Contents lists available at ScienceDirect



Review Article

Journal of Ayurveda and Integrative Medicine

journal homepage: elsevier.com/locate/jaim



Millets as a dietary supplement for managing chemotherapy induced side effects

Swagata Dilip Tavhare

Department of Dravyaguna, Dr. D. Y. Patil College of Ayurved & Research Center, D.Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune, 411018, India

ARTICLE INFO

Chemotherapy induced side effects

Keywords:

Ayurveda

Adjuvant

Cancer

Millets

NCDs

SDG 3.4

Diet

ABSTRACT

Millets, the nutria-cereals, are one of the oldest utilized grain. Millets are reported to possess nutraceuticals health benefits which include improvement in functioning of digestive system, reduction in cholesterol, prevention of heart disease, protection against diabetes, lowering risks of cancer etc. With the widespread commemoration of the International Year of Millets in 2023, the Indian government is moving towards the global recognition of millets in light of its medicinal value in correction of lifestyles diseases. One of the common non-communicable diseases is cancer. Chemotherapy is used as adjuvant, neo-adjuvant or as a combination, in metastatic settings. It is linked to outcomes, but it also has unfavorable side effects that lower a patient's quality of life. The reported chemotherapy side effects includes loss of appetite, nausea, vomiting, weakness, hair loss, osteoporosis, immunological suppression and gastric disturbances such as dry mouth, altered taste, ulcers, constipation etc. The effectiveness of tumor therapy and the extension of treatment are both influenced by side effect management. New you help cancer patients with their polypharmacy load is through dietary management. Rich in phytochemicals, fiber, vitamins, and minerals, millets can be suggested as a dietary therapeutic intervention in addition to chemotherapy. Being widely accessible, cost effective, nutrient-dense, high in fiber, gluten-free, anti-inflammatory, antioxidant, lipid lowering, gastro-protective, immunomodulator in action, millets can serve as a good diet choice to minimize side effects of chemotherapy.

1. Introduction

Millets (*Trunadhanya*), are small annual grasses with seeds that belong to the Poaceae family. They are one of the earliest crops farmed for grain production. The majority of millets are grown in Asian and African countries [1]. Traditionally, millets were used as staple diet till mid-21st century. After 1960, there was an almost 800% growth in the production of wheat, rice, and corn; in contrast, millet production remained at low levels, stagnating [2]. The fall in the number of millet-based dishes in the Indian food basket was also attributed to perceived low prestige towards millet foods and a shift in dietary patterns brought on by the increasing availability of different food choices linked with higher economic growth.

The United Nations General Assembly (UNGA) officially proclaimed March 5, 2021, as International Year of Millets (IYOM), in accordance with a proposal forwarded by Indian government. Upon acceptance of it, Indian government has taken action for IYOM 2023 in order to promote the moment for the acknowledgment of millets, their recipes, and valueadded products on a global scale. WHO information sheet 2023; on noncommunicable diseases (NCDs) states, 41 million annual deaths worldwide are accounted due to lifestyle diseases contributing to 74% of all deaths [3]. Of all; 77% of NCD-related deaths occur in low- and middle-income nations. To achieve agenda 2030 on Sustainable Development Goals (SDG) 3.4 related to non-communicable disease and mental health, governments are developing preventive and curative strategies to reduce by one third premature mortality from NCDs.

One of the most common and fearful diseases among NCD is cancer. For cancer management, chemotherapy is one of the treatment protocol, used as independent treatment, or as an adjuvant or neo-adjuvant or in combination. Results of chemotherapy are linked to side effects that frequently occur both during and after the course of treatment. If severe, it influences the continuation of treatment, exerts negative impact on a patient's quality of life (QOL) or even poses a threat to their life. Chemotherapy-induced side effects include nausea, vomiting, loss of appetite, exhaustion, hair loss, osteoporosis, immunological suppression, cardiac dysfunction, and gastrointestinal disturbances such as dry mouth, altered taste, ulcers, and constipation. Management of side effects helps in continuation and effectiveness of tumor therapy. It is

* Department of Dravyaguna, Dr. D. Y. Patil college of Ayurved & Research Centre, Pimpri, Pune, 411018, India. *E-mail address:* drswagata32@gmail.com.

https://doi.org/10.1016/j.jaim.2024.100901

Received 23 March 2023; Received in revised form 31 January 2024; Accepted 5 February 2024

0975-9476/© 2024 The Authors. Published by Elsevier B.V. on behalf of Institute of Transdisciplinary Health Sciences and Technology and World Ayurveda Foundation This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

important to practice and implement treatments to alleviate side effects caused by chemotherapy in order to improve the QOL of cancer patient. As cancer patients are likely to experience side effects from their illness and treatment, it is highly beneficial if these adverse effects may be lessened through nutrition or non-pharmacological methods. Natural phytochemicals from dietary sources or non-pharmacological treatments serves a good treatment plan due to their comparatively less side effects, ease of accessibility, and affordability.

Millets are cereals, rich in nutrition, bestowed with many pharmacological actions namely digestive, anti-hypercholesteremic, hypoglycemic, cardio-protective etc. [4] Ayurvedic classics outline dietary regimens for millets; however, contemporary research is needed to close the knowledge gap about herbal remedies with substantial evidences [5]. An integrative strategy is necessary for the treatment of cancer diseases, chemo-radiation induced side effects [6]. In order to raise awareness about the use of millets in the management of adverse effects caused by chemotherapy, the present article is drafted depicting Ayurveda evidences supported by contemporary research.

