The Protective and Therapeutic Effect of Costus Specious on Some Liver Enzymes in Serum of Adult Male Rats that Treated with a Carbamazepine Drug

Dalal Awad Almuzaini, Hayat Ali Asmail and Haleema Yousef Alnahari

Physiology Department, Faculty of Science, Jeddah University, KSA
daldal-8@hotmail.com

Abstract: The aim of this study is to investigate the protective and therapeutic effect of Costus Speciosus against Carbamazepine toxicity on some biochemical parameters of liver. The rats were given carbamaze pine with a dose of 200 mg / kg, and the extract of the Costus Speciosus with a dose of 200 mg / kg. The following parameters were measured in blood serum: Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT) and Lactic Dehydrogenase (LDH). Carbamazepine caused an increase in serum, AST and LDH enzymes, while the protective and therapeutic effect of Costus Speciosus reduced these parameters to a level near to their normal values.
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Keywords: Carbamazepine, Costus Speciosus, Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT), Lactic Dehydrogenase (LDH). Liver.

1. Introduction

Carbamazepine was discovered by pharmacist Walter Schindler in Basel, Switzerland in 1953 [1], and was approved for seizure management in 1974 [2].

Carbamazepine is used primarily in the treatment of epilepsy and is effective in preventing simple and complex partial seizures and preventing them from becoming generalized seizures [3].

Scientists Foster et al [4] determined that chronic use of anticonvulsants leads to liver cell damage. Forbes et al. [5] reported that hepatic toxicity is known to be acute, serious and specific after carbamazepine.

Willmorem [6] confirmed that oxcarbazepine, a synonym for carbamazepine, affects liver enzymes when the dose is increased. Side effects of this drug have been reported on the liver. The liver is the main organ of the drug metabolism and the elimination of many antiepileptic drugs and therefore is toxic to drugs. There are a wide range of hepatic reactions, from mild and transient elevations of hepatic enzymes to hepatic liver failure [7]. Liver enzymes such as the enzyme alanine aminotransferase (ALT) and aspartate aminotransferase (AST) as a marker of hepatic injury [8].

Costusspeciosus is a medically important plant known as Wild ginger, which spreads spontaneously in South and Southeast Asia and is cultivated in India [9].

Costusspeciosus belongs to the Zingiberaceae family and is taken from the Costus plant, which is 1.5 meters long and has leaves, stems and roots. Costusspeciosus contains several active compounds, some of which have been identified: Saponins, Minerals, Alkaloid, Carbohydrates, Glycosides, Phenols & Vitamin C [10].

Costus has been found to have many medicinal activities, such as anti-bacterial, antifungal, anti-oxidant, anti-hyperglycemic and antihypertensive, while it is known to be anti-fertility and structural properties in the body [11].

The results of a study by Abdel-Maksoud et al. [12] found that the roots of Costus speciosus are effective against cancer and have a strong chemical protective activity against a wide range of tumors. The roots of the plant can improve biochemical measurements in the blood and prevent apoptosis.

2. Materials and Methods

1) Carbamazepine:

The animals will be given a dose of 200 mg / kg per day daily for 6 weeks [13].

2) Costus speciosus:

The animals will be given a dose of 200 mg / kg per day daily for 6 weeks [14].

Preparation of extract:

The roots of the Costusspeciosus were washed, dried and then grinded, Preparation of the extract by adding 100 ml of boiled water to 10 g of Costusspeciosus roots powder in a pot darked and cover it and leave it for 24 hours, Then filtratedand saved in dark glass at 4° [14].

3) **Experimental groups:**

1-The first group: control contains 5 rats given physiological solution daily for 6 weeks.

2-The second group: treatment with Carbamazepine contains 5 rats injected with a dose of 200 mg / kg per day daily for 6 weeks.

3-Protective group: containing 5 rats were given the extract of Costusspeciosus dose of 200 mg / kg per day for two weeks and then treated with Carbamazepine dose of 200 mg / kg daily for 4 weeks.

4-Therapeutic group: consisted 5 rats injected with Carbamazepine dose 200 mg / kg / day for 2 weeks and then administered with Costusspeciosus at a dose of 200 mg / kg daily for 4 weeks.

The animals to be sampled were weighed and they are 20 animals as of 5 animals from each group. Blood sampling was by animal slaughter and blood was collected in test tubes for each animal without adding anticoagulant and serum was extracted to be used in the required measurements.

