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Review Article

Multitude potential of wheatgrass juice (Green Blood): An overview

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Abstract	Wheatgrass is the young grass of the common wheat plant Triticum aestivum Linn., family Poeaceae (Graminae).
	It is commonly known as the "green blood" due to its high chlorophyll content which accounts for 70% of its
	chemical constituents. It contains a plethora of vitamins, minerals, amino acids and vital enzymes like superoxide
	dismutase and cytochrome oxidase. The vitamin content makes it an important adjuvant in anti-allergic and anti-
	asthmatic treatment, while the enzymes play a pivotal role in the anticancer approach of this herbal drug. A notable
	feature of the wheatgrass juice is its bioflavonoid content which are the naturally occurring antioxidants and ac-
	count for many of its clinical utilities such as management of inflammatory bowel disease and as a general detoxi-
	fier. However, the most remarkable feature of the wheatgrass juice is its high chlorophyll content. Chlorophyll
	bears structural similarity to hemoglobin and has been found to regenerate or act as a substitute of hemoglobin in
	hemoglobin deficiency conditions. This might be the reason behind the utility of wheatgrass in clinical conditions
	like thalassemia and hemolytic anemia. The present article focuses onto the various studies emphasizing the multi-
	tude potentials of wheatgrass.

Keywords: Triticum aestivum Linn., chlorophyll, green blood, bioflavonoids, antioxidant.

Introduction

Wheatgrass refers to the young grass of the common wheat plant, *Triticum aestivum* Linn., family Poeaceae (Graminae), [1] which is freshly juiced or dried into powder for animal and human consumption – both the forms provide chlorophyll, amino acids, minerals, vitamins, and enzymes. It is also known as "living food" and is a superior source of chlorophyll – appropriately referred to as the "green blood" .Various chlorophyll-rich greens are being used from variable sources, since prehistoric times, as blood builders. Thus, wheatgrass, containing about 70% chlorophyll, has been proclaimed to improve blood flow, aid in digestion and in general detoxification of the body.

Source

Although the major Indian source is *Triticum aestivum*, there are several other varieties of wheatgrass in the following plant genera: *Agropyron spicatum* (bluebunch wheatgrass), *Agropyron cristatum* (Crested wheatgrass), *Agropyron trachycaulum* (slender wheatgrass), *Elytrigia, Eremopyrum, Pascopyrum,* and *Pseudoroegneria* which are commonly found in temperate regions of Europe and the United States.

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Swati Padalia Maharaja Surajmal Institute of Pharmacy, C-4, Janakpuri. New Delhi- 110058 E-mail: swati622@gmail.com The environment in which wheatgrass grows determines its vitality and is thus sown in late autumn for maximum concentration of the active principles. The nutritional vibrancy of wheatgrass is encouraged by supplementing the soil with rich vegetable compost and seaweed. At the onset of the spring season, the simple sugars produced as a result of photosynthesis, undergo conversion into proteins, carbohydrates and fats, with the aid of the various enzymes and minerals absorbed by the plant via its roots. Due to the comparatively lower temperatures in the spring, the grass grows slowly enough for this conversion to occur before the critical jointing stage of growth. At jointing, or the reproductive stage of the plant, the nutrients and energy of the plant are redirected to seed formation. Wheatgrass is harvested just prior to this jointing stage, when the tender shoots are at their peak of nutritional potency.

Chemical constituents

The name "green blood" of wheatgrass is attributable to its high chlorophyll content which accounts for 70% of its total chemical constituents. Wheatgrass juice is a rich source of Vitamins A, C, E and B complex. It contains a plethora of minerals like calcium, phosphorus, magnesium, alkaline earth metals, potassium, zinc, boron, and molybdenum. The various enzymes responsible for its pharmacological actions are protease, amylase, lipase, cytochrome oxidase, transhydrogenase, super oxide dismutase (SOD). The other notable feature of wheatgrass is its high proportion of amino acids such as aspartic acid, glutamic acid, arginine, alanine and serine.

