Toxicological studies of ethanol leaf extract of *Lavandulastoechas* on kidney of Wistar rat.

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Abstract

The medicinal ingredients in herbal remedies are derived from plants. Despite the fact that they could offer a wide range of health advantages, they are thought to have a lower likelihood for adverse effects. The medicinal herb lavender (*Lavandulastoechas* L.) is widely utilized for a variety of medical conditions. The aim of this investigation is to evaluate the toxicological effect of *Lavandulastoechas* on Wistar rat kidney.Twenty four (24)Animals of either sex were used. Group 1 was given distilled water (10 ml/kg), while groups 2, 3, and 4 were given 50, 100, and 200 mg/kg of *Lavandulastoechas*, respectively for 28 days. Animals were housed in typical cages and given oral access to the extract for 28 days before being weighed and put to death. A heart puncture was used to get blood, which was then promptly taken for testing.Red blood cell, Hemoglobin, and Mean corpuscular volume levels decreased significantly (P<0.05), but neutrophils, basophiles, eosinophils, and platelets remained constant. At 100 and 200 mg/kg, *Lavandulastoechas* significantly (P<0.05)loweredK+ levels. Na+ increased significantly (P<0.05)at a dosage of 200 mg/kg. Across doses given, the levels of creatinine, chloride, and urea were not substantially (P<0.05)impacted. A histological analysis shows minimal tubular deformation.The study's findings indicated that the plant might have a negligible impact on the kidney, indicating that it should be used with caution if consumed over an extended period of time.

Key: *Lavandulastoechas*, blood, rats, kidney

Introduction

Modern medicine has its roots in the ancient therapeutic practices that have been practiced long before recorded human history. Numerouscommon medications, including morphine (opium poppies), digoxin (foxglove), quinine (cinchona bark), and aspirin (willow bark), were developed using plant materials (Solomon et al., 2015). The usage of natural medicines has dramatically expanded across the globe. Since prehistoric times, medicinal plants have been discovered and used in traditional medical procedures. Manychemical compounds are produced by plants for a variety of purposes, including

defense against herbivorous mammals, fungus, insects, and illnesses (Ojochegbe et al., 2019; Joseph and Joseph 2018). Differentphytochemicals with potential or established biological activity have been identified(Joseph et al., 2018; Timothy et al., 2018).The results of taking a complete plant as medication remain unclear, though, because a single plant includes a vast variety of phytochemicals. Furthermore, extensive scientific research to determine the phytochemical composition and pharmacological effects of many plants with therapeutic promise is still lacking (Aprioku et al., 2016; Okokon et al., 2017). In non-industrialized communities, medicinal plants are frequently employed, mostly because they are more accessible and affordable than modern treatment (Gaitonde, 2017).Testing for sub-acute toxicity is used to evaluate toxicity in the target species. It provides insight into the relative toxicity of compounds, allowing them to be categorized as mild, moderate, very hazardous, and almost non-toxic. Additionally, it offers details on the process by which drugs exert their hazardous effects and offers a foundation for selecting doses for efficacy studies as well as long-term toxicity research (Joseph et al., 2020; Simeon et al., 2020).

Subacute toxicity test is defined by the globally harmonized system (GHS) as specific target organ/system toxicity resulting from 28 days of recurrent chemical exposure in rodents (Builder et al., 2019; Joseph et al., 2019). Testing for sub-acute toxicity is performed to assess impacts primarily on different organ systems and to determine a no observed effect level (Eknoyan et al., 1997; Haruna et al., 2020). The evaluation of clinical observation, blood analysis, a full body gross necropsy, and a microscopic examination of all organs and tissues make up the end points (Wazis et al., 2020; Builder et al., 2020).Herbal plants have been used for many years for therapeutic and health purposes. Local people frequently ingest medicinal plants without following a prescribed dosage schedule or time frame (Zubairu et al., 2021; Joseph et al., 2021). This may have unintended consequences for the tissue, organ, or biological system (Nahon et al., 2011).

