

THE EFFECTS OF AQUEOUS LEAF EXTRACT OF *SYMPHYTUM OFFICINALE* (COMMON COMFREY) ON THE LIVER ENZYMES OF ADULT WISTAR RATS.

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ABSTRACT

Symphytum officinale (common comfrey) has been used as herbal to treat wounds and to decrease pain and inflammation. Its effect on the liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were the main focus of this study. Twenty wistar rats of an average weight of 219g were used for the study and were divided into four (4) groups (A, B, C and D) of five animals each. Group A served as the control and received 0.3ml of distilled water; the experimental groups B, C and D were orally administered 0.4ml, 0.6ml and 0.8ml of aqueous extract of *symphytum officinale* leaf for twenty eight (28) days respectively. Twenty four (24) hours, after the last administration, the animals were anaesthetized under chloroform vapour and dissected. About 5ml of blood was collected from animals in all the groups by cardiac puncture

using sterile syringe and needles, liver organs were also harvested and weighed, blood for serum preparation was collected into sterile plain tubes and stored in the refrigerator for analysis. The activities of serum aspartate aminotransferase (AST), Alanine aminotransferase

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(ALT) and alkaline phosphatase (ALP) were determined using radox kit method. The results showed that there was a significant increase ($P < 0.005$) in the activity levels of aspartate aminotransferase (AST), alanine aminotransferase, (ALT), and alkaline phosphatase (ALP) in groups C and D relative to group A (Control). Alkaline phosphatase (ALP) activity level of group B also increases significantly. Group B also recorded a little increase in activity levels of AST and ALT but it is not statistically significant. Thus, chronic consumption of aqueous extract of *symphytum officinale* (common comfrey) may cause biochemical alterations in the liver enzymes.

KEYWORDS: *Symphytum officinale*, Wistar rats, Blood samples, liver organ, Biochemical alterations.

INTRODUCTION

Liver involve almost in all biochemical pathways related to growth, fight against disease, nutrient supply, energy production and reproduction. Because of it unique metabolism and relationship to the gastrointestinal tract, the liver is an important target for toxicity produced by drugs, xenobiotics, and oxidative stress.^[1]

Liver is the largest, complex organ that is well designed for its central role in metabolizing different food products. The position of liver in the circulatory system is optimal for gathering, transforming and accumulating metabolic and for neutralizing and eliminating toxic substances.^[2]

Researchers have shown that herbal extracts including spices, have the potential to produce adverse effects, especially when used in concentrated forms. Further, these products may interact with other herbal products as well as drugs^[3] and more than 900 drugs, toxins and herbs have been reported to cause liver injury and drugs account for 20-40% of all instances of fulminant liver failure.^[4]

In modern herbalism, comfrey is most commonly used tropically, some expert said that comfrey should be restricted to tropical use, and should never be ingested, as it contains dangerous amounts of hepatotoxic pyrrolizidine alkaloids (PAs).^[5, 6]

Pyrrolizidine alkaloids (PAs, sometimes referred to as necine bases) are a group of naturally occurring alkaloids been on the structure of pyrrolizidine, Pyrrolizidine alkaloids are produced by plants as a defense mechanism against insect herbivores. More than 660 PAs

and PA N-oxides have been identified in over 6,000 plants, and about half of them exhibit hepatotoxicity.^[7]

The most serious risk of pyrrolizidine alkaloid poisoning in herbal practice in the U.S. appears to be the use of comfrey root for chronic digestive conditions. Such treatment assumes long-term use, and patients are often weakened from the disease. At least one company has recently removed comfrey from its Robert's formula; a traditional anti-ulcer formula. The lack of warning information about consumption during pregnancy and for small children is also cause for concern. It should be noted that the Henry Double day Research Association (growers & marketers of comfrey in the United Kingdom) issued a public statement 1978 which concluded that until further research clarifies the long-term health hazard from comfrey injection, no human being or animals should eat, drink or take comfrey in any form.^[8]

MATERIALS AND METHOD

Breeding of Animals

Twenty healthy adult wistar rats were procured from the animal house of Department of Applied Biochemistry, Faculty of Biological Sciences, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria. They were allowed to acclimatized under normal temperature (29°C – 31°C) for a period of seven days, before their weight were taken and recorded. They were fed with normal rat feed pellets from livestock feed Nig. Ltd. Lagos, Nigeria.

