A Review on Phytochemical and Pharmacological Activities of Eleusine Coracana

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ABSTRACT

Eleusine coracana is a significant millet that is a staple meal for many Asian and African populations that are struggling economically. India is home to several locations of it, including Punjab, Kerala, Assam, Madhya Pradesh, and Odisha. Commonly called as Finger millet, Ragi seed grain is traditionally utilized for ulcer, diabetes, osteoporosis, depression, insomnia and anemia. Additionally, it is supposed to help nursing moms produce more milk. Dietary fibers, vitamins, proteins, alkaloids, steroids, terpenoids, tannins, carbohydrates, minerals, lipids, and polyphenols are all abundant in finger millet. Additionally, it has been shown to have antioxidant, diuretic, anticancer, antimicrobial, and antidiuretic, hypolipidemic, and anti-inflammatory qualities. This paper provides a comprehensive analysis of the polyphenols and dietary fiber found in finger millet, focusing on their impact on the health benefits associated with consuming millet.

KEYWORDS: *Eleusine coracana*, Finger millet, Polyphenols, Antioxidant, anti-inflammatory.

INTRODUCTION

Plants have been used for centuries in the control and prevention of a several different medical conditions such as diabetes, arthritis, ulcers, tumors, malaria, hypertension, and many more. Medicinal plants have been the source of lead chemicals utilized in the creation of new drugs with great effectiveness and few negative effects (Juárez-Rojop et al; 2014). Aside from their abundance in vitamins and minerals that are necessary for a healthy body's metabolism, plants often referred to as having secondary metabolites like steroids, tannins, flavonoids, phenols, saponins, and alkaloids, cardiac glycosides. These phytochemicals have been shown to have therapeutic benefits when utilized in moderation (Edeoga et al; 2005). Millets are tiny annual cereal crop species with seeds that are members of the Poaceae family. The term "millet" is of French origin, coming from the word "Mille" which meaning thousands (Ramashia et al; 2019).

Eleusine coracana, commonly referred to as finger millet in India as mandua or ragi, is a remarkable kind of millet belonging to the grass family Gramineae or Poaceae (Singh et al; 2016). Although it originated in the Ethiopian area, it is now mostly cultivated in Asia and Africa.

It is a crop species that self-pollinates and has chromosomes number 36 (allotetraploid), that is spread among around 10 genera and 20 species overall (Karki et al; 2020). With over 60% of the world's production, India is the top producer of finger millet, followed by Ethiopia. (Gull et al; 2014). The globular grains of finger millet have a diameter ranging from 1.0 to 1.5 mm. The finger millet kernel is divided into three main parts: the endosperm, the embryo, and the seed coat. The phrase "pericarp" or "glume" refers to the uppermost layer of millet which has little nutritional significance (Ramashia et al; 2019). The millet is rich in phytochemicals due to the presence of polyphenols in its seed coat, germ, and endosperm cell walls (Shobana et al; 2013). There are several health advantages associated with finger millet, including anti-aging, antioxidant anti-diabetic, anti-hyperactivity, healing, and anti-cancer properties (Antony et al; 2018). Finger millet flour may be utilized for the manufacture of numerous nutrient rich or dense dishes which can be used for supplement feeding. Finger millet flour give numerous health advantages including finger millet for reducing weight, healthy bone, decreasing blood cholesterol, for anemia and other health concerns. Finger Millet is the excellent source of calcium, phosphate and iron (Wadikar et al; 2007). Finger millet contains excellent quality protein combined with the presence of key amino acids, vitamin A, vitamin B (Gopalan et al; 2004).