2. Material & methods

The data have been reviewed from *Samhita* (classical texts), *Nighantu* (lexicons), books and recent research evidences on millets. The information relevant to management of chemotherapy induced side effects searched from databases like 'PubMed', 'Web of Science', 'Scopus', 'Google Scholar' and with keywords like 'chemotherapy induced side effects', 'chemotherapy induced hairfall', 'chemotherapy induced osteoporosis', 'chemotherapy induced ulcers', 'millets and nutrition', 'millets and gastro protection', 'millets and immunosuppression', 'chemotherapy induced cardiac dysfunction, 'chemotherapy induced nephrotoxicity', 'millets uses' etc. The data relevant to present topic is discussed.

3. Results & discussion

Ayurveda has mentioned millets as grains with fewer calories as compared to wheat, rice, maize etc. The initiative of government has made impact about rethinking and reconsideration of this lost grain as evident through various education, research activities and business activities of millets. As proven superiorly beneficial, millets are termed as Shridhanya (a grain of superior qualities). The commonly used millets used are adaly millet [Coix lachrymal jobi L.] (Gavedhuka), barnyard millet [Echinochloa frumentacea L.] (Shyamaka), buck-wheat [Fagopyrum esculentum] (Kuttu), finger millet [Eleusine coracana Gaertn] (Nachani/ Ragi), amaranth [Amaranthus cruentus L] (Rajgira), foxtail millet [Setaria italica Beauv] (Kang), kodo millet [Paspalum scrobiculatum L] (Kodrava), little millet [Panicum sumatrense Roth], pearl millet [Pennisetum glaucum L] (Bajra), sorghum [Sorghum vulgare L] (Jowar). The pharmacological actions that should be taken into account while applying a diet based on millets to treat side effects caused by chemotherapy are listed in Fig. 1 [7–9].

4. Chemotherapy induced mucositis and ulcer

Oral mucositis is a major concern among patients undergoing chemotherapy. Overall 30–40% patients undergoing chemotherapy develops mucositis. Approximately 51% patients suffering for solid tumors or lymphoma develops mucositis [10]. About 60–85% patients undergoing an hematopoietic stem cell transplantation (HSCT) and almost 90% who get treated by radio and chemotherapy for head and neck cancer (HNC) patients develop mucositis or ulcers [11,12].

Chemotherapy-induced reactive oxygen species (ROS) and DNA damage cause basal or suprabasal epithelial cell death, erythematous or ulcerative lesions, atrophy, disruption in mucosal lining, leading to pain sensation and nausea. Due to this, patients suffer from poor nutrition,



Fig. 1. Pharmacological activities of millet.

weight loss, systemic/local infections, high grade mucositis etc. This occasionally causes discontinuation of chemotherapy protocol [13].

Adlay seeds possess a phenolic antioxidant that imparts gastroprotective properties by exerting preventative and protective role against ulcers [11]. Research states, a product including licorice root, foxtail millet, and adlay reduces stress induced ulcers in rats.

Adlay processed diet and foxtail millet increases stomach nonprotein sulfhydryl (NPSH) content of stomach thereby increasing the activity glutathione (a powerful antioxidant); which helps to reduce progression of cancer. The oxidative stress is reduced as these millets also decrease plasma and mucosal thiobarbituric acid reactive substances (TBARS). Millets exerts antioxidant potential, due to presence of phenolic acid, ferulic acid, tannins, and other nutrients, essential for a strong immune system [14]. Adaly possesses bioactive components such as lignans, flavonoids, and phenolic acids, which exhibits anticancer and anti-proliferative properties in addition to its antiulcer properties [15–17].

For ulcer protective effect of millets, use of unrefined flours is recommended. Horsegram, being rich in sterol and phospholipid compounds exerts ulcer-protective effect. Phytosterols enhance activity of membrane-bound enzymes and maintain its fluidity [18]. It also decrease sodium and proton ion leakage from cell membranes, and exerts anti-pyretic, anti-inflammatory, immune-stimulating properties etc. [19,20].

Foxtail millet is gastro-protective as its inner shell bran is rich in polyphenols. Polyphenols are reported to possess anti-inflammatory effects in LPS-induced HT-29 cells [in-vitro] and in nude mice [invivo] [21]. Polishing of grains are not advisable as polishing causes loss of protective buffer and lipids content[22,23], Research reports, higher prevalence of ulcers in the population taking principally refined wheat, milled rice and lower prevalence where unrefined wheat, millet based food are in used diet. [24] Refined flour of wheat and rice lacks protective buffer to gastric acid resulting in stimulatory effect on the gastric antrum causing higher acid outputs and thus becomes risk for ulcer formation.

5. Chemotherapy induced fatigue

Cancer fatigue is multi-dimensional which includes physical, mental,

and emotional manifestations like generalized weakness, loss of concentration, decreased motivation or interest to engage in usual activities, and emotional lability. It is a common symptom among patients receiving chemotherapy manifested due to decline in skeletal muscle mass and strength. It is responsible for deteriorating QOL of patient and has detrimental physical, psychological and financial consequences; leading to 30% of cancer-related deaths [25,26]. Skeletal muscle wasting and weakness is a complication of common chemotherapeutic drugs. Thus, nutritional support in the form of vital amino acids to replenish protein loss is essential for managing fatigue. Finger millet is a good source of tryptophan, isoleucine, methionine, valine, threonine and amino-acids. Isoleucine is useful in blood formation and repairing of muscles. Valine stimulates metabolism, assists in muscle coordination; repairs body tissue and maintains nitrogen balance in the body. Methionine is an essential amino acid present in ragi which helps in production of glutathione; a natural antioxidant [27]. Looking at the nutritional importance, finger millet based recipes should be included in the diet of cancer patients.

