IAMJ

Review Article *International Ayurvedic Medical Journal* *ISSN:2320 5091*

THERAPEUTIC POTENTIAL OF WHEATGRASS (*TRITICUM AESTIVUM)* AGAINST OXIDATIVE STRESS BY PLATINIUM CONTAINING DRUGS DURING CANCER CHEMOTHERAPY: A FUTURE PROSPECTIVE

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ABSTRACT

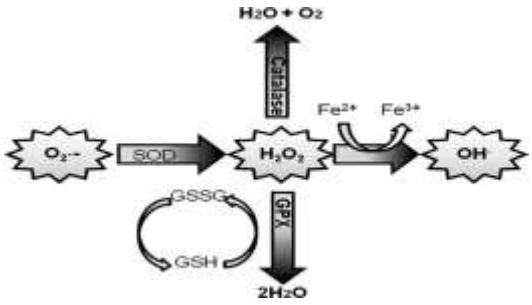
Oxidative stress is thought to be involved in the development of many diseases or may exacerbate their symptoms including cancer in human. Free radicals can cause toxicity and damage to many components of cells including proteins, DNA and lipids by the production of peroxides. Platinium containing drugs such as Cisplatin and Carboplatin can produce reactive oxygen species during their activity on the cancerous cell, which ultimately leads to an increased levels of oxidative stress during chemotherapy which slows down the replication of Cancerous cells, however, chemotherapeutic drugs are able only to kill highly dividing cells, so it ultimately interferes the antineoplastic activity of the drug. Oxidative stress also causes necrosis, depletion of ATP, prevent the control apoptotic death and causing the cells to simply fall apart, which can lead to a tumor formation further. Wheatgrass (*Triticum aestivum)* contains high amount of antioxidants, and almost no side-effects, so it can be use as an antioxidant phytomedicine against oxidative stress caused by chemotherapeutic drugs and can also increase the antineoplastic activity of the drug.

Keywords: Oxidative stress, Antioxidant, Chemotherapy, Wheatgrass

INTRODUCTION

1. Oxidative stress and antioxidants

A collapse in the sensitive balance between the free radicals and the antioxidant defense can lead to oxidative stress.[1] Any disturbance in the normal redox state of cells can cause toxic effects by the production of peroxides and free radicals which can damage components of the cell, including proteins, lipids and DNA.[2] In humans, oxidative stress is thought to be play an important role in the development of many disease such as cancer or may make worse their symptoms.[3] Enzymatic antioxidants such as Catalase, Superoxide dismutase and non enzymatic such as vitamins A and E, block the initiation of free radical chain reactions and breaks the chain reaction of lipid peroxidation which cause the tissue damage.[4]



(Fig-1) Balance of ROS and antioxidants. Oxidative stress is the imbalance between the production of ROS and antioxidants. The antioxidant properties of GPX, SOD, and catalase control the production of oxygen species. Abbreviations: GPX, glutathione peroxidase; GSH, reduced glutathione; GSSG, glutathione disulfide; H_2O_2, hydrogen peroxide; O_2^-, superoxide; OH^-, hydroxyl radical; ROS, reactive oxygen species; SOD, superoxide dismutase.[5]

2. Cisplatin

Cisplatin is a chemotherapy drug that is widely used to treat different types of cancer, including testicular cancer, germ cell cancer, head and neck cancer, bladder cancer and lung cancer. At the centre of this drug is an atom of the metal platinum.

2.1. Oxidative stress caused by Cisplatin and its combination

Cisplatin combination chemotherapy increase the levels of lipid peroxidation and nitrite it also decrease the levels of superoxide dismutase and reduced glutathione which ultimately increase the levels of oxidative stress in advance non small cell lung cancer patients at different cycles of chemotherapy.[6] A study shows that Cisplatin- combination chemotherapy induce a fall in plasma antioxidant levels in osteosarcoma and testicular carcinoma patients, which may cause failure of antioxidant defense mechanism against oxidative damage caused by commonly used anticancer drug.[7] The Malonaldehyde (MDA) levels were elevated and Catalase and Superoxide dismutase activities are decreased significantly after 24 hours of administration of polychemotherapy consisting of Doxorubicin, Cisplatin and Cyclophosphamide in ovarian cancer patients.[8] Two studies shows that hepatic MDA levels are increased, and levels of antioxidant enzymes are found to be decreased in rats treated by Cisplatin.[9,10] Cisplatin induce oxidative stress by altering the glutathione redox status, reduced glutathione levels and oxidized glutathione and reduced glutathione ratio it also increase lipid peroxidation in rat liver.[11]