Drug Preparation

Common comfrey (*symphytum officinale*) leafs were plucked from Okitipupa in Ondo State. It was identified at herbarium unit, Botany Department, Nnamdi Azikiwe University, Anambra State. It was sun-dried and then milled to a powder. 300mg/kg body weight was dissolved in 10mls of distilled water and administered to the animals.

Experimental Protocols

Twenty healthy adult wistar rats were weighed and allocated into four groups (A, B, C & D) of five animals each. Group A serve as the experimental control and administered 0.3ml of distilled water, the experimental groups B, C and D received 0.4ml, 0.6ml & 0.9ml of aqueous extract of *symphytum officinale* (Common comfrey) leaf orally respectively for twenty eight days. After the last administration (24 hours), the animals were weighed and recorded. Animals were sacrificed using chloroform inhalation method. About 5ml of blood

was collected from all the groups through cardiac puncture using sterile syringes and needles. Blood for serum preparation was collected into sterile plain tubes without ant-coagulant. Serum samples were separated into sterile plain tubes and stored in the refrigerator for analysis. The activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) & alkaline phosphatase (ALP) were determined using randox kit method. Liver tissues were also removed and weighed.

RESULT

Morphometric Analysis of Body Weight

Table 1: Comparison of mean initial, final body and weight changes in all the groups (A, B, C and D).

(Meant \pm SEM given for each measurement)

Groups	Group A	Group B	Group C	Group D	F-Ratio	Prob. of Sig.
Initial body Weight	179.20 \pm 2.10	182.60 \pm 2.10	87.30 \pm 4.30	193.21 \pm 2.60	50.170	<0.005
Final body Weight	200.10 \pm 3.40	196.70 \pm 4.30	76.40 \pm 1.70	171.30 \pm 1.40	38.140	<0.005
Weight changes	20.90 \pm 1.30	14.30 \pm 2.20	-10.90 \pm 2.60	-21.91 \pm 1.20	8.310	<0.005

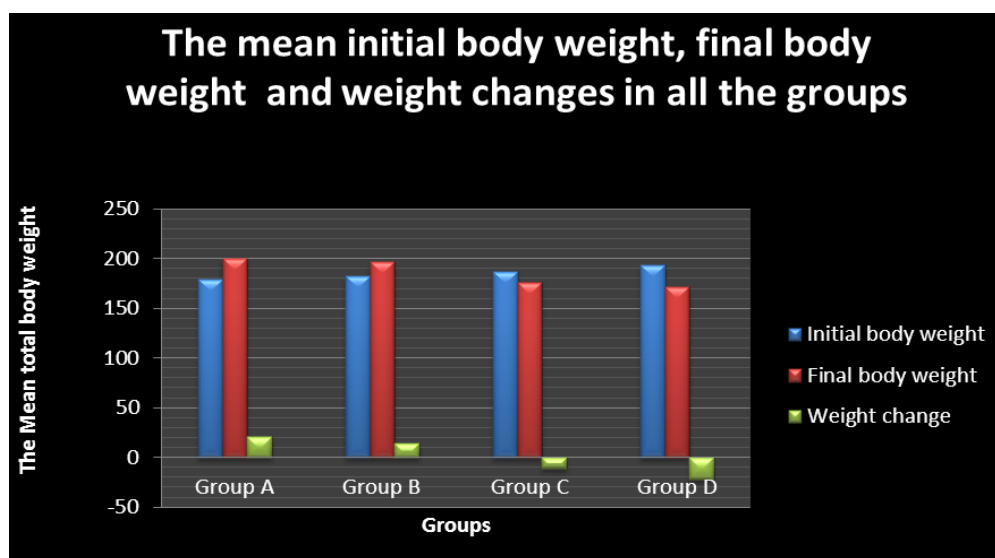


Figure 1: Bar chart showing the mean initial body weight, final body weight and weight changes in all the groups

Morphometric Analysis of liver weight

Table 2: Comparison of mean relative liver weight of all the groups (A, B, C and D).