Millets offers abundant micronutrients like vitamins, beta-carotene etc. Some times, this nutrition is supplemented in synthetic form. Foxtail and little millet contain comparatively high iron content than rice. All the millets are extraordinarily superior in macro and micro-nutrition and are therefore, the solution for the fatigue. It can be preferred in the form of different recipe fortified with jaggery, cow's ghee, honey etc. Recipe like ragi *dosa*, ragi malt, ragi *ladoo*, horsegram dal, *jowar upma*, *bajra khichadi*, *roti* prepared from *jowar*, *bajra*, ragi etc. can be advised for patients undergoing chemotherapy for nutritional benefits.

6. Chemotherapy induced hair loss

Hair loss is one of the most commonly reported and psychologically distressing side effects of chemotherapy. It is due to cessation of mitotic activity in hair matrix resulting in narrow and weakened portion of hair shaft which becomes prone to fracture [28]. Research study reports that, millet extract powder (containing silicon and rosmarinic acid) given to patients for 12 weeks of hairfall helps in improvement of human hair. Silicon strengthens the combination of collagen; lack of silicon accelerates fallout of the hair or nail splitting. Rosmarinic acid is an anti-oxidant and helps in blood circulation [29].

According to Ayurveda concepts, hair is an *Upadhatu* of *Asthi Dhatu* (Bone). If *Dhatu* formation and functions are well, there will be supreme quality production of *Upadhatu*. For normal growth, development, and strengthening of bones, calcium is an important mineral [30]. Ragi and various ragi based recipes can be prescribed as calcium supplement [31]. However, there are no direct clinical evidences available in context of millets and chemotherapy induced hair loss.

7. Chemotherapy induced constipation

Constipation is a common and disturbing problem among many cancer patients during chemo-radiation, palliative care, and perhaps even during survivorship. Among patients of colon cancer, 49% develops incidence of post-chemotherapy chronic constipation [32]. The underlying mechanism is unclear. Millets being fiber rich are useful to relieve constipation.

The edible component of millet kernel is the rich source of dietary fibers. Intake of high fibers in foods helps in improvement of gut health and is important in the prevention of heart disease, colon cancer and diabetes. Finger millet and foxtail millets possess highest content of dietary fiber. If recipes are prepared from millets its dietary fiber content is increased. Among millet recipe, foxtail *idli* and proso millet *dosa* possess high fibers [33].

8. Chemotherapy-induced diarrhea

Chemotherapy-induced diarrhea is reported in 50-80% of patients

undergoing chemotherapy. It can cause depletion of electrolytes and thereby causing dehydration. This can lead to cardiovascular compromise and death. Additionally, diarrhea can interfere with cancer treatment due to dose delay and reduction [34]. Chemotherapeutic agents particularly, fluorouracil, capecitabine and irinotecan are responsible for diarrhea.

As per guidelines, initial management of mild to moderate diarrhea to be done by dietary modifications. Food with soluble fibers and rich in pectin are useful in diarrheal condition. e.g. sorghum helps to reduce motions frequency [35]. Finger millets starch is primarily [approximately 80–85%] composed of amylopectin [36]. Studies reports, on fermentation of millet bran, total phenols and total flavonoids content increases by 59.2% and 56.6%, respectively and soluble dietary fibers increases by six times [37]. Fermentation process increases the tryptophan content of millet bran, thus helps to improve intestinal inflammation and controls diarrhea [38].

Dietary fibers undergo fermentation in the large intestine and produces short-chain fatty acids like butyrate, propionate and acetate. Butyrate helps in the regeneration of colon mucosal cells and thereby reduces the risk of inflammatory bowel disease. Sometimes, in such patients constipation and diarrhea are observed alternately. As per Ayurveda; chronic altered bowel movements comes under the pathological condition called as *Grahani* (Irritable bowel syndrome, gluten enteropathy). Most of millets are gluten free and fiber rich hence helps in control of an immune mediated enteropathy or celiac disease.

9. Chemotherapy induced immune-suppression

Chemotherapeutic drugs are used commonly for conditions where diminution of the host immune response is a goal.An unfortunate side effect of chemotherapy-induced immunosuppression is that the patient becomes more vulnerable to opportunistic infections [39].

It is established that, tumors can promote immunosuppressive cells, primarily regulatory T lymphocytes, myeloid-derived suppressor cells, alternatively activates macrophages, or immature/tolerogenic dendritic cells. These cells inhibit anti-cancer immunity and significantly compromise the efficacy of immune-based therapies [40].

It is task to keep patient immune during and after the treatment of chemotherapy. In this regards, bioactive nutrient-induced immunity is helpful for defense. Millets comprised of macronutrients like vitamins, minerals, amino acids, lipids, antioxidant which are responsible to boost up immune response. Various millets based nutrients are essential for enhancing immunity are described in Table 1.

l-Arginine has potent strong immune-enhancing properties. It has been reported that, arginine deficiency affects immune cell functions of tumor-infiltrating lymphocytes, such as macrophages, natural killer cells, cytotoxic T-cells, dendritic cells etc. Glutamine improves the function of the gut barrier by protecting intestinal epithelial tight junctions and preserve the mucosal integrity. This may help to control the development of cancer and prevent infections. Tryptophan is a potent modulator of both innate and adaptive immune responses which plays crucial role in immune tolerance.