Although there is little to no scientific evidence about the efficacy and safety of medicinal plants, long-term clinical experience has generally served as the basis for their use (Romer and Parsons 1977). The use of medicinal herbs as a remedy is only based on a long-standing, widespread traditional folk practice (Romer and Parsons 1977; Oluwakanyesola et al., 2018). A thorough scientific examination of these plants is essential given the rise in the use of herbal medicines and the necessity to support their traditional uses (Tosin et al., 2019; Simeon et al., 2019). Although herbs are supposed to be safe, there have been many reports of unsafe and fatal side effects (Emamian et al., 1993;Molina and DiMaio 2015).These could include overt toxicity, allergic responses, contaminant effects, and/or medicine and herb interactions. Because they are "natural," phytotherapeutic treatments are frequently wrongly thought to be less hazardous. However, those items have bioactive components that could have negative impacts (Boron 2004).

Various aesthetic and therapeutic uses for lavender (*Lavandula stoechas*), a plant belonging to the Labiatae family, are found in herbal medicine (Simeon et al., 2019; Sabastine et al., 2019; Joseph et al., 2019). *Lavandulastoechas*essential oil inhalation decreased cholesterol plaques in rabbits with atherosclerotic disease but had no impact on serum cholesterol levels (Samson et al., 2019). In rats, lavendar had a hypolipidemic impact (Simeon et al., 2019). Lavender aromatherapy has additionally shown vasodilatory benefits and increased coronary blood flow in people (Joseph et al., 2019). Isolated rat hearts were guarded against ischemia reperfusion (IR) damage by a lavender flower extract (Oyebadejo et al., 2019).In an experimental model of stroke, lavender oil had neuroprotective efficacy and antioxidant properties(Joseph et al., 2019b). In a recently completed study, therapy with lavender essential oil after myocardial infarction decreased ischemia injury in rats (Modupe et al., 2019). Several studies have been carried out on this plant but no report on safety or sub chronic toxicity study has been carried out. The aim of this investigation is toevaluate the toxicological effect of *Lavandulastoechas* on Wistar rat kidney.

Material and Method

Wistar rats, both sexes, were acquired from Bingham University's Animal House. They were fed typical animal pellets and given unlimited amounts of water. The College of Health Sciences Animal Ethics Committee at Bingham University granted permission and consent for the use of animals in research as BU/DR&D/REC/019/003.It plant was also given the voucher number *BUFP 3001*.

Plant collection

In the adjacent Karu village in Nasarawa State, Nigeria, leaves from the Lavandulastoechas plant were harvested from its natural environment in the morning during raining season. The Department of Botany at Bingham University in Nasarawa State, Nigeria, verified the plant's authenticity. It was given the voucher number BUFP 3001.

Plant extraction

For two weeks, the leaves were dried in the shadows. The ground-up dried plant material was further broken up and pulverized. The substance was pulverized and then macerated in 70% ethanol. Utilizing a rotary evaporator in a vacuum, the liquid filtrates were concentrated and evaporated to dryness at 40°C. Until it was used, the ethanol extract was kept at -4°C.

Animal study

Twenty four rats of either sex (weighing 174–257g) were chosen at random and divided into four groups of six rats each. Rats in groups 2, 3, and 4 got 50, 100, and 200 mg/kg of *Lavandulastoechas* extract, respectively, while group 1 acted as the control group and received normal saline (10ml/kg). At the start of the experiment and once a week, the weights of the rats were noted. The day of

sacrifice was given the designation D_{29}, whereas the first day of dosing was given the designation D_0.

Haematological analysis

On the day 29, of the trial, the rats were sacrified and blood was collected through Cardiac puncture. EDTA-containing sample bottles were used to collect a portion of the blood for hematological analysis, which included measuring hemoglobin concentration, white blood cell counts (WBC), differentials (neutrophils, eosinophils, basophils, lymphocytes, and monocytes), red blood cell counts (RBC), platelets, and hemoglobin (Hb) concentration (Cell-Dyn, Abbott, USA).

Chempathology analysis

Second portion of the blood was collected into plain bottle, allowed to clot and centrifuged at 300rpm for 10 minutes. The serum collected was used to estimate biochemical parameters.

Histological study

Thekidney of the animals were surgically removed and weighed and a part of each was fixed in 10% formaldehyde for histological processes.

Statistical analysis

Data were expressed as the Mean ±Standard Error of the Mean (SEM). Data were analyzed statistically using one-way Analysis of Variance (ANOVA) followed by Dunnett's post hoc test for multiple comparisons between the control and treated groups. Values of $P \leq 0.05$ were considered significant.

