282(C)
T3/1000	3.52±0.163(D)	0.735±0.046(D)	7.943±0.278(D)

Note: The divers letters (Capital letters for degradation in column and small letters for row degradation in value) mention to significant differences ($P> 0.05$) between means while similar letters mention to non-significant differences between means.

Figure 2 Illustrates the changing possibility out coming of the oral control in different doses of naproxen on relative weight of liver g/100g bw in female rats.

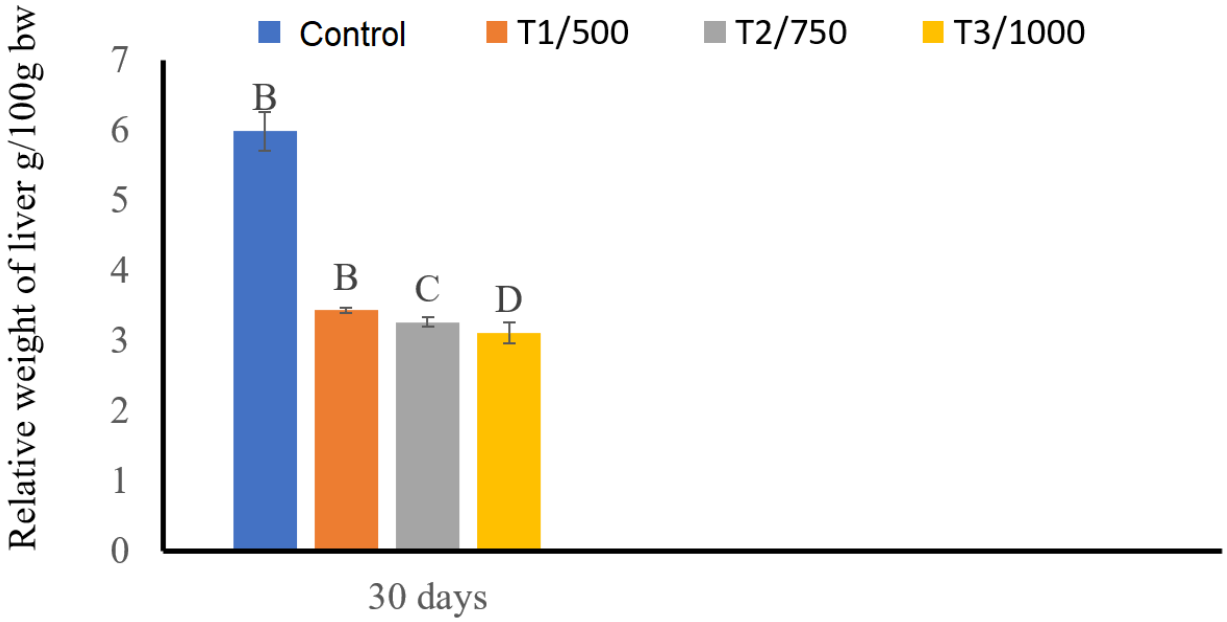


Figure 2. The changing possibility out coming of the oral control in different doses of naproxen on relative weight of liver g/100g bw in female rats.

Note: The different letters refers to significant differences (P< 0.05) between means while similar letters refers to non-significant differences between means.

