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EFFECT OF WHEATGRASS JUICE ON REDUCED GLUTATHIONE AND GLUTATHIONE RELATED ENZYMES IN LUNG CANCER PATIENTS DURING CHEMOTHERAPY

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ABSTRACT

Lung cancer is one of the major forms of cancer now days, leading to a large number of deaths throughout the world. Oxidative stress has been reported in most of the cancers including lung cancer. In the present study significantly decreased levels of reduced glutathione (**4.54±0.68)**, glutathione peroxidase enzyme (**3.50±0.11)** and glutathione reductase enzyme (**3.21±0.22)** has been reported as compared to healthy controls. The levels of of oxidative strees also increases significantly during chemotherapy as the levels of reduced glutathione decreases to (**3.46±0.34)**, glutathione peroxidase (**2.92±0.26)** and glutathione S transferase (**2.80±0.25)** after 3 cycles of chemotherapy. Wheatgrass juice during chemotherapy was found to be a natural antioxidant supplement during chemotherapy which decreases the levels of oxidative stress during chemotherapy and increases the effectiveness of chemotherapy drugs.

KEYWORDS: Oxidative stress, Reduced Glutathione, Glutathione peroxidase, Glutathione S transferase, wheatgrass, chemotherapy.

INTRODUCTION

At the beginning of the 20th Lung cancer was a rare disease but today it become one of the most common cancer types around the globe[1], now it is the leading cause of cancer deaths in both men and women throughout the world.[2] In 1997 lung cancer ranks as 10th cause of deaths throughout the world and is predicted that by 2020 it will rise to 5th cause of death.[3]

To protect the cells from damaging affect of reactive oxygen species a multiple defense system is present known as antioxidants. Antioxidants such as superoxide dismutase (SOD), catalase, glutathione peroxidiase (GPx) and glutathione (GSH) etc. are present in human serum and erythrocytes. To protect the cells from damaging affect of reactive oxygen species a multiple defense system is present known as antioxidants.[4]

Oxidative stress is a condition of imbalance between the generation of reactive oxygen species and antioxidant defense system of the cell oxidative stress is thought to be involved in development of many diseases including cancer.[5]

The young grass of wheat plant *Triticum aestivum* germinated over a period of 6-10 days is generally called wheatgrass. Wheatgrass is found to have a high antioxidant and anti cancer properties.[6] The juice extracted from mature sprouts of wheat seeds is known as wheat grass juice. The therapeutic purposes of WGJ was developed and popularized by Dr. Ann wigmore (1909-1996).[7]

Chlorophyll, one of the primary content of wheatgrass juice was found to strengthen the immune system through inhibition of metabolic activation of carcinogens. Wheatgrass juice also posseses the ability to inhibit oxidative DNA damage. The extract of wheatgrass was also found to decrease the cancer causing ability of certain chemical mutagens.[8]

The anti proliferative effect, total antioxidant capacity (TAC), Total Phenol Content (TPC), DPPH ((1, 1-diphenyl-2-picrylhydrazyl) and FRAP (Ferric reducing antioxidant power) of wheatgrass extract was studied on the selected model of breast cancer MCF-7 cell line. Significant anti proliferative effect and cell death was observed in a dose dependent manner of wheatgrass extract on MCF-7 cells. Wheatgrass was also found to have high anticancer and antioxidant activity.[9]

In another study the effects and oxidant/antioxidant status of aqueous and ethanol extracts of wheatgrass were tested in human chronic myeloid leukemia CML (K562) cell line, which shows that Wheatgrass extract has an antioxidant activity, it inhibits proliferation of leukemia cells, and induces apoptosis; thus, this finding may represent a novel therapeutic approach for the treatment of this type of leukemia.[10] A study conducted by Dey et al found that wheatgrass juice as supportive care drink which helps to improve the health status and lifespan in terminally ill cancer patients.[11]

MATERIALS AND METHODS

Blood samples of 100 lung cancer patients who were admitted to Cancer Hospital and Research Institute Gwalior (M.P.) and 50 healthy subjects were collected. Lung cancer patients were divided in two groups, group 1st received only chemotherapy and group 2nd received 50 ml of wheatgrass juice daily during chemotherapy. Blood samples were collected from both the groups of lung cancer patients before the chemotherapy and after the 3rd cycle of chemotherapy.