Results

Effect of 28 days oral administration of *Lavandulastoechas*on hematological parametersin rats

At a dose of 100 mg/kg, *Lavandulastoechas* considerably ($p<0.05$) decreased the levels of red blood cells, hemoglobin, and platelets; however, at a dose of 50 mg/kg, it significantly ($p<0.05$) increased the mean corpuscular hemoglobin concentration in rats compared to the control. However, the mean corpuscular hemoglobin concentration did not substantially ($p<0.05$) impact the level of basophiles, neutrophils, eosinophils, or lymphocytes. (Table 1).

Table 1: Effect of 28 days oral administration of ethanol leaf extract of *LavandulaLavandulastoechas*onhematological parameters in wistar rats.

			Treatment (mg/kg)	
Hematological parameters	DW(10ml/kg)	50	100	200
WBC (×10^9/L)	8.27±0.77	6.54±1.42	3.72±0.67*	7.20±1.83
RBC (×10^12/L)	8.30±0.36	8.65±0.64	6.17±0.25*	7.74±0.25
HGB (g/dL)	15.90±0.56	15.24±0.63	11.36±0.77*	14.58±0.36

HCT (g/dL)	55.18±2.02	56.61±3.56	34.67±3.29*	53.40±1.80
MCV (fL)	66.67±0.94	65.44±1.45	57.17±0.10*	69.60±1.72
MCH (pg)	19.16±0.16	17.80±1.19	18.83±0.38	18.80±0.22
MCHC (g/dL)	29.15±0.16	27.43±1.23	32.51±0.61*	27.10±0.67
PLT (×10^9/L)	620.83±52.81	567.00±96.28	252.00±50.14*	670.45±55.78*
LYM (%)	86.81±4.61	85.00±4.03	82.83±5.82	86.41±3.14
NEUT (×10^9/L)	10.81±3.64	10.82±3.61	15.40±5.41	11.00±3.23
EOSI (×10^9/L)	1.50±0.33	2.40±0.48	1.80±0.44	1.25±0.22
BASO (×10^9/L)	1.00±0.29	2.00±0.55	2.50±1.51	3.30±2.21

Data presents Mean ± SEM: n = 6, One way ANOVA, followed by Dunnett's post hoc for multiple comparison
*significantly different from the distilled water (DW) control at $p<0.05$. DW = distilled water (WBC = white blood cells, RBC = red blood cells, HGB = hemoglobin, HCT = hematocrit, MCV = mean corpuscular volume,
MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, PLT = platelet, LYM =
lymphocyte, NEUT = neutrophils, EOSI = eosinophils, BASO = basophils).

Effect of 28 days oral administration of *Lavandulastoechas*on renal indices and electrolytes in Wistar rats.

At 100 and 200 mg/kg, Lavandulastoechas significantly ($p<0.05$) lowered K+ levels. Na+ increased significantly ($p<0.05$) at a dosage of 200 mg/kg. Across doses given, the levels of creatinine, chloride, and urea were not significantly affected($p<0.05$).

Table 4.4: Effect of 28 days oral administration of ethanol leaf extract of *Lavandulastoechas*on renal indices in Wister rats.

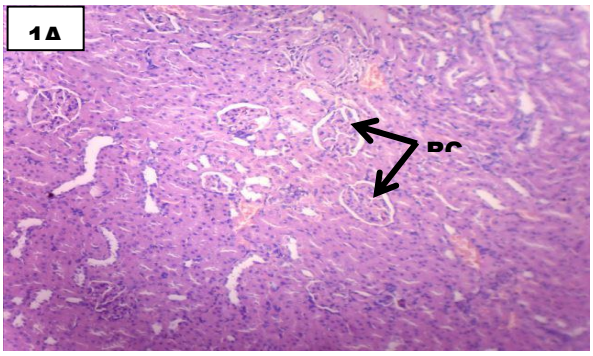
		Treatment (mg/kg)		
Renal indices and electrolytes (mmol/L)	DW(10ml/kg)	LS (50)	LS (100)	LS (200)
Potassium	7.00±0.55	7.60±0.70	5.30±0.48*	5.8±0.20*