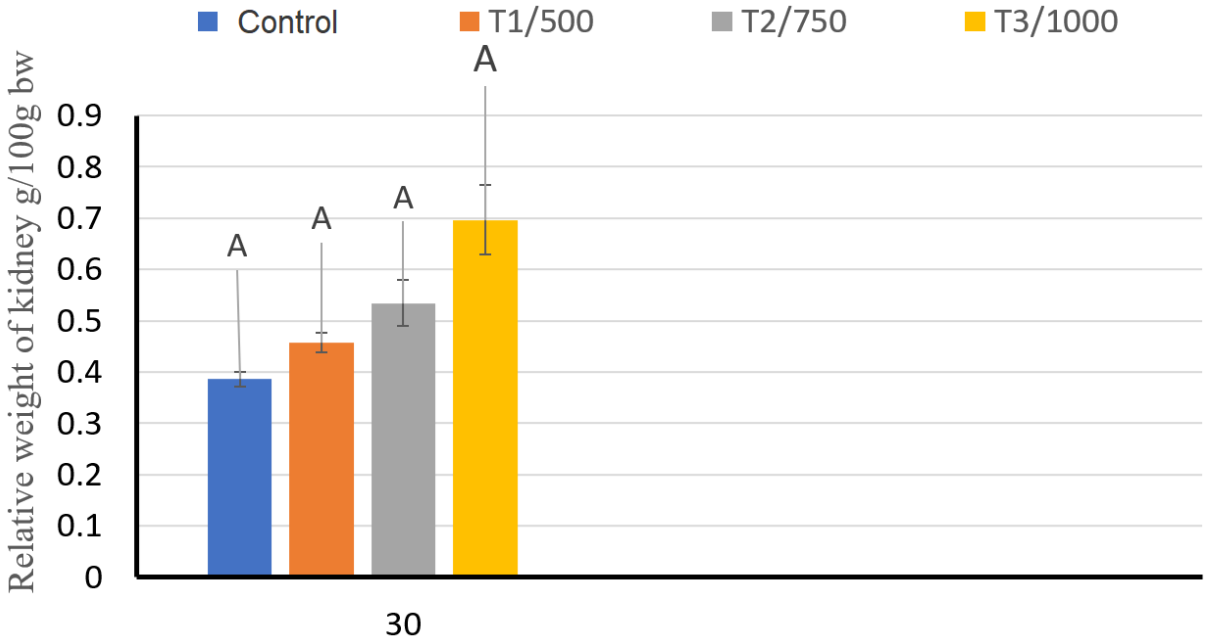


Figure 3. The Changing possibility out coming of the oral control in different doses of naproxen on relative weight of kidney g/100g bw in female rats.

Note: The different letters refer to significant differences (P< 0.05) between means while similar letters refers to non-significant differences between means.

Figure 3 Illustrates the changing possibility out coming of the Oral Control in Different Doses of Naproxen on proportional mass of kidney g/100g bw in female rats.

Figure 4 Illustrates the changing possibility out coming of the Oral Control in Different Doses of Naproxen on proportional mass of bone g/100g bw in female rats.

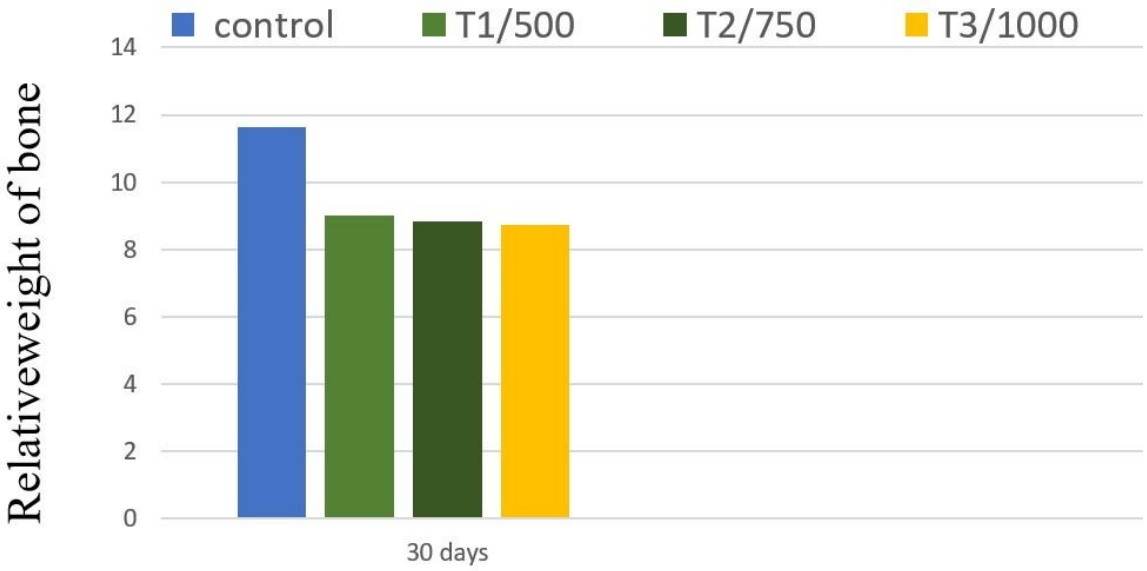


Figure 4. The changing possibility out coming of the oral control in different doses of naproxen on relative mass of bone g/100g bw in male rats.

