



Nutritional prospects of wheatgrass (*Triticum aestivum*) and its effects in treatment and chemoprevention

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Abstract

Nutraceuticals are organic and traditional foods consumed nowadays to maintain a healthy lifestyle and get rid of lifestyle diseases like obesity, cancer, diabetes, hypertension, etc. Globally, herbal products have become increasingly popular in recent years. Wheatgrass (*Triticum aestivum*) is a nutraceutical proven to be a dietary supplement and beneficial for cancer-suffering patients. Wheatgrass possesses many beneficial antioxidant properties: anti-cancer activity, anti-bacterial activity, anti-fungal activity, and anti-microbial activity. Due to the presence of resistant starch, lignans, phenolic acids, alkylresorcinols, and numerous antioxidant components, including carotenoids and tocopherols, this herbal plant is deserving attention as a source of dietary fiber. Patients consume wheatgrass during cancer treatment as an adjunct to reduce toxicity associated with drugs and chemotherapy and ultimately improve long-term outcomes. Studies have proved that wheatgrass helps treat pancreatic cancer, lung cancer, and breast cancer. So, the multi-targeted herbal drug—wheatgrass—is used as an adjunct therapy alongside conventional medicine to treat cancer and other diseases. A promising therapeutic nutraceutical for avoiding lifestyle disorders is wheatgrass.

Keywords

Triticum aestivum, wheatgrass, nutraceutical, anti-cancer, breast cancer, antioxidant, lifestyle disease

Introduction

Herbal plants have nutritional and therapeutic values as they possess active constituents so that consumers can benefit from their use. Due to fewer side effects, herbal products are widely accepted and consumed worldwide. Literature also confirms the safe use of traditional medicines. Wheatgrass, the most edible crop, has been selected for this review due to the high amount of nutritional phytoactive ingredients, which may be beneficial for treating many diseases like diabetes, hypertension, obesity, fungal infection, cardiovascular diseases, cancer, etc. Numerous bioactive substances are contained in wheatgrass (*Triticum aestivum*),

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including minerals, amino acids, vitamins A, B, C, E, and K [1, 2]. This review aims to compile the nutritional prospects of wheatgrass (young wheat plantlets [3]) and its use in chemoprevention. The review of literature was performed on the basis of searches done on PubMed, Google Patents, Google Scholar, etc. To further explore the nutritional potential of wheatgrass in treating various malignancies, data from many sources have been cited and summarised here in one location. This study includes the relevant literature survey impacting the use of wheatgrass in chemoprevention and its nutritional values from 1976 to 2022.

Nutritional prospects of wheatgrass

Wheatgrass possesses potent activity against many diseases due to bioactive compounds like vitamins, minerals, antioxidants, bioflavonoids, etc. The effectiveness of wheatgrass is duly attributed to the existence of these bioactive and nutritionally active ingredients. It has anti-fungal [4, 5], anti-bacterial [5, 6], anti-ulcer, anti-diabetic [6, 7], anti-inflammatory [8], anti-arthritic, antioxidant [9], anti-leukemic [10], anti-hypertensive [11], and anti-microbial properties [12, 13]. Wheatgrass helps with wound healing, digestion, and general detoxification of the body. It also acts as an adjuvant therapy in hemolytic anemia and helps blood-building activity in thalassemia [14]. It is suggested to include wheatgrass in the daily diet (powder, tablet, juice [15, 16], bread [17], or cookies) [18, 19] as it contains chlorophyll, which is almost similar to haemoglobin and strengthens the body's immune system [1, 20]. Wheatgrass is found to possess anti-bacterial, anti-microbial, and anti-fungal activity, and according to the literature available, the plant is effective against the following organisms as tabulated in Table 1 below:

Table 1. The potency of wheatgrass against microbes

Activity	Potent against organism	Reference
Anti-bacterial	<i>Bacillus cereus</i>	[21]
	<i>Staphylococcus aureus</i>	
	<i>Escherichia coli</i>	
	<i>Shigella flexneri</i>	
Anti-microbial	<i>Escherichia coli</i> MTCC 729	[12, 22]
	<i>Staphylococcus aureus</i> MTCC 96	
	<i>Yersinia enterocolitica</i> MTCC 859	
	<i>Listeria monocytogenes</i> MTCC 1143	
Anti-fungal	<i>Aspergillus niger</i>	[4, 12, 23]
	<i>Candida albicans</i>	
	<i>Aspergillus flavus</i>	
	<i>Trichoderma viride</i>	

Phytochemistry of wheatgrass

Modern science has accepted the potential benefit of wheatgrass as a source of bioactive constituents. Abundant literature is present showing the nutritive and therapeutic values of wheatgrass. This is all due to the presence of phytoconstituents present in the plant. According to its phytochemistry, wheatgrass contains a significant number of amino acids, antioxidants, minerals, and other vitamins. The presence of phenols, flavonoids, tannins, polysaccharides, and various enzymes that are responsible for pharmacological activities are detected during phytochemical screening of wheatgrass extract. Owing to the presence of high nutritive qualities, wheatgrass is now being explored as a “functional food” [14].

A study on the impact of wheatgrass juice therapy on haemoglobin levels in anaemic adolescent females found that it improved their symptoms and raised their haemoglobin levels. The conclusion is that wheatgrass juice consumption improves haemoglobin levels [24]. Various antioxidant compounds found in wheatgrass, such as carotenoids and tocopherols, as well as lignans, phenolic acids, resistant starch, and alkylresorcinols, render it an exceptional source of dietary fiber and lignans [25]. Due to its various nutritious components, it can also be called “functional food” [22]. The juice form of wheatgrass is an energy beverage and has been demonstrated to upsurge fertility in male albino rats, owing to the existence of a good amount of magnesium

in chlorophyll [26]. Chlorophyll is structurally composed of a tetrapyrrole ring, having a magnesium atom at the center and almost resembling the heme group in haemoglobin where the central atom is iron. Chlorophyll has substantial biological activity by inhibiting P450 cytochrome enzymes followed by synthesis of Phase II enzymes, thereby proving anti-inflammatory and anti-proliferative mechanisms and proving this herbal plant beneficial for humans [3, 27].

Due to wheatgrass' nutritional content and therapeutic properties, it is beneficial for the management of ailments including anemia, high glucose levels in the blood, blotting and constipation, joint inflammation and disorders, skin problems, swelling of the kidneys, cardiovascular problems [9, 28], and Alzheimer's disease [29]. It is also known as "Panacea on Earth" [30]. The inclusion of bioactive ingredients contributes to the effectiveness of herbal plant extracts and thus, the therapeutic and nutritional prospects of wheatgrass are tabulated in Table 2, as below:

Table 2. Therapeutic potential of wheatgrass due to potent chemical constituent

Therapeutic action	Chemical constituent	Reference
Anti-coagulant	Vitamin K	[1]
Antioxidant, anti-inflammatory action	Phenols, amylase	[1, 7]
	Apigenin and quercetin (bioflavonoid)	
Detoxification	Chlorophyll	[1]
Anti-hypertensive, anti-inflammatory	Luteolin (bioflavonoid)	[1]
Metabolism and digestion	Cytochrome oxidase, choline, proteins, lipids, threonine	[31–34]
Anti-thalassemic	Iron	[35]
Anti-cancer activity	Superoxide dismutase, cytochrome oxidase	[31]
Anti-diabetic	Fibers	[36]
Anti-aging effect	Lysine	[34]
Regeneration of kidney and liver cells	Methionine	[34]
Enhancement of men fertility	Arginine	[34]

Nutritive outcome of wheatgrass on gastrointestinal tract

Wheatgrass contains amino acids, carbohydrates, and lipids that are easily digested, absorbed, and metabolised by usual physiological methods [33]. The gastrointestinal tract's ease of functioning depends on its health, which may be promoted by adding fiber to our diet. The significant component of wheatgrass is dietary fiber, which increases stool bulk to keep the gastrointestinal tract happy. Therefore, wheatgrass is essential for maintaining a healthy gut. Wheatgrass also contains lignin and oligosaccharides [37, 38].