Zinc being immuno-modulator, strengthen host defense against initiation and progression of cancer. It is involved in cellular functions that are mainly related to cell cycle, apoptosis, and immune cell functioning. Deficiency of zinc affects the development of immune cells like B and T cells, natural killer cells, monocytes etc. Fibers are reported to modulate tissue immune responses and systemic inflammation [45].

Millets are a good source of polyphenols antioxidants, and fibers that helps to support gut microbiota function and, consequently, maintain gut immunity. Pearl millet is rich in iron, soluble and insoluble dietary fibers, minerals, and antioxidants, etc. Lysine, an important amino acid that is scarce in other cereals, is present in foxtail millet. Leucine, isoleucine, and methionine are among the necessary amino acids that are more abundant in proso millet's.

Foods recipes inclusive of millets are potent prebiotics and increase

Table 1

Dietary nutrients and their functions on immune cells.

No.	Nutrient	Function	Dietary sources & importnace	Ref
1	Arginine	Enhances immunity by upregulation of microRNA-155 and activation of CD8 T cells	Millets bran, finger millets. The bran germ proteins of millets contains approximately twice arginine as compared to endosperm. Finger millet is rich source of arginine.	[41]
2	Glutamine	Influence cell response by activating the GluR4 receptor on DCs	Millets endoderm contains double amount of glutamine as compared to bran germ	[42]
3	Tryptophan	Inducing effect on inflammatory cytokines	Found in pearl millet, finger millet, foxtail millet. Pearl millet contains good amount of tryptophan [average 2.4%]	[42]
4	Zinc	Development and functions	Found in <i>kodo</i> millet, pearl millet, sorghum. Sorghum flakes contains high zinc compared to its flour.	[43]
5	Fiber	Inhibit TNF- α , IL-8, -10 and -12 cytokines through SCFA, Increased activity of NK cells, Increased proportion of CD4 ⁺ and CD8 ⁺ cells	The dietary fiber of millets finger millet [11.24/100g],foxtail millet[11.24/100g], pearl millet [11/100g], sorghum[9.7/100g], proso millet [9.1/100g] and little millet [7.0/ 100g]. Highest fibers are noted in finger millets, foxtail millets. Fiber are important for hypoglycemic and hypo- lipidemic action thus inhibits atherosclerosis.It possess anti-toxic and anti-cancerous effect.	[44]

the viability of probiotics, which enhances health and strengthens immunity. Millets, being high in phytic acid and phytates, lowers cholesterol and reduce the risk of cancer. Sorghum and pearl millet contains good quantities of prebiotic components, viz. oligosaccharides, watersoluble fibers, and resistant starch which functions like probiotics [46]. Millets' is anti-inflammatory in properties aid in the prevention of inflammatory bowel disease and environmental enteropathy. By producing T cell cytokines, T helper cells contribute significantly to the function of other immune cells within the adaptive immune system. This suppresses or controls immunological responses, forming the initial line of protection.

10. Chemo induced osteoporosis and fractures

Significant bone loss is observed in 70% patients receiving chemoradiation. Treatment such as aromatase inhibitors, chemotherapy, and tamoxifen leads to accelerated bone loss and increased fracture risk [47]. Supplementing with calcium and vitamin D is crucial for preventing osteopenia and osteoporosis. Finger millet has an abundance of vital amino acids, phosphorus protein, and calcium [5–30 times more than other grains and 3 times more than milk [48,49]. It supplies the amino acid methionine, which is lacking in other cereals [46].

11. Diabetes

Diabetes increases the risk of infection in cancer patients, which

leads to chemotherapy dose reductions or discontinuations. Glycemic control is a crucial factor and affects level of health-related QOL and symptom severity experienced by a cancer patient.

Millets are an excellent tool for managing high blood sugar. Barnyard millet has very low, slowly digesting carbohydrate content. The predominantly found fatty acid like linoleic acid, palmitic and oleic acid shows a high degree of retrogradation of amylase, which further facilitates formation of higher amounts of resistant starches which helps to lower fasting blood glucose and insulin resistance and thus helpful to control diabetes. Barnyard millet helps to lower cholesterol and blood sugar levels; hence beneficial cardiovascular diseases and diabetes management and would be useful for overall survival of cancer patients [50].

Slow digesting starches aid in the control of metabolic disorders namely diabetes and hyperlipidemia. Prolonged digestion and absorption of carbohydrates is beneficial for controlling high glucose associated problems. Thus cooked millet flour is beneficial over flours of rice, maize, wheat etc. [50].

Millet bran is rich source of dietary fibers. Fiber, being slow in digestion, it increases the transit time and reduces the blood glucose [51, 52]. From studies it is reported that, *Jowar bran papdi* reduces blood glucose level in non-insulin dependent diabetic patient [53]. In-vivo studies reports feeding of proso millets improves levels of plasma adiponectin and HDL in genetically obese type-2 diabetic mice experimentally stressed under high fat conditions [54].