Fig 1: Plants and seeds

Phytochemical Constituents:

Hexane, ethyl acetate and ethanol extraction of seeds, demonstrated the presence of terpenoids, alkaloids, phenols, and steroids, tannins, phenols, cardiac glycosides, balsams (David et al, 2014). Hexane extracts of three distinct cultivar of finger millet also the presence of tannins alkaloids, terpenoids, (Shukla et al; 2015). The oil content of this grain is determined to be 0.74% consisting of oleic acid (47.16%), linoleic acid (24.79%) and palmitic acid (23.07%) (Poonia et al; 2012). Aqueous extract of the powdered seed of *Eleusine coracana,* indicating the presence of carbohydrates, alkaloids, proteins, reducing sugars, saponins, tannins, phenols, flavonoids, and terpenoids (Oseghale et al; 2020). Finger millet contains amino acids such as, Valine, Methionine, Isoleucine, Leucine, Tyrosine, Phenylalanine, Histidine, Lysine, Arginine, Proline, Glycine, Alanine, Cystine, Aspartic acid, Threonine, Serine, Glumatic acid, Proline, Glycine, Alanine, Cystine, Valine,

Methionine (Ravindran G; 1992). In addition, finger millet contains vitamins, B vitamins, ascorbic acid, thiamin, riboflavin, and niacin (Amir et al; 2016). The polyphenols found in finger millet, include quercetin, vanillic, syringic, ferulic, p-hydroxy benzoic, p-coumaric, and gallic and protocatechuic acids are present in ragi seed coat (Chethan et al; 2008). Finger millet contains minerals such as Ca (0.33%), P (0.24%), K (0.43%), Na (0.02%) Mg (0.11%) Fe (46.0%) Mn (7.5%) Zn (15.0%) (Devi et al; 2011). Gallic acid, tannic acid, vanillic acid, ferulic acid, caffeic acid, and chlorogenic acid are polyphenols that are thought to be found in the seed. The crude polyphenols of Eleusine coracana extracted by HCl-methanol were fractionated using High Performance Liquid Chromatography (HPLC), more polyphenols found in the finger millets' seed coat were identified, including Gallic aid (12.61%), trans-cinnamic acid (3.6%), p-coumaric acid (4.40%), syringic acid (4.0%), proto-catechuic acid (15.32%), P-hydroxyl benzoic acid (17.91%), ferulic acid (32.82%), and vanillic acid (3.81%). 4-O-Methyl gallic acid, prodelphinidin dimer, diadzein, catechin gallates, trimmers of catechin, tetramers of catechin, kaempferol, naringenin, phoroglucinol, apigenin, (+)-catechin, epicatechin, luteolin glycoside (orientin), trans feruloyl-malic acid, are the polyphenols that were previously found (Oseghale et al; 2017).