Sample collection and processing

The blood samples were drawn from the antecubital vein nenopuncture. The blood was collected in tubes containing EDTA (an anticoagulant, 2mg/ml) and sodium fluoride (an inhibitor of glycolysis, 2mg/ml). Each blood sample was centrifuged for 10 min at 3000rpm. The plasma was collected and stored at -20^0 C, which is used for further investigation.

Estimation of blood GSH was performed with method described by Ellmen (1959)[12] and modified by Jollow *et al*, (1974).[13] Glutathione peroxidase activity was measured by the procedure of Rotruck *et al.*,(1973).[14] Glutathione transferase activity in haemolysate was measured by method of Beutlar (1984).[15] Statistics was done by using SPSS software.

RESULTS

Table-1. Levels of oxidative stress markers lung cancer patients before and after chemotherapy.

Oxidative stress markers	Before chemotherapy (0 cycle) N= 50	After 3 cycles of chemotherapy N= 36	Percentage (%) change	Healthy controls
Reduced glutathione (GSH)	4.54±0.68[a]	3.46±0.34[ab]	23.78%	9.10±0.82
Glutathione peroxidase (GPx)	3.50±0.11[a]	2.92±0.26[ab]	16.57%	4.45±0.54
Glutathione S transferase	3.21±0.22[a]	2.80±0.25[ab]	12.77%	4.01±0.30

Values are expressed mean± SD

Units: GSH-mg/ml; GPx; units/min/mg protein: GST; units/min/mg protein

[a]P<0.01 in superscript showed comparison of controls group with patients groups and were significant at P<0.01

[ab]P<0.01 in superscript showed comparison of patients group with patients groups (after 3 cycle) and were significant at P<0.01

Table-2. Levels of oxidative stress markers lung cancer patients before and after chemotherapy with wheatgrass juice.

Oxidative stress markers	Before chemotherapy (0 cycle) N= 50	After 3 cycles of chemotherapy N= 44	Percentage (%) change
Reduced glutathione (GSH)	4.49±0.28[a]	4.02±0.36[ab]	10.46%
Glutathione peroxidase (GPx)	3.39±0.21[a]	3.11±0.28[ab]	8.25%
Glutathione S transferase	3.16±0.25[a]	2.91±0.19[ab]	7.93%

Values are expressed mean± SD

Units: GSH-mg/ml;

GPx; units/min/mg protein

GST;units/min/mg protein.

[a]P<0.01 in superscript showed comparison of controls group with patients groups and were significant at P<0.01

[ab]P<0.01 in superscript showed comparison of patients group with patients groups (after 3 cycle) and were significant at P<0.01

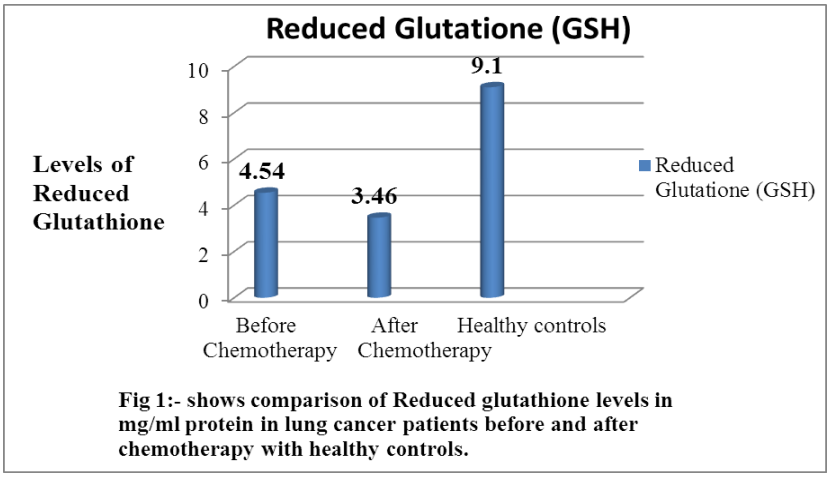

Fig 1:- shows comparison of Reduced glutathione levels in mg/ml protein in lung cancer patients before and after chemotherapy with healthy controls.