(Meant \pm SEM given for each measurement)

Groups	Group A	Group B	Group C	Group D	F-Ratio	Prob. of Sign.
Liver Weights	4.30 \pm 0.141	4.33 \pm 0.310	4.49 \pm 0.120	.75 \pm 0.430	43.60	<0.005

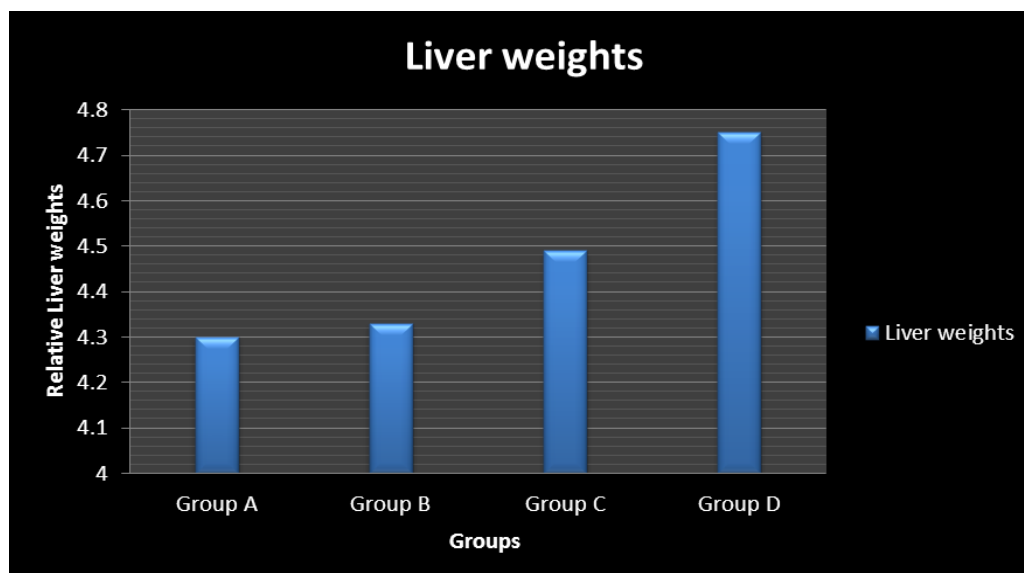


Figure 2: Bar chart showing the organ weights of all the groups

Activities of Serum Levels of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP).

Table 3: Comparison of activities of serum levels of AST, ALT, and ALP in all the groups (A, B, C and D).

(Mean + SEM given for each groups)

Groups	Group A	Group B	Group C	Group D	F- Ratio	Prob. of Sign
AST	81.30 \pm 4.10	83.10 \pm 2.60	88.90 \pm 4.90	95.00 \pm 2.10	36.30	<0.005
ALT	70.30 \pm 3.10	73.90 \pm 3.20	81.30 \pm 4.00	89.10 \pm 1.60	43.10	<0.005
ALP	160.30 \pm 3.70	163.10 \pm 2.50	174.10 \pm 4.10	189.10 \pm 5.30	15.00	<0.005