Effect of wheatgrass on metabolic disorders

It is believed that metabolic diseases result from disturbances in normal metabolism caused by enzyme deficiencies or buildup of enzymes or toxic agents caused by endocrine disorders, organ malfunctions, and nutritional deficiencies [39]. To attain good enzyme levels in the body, it has been suggested to take wheatgrass in any form, as it contains essential and non-essential enzymes and has antioxidant and anti-inflammatory properties. Wheatgrass is crucial in regulating enzymatic balance in the body [25, 40]. It contains enzymes like lysine, isoleucine, threonine, methionine, arginine, glycine, proline, and tyrosine. Anti-aging effects and the immune system are improved by lysine, present in wheatgrass. Overall, body metabolism and digestion may be stimulated by threonine. Valine activates the brain and calms nerves. Methionine helps in the regeneration and cleaning of kidney and liver cells. Arginine helps enhance the seminal fluid of men to increase fertility. Aspartic acid and glutamic acid help provide energy and improve the body's metabolism [34].

Wheatgrass can act as a powerful antioxidant, which may be beneficial in treating many metabolic disorders. The antioxidant potential of wheatgrass has been reviewed in a study where wheatgrass juice was encapsulated by means of whey protein and maltodextrin as a covering layer. The total phenolic content and antioxidant activity of extracted powder were examined, which showed that powder encapsulation could protect and enhance the plant's phenol level and activity to fight against free radicals [41]. A study

on rats suggests that wheatgrass extract showed direct protection against liver damage by preventing lipid peroxidation in the phospholipid bilayer and reducing the modifications of fatty acids in the liver membrane [42]. A study on mice showed that wheatgrass exhibits potential hepatoprotective activity (a hepatotoxic effect caused by acetaminophen) by preventing oxidative stress, irritation, apoptosis, and liver damage. Wheatgrass extract was given orally daily to mice. The positive control group was assigned silymarin, and the negative control group was on a saline dose for seven days before injecting acetaminophen intra-peritoneally. The liver condition was analysed by enzyme-linked immunosorbent assay (ELISA) testing, western blotting, and polymerase chain reaction (PCR) analysis. It has been observed that the liver of the mice group had wheatgrass extract, showed the inhibited expression of cytochrome P4502E1 (an enzyme responsible for acetaminophen induced hepatotoxicity) and thereby suppressed hepatocyte apoptosis [43].

Effect of wheatgrass in lowering cholesterol

To eliminate cholesterol from the body, faecal bile acid represents an essential pathway. It has been reported that taking more calcium and fiber in the diet reduces the concentration of faecal bile acids [44]. According to a study, arabinoxylans from wheat lower low-density lipoprotein cholesterol levels in hamsters with high blood cholesterol levels as long as they are on a feed diet containing 0.5% arabinoxylans. Moreover, arabinoxylans inhibited the absorption of cholesterol in the intestine and augmented the elimination of bile acids. This study suggests that there are numerous approaches to prevent cardiovascular problems, and one of them could be increasing consumption of arabinoxylan (present in wheatgrass) [25, 45]. Wheatgrass is also used to treat hyperlipidemia, as confirmed in a study on Long-Evans rats. The serum triglyceride levels in experimentally induced hypercholesterolaemic rats were measured after consuming wheatgrass juice. The rats were divided into eight groups for the study. The study showed that a group of rats taking wheatgrass juice daily showed a significant reduction in serum triglycerides, thus indicating a preventive role of wheatgrass juice against increased levels of triglycerides in the blood [46].