Millets include magnesium, which improves the body's ability to use insulin and glucose receptors, hence regulating blood sugar levels. Finger millets reduces the glycaemic response by inhibiting alpha amylase, being rich in fiber, it slow down the absorption and digestion of starch [55]. Sorghum and pearl millets contain fiber, magnesium, phenolic compounds, vitamin E and tannins which helps to reduces the risk of diabetes by lowering the sudden increase of blood glucose and insulin levels [56].Finger millets possess antioxidant and anti-diabetic properties due to their polyphenol content [57]. The anti-hyperglycemic properties of foxtail millets aqueous extracts are quite encouraging [58].Clinical trials have reported blood glucose lowering effect of foxtail millet [59].

12. Chemotherapy induced amenorrhea

In pre-menopausal women, if undergoing chemotherapy there is possibility to develop chemotherapy-associated amenorrhea. Newadjuvant therapies are essential in women of child-bearing age to deal with the threat of infertility. Roughly 25% of women diagnosed with breast cancer; 15 % of which falls under age of 45 years. Upon developing chemotherapy induced amenorrhea, women aging process gets fasten. Chemotherapy can lead to the induction of apoptosis in primordial follicles [60].

The condition, may get represented with fall in estradiol level, increases FSH and, or decline in inhibin-B and AMH levels. This is due to disturbance in hypothalamic-hypophyseal-ovarian axis leading to metabolic disturbances, weight changes, elevated androgen levels presenting with hirsutism, development of osteopenia and osteoporotic changes. Millets are useful for weigh management. Finger millet, undoubtedly, a rich source of calcium, protein, and essential amino acids thus useful to manage osteoporotic changes. Overall millets are good source of fibers so helpful for gut health and metabolic corrections. Being rich antioxidants, they help to protect body from oxidative damage changes

13. Chemotherapy induced cardiac dysfunction

Cardiac dysfunction is one of the undesirable side effects of chemotherapy, occurring in approximately 10% of the patients [61]. Millets' possess comparatively higher dietary fibers than other staple cereals. The soluble dietary fibers are good for maintaining cardiac health.as they reduce total serum and low-density lipoprotein cholesterol concentrations [62].

14. Chemotherapy induced nephrotoxicity

Certain chemotherapeutic agents such as cisplatin and ifosfamide cause nephrotoxicity due to damage of the nephron architecture leading to impairment in normal filtration, detoxification, and excretion functions of the kidneys. Through animal experimentation, it is reported that finger millet's seed coat extract possess nephroprotective action as it reduces alkaline phosphatase, aspartate transaminase, and alanine transaminase serum levels [63].

15. Millets and digestive capacity [Agni]

Though, millets have potential therapeutic benefits. It shall be advised as per patient's digestive capacity (*Agnibala*). Some millets namely *Kangu*, *Cheenaka* are difficult to digest. Overall all millets; due to its high fiber are difficult to digest. Millets possess balanced composition of fiber, vitamin and minerals; they serve as a good choice food to avoid over nutrition which is a cause of *Santarpana* diseases (diseases due to over nutrition or faulty lifestyle habits).

16. Millets and qualities required for digestion [Guna]

Ayurveda defines Rasapanchaka based pharmacodynamics of millets. Though, research based evidences has been discussed, while using at clinics, the basic principles of drug selection i.e. by considering the inhabitant qualities (Guna) in relation to constitution (Prakruti), habit (Desha), season (Kala), age (Vaya) etc. are ought to consider. A personalized medicine approach cannot be overlooked while prescribing millets administration for therapeutic ailments [64]. Millets namely, foxtail, kodo, proso millets are heavy (Guru) for digestion due to rich fiber content. Hence, it shall be advised for patients whose hunger is high or may be preferred during day time meal. On the basis of Guna, all millets are Ruksha ([provides roughness, assist scraping action). Hence, it is common guideline that millets based recipes shall be consumed with ghee or oil. Finger millet serves as exception as it is *Snigdha* (unctuous) in nature. Millets cultivation does not require use of pesticides and hence an organic pest free grain which can significantly contribute to improve QOL of a cancer patient.

Adlay millets are highly *Ruksha*, hence, shall be given only to obese patients having excessive accumulation of lipids (*Meda*). Processing methods such as dehulling, decortication, grinding, and extrusion reduce the amount of dietary fiber, total proteins, and micronutrients [4].

Over consumption of ragi may enhance the level of oxalic acid; so shall be cautiously given to patient suffering from renal stones. Millets being *Ruksha* and *Vatakara* (aggravates *Vata dosha*) shall not be consume for long time. It should be used in the form of different recipe prepared by adding milk, ghee, jaggery and spices etc. *Kodrava* is *Avrushya* (antiaphrodisiac) and also quoted as *Vikashi* (may affects the joints lubrication and stability). It shall be given with cautions or in less quantity for short duration.

17. Anticancer potential of millets

Foxtail millet bran possess anti-cancer potential on colon cancer due to presence of peroxidase of class III protein. Ethanol extract of foxtail millet exhibits anti-proliferative effects on breast cancer cell lines by causing cell cycle arrest in the G2/M phase, increased DNA fragmentation and an increase in the number of cells in Sub-G1 phase [65]. Phenolic extract of dehulled pearl grain possess anti-carcinogenic activity. Phenolic compounds isolated from whole pearl millet grain (52.7%) and dehulled grain (43.8%) exhibited greater inhibitory effects against the colon cancer cell line HT-29 [66]. Vanillin (4-hydroxy-3-methoxybenzaldehyde) extracted from proso millets showed significant suppression of cellular proliferation of HT-29 cells line [67]. Vanillin extracted from proso and barnyard millet significantly inhibits proliferation of MCF-7 cells through G0/G1 phase cell arrest and increases the apoptotic cells in the sub-G₀ phase in a dose-dependent manner [68].

