The effect of aqueous leaf extract of *Symphytum officinale* (common comfrey) on the liver of adult wistar rats


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**ABSTRACT**

The aim of this study is to investigate the effect of aqueous extract of *symphytum officinale* leaf (common comfrey) on the liver of adult wistar rats. Twenty adult wistar rats of an average weighing 219g were used for the study. They were apparently divided into four groups of five animals each. Group A served as the experimental control and were orally administered 0.3ml of distilled water; the experimental groups B, C & D were orally received 0.4ml, 0.6ml and 0.8ml of aqueous extract of *symphytum officinale* leaves for twenty eight (28) days respectively. Twenty four hours after the last administration, the animals were weighed and weights were recorded. The animals were sacrificed under the influence of chloroform vapour and dissected. The liver organ were harvested, weighed and trimmed down to a size of 3mm x 3mm and fixed in 10% formalin for histological studies. The results of this study revealed that consumption of *symphytum officinale* in low dose or small amount had no effect on the histological appearance of the liver but when consumed in high dose or excessive induced mild distortion of histological liver appearance which includes mild central vein hypertrophy, increased cellularity and periportal fibrosis of liver cells.

**Keywords**: *Symphytum Officinale*, *Wistar Rats*, Liver Weight, Distilled Water, Body Weight

**INTRODUCTION**

The world Health Organization (WHO) estimates that 80 percent of the population of some Asian and African Countries presently uses herbal medicine for some aspect of primary health care. Many of the pharmaceuticals currently available to physicians have a long history of use as herbal remedies, including opium, aspirin, digitalis, and quinine.

According to the world Health Organization approximately 25% of modern drugs in the United States have been derived from plants (World Health Organization, 2008). At least 7000 medical compound in the modern pharmacopoeia are derived from plants (Interactive European Network for industrial Crops and their Application, 2000-2005). A number of herbs are thought to be likely cause adverse effects (Talalay, 2001). Further, “adulteration, in appropriate formulation, or lack of understanding of plant and drug interactions have led to adverse reactions that are sometimes life threatening or lethal (Elvin-Levis, 2001).

Contemporary herbalists have a mixed view of comfrey, despite widespread historical use. Its traditional names of kritbone, boneset and the derivation of its Latin name *symphytum* (from the Greek Symphys, Meaning growing together of bones, and phyton, a plant) speak to its long standings reputation as a therapeutic herb (Staiger, 2013; Yarnell, 1999).

The plant contains the small organic molecule allantoin, which is thought to stimulate cell growth and repair while also depressing inflammation (University of Maryland Medical Center, 2012).
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More than 900 drugs, toxins and herbs have been reported to cause liver injury. Attempts are made globally to get scientific evidence for these traditionally reported herbal drugs. This scenario provides a necessity to carry out research on hepatotoxicity (Jaeschke et al., 2002). Therefore, this study aims at investigating the effect of aqueous leaf extract of *symphytum officinale* (common comfrey) on the liver of adult wistar rats.

MATERIALS AND METHODS

Breeding of Animals
Twenty four apparently healthy adult wistar rats were purchased from the animal house of Anatomy Department, University of Calabar, Cross River State, Nigeria and bred in the animal house of University of Uyo, Akwa Ibom State. The rats were maintaining ad libitum on water and growers mash bought from Nkwo Nnewi Market Anambra State, they were acclimatized for two weeks under normal temperature (27°C-30°C) before the experiment. Ethical committee permission was gotten from Faculty of Bioscience Nnamdi Azikiwe University Ethical committee.

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
The twenty adult wistar rats were weighed and allocated into four groups (A, B, C & D) of five animals each. Group A served as the control while the other groups (B, C & D) serve as the test groups. The animals were fed with grower mash; a product of livestock feed Nig. Ltd. Lagos, Nigeria. The experiment lasted for twenty eight days (28) and throughout the duration of the experiment, Group A was fed with 72g of normal feed (grower mash without *symphytum officinale* extract) while test groups B, C and D were fed with 72g grower mash plus 0.4ml, 0.6ml & 0.8ml of aqueous extract of *symphytum officinale* leaf (common comfrey) respectively for each day. Twenty four hours after the last administration, the animals were weighed and recorded. The animals were then sacrificed under the influence of chloroform vapour and dissected, liver organ were harvested and weighed.

Tissue Processing
For easy study of sections under microscope, the tissues passed through several processes of fixation, dehydration, clearing, infiltration, embedding, sectioning and staining. Fixation was carried out in 10% formal saline for 10 hours. After fixation, the tissue washed in stream tap water. Dehydration of fixed tissue was done using ascending grade of alcohol, 50%, 70%, 90% and 95% absolute alcohol. The tissue was clear in xylene after which infiltration was done in a molten paraffin wax at 60°C for two hours each in two changes. The embedding of the tissue was done in molten paraffin wax and was sectioned afterwards. Haematoxylin and eosine method was used in staining.

