Antioxidant effect and protects the Turnip Root on Liver Enzyme Changes in Rats Undergoing Chemotherapy with Cyclophosphamide

1 Davari Hamideh, 2alaeyan Jahromi Nahid, 3alaeyan Jahromi Zahra, 4Jamali Houshang, 5alaeyan Jahromi Majid, 6alaeyan Jahromi Ali Reza

ABSTRACT

Background and purpose: Cyclophosphamide is an anticancer drug that passes through the blood-brain barrier. Turnip extract contains some antioxidants such as flavonoids, vitamin C and many others, and eliminates free radicals produced from the metabolism of other compounds in the body. The purpose of this study was to evaluate the antioxidant and protective effects of turnip roots on the liver and on changes in liver enzymes of rats undergoing chemotherapy with cyclophosphamide.

Materials and methods: In this study, 36 large laboratory rats (200 g) of the Vistar race were divided into six equal groups. The control group did not receive any solvent or drug. The sham group received 0.2 ml of the drug solvent by intraperitoneal injections. The experimental group I received the hydroalcoholic extract of turnip with the dose of 250 mg/kg/B.W. by gavage. The experimental group II was given cyclophosphamide with the dose of 5 mg/kg/B.W., and the experimental groups III and IV cyclophosphamide with the dose of 5 mg/kg/B.W. by intraperitoneal injections and 125 and 250 milligrams per kilogram of body weight of turnip extract, respectively, by gavage for 21 days. Results: Concentrations of the enzyme alanine aminotransferase (ALT) in the experimental groups II and III, and of the enzymes aspartate aminotransferase (AST) and alkaline phosphatase (ALP) in the experimental group II increased significantly compared to the control group (p<0.01). Moreover, serum protein in the experimental groups II and III and serum albumin in the experimental group II significantly increased compared to the control group at the five percent probability level.

Conclusions: Turnip extract has antioxidant properties and somewhat decreases the negative effects of cyclophosphamide. Therefore, it is recommended that turnip extract be used to reduce toxicity resulting from the administration of cyclophosphamide to cancer patients.

KEY WORDS: turnip, cyclophosphamide, liver enzymes, antioxidant.

INTRODUCTION

Cyclophosphamide is one of the alkylating agents that are widely used as anticancer drugs (Androli, T., et al., 2007), and has been administered for the treatment of the nephritic syndrome and multiple myeloma too (Bennett, RN., et al., 2006). In rats, cyclophosphamide causes apoptosis in cancer, embryonic, lung, and thymus cells (Das, UB., et al., 2002; DeLeve, L.D., 2003). Although this drug has good anticancer properties and reduces tumor volume, its high doses weaken the body’s immune system. This usually leads to suppression of immunological responses, causes the growth of opportunistic infections, and results in recurrence of the cancer (Diasio, RB. and LO.AF. Buglio, 2003; Ghosh, D., et al., 2002). Despite the benefits derived from using this drug against various cancers, researchers have proved its administration is associated with adverse side effects and complications for various organs of the body such as the liver and the kidneys (Hassanzadeh, H., 1991). Medicinal compounds, especially those of plant origin that can neutralize the pathologic effects of cyclophosphamide, may be used in treating patients, and for people who take this group of drugs, to reduce complications.
Turnip (Brassica rapa L.) contains compounds including glucosinolates and phenolic substances such as flavonols and hydroxycinnamic that are antioxidants and eliminate free radicals and inhibit the activity of toxic cyclophosphamide metabolites in the body (Jung, UJ., et al., 2008; Katzung, et al., 13378). Antioxidant properties of turnip extract are due to the presence of phenolic compounds such as flavonoids. Phenolic compounds destroy and suppress free radicals and thus play their antioxidant role (Kern, JC., JP. Kehrer, 2002). Given the importance of the liver, and considering the high prevalence of liver diseases, this research was conducted with the purpose of evaluating the antioxidant and protective effects of turnip roots in reducing toxicity resulting from the administration of cyclophosphamide on liver enzymes in rats undergoing chemotherapy.

MATERIALS AND METHODS

Large lab rats (200 ± 200 grams) of the Vistar race used in this research were provided by the Islamic Azad University of Jahrom. They were randomly divided into the following six groups of six: the control, the sham, and the experimental groups I- IV. Each group was kept in a separate cage.

Drug preparation and injection:

After adding distilled water to cyclophosphamide powder and preparing the suspension, 5 mgs/kg/B.W. of the suspension were injected daily with an insulin syringe into the peritoneum of each rat for 21 days.

We washed 100 grams of fresh turnip roots thoroughly with clean water, sliced, and extracted the turnips (three times) with ethanol to prepare turnip extract. We then purified the obtained solution and completely dried it by using a rotary vacuum dryer. The extract was put in a refrigerator and the required quantities of it were taken every day and administered orally to the rats in the experimental groups for 21 days.