Millets based foods are predominantly used in Asia and Africa countries. In India, the traditional recipes like roti, *dosa, upama*, porridge, *laddo* are routinely consumed. In Africa, recipes like bread, oshikwila, injera, banku, kenkey, jollof etc. recipes are prepared. However, in current era, millets bread, cookies, noodles, biscuits etc. are used.

18. Conclusion

Millets are super food, rich in nutritional phytochemicals, fiber, vitamins, minerals, gluten and pesticide free. Millets being gastroprotective, anti-oxidant, anti-inflammatory, lipids lowering, antibacterial, immunomodulatory in actions serve as a smart choice as an adjuvant diet for a patient undergoing chemotherapy or suffering from chemo-induced side effects. The use of millet-based dishes, which are readily available, affordable will definitely help patients experiencing side effects due to chemotherapy by reducing symptoms severity and improving their overall quality of life.

Financial support

Nil

Declaration of competing interest

None

Credit author statement

ST is the sole author of this paper and she handled all the roles Cconceptualization, methodology, data collection, data curation, data analysis, writing original draft, review and editing, validation, final draft review and supervision.

Acknowledgements

Author acknowledges Management of Dr D Y Patil College of Ayurved & Research Center, Dr D Y Patil Vidyapeeth (deemed to be university), Pimpri, Pune for support and encouragement.

References

- Vetriventhan M, Azevedo VCR, Upadhyaya HD, Nirmalakumari A, Kane-potaka J, Anitha S. Genetic and genomic resources, and breeding for accelerating improvement of small millets: current status and future interventions. Nucleus 2020;63:217–39.
- [2] Kane-Potaka J, Kumar P. Smart food food that is good for you, the planet and the farmer, vols. 71–82. in State of India's Livelihoods Report 2019 [New Delhi: Access Development Services]; 2019. Available online at: https://livelihoods-india.org/p ublications/all-page-soil-report.
- [3] Ramesh S, Kosalram K. The burden of non-communicable diseases: A scoping review focus on the context of India. J Educ Health Promot 2023;28(12):41.
- [4] Amadou I, Gounga ME, Millets Guo-Wei L. Nutritional composition, some health benefits and processing—a Review. Emir J Food Agric 2013;25(7):501–8.
- [5] Arnold JT. Integrating ayurvedic medicine into cancer research programs part 2: Ayurvedic herbs and research opportunities. J Ayurveda Integr Med 2022;16: 100677.
- [6] Vaidya Charaka In: Jadavaji Trikamji Acharya, editor. Charaka samhitha. Delhi: chaukhamba prakashan; sutrasthana, annapanavidhi adhyaya; 2011;154–155.
- [7] Bhavamishra. Bhavaprakasha Samhita edited by srikantha murthy,K.R. Chowkhamba krishna das academy; varanasi. Dhanya varga; 2011; p. 374–7.
- [8] Kaiyadeva Kaiyadeva Nighantu [Pathyaapthya vibhodika] edited by Prof priya vrat sharma, Dr guru prasada sharma, Dhanya varga, Varanasi: Choukambha Orientalia; 2009;318–321.