3. Carboplatin

Carboplatin, or cis-Diammine (1,1-cyclobutanedicarboxylato) platinum(II) (trade names Paraplatin and Paraplatin-AQ) is a chemotherapy drug used against some forms of cancer (mainly ovarian carcinoma, lung, head and neck cancers).[12]

3.1.Oxidative stress caused by Carboplatin and its combination

Oxidative stress markers levels has been tested in small cell lung cancer patients in one study, which showed that the increased levels of lipid peroxidation markers are associated with better overall survival in cancer patients receiving Carboplatin, Vinccristine and Etoposide combination chemotherapy however, only

TBARS and Schiff's bases are examined in the study.[13] Carboplatin also leads to an increase in nitric oxide and malondialdehyde levels, Xanthine oxidase and manganese-superoxide dismutase activities in the cochlea indicating the increased levels of free radicals in the cochlea and renal cells of rat.[14,15]

4. Wheatgrass (*Triticum aesitivum*)

Wheatgrass (*Triticum aesitivum*) belongs to Poaceae family. Wheatgrass, has been an integral part of Indian culture for thousands of years, and has been known to have outstanding healing properties. some studies shows that wheatgrass has chemical constituents such as Vitamin A, B1, 2, 3, 5, 6, 8, and 12, Vitamin C, E and K, Ascorbic acid, Carotene, Sulfur, Sodium, Copper ,Calcium, Phosphorus, Iodine, Magnesium, Selenium, Zinc, Boron and Molybdenum , wheatgrass also contains many enzymes including protease, amylase, lypase, superoxide dismutase (SOD) cytochrome oxidase and transhydrogenase, there are also some other particular components present in wheatgrass are amino acids such as aspartic acid, threonine, asparagines, glutamine, proline, glycine, arginine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, tryptophan and serine, P4D1 (gluco-protein), muco-polysaccharides, and chlorophyll, bioflavonides like apigenin, quercitin and luteonin, indole compounds, choline and lactrile (amygdalin) which provides a excellent therapeutic potential to it.[16-18]

4.1.Antioxidant activity of Wheatgrass

Wheatgrass is found to have elevated amount of chlorophyll which act as an antioxidant and can prevent cancer. Selenium and lactrile found in wheatgrass have anticancer activities and can diminish risk of cancer.[19] Aqueous and ethanol extracts of wheatgrass were found to inhibit the growth of leukemia cells in a time dependent manner. Also an increase in CAT, SOD, and ADA activities were calculated in the cell lines treated with wheatgrass extracts.[20] The concentration of vitamin C and E, beta carotene, ferulic acid and vanilic acid present in wheatgrass increases with the germination period of wheatgrass.[21] Chlorophyll present in wheatgrass inhibits the metabolic activation of carcinogens[22,23], wheatgrass was also found to inhibit the oxidative DNA damage.[24] A study done on MCF-7 breast cancer cell lines with different extracts of wheatgrass found that crude ethanolic extract show highest free radical scavenging activity and the highest cell killing property.[25] The antioxidant activity of Wheatgrass has been measured which are grown under different conditions (1) tap water, (2) tap water with nutrients, (3) soil and tap water, and (4) soil with nutrients, it has been found that the ethanol extract of wheatgrass has highest FRAP values day 15 of growth under condition 4 also the highest ORAC has been found with ethanol extract of wheatgrass on day 10 with condition 4.[26,27] Wheatgrass contains antioxidant enzyme superoxide dismutase (SOD) which converts dangerous free radical reactive oxygen species (ROS) into hydrogen peroxides, which is not destructive as superoxide molecule and an oxygen molecule.[28]

5. Summary and future directions

Cisplatin and Carboplatin generally increase the levels of oxidative stress, which can affect the antineoplastic activity of the chemotherapeutic drug by slowing down the growth of the cancer cells and also prevent control apoptosis and can regenerate the

tumour. Wheatgrass contains both enzymatic and non enzymatic antioxidants and has almost no side effects, so it can be use as a supplement to the cancer patients during chemotherapy to reduce the oxidative stress caused by platinium containing chemotherapeutic drugs and it can also increase the antineoplastic activity of the drug and illustrate better results.

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Source of support: Nil

Conflict of interest: None Declared