Blood was collected then serum was distributed in small glass bottles for each animal and were kept in the freezer at:

-18°C to be used for biochemical measurements.

- Liver function includes measurement of Aspartate Amino Transferase (AST), Alanine Amino Transferase (ALT) and Lactate dehydrogenase (LDH).

Statistical study:

Mean will be calculated for control group and treated groups, also the standard deviation S.E. for means and T-Test at a 5% significant level.

3. Results

1) **Aspartate aminotransferase (AST):**

Table (1) and Figure (1) show the protective and therapeutic effect of Costusspeciosus200 mg / kg against carbamazepine damage 200 mg / kg on enzyme (AST) U/ L:

Where a significant decrease occurred in the sixthweek in both the protective group And the therapeutic group when compared to the control group And the carbamazepine-treated group.

2) **Alanine aminotransferase (ALT):**

Table (1) and Figure (2) show the protective and therapeutic effect of Costusspeciosus200 mg / kg against carbamazepine damage 200 mg / kg on ALT (U / L):

There was no significant effect in the sixth week in both the protective and therapeutic group when compared to the control group and the carbamazepine-treated group.

3) **Lactate dehydrogenase (LDH):**

Table (1) and Figure (3) show the protective and therapeutic effect of Costusspeciosus 200 mg / kg against carbamazepine damage 200 mg / kg on LDH (U / L):

There was a significant decrease in the sixth week in both the protective group and the therapeutic group when compared to the control group And the carbamazepine-treated group.

Table (1): The protective and theraputic role of Costus Speciosus (200mg/kg) on Aspartate Amino Transaminase (AST) (U/L), Alanine Amino Transaminase (ALT) (U/L) and Lactate Dehydrogenase (LDH) (U/L) in serum of adult male rats during 6 weeks.

	NO. Week	Control Mean ± S.E	Carbamazepine Mean ± S.E	Protective Mean ± S.E	Therapeutic Mean ± S.E
Aspartate Amino Transaminase (AST) (U/L)	6	35.63± 2.26	54.05± 3.53 [a]	26.08± 1.05[a,b]	27.55± 1.71[a,b]
Alanine Amino Transaminase (ALT) (U/L)	6	32.92± 3.20	43.62± 3.91	34.76± 1.59	34.68± 1.75
Lactate Dehydrogenase (LDH) (U/L)	6	872.93± 73.82	1201.54± 49.70 [a]	602.78± 60.26[a,b]	419.33± 20.99[a,b]

Statistical analyses were performed between control (C=5) and treated (T=5) animals by using:

a: Statistically significant ($p< 0.05$) compared to control.

b: Statistically significant ($p< 0.05$) compared to Carbamazepine.

Protective: 2 weeks of Costus Speciosus followed by 4 weeks of Carbamazepine.

Therapeutic: 2 weeks of Carbamazepine followed by 4 weeks of Costus Speciosus.

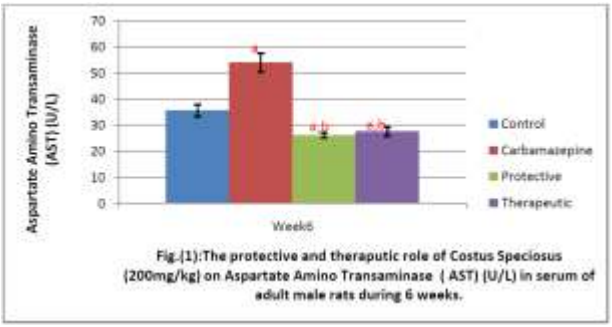

Fig.(1):The protective and theraputic role of Costus Speciosus (200mg/kg) on Aspartate Amino Transaminase (AST) (U/L) in serum of adult male rats during 6 weeks.

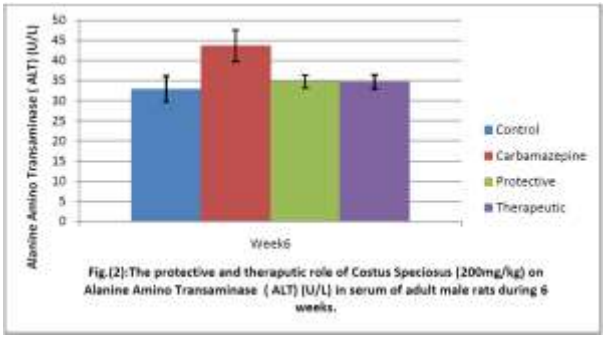

Fig.(2):The protective and theraputic role of Costus Speciosus (200mg/kg) on Alanine Amino Transaminase (ALT) (U/L) in serum of adult male rats during 6 weeks.