S.D. Tavhare

Journal of Ayurveda and Integrative Medicine 15 (2024) 100901

- [9] Lalla RV, Sonis ST, Peterson DE. Management of oral mucositis in patients who have cancer. Dent Clin 2008;52(1):61–77.
- [10] Chung CP, Hsia SM, Lee MY. Gastroprotective activities of adlay [Coix lachrymajobi L. var. ma-yuen Stapf] on the growth of the stomach cancer AGS cell line and indomethacin-induced gastric ulcers. J Agric Food Chem 2011;59:6025–33.
- [11] Villa A, Sonis ST. Pharmacotherapy for the management of cancer regimen-related oral mucositis. Expet Opin Pharmacother 2016;17:1801–7.
- [12] Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, Morrone A, et al. Oral mucositis: the hidden side of cancer therapy. J Exp Clin Cancer Res 2020;39:210.
- [13] Chandrasekara A, Shahidi F. Content of insoluble bound phenolics in millets and their contribution to antioxidant capacity. J Agric Food Chem 2010;58:6706–14.
 [14] Kuo CC, Shih MC, Kuo YH, Chiang W. Antagonism of free-radical-induced damage
- of adlay seed and its antiproliferative effect in human histolytic lymphoma U937 monocytic cells. J Agric Food Chem 2001;49:1564–70.
 [15] Lee MY, Tsai SH, Kuo YH, Chiang W. Anti-tumor and anti-inflammatory activity of
- the methanol extracts from adlay bran. Food Sci Biotechnol 2008;17:1265–71.
- [16] Li SC, Chen CM, Lin SH, Chiang W, Shih CK. Effects of adlay bran and its ethanolic extract and residue on preneoplastic lesions of the colon in rats. J Sci Food Agric 2011;91:547–52.
- [17] Hennessy TM. Effect of membrane plant sterols on excitable cell function. Comp Biochem Physiol 1992;101:1–8.
- [18] Gupta MB, Nath R, Srivastava N, Shanker K, Kishor K, Bhargava KP. Antiinflammatory and antipyretic activities of beta-sitosterol. Planta Med 1980;39(2): 157–63.
- [19] Bouic PJ, Lamprecht JH. Plant sterols and sterolins: a review of their immunemodulating properties. Alternative Med Rev 1999;4(3):170–7.
- [20] Tovey FI, Capanoglu D, Langley GJ, Herniman JM, Bor S, Ozutemiz O, et al. Dietary phytosterols protective against peptic ulceration. Gastroenterol Res 2011 Aug;4(4):149–56.
- [21] Shi J, Shan S, Li H, Song G, Li Z. Anti-inflammatory effects of millet bran derivedbound polyphenols in LPS-induced HT-29 cell via ROS/miR-149/Akt/NF-κB signaling pathway. Oncotarget 2017;8:74582–94.
- [22] Jayaraj AP, Tovey FI, Clark CG. The possibility of dietary protective factors in duodenal ulcer. II. An investigation into the effect of pre-feeding with different diets and of instillation of foodstuffs into the stomach on the incidence of ulcers in pylorus-ligated rats. Postgrad Med 1976;52:640–4.
- [23] Tovey FI, Hobsley M. Milling of wheat, maize and rice: effects on fibre and lipid content and health. World J Gastroenterol 2004;10(12):1695–6.
- [24] Iop A, Manfredi AM, Bonura S. Fatigue in cancer patients receiving chemotherapy: an analysis of published studies. Ann Oncol 2004 May;15(5):712–20.
- [25] Melstrom LG, Melstrom Jr KA, Ding XZ, Adrian TE. Mechanisms of skeletal muscle degradation and its therapy in cancer cachexia. Histol Histopathol 2007;22: 805–14.
- [26] Huot JR, Essex AL, Gutierrez M, Barreto R, Wang M, Waning DL, et al. Chronic treatment with multi-kinase inhibitors causes differential toxicities on skeletal and cardiac muscles. Cancers [Basel 2019;11:571.
- [27] Gull A, Jan R, Navik GA, Prasad K, Kumar P, Longowal S. Significance of finger millet in nutrition, health and value-added products: a review. J Environ Sci Comput Sci Eng Technol 2014;3(3):1601–8.
- [28] Batchelor D. Hair and cancer chemotherapy: consequences and nursing care. A literature study. Eur J Cancer Care 2001;10:147–63.
- [29] Najima Masatomo, Miyara Akinobu, Inotsume Yuko. Hair restoration efficacy of a food containing millet extract with keratin powder, vol. 2; 2016. p. 43.
- [30] Vannucci L, Fossi C, Quattrini S, Guasti L, Pampaloni B, Gronchi G, et al. Calcium intake in bone health: a focus on calcium-rich mineral waters. Nutrients 2018;10 (12):1930.
- [31] Devi PB, Vijayabharathi R, Sathyabama S, Malleshi NG, Priyadarisini VB. Health benefits of finger millet (Eleusine coracana L.) polyphenols and dietary fiber: a review. J Food Sci Technol 2014;51(6):1021–40.
- [32] Denlinger CS, Barsevick AM. The challenges of colorectal cancer survivorship. J Natl Compr Cancer Netw 2009;7:883–94.
- [33] Mounika M, Uma Devi K. Dietary fibre content in healthy millet based recipes. Int J Curr Microbiol App Sci 2019;8(7):1829–34.
- [34] Stein A, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management. Ther Adv Med Oncol 2010;2(1): 51–63.
- [35] Wursch P. The role of viscous soluble fiber in the metabolic control of diabetes. Diabetes Care 1997;20(11):1774–80.
- [36] Bhatt A, Singh V, Shrotria PK, Baskheti DC. Coarse grains of Uttaranchal: ensuring sustainable food and nutritional security. Indian Farmer's Digest; 2003. p. 34–8.
 [37] Min Z, Jia X, Xie T, Zhou Y, Gong M, Xu X, et al. Extraction of soluble dietary fiber
- [37] Min Z, Jia X, Xie T, Zhou Y, Gong M, Xu X, et al. Extraction of soluble dietary fiber in rice bran meal by microbial fermentation method. China Brew 2017;36:59–62.
 [38] Islam, Sato S, Watanabe K, Watanabe T, Hirahara K, Aoyama Y, et al. Dietary
- tryptophan alleviates dextran sodium sulfate-induced colitis through aryl hydrocarbon receptor in mice. J Nutr Biochem 2017;42:43–50.
- [39] Rasmussen L, Arvin A. Chemotherapy-induced immunosuppression. Environ Health Perspect 1982;43:21–5.
- [40] Zitvogel L, Tesniere A, Kroemer G. Cancer despite immunosurveillance: immunoselection and immunosubversion. Nat Rev Immunol 2006;6:715–27.