4. DISCUSSION

4.1. Body Mass and Organ's Mass

The sitting seek give away significant undergo fall ($p<0.05$) in body mass and Organ's mass of female rats follow the oral control with 500, 750, 1000 mg/kg/day of naproxen as balanced with the prime body mass at closing program, whereas there was significant decrease ($p<0.05$) in both final body mass and proportion of mass gaining as balanced with control category follow up oral managing with 500, 750, 1000 mg/kg/day of naproxen.

Recently study, use of Naproxen concomitant with increased risk of bleeding recorded in many individuals of currant groups. The distinctive of suppression all the isoenzymes cyclooxygenase (COX) is marked off as the first spark for the cardio-vascular healthy by naproxen. in spite of the two COX iso-forms have a similar build but a many functional role [10].

COX-s is intricated in maintains the basal pro steroids level, especially at the gastrointestinal tract, to provide the safeguard at the line of mucosa in stomach in defiance and support of the gastrointestinal homeostasis in secreting the gastric acid the suitable milieu, the main Adverse side effect akin with naproxen are linked with risk for erosive destruction along the gastro-intestinal tract [11].

On the other side, the responsibility of COX-2 fabrication of proteinoids along with the inflammatory response and Vaso protection [12]. The selective of naproxen suppress the chiefly COX-2, in this way minimize the hurtful effects on the upper gastrointestinal tract (GIT) mucosa. It is known, though that the higher COX-2 carefully choosing the target site is correlating with significantly greater cardiovascular risk [13].

This result concomitant with Stiller & Hjemdahl, 2022. reported that a remarkable decrease in percentage of weight gain of male rats occur due to naproxen administration 500, 750, 1000 mg/kg/day compared with control group.

A caliber integrity concern connected with the management of each naproxen pattern is their upshot on liver, kidney function and exactly renal homeostasis. Naproxen is capitulated to almost full liver metabolism. The deliberation for liver sufferance linked with naproxen are met by the proof as long as by the system for drug safety

spying. The statistical evaluation of spontaneous reports for occurring liver failure following the use of naproxen unambiguously observed that naproxen has the stubby rate of noted liver failure balanced to other popular representatives of tNSAIDs [14].

From the mentioned, we conclude a sizeable ulcerative bruise in the gastrointestinal tract may be led to limit blossoming and mass gain be in debt to turn down hunger, imbalance in electrolyte, and increased bleeding blood in urine, as shown by the lower percentage of weight gain in male rats [15].

It is clear that naproxen causes a significant scaling down in metabolically activation cells as well as a rise in cell death. several cell lines were used to reinforce the findings. It's worth noting that these findings came from two separate cell lines, both of which are known to be charier than normal cells [1].

Naproxen be worthy of causes as the most likely to cause significant brake down to DNA and other biological structures from a strictly mechanistic standpoint. Because of the low energy barrier, naproxen barrierless ultrafast dissociation may be more loath than other tNSAIDs triplet population or split from the singlet manifold [16].

5. CONCLUSION

Last but not least, I would like to point out that naproxen is a physical and chemical toxic substance that exposes the internal environment to profound physiological and tissue changes, which reverses the response to atrophy in cells in general, causing a loss of overall weight and, consequently, organ weight when taken orally on a regular basis. Statistical data have shown that naproxen causes a marked imbalance in overall body mass, leading to a significant decrease in the actual mass of organs. The goal is to use naproxen cautiously, after ensuring a healthy digestive system, and for intermittent, non-prolonged periods to allow for the restoration of metabolic sites.

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