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ORIGINAL ARTICLE

Hepatoprotective Role of Virgin Coconut Oil and Neem Extract in Acetaminophen Induced Liver Toxicity

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ABSTRACT

Aim: To study the comparative hepatoprotective effect of Virgin Coconut Oil (VCO) and Neem (Azadirachta indica) leaf extract in acetaminophen (Paracetamol) induced liver toxicity.
Methods: About 60 mixed population of rats (male/female) of Wistar and Sprague-Dawley species were randomly selected for the proposed study and are segregated into four equal groups. Every group contains 15 animal subjects. Group A was the control group given normal diet. In Group B, the rats were treated with a single dose of 2gm / kg body weight paracetamol, orally. Simultaneously, Group C were given an oral Neem extract of 500mg/kg body weight for 2 weeks days in combination with single dose of Paracetamol, while Group D were provided with 6.7ml/Kg/body weight Virgin Coconut Oil (VCO) for 15 days. Data was analyzed using SPSS Version 20.0 with level of significance being kept at p-value ≤0.05.
Results: The mean values of ALT were 23.1, 100.5, 29.85, and 31.09 U/L in Group A, B, C, and D respectively. While, the mean values of AST were 25.6 U/L (Group A), 41 U/L (Group B), 19.3 U/L (Group C), and 15.2 U/L (Group D). The ALP showed maximum response indicated by the mean values of 221 U/L, 444 U/L, 241 U/L, and 243 U/L in Group A, B, C, and D respectively. Group B suggested the paracetamol induced liver toxicity indicated by the increase in hepatic DMEs right after the acetaminophen induction.
Conclusion: Azadirachta Indica and Virgin Coconut Oil displayed hepatoprotective effects on the Wistar and Sprague-Dawley rats that were subjected to Paracetamol.
Keywords: hepatic, Drug Metabolizing enzymes, Acetaminophen, Virgin coconut oil, Neem extract, Paracetamol, Wistar

INTRODUCTION

Liver is a vital organ in a human body and it plays a significant role in the drug metabolism and its regulation in the body. A group of enzymes called Drug metabolizing enzymes (DMEs) are activated while detoxifying a drug or Xenobiotics (non-self-exogenous substances unrecognized by the body). Body does this process for its maintenance or homeostasis. A change in the homeostasis cycle generates Reactive Oxygen Species (ROS) or lipid peroxidation that in return builds oxidative stress and liver dysfunctioning inside the body, making it toxic and vulnerable. Some drugs (such as Acetaminophen) are very dangerous for the liver[1]. It must be consumed in the prescribed doses (<4000 milligrams or 4 grams per day), otherwise it may pose serious liver damages (like liver cirrhosis, acute liver damage, liver failure etc.) and sometimes can be fatal too[2].

Acetaminophen (AAP) induces liver impairment by suppressing the immune system, making the body hypertensive and contributing to the hepatocytes necrosis. Therefore, it is the need of an hour to upright such destructive effects and to save the body from such deadly repercussions as indicated in the schematic representation of Fig. 1[3].

Virgin Coconut Oil (VCO) has many unique attributes and health benefits; therefore, it is recommended by many scientists and medical practitioners for public use. Virgin Coconut Oil is also a potent and naturally occurring anti-oxidant[4]. It is the best source of phytochemicals such as terpenoids, flavonoids, Polyphenols, triglycerides etc. which are used to treat the cellular damages and in improving the immune responses. Recently, it's Hepatoprotective, cardio-protective and anti-microbial responses has gained much attention[5,6].

Azadirachta indica (A. indica) commonly referred to as neem plant is also a traditional medicinal plant found in South-Asia. It is used extensively by the local residents because of its several therapeutics activities such as in treating fevers, syphilis, ulcers, diabetes, cancers, chest, and liver infections etc[7,8].

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Treatment of hepatotoxicity is possible by using natural products such as Virgin coconut oil and Neem extract. They are easily available and can be used in diet to supplement the cellular toxicity and cell damage. These natural products have the ability to neutralize the free radicals or reactive oxygen species (ROS) that are responsible for the lipid peroxidation and liver dysfunctioning[9]. Thus, it is a common consensus that drug-Induced hepatotoxicity can be reversed by using natural compounds from neem extracts and VCO.

This study aims to explore the therapeutic role of natural and organic products like VCO and Neem extract in reducing the acetaminophen-induced hepatotoxicity[10].

METHODOLOGY

Total 60 (male and female) Wistar and Sprague-Dawley strains weighing 150-250gms were randomly obtained from the Animal House of Indus Medical College, Tando Muhammad Khan, after taking the approval of institutional Ethical Committee. The designed experiment was conducted for about 6 months in the Anatomy Department of Indus Medical College, Tando Muhammad Khan after permission from IRB. All the experimental subjects were divided into four groups such that every group contains 15 individuals. They were kept at room temperature (+/-25°C) with relative humidity (45 to 55%), and 12/12 h light/dark cycle. Following therapeutic groups were made.

Group A: It is the control group for validating the experiment. The individuals of this group were injected with Normal saline (1 unit each) along with the regular normal diet.

Group B: In this group, the experimental animals were injected with single dose of Paracetamol at 2gm/Kg body weight oral dose in their intraperitoneal cavity.

Group C: Rats of this group were treated with an oral Neem extract of 500 mg / kg body weight for 2 weeks days in combination with single dose of Paracetamol (2gm/Kg by b/w).

Group D: This group comprises of the animals that were fed with 6.7ml/Kg/body weight Virgin Coconut Oil (VCO) for 15 days.