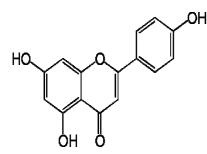
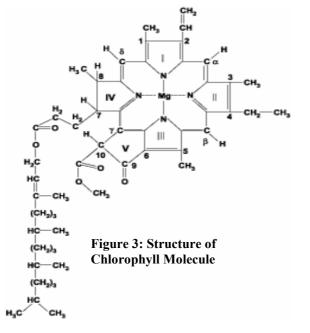


Figure 1: Structure of Apigenin



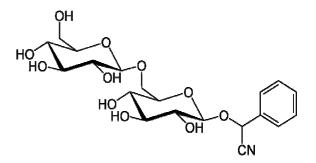


Figure 2: Structure of Laetrile

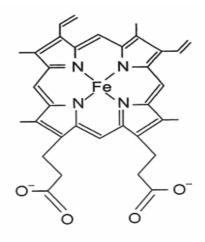


Figure 4: Structure of Tetra Pyrrole Head of Hemoglobin

Table 1: Different constituents o	of wheatgrass occur in the	e following proportion in the plant

Basic Nutrients	Minerals	Vitamins
Calories: 21.0 Cal	Iron: 0.61 mg	Vitamin C :3.64mg
Water: 95g	Magnesium: 24mg	Vitamin A: 427 IU
Fat: 0.06g	Potassium: 147mg	Vitamin B1: 0.08mg
Carbohydrates: 2.0g Dietary	Phosphorous: 75.2mg	Vitamin B2: 0.13mg
Fiber: <0.1g Chlorophyll: 42.2mg	Zinc: 0.33mg	Vitamin B3: 0.11mg
Choline: 92.4mg	Calcium: 24.2mg	Vitamin B5: 6.0mg
Glucose: 0.80g	Sodium: 10.3mg	Vitamin B6: 0.2mg
	Selenium: <1ppm	Vitamin B12: <1mcg
		VitaminE:15.2IU
		Folic Acid: 29mcg

The major clinical utility of wheatgrass juice is due to its antioxidant action which is derived from its high content of bioflavonoids like apigenin, quercitin and luteolin. Other compounds present, which make this grass therapeutically effective, are the indole compounds, choline and laetrile (amygdalin). (Figure 1 and 2) The different constituents of

wheatgrass occuring in different proportions are represented in Table 1.

In a study conducted to determine the elemental concentration profile of wheatgrass using instrumental neutron activation analysis, it was found that the concentration of elements such as K, Na, Ca and Mg increased linearly in the shoots with the growth period whereas the concentrations of the elements namely Zn, Mn and Fe remained constant in shoots after 8th day of plant growth for all three conditions of growth. However, it was observed that the shoot to root concentration ratio in all the conditions increased linearly for K, Na, Ca, Mg and Cl and decreased for Zn, Fe, Mn, and Al with growth period. [2]

Chlorophyll as green blood

The analogy between chlorophyll and hemoglobin can be demonstrated with respect to the structure of their porphyrin heads. (Figure 3, 4) The structure of both the compounds depicts a striking similarity in having a tetra pyrrole ring structure, the only difference between the two being the nature of the central metal atom – magnesium (Mg) in chlorophyll and iron (Fe) in hemoglobin. The apparent resemblance between the two is thus considered to be responsible for the therapeutic effects shown by chlorophyll in conditions involving deficiency of hemoglobin.

Hemoglobin and its congeners are protein bodies which act as the oxygen carrier in higher animals by binding two electrons attached to the oxygen molecule, whereas chlorophyll is the active metabolic agent in plants which assimilates carbon from the carbon dioxide of the atmosphere by producing two electrons which are then transmitted through electron transport chain. The structural similarity between the two compounds is stipulated to be the reason behind the limited use of chlorophyll as a blood substitute in conditions like chronic anemia, tissue hypoxia, thalassemia and other hemolytic disorders etc.