Effect of wheatgrass in chemoprevention

Cancer is a disease that is life-threatening and comes from a family of complex diseases. Different forms of cancer are prevailing worldwide. It is known as a multifactorial disease. One of the causes of cancer is oxidative stress, which is the second leading cause worldwide, for many reasons pertaining to the expansion of the disease [47]. Although chemotherapies might successfully treat cancer, the toxic side effects and pain associated with chemotherapies synthetic alternatives may deteriorate a patient's health. Free radicals are produced as a result of natural metabolism, causing oxidative stress and ultimately leading to the development of many diseases [48]. So, to be on the safe side, one must include antioxidants in a daily diet. Although there are many synthetic antioxidants on the market, they could be hazardous. Plant-based nutraceuticals have been utilised to cure, lessen, and prevent cancer in recent years. For cancer patients with prostate, breast, and colorectal cancers, functional diets and herbal therapies are complementary medicines [49].

Wheatgrass contains natural antioxidants, which are recommended and proven to be potent in preventing cancer. Wheatgrass has many vitamins, β -carotene, and enzymes that help scavenge free radicals and provide anti-oxidative activity. The study assessed the cytotoxicity of wheatgrass and the activation of apoptosis using fluorescent propidium iodide (PI) staining. The presence of antioxidants was confirmed by tests for hydrogen peroxide scavenging, hydroxyl radical scavenging, and anti-proliferative activity, which decreased the spread of Hep2 cell lines. Gas chromatography-mass spectroscopy (GC-MS) analysis of wheatgrass extract confirmed the existence of 9 biologically active constituents having hydroxyl groups and double bonds to stabilise free radicals and thereby possess anti-oxidative action [50]. Free radical reactive oxygen species are changed into hydrogen peroxide and an oxygen molecule by the antioxidant enzymes super oxide dismutase and cytochrome oxidase. This transformation destroys cancer cells [31, 50]. The anti-leukemic potential of wheatgrass has been proven by the presence of polyphenolics [10] and flavonoids [51]. It has also been discovered that components found in fresh wheatgrass juice scavenge free radicals, neutralise toxins and carcinogens, reduce chemotherapy-induced myelotoxicity, and regulate the levels of specific pro-inflammatory cytokines like interleukin-6 (IL-6), IL-8, IL-10, and IL-12 [52]. Wheatgrass possesses plant

hormones in huge quantities. When used after 4 h of cutting wheatgrass, abscisic acid can neutralise the effect of cancer-causing fragments [1, 53]. Graphical representation of wheatgrass used in chemoprevention is shown in Figure 1.