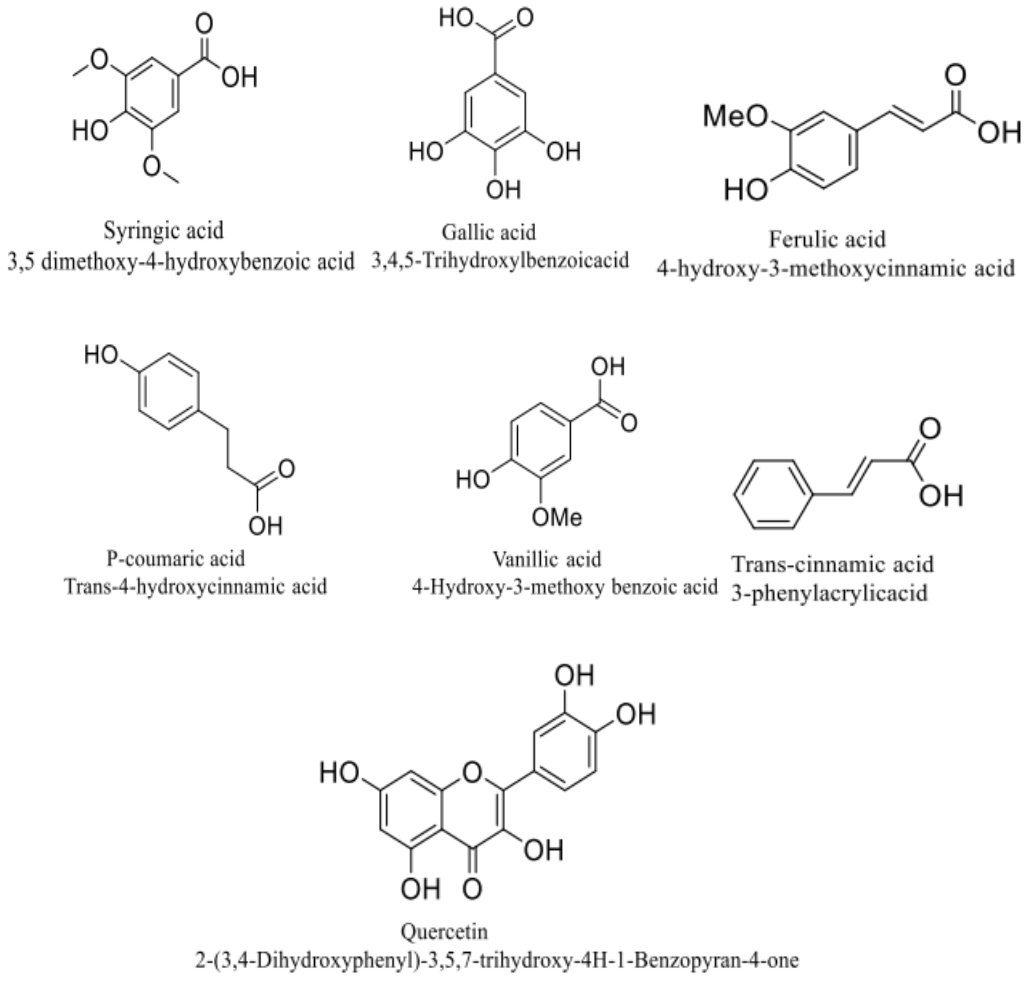

Fig 2: Compounds present in *Eleusine coracana Linn*.

Ethnomedicinal uses:

In the many communities where they are located, the plant's seed grain, *Eleusine coracana Linn*, is utilized to treat certain illnesses. It is reported to be utilized in the treatment of diabetes, avoiding of osteoporosis and anemia. It's also said to help women who are nursing but are having trouble lactating by increasing the flow of milk. When consumed, finger millet is supposed to promote relaxation and be helpful in the treatment of anxiety, and insomnia, depression. In addition, the seeds (grains) are utilized as an anti-aging agent, to improve weight loss, lower cholesterol, and heal damaged tissues (Mall et al; 2016).

PHARMACOLOGICAL ACTIVITIES

1. Antilithiatic activity:

Finger millet was shown to have the ability to both enhance kidney function and prevent the development of crystal growth in both its aqueous and ethanol fractions (Mathanghi et al; 2012). Reported the effect of *Eleusine coracana* grain aqueous and alcohol extracts about male albino rat nephrolithiasis caused by calcium oxalate. Both hyperoxaluria and elevated excretion of calcium and phosphate by the kidneys were seen in the case of ethylene glycol feeding. Supplementation with aqueous and alcohol extracts (300 mg/kg b.w., p.o.) considerably decreased the increased urine oxalate, demonstrating a regulatory influence on endogenous oxalate production. Aqueous and alcohol extracts were used as a therapeutic and preventative therapy, which considerably reduced the elevated deposition of stone-forming components in the kidneys of calculogenic rats. Therefore, the preventative and therapeutic therapy with aqueous and alcohol extracts exhibited cytoprotective and kidney-function-improving properties while inhibiting the development of crystals (Bahuguna et al; 2009).

2. Diuretic activity:

Reported the ethanolic and aqueous extracts of grains of *E. coracana* (300 mg/kg, b.w., p.o.) were examined for diuretic action. The activity was compared with furosemide (20 mg/kg, i.p.) as standard medication. Results demonstrated that both the extracts displayed considerable diuretic action as shown by the total volume of urine and the urine contents of Na+, K +, Cl (Bahuguna et al; 2009).