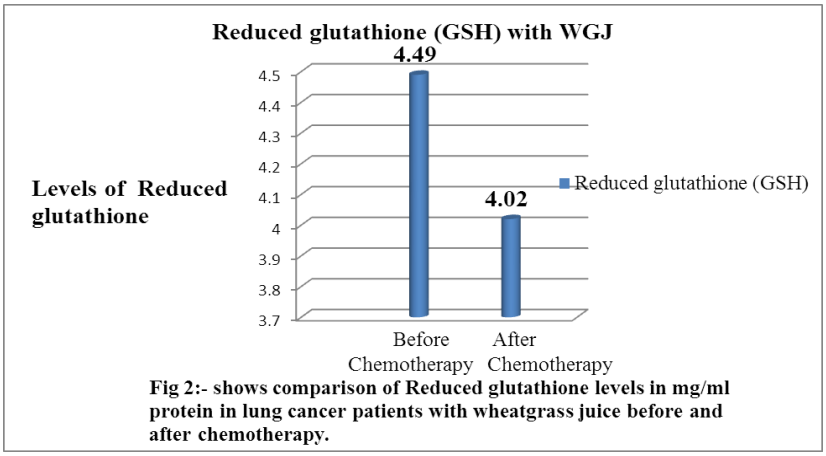

Fig 2:- shows comparison of Reduced glutathione levels in mg/ml protein in lung cancer patients with wheatgrass juice before and after chemotherapy.

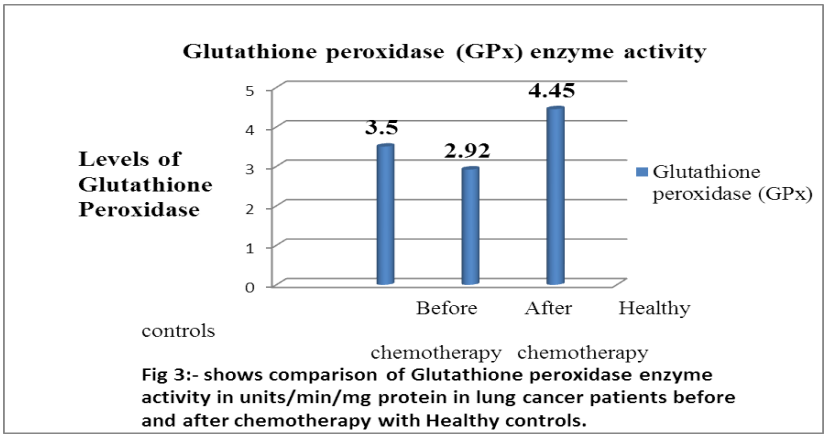

Fig 3:- shows comparison of Glutathione peroxidase enzyme activity in units/min/mg protein in lung cancer patients before and after chemotherapy with Healthy controls.

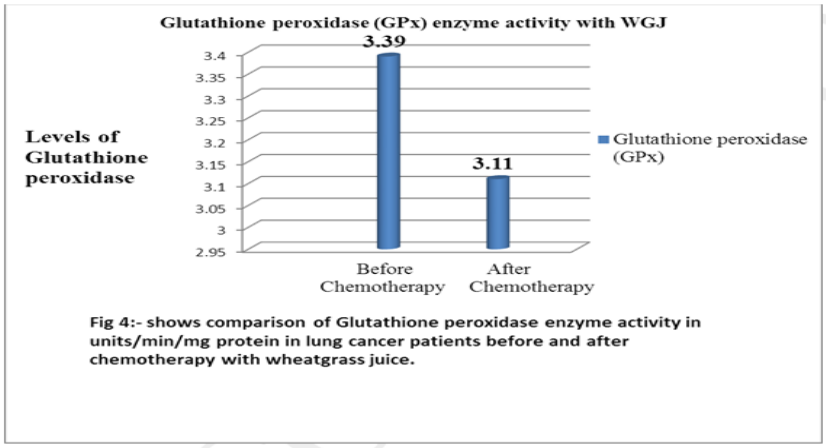

Fig 4:- shows comparison of Glutathione peroxidase enzyme activity in units/min/mg protein in lung cancer patients before and after chemotherapy with wheatgrass juice.

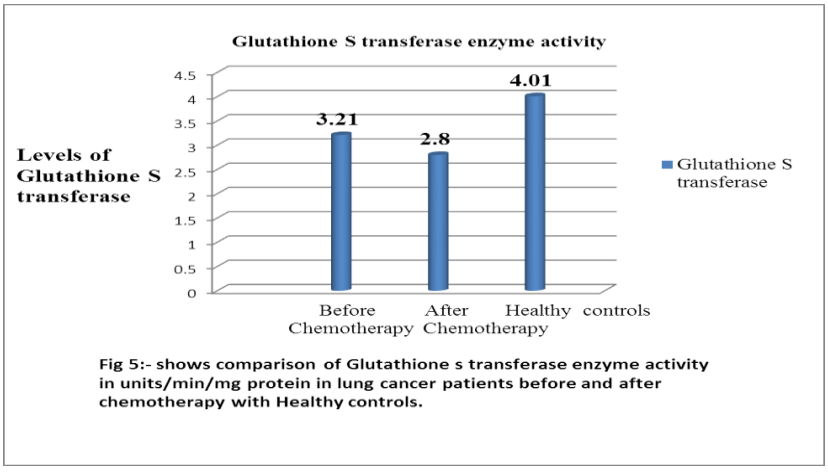

Fig 5:- shows comparison of Glutathione s transferase enzyme activity in units/min/mg protein in lung cancer patients before and after chemotherapy with Healthy controls.