Clinical utilities of wheatgrass

1. Blood builder in thalassemia major

Beta-thalassemia is a genetically inherited disorder that arises due to abnormal beta globin chains which are required for the synthesis of adult hemoglobin (HbA). The characteristic deficiency of beta globin chains, seen in thalassemia, results in the production of abnormal red blood cells (RBCs) having a preponderance of alpha globin chains. This leads to destruction of such RBCs in the spleen and a decreased number of RBCs in the blood. Individuals with thalassemia may continue to produce gamma globin chains in an effort to increase the amount of fetal hemoglobin (HbF) and compensate for the deficiency of HbA.[3] Thus, induction of fetal hemoglobin in thalassemia can improve the patient's clinical condition. Drugs exhibiting this function like hydroxyurea are not used conventionally due

to lack of specificity and greater degree of side effects. [4] 3-5 fold increase in the production of HbF on consumption of wheatgrass has been reported using a cellular assay. This has now been confirmed by the development of a specific assay method for HbF, which is based on detecting its production in human erythroleukemia cells using a fluorescent protein gene that replaces the genes for HbF. [5] The level and speed of induction of HbF by the wheatgrass extract is significantly greater than any of the pharmaceutical inducers available. Chlorophyll extracted from the wheatgrass plant or its synthetic derivative chlorophyllin has also been implicated in this clinical condition. The antioxidant

mechanism of the various wheatgrass constituents may be responsible for the beneficial effects. The enhanced antioxidative capacity of the RBCs may prolong the survival time of not only the newly formed cells, but also of the transfused RBCs. [6]

In a clinical study, wherein the thalassemic patients were administered wheatgrass juice on a daily basis, the following conclusions were drawn –

- a. 50% patients showed upto 25% reduction in transfusion requirement.
- b. The mean time interval between transfusions increased to 29.5%
- c. Hemoglobin levels were not compromised by reduced transfusion volumes.
- d. The patients reported general well-being, improved appetite and reduced musculo-skeletal aches and pains. [7]

2. Adjuvant therapy in hemolytic anemia

It was seen that wheatgrass juice therapy decreased the total volume of blood transfused and increased the intervals between blood transfusions of the entire study cohort. These analyses suggested that not only is this therapy effective, but also that the benefit is related to the duration of the wheatgrass juice therapy. The beneficial effects of this therapy have been attributed to its rich nutritional content that includes antioxidant vitamins (C&E) and bioflavonoids. The effects of the wheatgrass juice therapy may be due to the action of natural antioxidants on red blood cell (RBC) antioxidant function and corresponding effects on cellular enzyme function and membrane integrity. This thought is supported by studies that show decreased antioxidant capacities of RBCs of patients with hemolytic disorders as well as beneficial effects on RBC life-span by supplementation of antioxidants in vivo. [8]

The response to this therapy took some months (called as the "neutral period") which may suggest that the natural antioxidants contained in the wheatgrass juice are better able to prevent cellular injury than to repair RBC enzymes/membranes once damaged. Hence, RBCs, once damaged, would be cleared from the circulation by the reticuloendothelial system as they would prior to the onset of this therapy, but newly formed RBCs would not be damaged and would have a longer life-span.

While clinical trials are currently underway to find suitable blood substitutes for patients needing blood transfusions, they may not be readily available in developing countries nor would they be preferable to natural therapies aimed at preserving a patient's own RBCs. Therefore, wheatgrass juice and other nutritional therapies may be considered as adjuvant to drug therapy.

3. Supportive care for terminally ill cancer patients

Wheatgrass juice is an integral part of the macrobiotic diet under the complementary and alternative medicine (CAM) approach of anticancer therapy, due to its high antioxidant content. Wheatgrass juice is a highly placed source of chlorophyll, laetrile and antioxidant enzyme Superoxide dismutase (SOD). Wheatgrass intake enhances hemoglobin synthesis as chlorophyll bears a structural analogy to hemoglobin. This results in augmented oxygen supply to all body cells including cancer cells which are highly vulnerable to high oxygen concentration due to the deleterious effects caused by the generation of reactive oxygen species (ROS). The enzyme SOD catalyses the generation of hydrogen peroxide from superoxide radicals, and thus further ads onto this effect. [9]