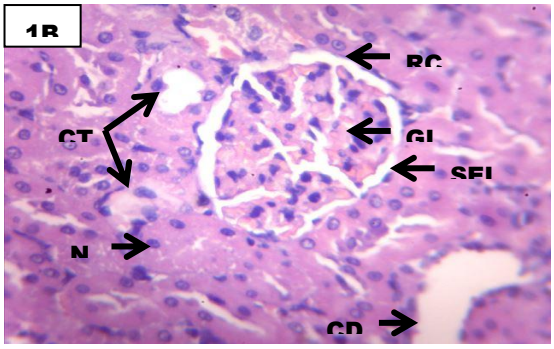
Sodium	158.00±2.90	168.20±2.91	169.10±1.90*	164.20±1.79
Chloride	101.30±5.81	99.72±6.61	111.23±2.46	100.55±3.21
Urea	9.43±0.29	9.54±0.55	8.90±0.25	8.75±0.53
Creatinine	63.44±9.62	80.22±12.41*	55.11±16.932	73.71±6.11

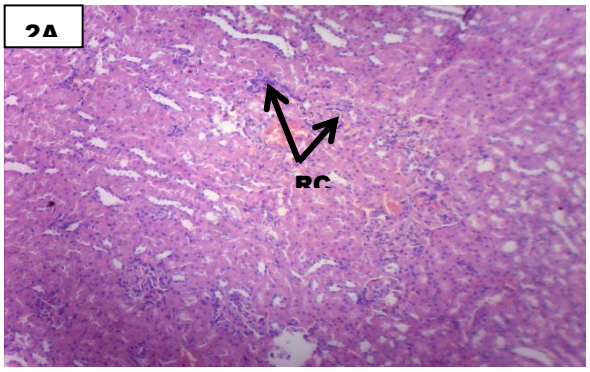
Data presents Mean ± SEM: n = 6, *significantly different from the distilled water (DW) control at p <0.05. DW = distilled water.

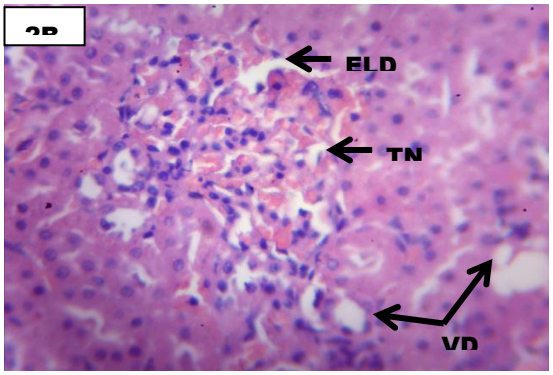
Histopathological Investigations of the effect of 28 days oral administration of *Lavandulastoechas*on renal indices and electrolytes in Wistar rats.

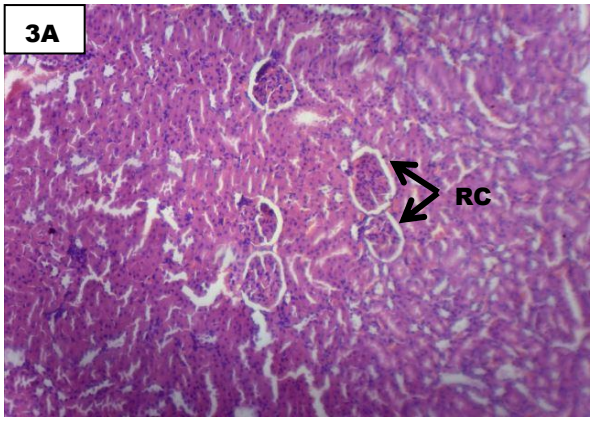
At 100 mg/kg and 200 mg/kg, the kidney exhibited mild tubular deformation and glomerular necrosis. Additionally, there was mild tubular necrosis along with lymphocyte hyperplasia at 50 mg/kg dose. Histology characteristics of Kidney of rats in the control group were normal.