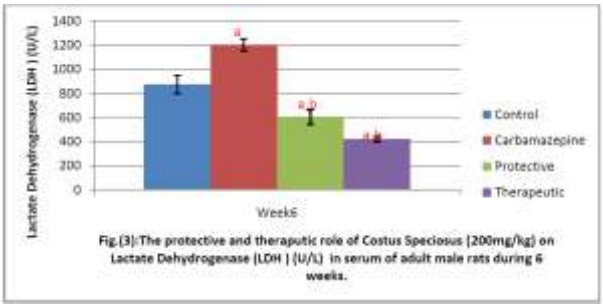

Fig.(3):The protective and theraputic role of Costus Speciosus (200mg/kg) on Lactate Dehydrogenase (LDH) (U/L) in serum of adult male rats during 6 weeks.

4. Discussion

The activities of serum liver function enzymes: aspartate aminotransferase (AST) and Lactate dehydrogenase (LDH) were increased by the Carbamazepine (Table1, Figure1,3).

That agrees with the studies of Ueda et al. [15] Which found that carbamazepine causes elevated level of ALT, AST in serum, and agrees with what was found by Callaghan et al. [16] and Cepelaket al. [17], that carbamazepine causes elevated level of AST in serum.

Cepelak et al. [17] and Benedetti et al. [18] reported that the Symptoms of elevation of liver enzymes rare and occur in 25-61% in patients taking carbamazepine.

CYP P450 is a family of 40-50 isoenzymes responsible for the biotransformation of several drugs. These isoenzymes are membrane proteins, which are located in the smooth endoplasmatic reticulum of several tissues. CYP3A4 and CYP3A5 represent 65% of isoforms in the cytochrome P450 enzyme system and they interact with more than 60% of licensed drugs [19].

CYP3A4 has the greatest abundance in the liver and intestine and is responsible for the metabolism of the largest number of clinically used drugs, as well as range of endognous substrates such as prostaglandines, steroid hormones and fatty acids. Carbamazepine is potent inducer of CYP 450 enzymes. Enzyme induction is mediated through the binding of one or more chemical activators to CYP isoenzyme intracellular receptors, ultimately producing increased transcription of CYP genes, increasing metabolism and increasing liver enzymes [20].

The results of the study showed a significant decrease in the level of LDH and AST enzymes in both the protective and therapeutic group when compared to the control group and the group treated with carbamazepine (Table1, Figure1,3). That agrees with the studies of Verma and Khosa [21] Where the Costusspeciosus caused a significant reduction and prevented a significant increase in levels of serum enzymes of AST, ALT in rat serum treated with carbon tetrachloride, The extract was effective in preventing liver toxicity caused by carbon tetrachloride. This effect is due to the availability of Saponin and glycosides associated with liver protection. These chemical compounds are the most common in the extract of the Costus.

El-Demerdash et al. [22] and Alamoudi et al. [23] found that the treatment of diabetic rats with the Costusspeciosus caused the restoration the level of enzymes AST, ALT to almost normal levels compared with the diabetic group in Which showed a rise in the level of these enzymes.

The results showed no significant effect of ALT level in both the protective and therapeutic group when compared with the control and the carbamazepine group (Table1, Figure 2). That agrees with the studies of El-Far and Abou-Ghanema [24] and Subasinghe et al. [25] That the extract of the Costus did not lead to a significant difference in the level of enzymes AST and ALT, which indicate that the extract did not harm the liver cells. Eliza et al. [26] reported the presence of two active chemical compounds costunolide and eremanthin isolated from the roots of the Costus and effective in reducing the elevation of AST, ALT. The study Nascimento [27] showed that the antioxidant effects of the Costus are not yet well known, but studies suggest that many types of Zinziberaceae it can remove free radicals.

Conclusions:

The present study demonstrated that The aqueous extract of Costusspeciosus was able to ameliorate some serum enzymes in Rats treated with carbamazepine, Therefore, this study recommends the

use of Costusspeciosus when taking anti-epileptic drugs To reduce the side effect of the drug on these enzymes.

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