All the subjects after above-mentioned treatment were kept overnight (24 hrs.) of observation followed by the withdrawal of

blood samples from the representatives of each group to analyze the hepatic Drug Metabolizing Enzymes (i.e., AST, ALT, ALP), biochemically.

Neem leaves used in this experiment were purchased from the local nursery of Tando Muhammad Khan, Pakistan. They were rinsed thoroughly before induction to wash-away any possible contaminant that may cause hindrance in the experiment. The sterilization of neem leaves involved the fine cutting of leaves and washing them with double distilled water. Afterwards, they were boiled (~100°C) for 30 minutes. The temperature was then lowered and the extract was cooled followed by the filtration using Whatman's filter paper. The filtrate was then used to fed the respective group. The data of the liver enzymes (ALT, AST, and ALP) was evaluated through one way ANOVA. Data was analyzed using SPSS Vr 20 with level of significance being kept at p-value ≤0.05.

RESULTS

Figure1 suggested the trends of three Drug Metabolizing Enzymes (DMEs) i.e., Alanine transaminase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase (ALP). It was observed that there was a significant increase in their activities in Group B when they were induced with acetaminophen (Paracetamol) toxicity. Simultaneously, the activity of these liver enzymes was reduced in the later groups, showing the therapeutic effects of Virgin Coconut Oil (VCO) and Neem (Azadirachta indica) leave extracts. Table 1 shows mean value of significance of three tested DMEs in liver (ALT, AST, ALP). The mean cut-off values validating the results taken were P=<0.05.

Figure 1: Activity of Drug Metabolizing Enzymes (DMEs) in different therapeutic groups (U/L).

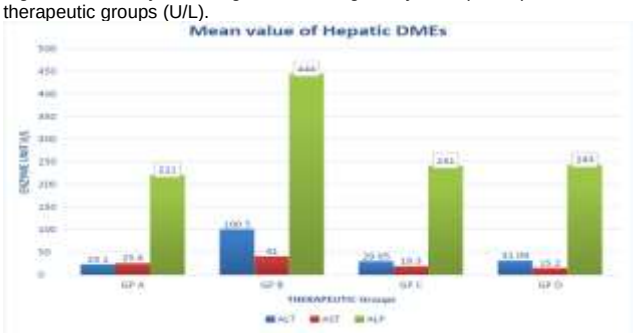

Table 1: Indicating the Level of significance of hepatic DMEs among different therapeutic groups

Hepatic biomarkers	GP B vs A	GP B vs C	GP B vs D
ALT	≤0.001	≤0.001	≤0.001
AST	≤0.001	≤0.001	≤0.001
ALP	≤0.001	≤0.001	≤0.001
One way ANOVA (post hic Tukey's test) applied P=<0.05 Liver Biomarkers: ALT: ALANINE TRANSAMINASE, AST: ASPARTATE AMINOTRANSFERASE, ALP: ALKALINE PHOSPHATASE			

DISCUSSION

Liver is the centralized organ of the body where all the toxic content is catabolized and then processed for further absorption in the Gastro-Intestinal (GI) tract. Every drug is metabolized in liver in the similar fashion. Liver is susceptible to acetaminophen (AAP) induced hepatotoxicity. Paracetamol is responsible for the same causing reduction in the levels of COX enzyme in liver, which ultimately instigate the production of radical intermediates triggering cellular damage (necrosis) of kidney and liver cells. Meanwhile, the body is getting deprived of the Glutathione (GSH) leading to the development of oxidative stress which eventually causes the hepatocytic apoptosis.

Virgin Coconut Oil (VCO) is one of the most widely used organic plants in Pakistan that is involved in the phytotherapy. It exhibits medicinal properties such as anti-oxidant, anti-microbial, anti-inflammatory, anti-hypercholesterolemia, and anti-thrombotic activities due to the presence of antioxidants. The anti-oxidative enzymes in VCO are responsible for the reduction in lipid peroxidation. Tocopherols, Sterols and Squalene are the most active constituents of Virgin Coconut Oil (VCO). The polyphenols present in Virgin coconut oil have the tendency to capture free radicals generated by the metabolism of unwanted xenobiotics, resulting in the production of N-acetyl-p-benzoquinone imine (NAPBQI), its by-product which is again the subsequent response of acetaminophen over-dosage.

Neem (Azadirachta indica) leave extract displayed the similar responses as VCO. The damage caused by the free radicals generated by the metabolism of metabolic waste is neutralized by the anti-oxidants present in these natural products, providing protection to hepatocytes. Experimental subjects of both the groups i.e., Group C and D displayed the significant potent antioxidative efficacy and hepatoprotective potency of the used natural extracts as demonstrated by P-value ≤0.05 in comparison with the Group B. The levels of Drug metabolizing Enzymes (DMEs) i.e., ALT, AST, and ALP were reduced significantly in these therapeutic groups showing the anti-oxidative strength of neem extract and VCO that scavenges the NAPQI molecules to reduce the chronic hepatocellular damage.

Moreover, the combine effect of Virgin Coconut Oil and neem (Azadirachta indica) leave extract can further explain the exact mechanism of how these liver enzymes functions to restrict the parenchymatous cell formation inside the liver. The association between these natural products and DMEs to limit the hepatocellular death (necrosis and apoptosis) can be further studied with the histological point of view that will confirm the regenerative potential of these natural extracts.

CONCLUSION

Acetaminophen such as Paracetamol is threatening to the hepatocytes. Whereas, the anti-oxidative potential of Azadirachta Indica and Virgin Coconut Oil can be utilized to reduce the drug induced hepatotoxicity.

Conflict of interest: None to declare

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