Chlorophyll, like other tetrapyrroles, has the ability to induce mammalian phase 2 proteins that protect cells against oxidants and electrophiles. The capacity of this compound to induce the phase 2 response depends upon its ability or that of its metabolites to react with thiol groups. Its pseudo second-order rate constant is correlated with its potency in NAD inducing the phase 2 enzyme (P) H:quinone oxidoreductase 1 (NQO1) in murine hepatoma cells. One of the most potent inducers was isolated from chlorophyllin, a semisynthetic water-soluble chlorophyll derivative. Although chlorophyll itself is low in inducer potency, it may nevertheless account for some of the disease-protective effects attributed to diets rich in green vegetables like wheatgrass because it occurs in much higher concentrations in these plants. [10]

Another constituent of wheatgrass implicated as an anticancer agent is the plant hormone abscisic acid (ABA) or dormin. This hormone is 40 times more potent 4 hours after cutting the wheatgrass plant. ABA can neutralize the effect of the hormone chorionic gonadotropin and a compound similar to this hormone has been found to be produced by the cancer cells. [11]

A novel anticancer approach utilizes high alkalinity in the cancer chemotherapy. Firstly, an alkaline diet helps to reduce the number of microbes in the diet. This attenuates the incidence of secondary infections to a certain degree in the patient. Secondly, the cancer cells succumb in a highly alkaline environment. As the pH of the wheatgrass juice is around 7.4, it is being considered a viable option under this approach. [12] Other postulated mechanisms by which wheatgrass juice appears beneficial include antioxidant activity preventing oxidative damage to deoxyribonucleic acid (DNA) and lipid peroxidation, stimulation of gap junction communication, effects on cell transformation and differentiation, inhibition of cell proliferation and oncogene expression, effects on immune function and inhibition of endogenous formation of carcinogens. [13]

4. Management of inflammatory bowel disease

Inflammatory Bowel Disease (IBD) refers to the inflammation of the intestines and includes two chronic conditions namely ulcerative colitis and Crohn's disease, both being characterized by rectal bleeding, diarrhea and abdominal pain. Although IBD is idiopathic, an increased incidence of IBD has been noted in urban areas due to the higher concentrations of microparticles in the urban diets such as titanium dioxide and aluminosilicates which may combine with other substances in the intestine (such as bacterial components) and form antigenic particles. The antigenic particles so formed trigger the inflammatory cascade by stimulating gene encoding for the NOD2 protein. NOD2 is believed to play a role in the recognition of bacterial particles and subsequent activation of the inflammation cascade by the activation of protein NF-kappa B. This results in the release of various mediators of inflammation such as cytokines, Tumour Necrosis Factor (TNF) etc. [14]

Wheatgrass juice is currently under investigation as a possible therapy for ulcerative colitis as it is rich in bioflavonoids which are believed to possess both anti-inflammatory and antioxidant properties. One of these bioflavonoid, apigenin, has been shown to in TNF induced transactivation [15]

In an experiment conducted on rats to establish its role as an anti-carcinogenic compound, the animals exposed to the carcinogen N-nitrosodiethylamine were administered apigenin for 14 consecutive days. The level of lipid peroxidation markedly increased in carcinogen administered animals, which was brought back to near normal by apigenin treatment. In contrast the activities/levels of the antioxidant status both in liver and kidney were decreased in carcinogen administered animals, which was recouped back to near normal upon apigenin administration. [15]

A randomized controlled trial of wheatgrass juice in the management of ulcerative colitis has demonstrated that there was a significant improvement in the symptomatic indicators of disease activity. In this double-blind, placebocontrolled study, 24 people with ulcerative colitis was given a daily dose of 100 cc of wheatgrass juice daily for one month .Efficacy of treatment was assessed by a 4-fold disease activity index that included rectal bleeding and number of bowel movements as determined from patient diary records, a sigmoidoscopic evaluation, and global assessment by a physician. In the said study, 78% of the treatment group showed improvement compared to 30% of the control group. [16] However, the results of this trial were not considered convincing as the bitter taste of wheatgrass juice is difficult to reproduce and thus the study cannot be considered as truly blind.

Therefore, although the efficacy of wheatgrass juice as a primary approach in the management of IBD is questionable, it can be considered as a part of adjuvant therapy which may help in cost reduction of the primary treatment.