3. Anticancer activity:

Differences in the Free and Bound Phenolics of *Eleusine coracana* Seeds' Anticancer Activity have been reported. The FM-FP and FM-BP fractions contained phenolics, phenolic acid derivatives, flavonoids, and amino acids, according to an analysis of the UPLC-QTOF-MS data. Both fractions showed the ability to lower ferric ions and scavenge DPPH radicals. Nonetheless, there were significant differences in how FM-FP and FM-BP affected the proliferation of various cell types. When FM-FP and FM-BP were examined in relation to breast cancer cell lines, FM-FP had more cytotoxic capability. Cytotoxic FM-FP increased DNA fragmentation, which resulted in an accumulation of cells in Sub-G1 phase, and G0/G1 or G2/M arrest in a cell line-dependent manner (Mahadeva swamy et al; 2022). After being separated as fractions in an organic solvent, phenolic acids from finger millet (*Eleusine coracana*) were assessed for their potential anticancer effects.

To check for anticancer effectiveness against HepG2 hepatic cancer cell lines, a cytotoxicity experiment was performed (Singh et al; 2015). The purpose of this study was to examine the effects of a protein extracted from seeds on the chronic myeloid leukemia cell line K562, namely its ability to induce apoptosis and inhibit proliferation. Using flow cytometric analysis, the extract's ability to induce apoptosis was evaluated. The K562 cells' apoptosis was triggered and their proliferation was reduced in a dose-dependent manner by the protein extract from ragi seeds. In contrast, the anti-proliferative activity of the seed extract was not able to affect normal human peripheral blood mononuclear cells. The extract's value was found to be 2 mg/ml. This research therefore reveals that the ragi seed extract has selective anticancer effect, as it can target and reduce K562 cells (Singh et al; 2011).

4. Antifungal activity:

Discovered an endophytic fungus that was separated from *Eleusine coracana*, a plant that yields a lot of naturally occurring anti-fungal compounds. Five different fungus species were separated from roots and classified according to their taxonomic range using 18S rDNA sequencing. *F. graminearum* and 3 (three) additional pathogenic Fusarium species had their growth suppressed by extracts from three potential endophytes. Using pathogenicity and confocal imaging investigations, it was determined that the mostly effective anti-Fusarium strain (WF4, presumed to be a Phomasp.) behaves as an endophyte. By fractionating the WF4 extract under the guidance of bioassay, four anti-fungal substances were identified: alternariol monomethyl ether, viridicatol, tenuazonic acid. In vitro, *F. graminearum* hyphae broke dramatically under the influence of all the isolated chemicals. Thus, it may be concluded that the storied, disease-resistant finger millet crop represents a brand-new source of natural compounds with endophytic anti-fungal properties (Walaa et al; 2015).

5. Antidiabetic activity:

Reported the ethanolic extract of *Eleusine coracana* hyperglycaemia was effectively created in this research as demonstrated by the considerably high blood glucose levels confirmed for the groups that experienced hyperglycemia due to alloxan during the course of the 14-day study period. Comparing the blood glucose levels of the graded doses of E. coracana extract (250, 500, and 1000 mg/kg)-administered rats to the hyperglycaemic control rats throughout the course of the 24-hour studies produced significant reductions. When comparing the blood glucose levels of the hyperglycaemic control group on the seventh and fourteenth day of the 14-day trial, E. coracana extract, at all tested doses, resulted in a significant and dose-dependent decrease. Similarly, the conventional medicine (Metformin, 125 mg/kg) dramatically dropped the blood glucose levels (Yaro et al; 2018). The study conducted on finger millet varieties from Sri Lanka revealed that the Ravi, Rawana, and Oshadha varieties exhibited anti alpha amylase, anti-alpha glucosidase, antiglycation, and glycation reversing activities. Additionally, the varieties showed promise in reducing postprandial hyperglycemia and preventing diabetic complications mediated by advanced glycation end products. (Jayawardana et al; 2022). There has been research on the impact of feeding finger millet and kodo millet on the glycaemic and antioxidant state of diabetic rats produced by alloxan. The results showed a 36 and 42% decrease in blood glucose levels. (Shobana et al; 2010). Feeding FM or KM for 28 days to alloxan-induced diabetic rats' greater reduction in blood glucose level 42% (Hegde et al; 2005).

