# Gabapentin effects on lipid profile, Blood electrolytes, and functions of kidney and liver of laboratory mice (Mus musculus)

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## Abstract

This study was done to find out the effects of oral use of gabapentin on different parameters of laboratory mice. In this study, three groups were used of twelve male mice each. The animals of the control group were maintained on a standard ration. The treated groups were also maintained on a standard ration, but they were daily dosed orally with gabapentin. The first treated group (GABA low) were dosed orally with one ml of distilled water containing gabapentin as (25mg/ml/mice) daily. The second treated group (GABA high) were dosed orally with one ml of distilled water containing gabapentin as (50mg/ml/mice) daily. The experiment protocol continued for two months. The results revealed that the use of gabapentin of different doses causes the TAGs, TCH, LDL, VLDL of both treated groups to increase significantly as compared with control group and those values of the GABA high group were significantly higher than that of the GABA low group. The HDL was significantly reduced in both treated groups and it was more significantly reduced in that of GABA high group as compared with control and GABA low groups. Blood urea, creatine, and sodium were significantly increased in both treated groups as compared with the control one, but blood urea of GABA high was significantly higher than that of GABA low group. No significant differences were seen for the blood potassium of all the groups. AST, ALT and ALP were also significantly increased in both treated groups comparing with that of the control one, but ALT of GABA high was significantly less than that of GABA low group. For the albumin and bilirubin, there was no significant differences among all the groups at ($P \leq 0.05$).

**Keywords**: Gabapentin; Lipid; Electrolyte; Kidney and liver

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## Introduction

Most of the researches on gabapentin have focused on its role as an anti-epileptic and anti-nociceptive agent and many papers have described this. Examples of these studies, the role of gabapentin to reduce postoperative pain, nausea, and vomiting in patients who undergo laparoscopic cholecystectomy [1], gabapentin is used to relieve a pain caused by an anti-cancer agent [2], to relieve neuropathic pain in rats [3], a study on gabapentin pharmacology and its role in pain management [4], its anti-nociceptive effect when used in a synergism manner with other compound [5], and many others. Our study aims to spot a light on the side effects of gabapentin on other body functions and biomarkers. Gabapentin is well known as an analogue of gamma amino butyric acid (GABA). Gabapentin does not act on the receptors of GABA, neither fortifies its action nor converted into GABA and its exact mechanism of action is not fully understood [6]. Instead, gabapentin is a ligand of calcium channels specifically as calcium channel α2δ ligand [7]. Gabapentin has a high affinity to bind to a protein in cortical membranes with an amino acid sequence identical to that of the Ca2+ channel subunit α2δ-1 and it has been postulated that the anticonvulsant effects of gabapentin are mediated by α2δ-1 protein, but whether and how the binding of gabapentin to the α2δ-1 regulates neuronal excitability remains unclear. Gabapentin is absorbed after oral administration and are not metabolized in humans. Gabapentin is not bound to plasma proteins and is excreted unchanged, mainly in the urine. Its half-life, when used as monotherapy, approximate 6 hours [8]. Gabapentin has many adverse effects such as dizziness, ataxia, somnolence and fatigue [9] and was found to affect the hemodynamics of rats [10].

## Materials and methods

### *Animals of the experiment*

The experiment was done at the animal house of the College of Medicine, Al-Muthanna University. Thirty-two male mice (Mus musculus), twelve weeks old, and of 20 – 25 grams weights were used. The experiment conditions were fit for all animals. Room temperature was set 20 – 25 C˚ using air conditioners, and the humidity rate was about 50 %. Food and water were provided daily (ad libitum).

*Protocol of experiment*

1- Control group: Twelve male mice were maintained on a standard ration for two months.
2- GABA low (GABA L) treated group: Twelve male mice were dosed orally (25mg/ml/mouse) of gabapentin using oral gavage daily for two months.
3- GABA high (GABA H) treated group: Twelve male mice were dosed orally (50mg/ml/mouse) of gabapentin using oral gavage daily for two months. Gabapentin was dissolved in distilled water and dosed to the mice in both treated groups.

** Oral LD50 of gabapentin for mice = 8000 mg/kg (11).

*Preparation of specimens*

At the end of the experiment period, mice were anaesthetized using chloroform and blood samples were withdraw from myocardium directly. Blood samples were put in Ependorf gel tubes to separate and obtain sera.

*Parameters of the study*

All the tests of the study were done using PKL (POKLER ITALIA) device and its special included kits.

*Statistical analysis*

ANOVA one-way test was used to find out the least significant difference (LSD) among groups depending upon IBM SPSS program, version 20.