Statistical Analysis
The data of this study were analyzed using T-test of SPSS version 16 software packages and P<0.005 was considered as the level of significance.

RESULTS AND DISCUSSION

Physical Observation
The animals used during this experiment were thoroughly observed and all survived to the end, except the animals in groups D which appeared weak and less active at the later stage of the experiment.

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Morphometric Analysis of Body Weight

Table 1: The result obtained from calculation of initial, final and weight changes of the various groups are presented in the table below (Mean ± SEM Given for Each Measurement)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
<th>F-Ratio</th>
<th>Prob. of Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Body Weight</td>
<td>177.40±3.10</td>
<td>180.70±1.10</td>
<td>186.30±3.00</td>
<td>191.30±3.30</td>
<td>60.010</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Final Body Weight</td>
<td>200.00±3.70</td>
<td>196.70±2.10</td>
<td>174.60±2.60</td>
<td>168.00±1.40</td>
<td>47.360</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Weight Changes</td>
<td>22.60±0.60</td>
<td>16.00±0.40</td>
<td>-11.70±0.10</td>
<td>-23.30±1.90</td>
<td>11.310</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

The mean initial body weight, final body weight and weight changes in all the groups

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 & D). (Mean ± SEM Given for Each Measurement)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
<th>F-Ratio</th>
<th>Prob of Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver weight</td>
<td>5.28±0.310</td>
<td>5.31±0.316</td>
<td>5.47±0.140</td>
<td>5.64±0.561</td>
<td>41.30</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>
Histopathological Findings

Photomicrograph 1: (Control group A) showing normal architectural structure of the liver-central vein surrounded by hepatocytes, with sinusoids

Figure 2: Bar chart showing the organ weights of all the groups
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Photomicrograph 2: (Group B, treated with 0.4ml of aqueous extract of *symphytum officinale*) showing normal liver architecture, displaying normal central vein and hepatocytes.

Photomicrograph 3: (Group C, treated with 0.6ml of aqueous extract of *symphytum officinale*) showing hypertrophy of central vein and increased cellularity.
Photomicrograph 4: (Group D, treated with 0.8ml of aqueous extract of *Symphytum officinale*) showing periportal fibrosis and hypertrophied hepatocytes of the liver tissues

**Discussion**

Comfrey was historically used to treat a wide variety of ailments ranging from bronchial problems, broken bones, sprains, arthritis, gastric and varicose ulcers, severe burns, acne and other skin conditions. It was reputed to have bone and teeth building properties in children, and have value in treating “many female disorders” comfrey plants constitute mucilage, steroidal saponins, tannins, pyrrolizidine alkaloids, inulin and proteins (Nick, 2014).

Studies associating comfrey with veno-occlusive disease (VOD), do not differentiate between Russian and common comfrey, plants with different level of pyrrolizidine alkaloids (PAS). Veno-occlusive disease (VOD) can in turn lead to liver failure and comfrey has been implicated in at least one death, though type of comfrey being consumed, and other dietary, physiological and pharmacodynamic factors were not accounted for (Stallings, 2014).

In 2001, the United State Food and Drug Administration issued a ban of comfrey product marketed for internal use, and warning label for those intended for external use (FDA/CFSAN-FDA, 2009; Koll and Khingenburg, 2002). In additional to restriction on oral use, some expert recommended applying comfrey extracts no longer than 10days in a row, and no more than 4-6weeks a year (University of Maryland Medical Center, 2012; Stickel, 2000).

It has been reported that comfrey plants (*Symphytum officinale*) contain pyrrolizidine alkaloids (Hirono and Mori, 1979); pyrrolizidine alkaloid poisoning causes a liver disorder in humans called hepatic veno-occlusive disease. The small and medium veins in the liver become obstructed, eventually leading to liver dysfunction, cirrhosis and death. Break down product of the pyrrolizidine alkaloids appear to bind to tissue in the liver, causing cell dysfunction and blockage of the veins by a proliferation of connective tissue (Maltocks, 1968).

In the present study, the final body weight of groups C and D decrease significantly (P<0.005) when compared with the control while group B Increase significantly (P<0.005) with the control group A.

The mean relative organ weight of groups C and D increase significantly when compared with the control while group B was statistically similar with control group A.
The histological findings revealed hepatocellular hypertrophy, periportal fibrosis and hepatrophied hepatocyte in the liver cells of groups C and D when compared with the control while group B showed normal cyto-architecture of the liver tissue.

**Conclusion**

From this present study, we therefore inferred that consumption of *symphytum officinale* (common comfrey) in low dose is not harmful to the liver but when consumed at high dose over a long period of time could cause histopathological lesions to the liver cells (hepatocytes).

**REFERENCES**


University of Maryland Medical Center (2012). *Comfrey* (University Press) 121-125.