After the 21- day period, the 36 rats were anesthetized with ether and five milliliters of blood were drawn from the heart of each one with a 5 cc syringe. After blood serum was separated, the activities of the ALP, AST, and ALT enzymes and serum albumin and protein were measured. ANOVA was used to compare the treatments and Duncan’s new multiple range test was employed for the comparison of the various groups. SPSS (version 18) was used for data analysis and for performing statistical tests.

RESULTS AND DISCUSSIONS

Cyclophosphamide is an alkylating agent belonging to the oxazaphosphorines group and has cytostatic, cytotoxic, and mutagenic properties. Turnips contain many compounds that affect the body in various ways; for example, they have antioxidant effects, eliminate free radicals, and reduce blood sugar. Results of this research show that concentrations of the enzyme alanine aminotransferase (ALT) in the experimental groups II and III, and of the enzyme alkaline phosphatase (ALP) in the experimental group II, increased significantly compared to the control group ( p <0.01). They also indicated that serum protein in the experimental groups II and III, and serum albumin in the experimental group II, increased significantly compared to the control group ( p <0.05). However, in the experimental groups III and IV, that had received turnip extract together with cyclophosphamide, turnip extract reduced the negative effects of cyclophosphamide and serum protein and albumin were close to the normal levels. Reduced serum total protein and albumin are one of the signs of chronic progressive liver diseases, and the intensity of this reduction shows the extent of liver damage (Matra, P., VR.OG. Rozados, 2000). The use of turnip extract raises serum total protein and albumin close to normal levels. Increased activity of liver enzymes in the serum is one of the main indices of liver damage caused by toxins. Return of the activity of liver enzymes close to the normal level, and increased serum total protein albumin, are one of the basic indices that show this important organ has been cured and has recovered its normal state (Mythili, Y., et al., 2004).

Comparison of various groups with respect to the studied parameters:

<table>
<thead>
<tr>
<th>Group Parameter</th>
<th>control group (C)</th>
<th>sham group (S)</th>
<th>empirical (T250) groups 1</th>
<th>empirical (CT250) groups 2</th>
<th>empirical groups 3 (CT125)</th>
<th>empirical groups 4 (CT250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (IU/Lit)</td>
<td>80.5000a</td>
<td>85.000a</td>
<td>83.8333a</td>
<td>139.000b</td>
<td>105.1667ab</td>
<td>114.5000ab</td>
</tr>
<tr>
<td>ALT (IU/Lit)</td>
<td>54.1667a</td>
<td>61.8333a</td>
<td>60.0000a</td>
<td>110.3333b</td>
<td>90.9667c</td>
<td>70.1667ac</td>
</tr>
<tr>
<td>ALP (IU/Lit)</td>
<td>181.3333a</td>
<td>185.8333a</td>
<td>194.3333ab</td>
<td>244.5000b</td>
<td>219.6667ab</td>
<td>197.5000ab</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.6667a</td>
<td>4.5000a</td>
<td>4.8500a</td>
<td>5.7417b</td>
<td>50.0833ab</td>
<td>4.483ab</td>
</tr>
<tr>
<td>Protein (g/dl)</td>
<td>6.0333a</td>
<td>5.9333a</td>
<td>6.2000a</td>
<td>8.5667b</td>
<td>8.31b7ab</td>
<td>7.6335ab</td>
</tr>
</tbody>
</table>

Columns that have at least one letter in common are not significantly different.
The antineoplastic effects of cyclophosphamide are due to the presence of phosphoramid mustard. Acrolein produces oxygen free radicals through interfering with the antioxidant defense system of tissues, and is responsible for the appearance of toxic effects such as cell death, apoptosis, formation of multiple tumors, and necrosis (Sethuraman, MG., et al., 2003; Sulkowska, M. and S. Sulkowski, 1998). Therefore, increased concentrations of the enzymes ALT, AST, and ALP in groups receiving cyclophosphamide are logical. Especially, concentrations of ALT in the C5, CT125, and CT250 groups increased significantly compared to the C group. These changes indicate the toxic effects of cyclophosphamide on liver enzymes. In rats that received turnip extract besides cyclophosphamide, the activity of these enzymes significantly increased (depending on the administered dosage of the extract) compared to the treatment in which only cyclophosphamide was given. Investigations of the effects of turnip extract showed that turnips had anti-inflammatory effects (Tzai, T.S., et al., 1996). Nowadays, by adding biological compounds with antioxidant properties, it is possible to protect various cells and tissues, including the liver, against disorders caused by active oxygen species and by free radicals (Wang, GJ, and L. Cai, 1999; Zhang, XH., et al., 2007). Flavonoids and derivatives of hydroxycinnamic acid that are abundantly found in turnip roots have strong antioxidant properties and eliminate free radicals (Tzai, T.S., et al., 1996).

Conclusions:
Findings of this study showed that turnip extract has antioxidant and protective properties and can somewhat reduce the negative effects of cyclophosphamide on liver enzymes.

REFERENCES