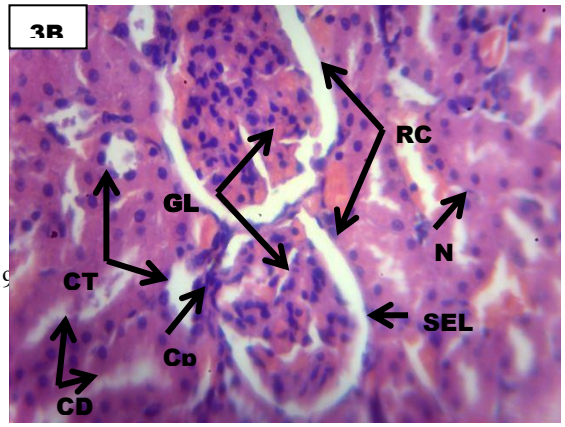












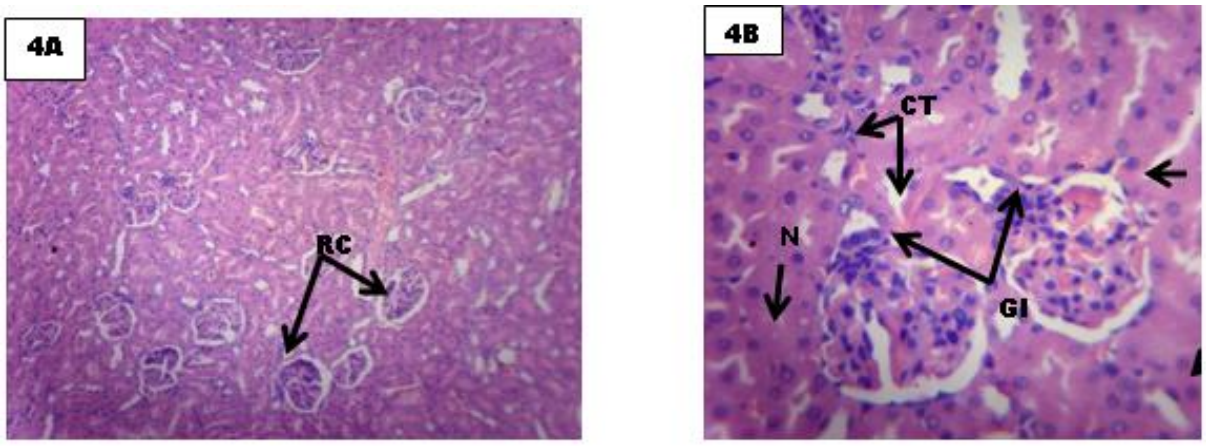


Plate XV: Histological sections of Kidneys of rats treated with Normal saline *10* ml/kg bw (1), LS 50 mg/kg bw (2), *LS 100* mg/kg bw (3) and LS 200 mg/kg bw (4) at magnification A (x100) and B(x400) Stained with H&E technique.

Keys: Renal corpuscle (**RC**) Convoluted tubules (**CT**), Collecting ducts (**CD**), Epithelial lining degeneration (**ELD**), Pyknotic nucleus **(Pn)** Glomerulus (**GL**), Nucleus (**N**) Tubular necrosis (**TN**) and vascular degeneration (VD)