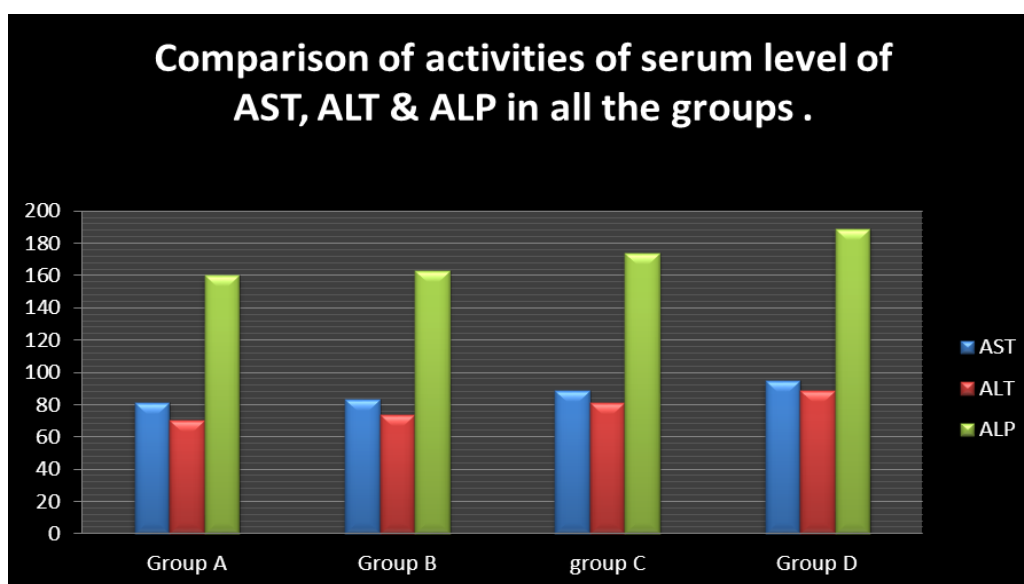


Figure 3: Bar chart showing the activities of serum level of AST, ALT, & ALP in all the groups.

DISCUSSION

The debate on the toxicity of comfrey and coltsfoot for internal use pits traditional herbalists against regulatory agencies. The traditional herbalist argues that these plants have been widely used for centuries without any absorbed ill effects. Regulatory containing plants, and comfrey and coltsfoot in particular, have caused liver disease in humans. Most cases of pyrrolizidine alkaloid poisoning in the scientific literature have involved third-wools epidemics among people who consumed contaminated grain over a long period.^[9, 10, 11, 12]

In 1985 and 1987, cases appeared in which comfrey (*S. Officinale*) itself was the offending agent.^[13, 14] Other articles have appeared which analyzed various commercially available comfrey product and showed that they had sufficient levels of pyrrolizidine alkaloids to cause toxicity with long term use.^[15, 16, 17]

It has been demonstrated that comfrey leafs (*S. Officinale*) and coltsfoot (*T. Farfara*-buds) have both caused liver tumors when introduced into the diets of mice.^[18, 19]

In the present study, the mean body weight result revealed decrease body weight in groups C and D with high dose of aqueous extract of *symphyntum officinale* while group B with low dose of aqueous extract of *symphyntum officinale* increase significantly with control group A.

The mean relative organ weight results revealed significant increase ($P < 0.005$) in groups C and D while group B had similar value with the control group A.

The comparison of activities of serum levels of the enzymes results showed that the level of aspartate aminotransferase (AST), alanine aminotransferase and alkaline phosphatase (ALP), increased significantly ($P < 0.005$) when compared with the control while group B (treated with low dose of aqueous extract of *symphyntum officinale* (common comfrey) level of aspartate aminotransferas (AST), alanine aminotransferase (ALT) and alkaline phosphate (ALP) were statistically similar with control group A.

CONCLUSION

From this study we therefore inferred that consumption of *symphyntum officinale* in low dose is not harmful to the liver but when consumed at high dose and over a long period of time could cause liver failure or damage. This is also seen from the elevated liver enzymes level which is one of biochemical indicator of liver injury. Thus, consumption of *symphyntum*

officinale in large amount caused injury to liver cells with subsequent release of these enzymes into the blood stream.

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