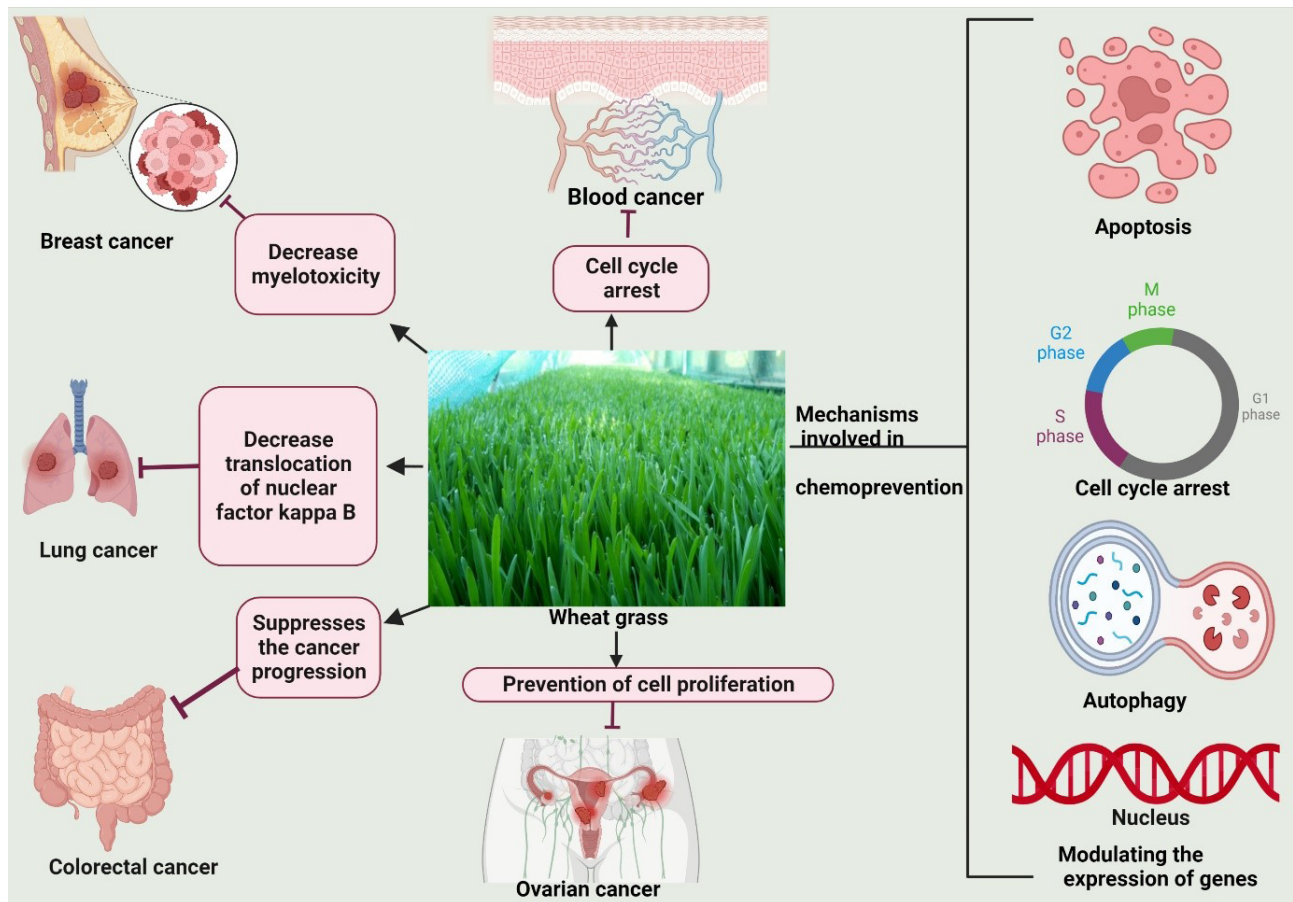


Figure 1. Graphical representation of wheatgrass in chemoprevention

According to literature availability, wheatgrass is useful in curing the following cancers:

- Colorectal cancer [41]
- Breast cancer [54]
- Cervical cancer [55]
- Oral cancer [56, 57]
- Ovarian cancer [58]
- Lung cancer [59]
- Laryngeal cancer [60]

The studies done on wheatgrass to prevent or treat different types of cancer are tabulated in Table 3.

Literature on wheatgrass shows that it inhibits metastasis and angiogenesis in Hep2 cell lines (human laryngeal squamous cell carcinoma). Metastasis is a significant hindrance in cancer treatment as cancer cells migrate, proliferate, and, through angiogenesis, reach other organs and ultimately infect them. A study focused on the anti-metastatic ability of methanolic extract of wheatgrass containing natural polyphenols was reported. The *in silico* docking studies were performed on the nine bioactive constituents and five polyphenolic compounds (reported by the authors in another study) identified by GC-MS and HPLC. Docking tests were conducted to assess how well these 14 drugs interacted with phosphatidylinositol 3-kinase (PI3K) and protein kinase B (AKT).