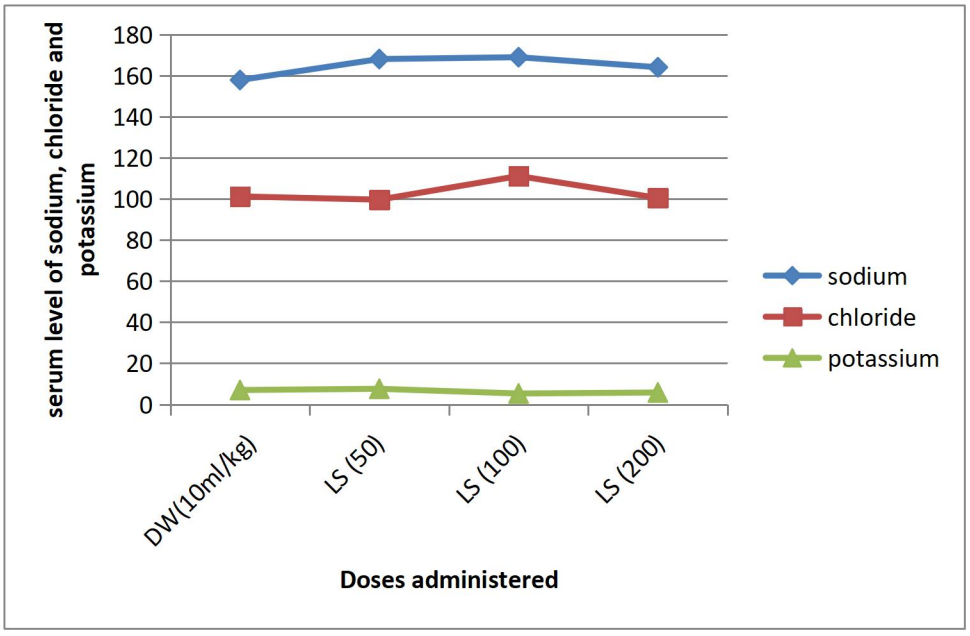


Fig 1: graph showingeffect of ethanol leaf extract of LSon rats' serum sodium, chloride and potassium levels.X axis represent doses administered while Y axis represent serum level of sodium, chloride and potassium.

Discussion

This study assessed how the plant affected the kidney after administering on rats for a period of time. When compared to the control group of rats, the ethanol extract of *Lavandula stoechas* caused a substantial decrease in the red blood cell, hemoglobin, and platelet counts.This suggested that the plant might affect the process and production of red blood cells, by shorten their life span, or affect how the body consumes iron. Anemia, or low red blood cell count, can make a person feel weak and worn out. The body has to work harder to supply enough oxygen to the cells when the red blood count is lower than normal. A low red blood cell (RBC) count can result in a wide range of symptoms and medical issues (Sabastine et al., 2021; Tosin et al., 2021).The blood's hemoglobin helps carry oxygen from your lungs to your tissues. In muscle cells, myoglobin takes up, stores, transports, and releases oxygen (Oyepata 2021). Additionally, the extract had no effect on the amount of basophiles, neutrophils, eosinophils, or lymphocytes. This suggests that the plant might not have an impact on the immune system

The study also demonstrated that while other parameters remained mostly unchanged, *Lavandula stoechas* slightly increased serum potassium ions and decreased serum sodium ions. This could suggest that the ethanol leaf extract of the plant does not affect electrolyte level when consumed for a sustained period. The extract had no effect on creatinine levels, indicating that itmay have no toxicological or therapeutic significant for causing or treating kidney-related disorders.According to several studies (Weinstein 1994; Joseph et al.; Kalantar-Zadeh et al., 2021; Kalantar-Zadeh et al., 2021),Some kidney diseases can cause an increase in creatinine level due to loss of the creatinine's normal excretory function, damage to the muscles, or after taking an unsuitable medication that interferes with the kidney's normal function (Simeon et al., 2022; Novick et al., 2006). Creatinine is mostly produced by tissue creatinine breakdown from endogenous sources (Thomas 2005). Also, in this study the level of Serum urea was unchanged when compared to the control group. .Serum urea concentration is frequently regarded as a more accurate indicator of renal function than serum creatinine. Serum/plasma urea concentration reflects the balance between urea production in the liver and urea elimination by the kidneys. An increased in plasma/serum urea can be caused by increased urea production, decreased urea elimination which affects the glomerular filtration rate, or a combination of the two(Oyepata and Simeon 2022; Maton et al., 1993). Result of the study suggests that the extract does not increase protein breakdown and has little significant on glomerular filtration rate. Hence, lethanol leaf extract of *Lavandulastoechas*does not affect the kidney functions.

The kidneys of the rats treated with *Lavandulastoechas*displayed slight

pathological symptoms of injury, including degraded microvesicles in the tubular lining cells among others, according to the histological results. Kidney sections of the control group rats examined showed normal glomeruli that were free of pathological symptoms. This agrees withother resultsprevious work (Weinstein 1994; Joseph et al.; Kalantar-Zadeh et al., 2021; Kalantar-Zadeh et al., 2021) and in that the extract may not possess severe toxicological significant when consumed for a particular period of time

Conclusion

The histological examination and biochemical parameters results revealed that *Lavandulastoechas* has chemical constituents that may somewhat modify the anatomical and physiological characteristics of the kidney, indicating that care should be taken while consuming it over an extended period of time.

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Conflict of interest

Author declares that there is no conflict of interest.

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