6. Anti-inflammatory activity:

Syringol separated from *Eleusine coracana* bran methanol extract was evaluated for Suppression in cPLA2, COX-2, IB, p38, and MPO signalling in sPLA2-induced mice paw oedema, which inhibits an inflammatory response. It was located Syringol considerably reduced in vitro the activity of the enzymes sPLA2 and 5-LOX. Substrate and calcium ion concentration had no effect on the inhibition. Fluorescence and molecular docking experiments have shown that it interacts with isolated sPLA2 enzymes. It also suppressed the growth of sPLA2 and edema caused by λ-carrageenan that was dose-dependent. Western blots also show that syringol reduces the expression of cPLA2, COX2 IκBα, p38, and MPO in swelling tissues [Vishwanath et al; 2022]. The demand for new sources of anti-inflammatory medicines is rising due to the rising prevalence of oxidative stress-related and inflammatory-mediated disorders globally. This work aimed to determine the in vitro inhibitory actions of oxidative burst, xanthine oxidase (XO), hyaluronidase, and arachidonate 5-lipoxygenase (A5-LOX) of the finger millet cultivars Rawana, Oshadha, and Ravi using ethanolic and methanolic extracts. The strongest A5-LOX and XO inhibitory actions were shown by the methanolic extract of Oshadha among all extracts. At a concentration of 1 mg/ml, the hyaluronidase inhibitory activity of all extracts was less than 50% (Sooriya Arachchige et al; 2021).

7. Hepatoprotective activity:

The goal of the current research is to assess the preventive effect of several extracts from *Eleusine coracana* grains against hepatotoxicity in rats caused by carbon tetrachloride (CCL4). Enzymatic analysis demonstrated that *E. coracana* significantly reduced the biochemical parameters altered by CCl4, indicating hepatoprotective action. Serum levels of alkaline phosphatase (ALP), total protein, serum glutamate pyruvate transaminase (SGPT), and serum glutamate oxaloacetate transaminase (SGOT) were all significantly reduced by the extracts 500 mg/kg by oral administration. The extract's activity was on par with that of the prescribed medication, silymarin (100 mg/kg, p.o.). Additionally, histopathological examinations showed that the animal was protected against CCL4 induced liver injury by treatment with extracts from *Eleusine coracana*. The findings suggest that the various *Eleusine coracana* grain extracts have hepatoprotective effects on rats' liver damage caused by CCL4 (Pingle et al; 2011).

8. Anticataract activity:

Ragi seed coat polyphenols have been shown to have cataract prevention and treatment potential. Aldose reductase is a monomeric reduced NADPH-dependent enzyme that belongs to the superfamily Aldo–keto reductase. Diabetic complications like as retinopathy, neuropathy, nephropathy, and cataractogenesis have been associated with it. In the presence of NADPH, this enzyme converts glucose to sorbitol (Scheme 1A–C). Aldose reductase (AR) is largely restricted to the lens epithelium, despite the fact that human lenses have been shown to have low quantities of the enzyme and high levels of polyol dehydrogenase (PD) in comparison to animal lenses. compared to adult lenses, two to three times greater in juvenile lenses which is enough to significantly increase osmotic pressure and promote cataractogenesis. It has been documented that the tissues of both diabetic animals and humans have elevated amounts of sorbitol.