Table 3. Studies on wheatgrass ameliorating chemoprevention

Type of cancer	Cell line used	Analysis method	Mechanistic approach for chemoprevention	Results	Reference
Laryngeal cancer	Hep2 cell lines	Hydrogen peroxide scavenging activity, hydroxyl radical scavenging activity, and anti-proliferative activity	Cell proliferation is via G1 arrest in the cell cycle and p53 induction. Isolated compounds inhibit cyclin D1/Cdk4 binding and thus inhibit cell proliferation.	The presence of polyphenolics has proved the anti-leukemic potential of wheatgrass.	[47]
Lung cancer	A549 human lung adenocarcinoma cells	MTT assay	Suppression of <i>HIF-1α</i> expression	Wheatgrass extract suppresses <i>HIF-1α</i> expression in airway epithelial cells and inhibits mucin overexpression induced by <i>HIF-1α</i> .	[59]
Cervical cancer	Human epithelial cells (HeLa)	MTT assay, cell cycle analysis, nuclear morphological examination, and RT-PCR	Cell arrest at G0-G1 phase of cell cycle	Wheatgrass possesses anti-cancer potential by inducing apoptosis and anti-proliferative action and is used to prevent and treat human cervical cancer.	[55]
Breast cancer	MCF-7	HPLC and GC–MS	Conducted immunomodulatory bioactive assays and observed delayed type hypersensitivity response and splenocyte proliferation assay	YWG and WG1 were discovered to show positive anti-cancer and immunomodulatory activity.	[54]
Prostate cancer	PC3				
Colon cancer	HCT-116				
Lung cancer	A549				
Pancreatic cancer	MIA PaCa-2				
Ovarian cancer	A2780 A2780cisR	XTT assays	XTT assays	Wheatgrass may lessen the cytotoxicity of carboplatin on ovarian cancer cells that are susceptible to the drug cisplatin.	[58]

MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide; *HIF-1 α* : hypoxia inducible factor; RT: reverse transcription; MCF-7: Michigan cancer foundation-7; A2780cisR: A2780 cisplatin resistant; XTT: 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide; YWG: 5-bromo-2-(5-bromo-chloro-1, 2-dihydroxy-4-methylcyclohexyl)-tetrahydro-2,6,6-trimethyl-2H-pran-3-yl-acetate; WG1: 2,28-diamino-3,27-dihydroxynonacosan-12-one; HPLC: high-performance liquid chromatography

Lung cancer

A study showed that wheatgrass had anti-inflammatory and protective properties against hypoxia in airway epithelial cells. Hypoxia is the pathogenic mechanism of sinusitis and causes inflammation. To check the influence of wheatgrass extract, A549 human lung adenocarcinoma cells were used in the study. Colorimetric assay using MTT was done to check the cell proliferation. Results of the study concluded that wheatgrass extract acts similarly to PD98059, which selectively inhibits the extracellular signal-regulated kinases 1 and 2 (ERK 1/2) pathway, decreasing the expression of the *mucin* gene in response to hypoxia. Wheatgrass extract downregulates *HIF-1 α* induced mucin overexpression by inhibiting *HIF-1 α* expression in airway epithelial cells. The study suggests that wheatgrass could have possible therapeutic significance [59].

Breast cancer

A study that confirmed the medicinal use of wheatgrass by studying the bioactivity of the plant was conducted. Two new compounds were isolated in this study whose bioactivities were not identified previously. The two new moieties were given reference codes as YWG [5-bromo-2-(5-bromo-chloro-1, 2-dihydroxy-4-methylcyclohexyl)-tetrahydro-2,6,6-trimethyl-2H-pran-3-yl-acetate] and WG1 [2,28-diamino-3,27-dihydroxynonacosan-12-one]. Both new molecules were tested for splenocyte proliferation, hypersensitivity assay, and cytotoxicity assay against five cancer cell lines, namely breast (MCF), prostate (PC3), colon (HCT-116), lung (A549), and pancreatic cancer (MIA PaCa-2). Through different assays and immunomodulatory

experiments, it has been stated that the two new moieties invented by the authors exhibit anti-cancer and immunomodulatory activity [54].

Cervical cancer

Human breast carcinoma cell line (MCF-7) and human cervical cancer cell line (HeLa) growth inhibitory effects of wheatgrass aqueous extract were examined, both alone and in combination with cisplatin. Supplements and nutrients were given in order to properly store and maintain cells. By using the MTT test, the anti-proliferative effects of cisplatin and wheatgrass extract were evaluated [55] (only detect the formation of tetrazolium salt [61]). Cell death brought on by aqueous wheatgrass extract was identified by nuclear morphological analysis and cell cycle analysis. By using RT-PCR, these effects were subsequently linked to the expression of the genes involved in apoptosis and proliferation [cyclin D1 and *Bax* (apoptosis regulator)], demonstrating wheatgrass' arrest of the G0-G1 phase of the cell cycle, which is connected to the variation of cyclin D1 and *Bax* expression in MCF-7 and HeLa cells. The study found that wheatgrass has anti-cancer potential and is utilised to prevent and treat human breast and cervical cancers because it induces apoptosis and anti-proliferative induction [55].