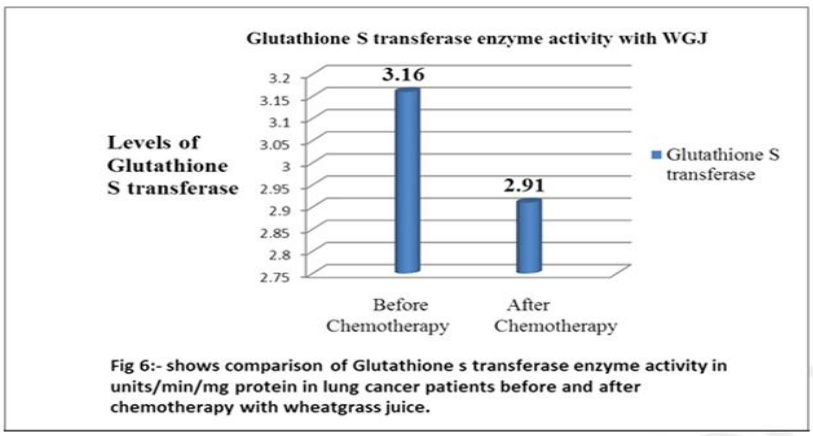

Fig 6:- shows comparison of Glutathione s transferase enzyme activity in units/min/mg protein in lung cancer patients before and after chemotherapy with wheatgrass juice.

DISCUSSION AND CONCLUSION

Lung cancer is known as the highest cause of cancer mortality all around the world in both men and women.[16] The incidences of lung cancer are rising every year by 0.5% which results in about 1.04 million new patients of lung cancer every year worldwide.[17] Glutathione is tripeptide with an unusual peptide linkage between the amine group of cystein (which is attached by normal peptide linkage to a glycine) and the carboxyl group of the glutamate side chain. It is an antioxidant, preventing damage to important cellular components caused by reactive oxygen species such as free radicals and peroxides.[18] Our findings also shows significantly decreased levels of reduced glutathione (**4.54±0.68)** in lung cancer patients as compared to healthy controls (**9.10±0.82) (**P<0.01), which further decreases to (**3.46±0.34)** about 23.78% after 3 cycles of chemotherapy. Significantly low activity of an antioxidant enzyme glutathione peroxidase is also found in lung cancer patients **(3.50±0.11)** as compared to control (**4.45±0.54) (**P<0.01), which decreased to (**2.92±0.26)** about 16.57% after 3 cycles of chemotherapy. Significant decrease in the activity of another antioxidant enzyme glutathione s transferase is also found in lung cancer patients (**3.21±0.22)** as compared to the healthy controls (**4.01±0.30) (**P<0.01), which further decrease to (**2.80±0.25)** after 3 cycles of chemotherapy (Table 1). Table 2 shows that the levels of reduced glutathione (GSH) Glutathione peroxidase (GPx), Glutathione S transferase, in lung cancer patients receive wheatgrass juice during chemotherapy. The levels of reduced glutathione (GSH) decreases from **4.49±0.28 to 4.02±0.36,** Glutathione peroxidase (GPx) **3.39±0.21 to 3.11±0.28** and Glutathione S transferase **3.16±0.25 to 2.91±0.19** after 3 cycle of chemotherapy. In the above study we found that the levels of reduced glutathione and glutathione related enzymes were found to be significantly decreased in lung cancer patients as compared to the healthy controls, which further decreases significantly after 3 cycles of chemotherapy which shows increased levels of oxidative stress during chemotherapy. Lung cancer patients receiving wheatgrass juice during chemotherapy were found to have lower levels of oxidative stress during chemotherapy as compared to the patients without wheatgrass juice. From the above results it can conclude that wheatgrass juice can be use during chemotherapy as an antioxidant supplement to decrease the levels of oxidative stress due to chemotherapy.

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