A thorough review of the literature revealed that using natural remedies, especially those derived from plants high in flavonoids, might either stop or decrease the rate of cataract development. Also, robust in vivo AR inhibitory impact and flavonoid hypoglycemic action discovered in the presence of greater levels of types of phenolics in finger millet encouraged us to examine the AR inhibitory potentials of the millet phenolics (Chethan et al; 2008). 1 % HCl in methanol extract of finger mellet, six weeks of 20% seed coat matter diet were provided to the rats following the induced of diabetes with a 40 mg/kg body weight dose of streptozotocin demonstrated less cataract progression than the control group, which was not given the seed coat matter treatment. The control group's cataracts were mature when the six-week diabetes induction period was monitored using a camera linked to a slit light (Shobana et al; 2010).

9. Antimicrobial activity:

Finger mellet phenolic compounds were investigated for their antibacterial properties using the agar well diffusion experiment. The test was performed using Mueller Hinton agar in accordance with Murray's technique with a few minor modifications. Following species used for antibacterial assay; *Pseudomonas aeruginosa*, *Y. enterocolitica*, Listeria monocytogen, *Staphylococcus aureus, B. cereus Streptococcus pyogenes, Proteus vulgaris, Escherichia coli, Klebsiella pneumoniae*, and the cultures were kept on Nutrient agar. A loopful of organisms was precultured in 10 mL nutrient broth for six hours. The culture's turbidity was brought down to 0.5 McFarland optical density. A 0.1 mL bacterial solution was spread-plated onto Mueller Hinton agar plates as an inoculant from the seed culture. Antibacterial activity was assessed using the width of the clear zone (mm) that resulted from growth inhibition during the triplicate testing. The gram-positive and gram-negative bacteria were controlled with oxacillin (20 µg/mL) and norfloxacin (200 µg/mL), respectively, as positive controls (Banerjee et al; 2012). finger millet of hexane extract reveled antimicrobial activities against *E. coli*, *Pseudomonas aeruginosa*, *Enterococcus sp. Staphylococcus aureus, and Salmonella sp* (Shukla et al; 2015). The well diffusion technique developed by Kirby Bauer was used to measure the antibacterial activity. After preparing the Muller-Hinton agar medium, the sterilized medium was added to the sterile Petri plates. Nine distinct bacterial isolates were used in cotton swabs for the spread plate approach. Following the cooling and solidification of the medium, 9 mm diameter wells were punched into the agar and filled with 25 µl, 50 µl, 75 µl, and 100 µl of each sample at a concentration of 25 mg/ml. At 37 °C, the plates were incubated for whole day. Following incubation, the diameter of the zone of inhibition was measured and examined (Singh et al; 2015).

10. Antihyperlipidemic activity:

Ragi leaf extract in hyperglycemic Wistar rats caused by alloxan Rats were given intraperitoneal injections of alloxan monohydrate (130 mg/kg) to induce hyperglycemia. The rats with hyperglycemia were given oral dosages of 250, 500, and 1000 mg/kg of ECE once a day for 14 days. Rats' levels of total cholesterol (TC), triglycerides (TG), HDL, and low-density lipoprotein (LDL) were evaluated in relation to ECE. Compared to normal rats, animals administered alloxan showed substantial increases in LDL, TG, and TC levels and decreases in HDL levels. In the hyperglycaemic rats, however, ECE markedly raised HDL and markedly lowered TG, TC, and LDL levels. All things considered; the findings imply that the leaf extract of E. coracana has anti-hyperlipidaemic characteristics.

(Yaro et al; 2018). A study was done to find out whether finger millet may help people lose weight and avoid becoming obese. High-fat fed mice were given finger millet as a dietary supplement, both whole grain and bran. In comparison to whole grain finger millet, the experiment's findings showed that ragi bran significantly decreased the body weight of the mice given a high-fat diet. This provided support for the use of ragi in reducing body weight and treating obesity (Murtaza et al; 2014).