- [41] Glew RS, Chuang LT, Roberts JL, Glew RH. Amino acid, fatty acid and mineral content of black finger millet [Eleusine coracana] cultivated on the Jos plateau of Nigeria. Food 2008;2(2):115–8.
- [42] Metz R, Smith C, DuHadaway JB, Chandler P, et al. Ido2 is critical for Ido1mediated T-cell regulation and exerts a non-redundant function in inflammation. Int Immunol 2014;26:357–67.
- [43] Bonaventura P, Benedetti G, Albarède F, Miossec P. Zinc and its role in immunity and inflammation. Autoimmun Rev 2015;14:277–85.
- [44] Bailón E, Cueto-Sola M, Utrilla P, Rodríguez-Cabezas ME, Garrido-Mesa N. Zarzuelo A.et al. Butyrate in vitro immune-modulatory effects might be mediated through a proliferation-related induction of apoptosis. Immunobiology 2010;215: 863–73.
- [45] Janakiram NB, Mohammed A, Madka V, Kumar G, Rao CV. Prevention and treatment of cancers by immune modulating nutrients. Mol Nutr Food Res 2016;60 (6):1275–94.
- [46] Shobana S. Finger millet [ragi, eleusine coracana L.]: a review of its nutritional properties, processing, and plausible health benefits. Adv Food Nutr Res 2013;69: 1–39.
- [47] Stumpf U, Kostev K, Siebenbürger G, Böcker W, Hadji P. Influence of chemotherapy and endocrine treatment on fractures in postmenopausal women with breast cancer - a retrospective cohort study. J Bone Oncol 2020;22:100292.
- [48] Nirgude M, Babu BK, Shambhavi Y, Singh UM, Upadhyaya HD, Kumar A. Development and molecular characterization of genic molecular markers for grain protein and calcium content in finger millet [Eleusine coracana [L.] Gaertn.]. Mol Biol Rep 2014;41(3):1189–200.
- [49] Anitha S, Givens DJ, Botha R, Kane potaka J, Saulaiman NLB, Tsusaka TW, et al. Calcium from finger millet-a systematic review and meta-analysis on calcium retention, bone resorption, and in vitro bioavailability. Sustainability 2021;13(16).
- [50] Asp NG Nutritional Classification and analysis of food carbohydrates. Am J Clin Nutr 1994;59(1):679–81.
- [51] Shobana S, Sreerama YN, Malleshi NG. Composition and enzyme inhibitory properties of finger millet [*Eleusine coracana* L.] seed coat phenolics: mode of inhibition of α-glucosidase and pancreatic amylase. Food Chem 2009;115(4): 1268–73.
- [52] Kavitha P, Easwaran P, Mageshwari US. Effect of different methods of cooking on the dietary fibre content of wheat and wheat products and their hypoglycemic effect on NIDDM patients. Indian J Nutr Diet 2001;38(6):173–81.
- [53] Kamble RM, Shinde UV. Utility of Bran products in non insulin dependent diabetes mellitus [NIDDM] patients. J Hum Ecol 2004;16(3):219–22.
- [54] Park KO, Ito Y, Nagasawa T, Choi MR, Nishizawa N. Effects of dietary Korean proso-millet protein on plasma adiponectin, HDL cholesterol, insulin levels and gene expression in obese type 2 diabetic mice. Biosc Biotech Biochem 2008;72(11): 2918–25.
- [55] Kumari PL, Sumathi S. Effect of consumption of finger millet on hyperglycemia in non-insulin dependent diabetes mellitus [NIDDM] subjects. Plant Foods Hum Nutr 2002;57:205–13.
- [56] Montonen J, Paul K, Ritva J, Arpo A, Antti R. Wholegrain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr 2003;77:622–9.
- [57] Chethan S, Dharmesh SM, Malleshi NG. Inhibition of aldose reductase from cataracted eye lenses by finger millet [Eleusine coracana] polyphenols. Bioorg Med Chem 2008;16:10085–90.
- [58] Sireesha Y, Kasetti RB, Swapna SAS, Apparao C. Anti hyperglycemic and hypolipidemic activities of Setaria italica seeds in STZ diabetic rats. Pathophysiology 2011;18(2):159–64.
- [59] Ren X, Yin R, Hou D. The glucose-lowering effect of foxtail millet in subjects with impaired glucose tolerance: a self-controlled clinical trial. Nutrients 2018;10:1509.
- [60] Bines J, Oleske DM, Cobleigh MA. Ovarian function in premenopausal women treated with adjuvant chemotherapy for breast cancer. J Clin Oncol 1996;14: 1718–29.
- [61] Cardinale D, Colombo A, Bacchiani G, Tedeschi I, Meroni CA, Veglia F, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation 2015;131:1981–8.
- [62] McRae MP. Dietary fiber is beneficial for the prevention of cardiovascular disease: an umbrella review of meta-analyses. J Chiropr Med 2017;16(4):289–99.
- [63] Okoyomoh K, Okere OS, Olowoniyi OD, Adejo GO. Antioxidant and antidiabetic properties of Eleusine coracana [L.] Geartn [finger millet] seed coat matter in streptozotocin induced diabetic rats. Int. J Adv Herb Altern Med. 2013;1:1–9.
- [64] Venil N. Sumantran and Girish Tillu. Insights on personalized medicine from Ayurveda. J Alternative Compl Med 2013:370–5.
- [65] Shan S, Li Z, Newton IP, Zhao C, Li Z, Guo M. A novel protein extracted from foxtail millet bran displays anti-carcinogenic effects in human colon cancer cells. Toxicol Lett 2014;227:129–38.
- [66] Chandrasekara A, Shahidi F. Bioactivities and antiradical properties of millet grains and hulls. J Agric Food Chem 2011;59:9563–71.
- [67] Ramadoss DP, Sivalingam N. Vanillin extracted from Proso and Barnyard millets induce apoptotic cell death in HT-29 human colon cancer cell line. Nutr Cancer 2020;72:1422–37.
- [68] Ramadoss DP, Sivalingam N. Vanillin extracted from proso and barnyard millets induces cell cycle inhibition and apoptotic cell death in MCF-7 cell line. J Cancer Res Therapeut 2021;17:1425–33.