**Results and discussion**

The study revealed that the oral use of gabapentin caused a significant elevation in the triacylglycerols (TAGs), total cholesterol (TCH), low density lipoprotein (LDL), and very low density lipoprotein (VLDL) of both the treated groups GABA low and GABA high as compared with the control group and it was obvious that these values were significantly more elevated when the dose of gabapentin increased in the GABA high group as compare with GABA low group. The HDL was significantly declined in both treated groups as compared with the control one but it was more significantly decreased in the GABA high group as it is shown in table (1). The results also show that

gabapentin causes significant elevations in the blood urea, creatine, and sodium of both treated groups comparing with the control group and the urea of GABA high group was significantly higher than that of GABA low too. For the potassium, there was no significant differences among the groups as it is clear from table (2). In addition to the previously mentioned effects, gabapentin also caused significant elevations in the values of AST, ALT, and ALP of both treated groups comparing with the control group and there were no significant differences between the treated groups. Besides, the bilirubin and albumin values were not affected by gabapentin and there was no significant difference among all the groups as it is seen in table (3). The bad effects of gabapentin in our study come in line with previous studies done by [12, 13, 14, 15] and 16). Gabapentin caused elevated liver function enzymes AST, ALT, and ALP beside bilirubin. This might be explained by the inducing effect of gabapentin on liver enzymes where it causes increased hepatic nitric oxide (NO) and here induces hepatotoxicity by increasing free radical's liberation [14, 15]. The lipid profile which was also significantly affected by gabapentin might be also involved to be caused by this mechanism. The increased levels of urea indicate renal malfunction and might be due to impaired renal glomerular filtration rate which caused by gabapentin [15] and we think this impairment or effect on GFR might be due to the renal over load which might be caused by the unchanged secreted gabapentin.

**Table 1.**

Effects of different doses of Gabapentin on lipid profile of laboratory mice. The numbers represent the mean ± standard deviation. Different letters refer to a significant difference among groups at ($P \leq 0.05$).

| GROUPS / Parameters | TAGs (mg/dl) | CHO (mg/dl) | HDL (mg/dl) | LDL (mg/dl) | VLDL (mg/dl) |
|---|---|---|---|---|---|
| Control | c 156 ± 15.6 | c 95.67± 6.02 | a 55± 5.4 | c 9± 2.8 | c 31.17± 3.1 |
| GABA low | b 220.33±17.8 | b 173.33±11.05 | b 39± 8.1 | b 90± 9.8 | b 44± 3.6 |
| GABA high | a 288.3± 26.3 | a 245.83± 32.9 | c 27.83±7.3 | a 160.33±32.6 | a 57.83± 4.9 |
| LSD | 64.33 | 72.5 | 11.16 | 70.33 | 12.83 |

**Table 2.**

Effects of different doses of Gabapentin on blood electrolytes of laboratory mice. The numbers represent the mean ± standard deviation. Different letters refer to a significant difference among groups at (P≤0.05).

| GROUPS /Parameters | Urea (mg/dl) | Creatine (mg/dl) | Sodium (mmol/l) | Potassium (mmol/l) |
|---|---|---|---|---|
| **Control** | c 39.67± 4.54 | b 0.41± 0.07 | b 161.17± 17 | a 3.67± 0.51 |
| **GABA low** | b 50.83± 7.46 | a 0.63± 0.1 | a 181.67± 7.03 | a 3.50± 0.54 |
| **GABA high** | a 67.67± 8.54 | a 0.63± 0.19 | a 189.83± 7.73 | a 3.83± 0.40 |
| **LSD** | 11.16 | 0.216 | 20.50 | ----- |

**Table 3.**

Effects of different doses of Gabapentin on Liver enzymes and proteins of laboratory mice. The numbers represent the mean ± standard deviation. Different letters refer to a significant difference among groups at (P≤0.05).

| Groups /Parameters | AST (U/L) | ALT (U/L) | ALP (U/L) | Bilirubin (mg/dl) | Albumin (g/dl) |
|---|---|---|---|---|---|
| **Control** | b 75.67± 8.77 | c 55± 8.80 | b 162.17± 10.16 | a 1.5± 0.54 | a 2.5± 0.83 |
| **GABA low** | a 378.50± 35.03 | a 282.5± 21.88 | a 193.5± 12.43 | a 1.5± 0.54 | a 3.01± 0.01 |
| **GABA high** | a 355.17± 53.12 | b 230± 53.68 | a 191.83± 14.34 | a 1.33± 0.51 | a 2.83± 0.75 |
| **LSD** | 279.50 | 52.50 | 29.66 | ------- | ------- |

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