11. Antioxidant's activity:

When compared to ibuprofen, methanolic extracts demonstrated a moderate level of suppress capacity on reactive oxygen species (ROS) produced by whole blood phagocytes, with values ranging between 26.91 and 27.71 μg/ml. Comparing all extracts to ibuprofen, they demonstrated strong suppression of ROS generated by polymorphonuclear neutrophils isolated from human blood; the values of the methanolic and ethanolic extracts were 0.29 to 0.47 μg/ml and 1.35 to 1.70 μg/ml, in that order. The concentrations of phenolic components in all extracts were notably high, and they included flavonoids and the ability to scavenge oxygen radicals, The cations 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic) acid (ABTS) and 2,2-diphenyl-1-picryl-hydrazyl (DPPH). Additionally, they were able to stop processes that produced radicals by chelating and reducing metal ions. The results showed that these finger millet extracts might be used as effective antioxidant sources. (Sooriya Arachchige et al; 2021). When compared to whole wheat, finger millet seed coat is an excellent source of polyphenols with a noticeably greater level of antioxidant activity. So, the seed coat of finger millet might be used as a natural antioxidant source (Viswanath et al; 2009). *Eleusine coracana* exhibited a greater total phenolic content than the other studied seeds, as well as the capacity to scavenge DPPH in a dose-dependent way, in light of the total phenolic content of the seeds given as gallic acid equivalent (Ademosun et al; 2015). The study revealed that the antioxidant activity of a combination of free and bound phenolic acids was greater than that of the latter. After malting for 96 hours, the antioxidant activity coefficient of bound phenolic acids dropped from 448.0 +_ 4.5 to 570.0 +_ 6.0, whereas the one for phenolic acids that are free increased from 770.0 +_7.8 to 1686.0 +_ 16.0. Consequently, throughout the malting of ragi, the antioxidant potential of phenolic acids varies. (Subba et al; 2002).

12. Antiaging activity:

Methanol fraction of *Eleusine coracana* disclosed adequate antioxidant capacity to block the process of cross-linking and glycosylation that happens with the aging process. This research is the first to show the prospective advantages of Kodo and Finger millet in decreasing crosslinking and glycation of collagen. The millets mentioned might serve as effective dietary supplements to avoid issues caused by glycation, such as those related to diabetes or aging (Hegde PS., et al; 2022).

13. Wound healing activity:

Studies on diabetic rats' wound healing processes have been conducted to demonstrate the impact of finger millet. A macroscopic analysis of the wound showed that in contrast to the FM diet-treated and control groups healed completely in around 14 and 15 days, respectively, the diabetes group needed a total of about 20 days**.** By the conclusion of the 15th day, the healing process was almost finished in the control rats, however the diabetic rats only showed 60% healing progress. Healing in diabetic animals was inconsistent as opposed to other groups (Rajasekarana et al; 2004).

14. Immunomodulatory activity:

It has been shown that the arabinoxylans extracted from finger millet possess immunomodulatory properties. The authors ascribed the observed impact to the millet's ferulic acid content. Their research revealed that arabinoxylans isolated from finger millet may considerably enhance mitogenic activity and activate macrophages (Prashanth et al; 2014).

15. Cardio protective activity:

Heart conditions are among the world's most serious issues. Finger millet high diet reduced the lipid peroxidation process, it diminishes the likelihood of arteriosclerosis and offers significant defence against myocardial infraction and strokes. In rat models with excessive cholesterol consumption, comparable recent research indicated that ragi-based multigrain diets were beneficial in regulating lipid and antioxidant metabolism (Vasant et al; 2014).

Conclusion:

Finger millet is so high in minerals and phytochemicals, it is employed as supplements in the food business. Its bioactive ingredients, which consist of cardiac glycosides, balsams, lignans, alkaloids, terpenoids, steroids, and tannins. Phytoestrogens, and phytocyanins, are also utilized in cuisine. Proanthocyanidins, ferulic acid, gallic acid, vanillic acid, caffeic acid, sinapic acid, and quercetin are among the substances that can be isolated for therapeutic purposes. Research has indicated that it can help prevent aging, diabetes, lipid peroxidation, cancer, osteoporosis, and hyperactivity. More research is needed to fully utilize and add value to the grain production.

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