Laryngeal cancer

According to a literature survey, there has been significantly less expansion in the treatment of laryngeal cancer in the past two decades. Hep2 cells are human laryngeal cancer cells. Early prognosis and treatment of cancer are needed in a world full of lifestyle disorders. In view of treating cancer, arresting cell cycle in its growth phase is the essential step, which allows human DNA to repair and discard the abnormal replicating cells. Hence, inhibiting the cell cycle stage is a prime target for cancer treatment therapy [60]. Tumour suppressive protein (p53), induces cell cycle arrest, apoptosis, and repairs DNA, thereby protecting normal cells from cancer [62]. In order to treat laryngeal cancer, a study was conducted to evaluate the cytotoxic and anti-proliferative effects of the methanolic extract of wheatgrass against the Hep2 cell lines. Using the MTT technique, cell proliferation was measured. In tissue culture plates, Hep2 cell suspensions were added after being pretreated with wheatgrass extract. The Hep2 cell lines' growth was significantly reduced according to the MTT assay results, and 200 g/mL of wheatgrass after 48 h was an inhibitory concentration. In order to determine the quantity of p53 and cyclin D1, western blotting was used. The main finding of the study demonstrated that Hep2 cells' cell cycle arrest at the G1 phase was associated with higher levels of p53 and lower levels of cyclin D1 expression. It has been concluded that active components present in wheatgrass can be actual moieties for cancer treatment [47].

Ovarian cancer

A study on 98 women with gynecologic cancer analysed the safety of the herbal medicine used in the course of chemotherapy by patients suffering with ovarian malignancy. Wheatgrass was selected to check its cytotoxic analysis. Cytotoxicity was measured using the XTT assay in non-cancerous kidney cells, cisplatin-sensitive and cisplatin-resistant ovarian cancer cell lines [A2780 (cisplatin sensitive), and A2780cisR (cisplatin resistant)] human embryonic kidney cells 293 (HEK-293). Results revealed that wheatgrass might increase the activity of carboplatin or paclitaxel on cisplatin-sensitive ovarian cancer cells and cisplatin-resistant cells while decreasing the cytotoxicity of carboplatin on cisplatin-sensitive ovarian cancer cells [58].

Conclusion

To maintain a healthy lifestyle, organic nutraceuticals and traditional foods are used to get rid of lifestyle diseases. Herbal plants and food supplements are used worldwide to maintain a healthy lifestyle. Wheatgrass is known as a powerful functional food because of its several minerals, vitamins, and enzymes and its potency in treating or preventing many diseases. Wheatgrass has numerous nutritional and therapeutic benefits. This review aims to provide collaborative information on the different dietary values of wheatgrass. One of the main diseases that kills people around the world is cancer. This study on wheatgrass has proved

the efficiency of this herbal plant in treating different types of cancer. Wheatgrass possesses anti-oxidative potential, which may arrest the life cycle of cancerous cells, thereby preventing and treating various types of cancer, like laryngeal cancer, ovarian cancer, and breast cancer. Thus, it has been stated that wheatgrass is a potent therapeutic nutraceutical.

Abbreviations

GC-MS: gas chromatography-mass spectroscopy

HIF-1 α : hypoxia inducible factor

IL-6: interleukin-6

MCF-7: Michigan cancer foundation-7

MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide

PCR: polymerase chain reaction

XTT: 2,3-bis-(2-methoxy-4-nitro-5-sulphophenyl)-2H-tetrazolium-5-carboxanilide

Declarations

Author contributions

NM drafted the paper; SS was responsible for supervision and methodology; PP supervised and helped in revision. All authors contributed to manuscript revision, read and approved the submitted version.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Consent to participate

Not applicable.

Consent to publication

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Availability of data and materials

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