5. Detoxifying agent

The vitality of liver is of high concern for the overall wellbeing of an individual as it is the major organ implicated in detoxification. In addition to the stimulating and regenerative properties of chlorophyll, other constituents of wheatgrass juice like choline and its high mineral content are responsible for the therapeutic benefit. In a study conducted to observe the effect of choline on liver, it was seen that choline prevents the deposition of fats in the experimental animals' liver when they were administered a diet rich in cholesterol. [17] Choline promotes the removal of the esters of both cholesterol and glycerol, with the effect on the glyceride fraction preceding that on the cholesterol esters. The lipotropic action of choline is attributed to its in vivo conversion to an active compound which is retained within the hepatic cells and enhances oxidation of fatty acids and formation of tissue lecithins. The latter effect augments lipoprotein synthesis which acts as a transport form of fatty acids in plasma and thus helps in removal of lipids from a fatty liver. [18]

It has been demonstrated experimentally that the dietary indoles like indole-3-carbinole and ascorbigen increase the activity of phase I and phase II xenobiotic metabolic enzymes in the liver and intestinal mucosa. [19] Thus the indole compounds of wheatgrass may have a role in the deactivation of carcinogens.

6. Anti-asthmatic and Anti-allergic agent

Allergy or hypersensitivity reactions are immunologically mediated responses that are triggered in certain individuals by the presence of a variety of stimuli, which are otherwise harmless to others. Asthma is a type of bronchial hyperreactivity which is characterized by dyspnoea and airway remodeling.

The rich vitamin and antioxidant content is accounted for the anti-allergic actions of wheatgrass juice:

- In an infection, phagocytic leucocytes become actia. vated and they produce oxidizing compounds which are released from the cell. By reacting with these oxidants, vitamin C may decrease the inflammatory effects caused by them. [20] In a study conducted to investigate the relationships between the intake of the antioxidant (pro)-vitamins C, E and \beta-carotene and the presence of respiratory symptoms and lung function, it was found that vitamin C intake was not associated with most respiratory symptoms (cough, wheeze, shortness of breath) but was inversely related with cough. Subjects with a high intake of vitamin C had a higher forced expiratory volume in one second (FEV1) and higher forced vital capacity (FVC) than those with a low vitamin C intake. [21]
- b. Low levels of antioxidant vitamin E have been associated with asthma and wheezing illness. The gammatocopherols protect against inflammatory cell recruitment and alterations to tissue cells during an antigen challenge. Allergy treatment with these tocopherols also appears to block certain inflammatory immune cells from entering the airspace and tissue spaces of the lungs, nose and sinuses. It reduces the IgE responses to allergic stimuli and thus reduces the frequency sensitization. [22] Vitamin E intake showed no association with most symptoms and lung function, but had a positive association with productive cough.
- c. The minerals present in this plant like Zinc reduces inflammatory cytokines in the airway while magnesium causes bronchodilatation and arrests airway inflammation. [23]
- d. The bioflavonoids like luteolin and quercitin inhibit the release of histamine, leukotrienes, prostaglandin D2 and granulocyte macrophage-colony stimulating factor (GM-CSF) from human cultured mast cells in a concentration-dependent manner. [24]

Pharmacokinetics

The proteins, lipids and carbohydrates in wheat grass are digested, absorbed and metabolized by normal physiological processes.

Contraindications

Wheat grass is contraindicated in those who are

hypersensitive to any component of a wheat grass containing supplement.

Precautions

- Pregnant women and nursing mothers should avoid wheat grass containing supplements.
- Wheatgrass supplements may contain high amounts of vitamin K. Those on warfarin should exercise caution in the use of wheat grass supplements.

Adverse reactions

Wheatgrass juice is safe and the incidence of side effects is very low. It may cause nausea and headache is excessive quantities are taken. Throat swelling may occur in hypersensitive individuals.

Conclusion

Comprehensive data from number of studies has revealed the multitude effects of wheatgrass in thalassemia, hemolytic anemia, cancer, asthma, allergy, inflammatory bowel disease and detoxification. The structural homology of chlorophyll with hemoglobin indicates the role of chlorophyll as a blood builder in various clinical conditions involving hemoglobin deficiency – thus the name "green blood". To conclude wheatgrass seems to be very promising herbal drug and extensive research work is needed in order to explore its therapeutic application in various diseases.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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