Moringa oleifera Accessions: Perspectives and Application as Nutraceuticals and Phytomedicines

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1 Introduction

Moringa oleifera Lam., commonly known as drumstick tree or horse radish tree, is an important tropical medicinal plant known for its multifarious nutritional and phytomedicinal property. It is frequently used by ethnic and local people of developed and emerging nations for their medicinal value and culinary use [1]. According to the report of World Health Organization (WHO), nearly 70–80% of the global population relies on herbal plants for their basic health care needs. The genus *Moringa* comprises 13 species, out of which *Moringa oleifera*, *Moringa stenopetala,* and *Moringa peregrina* are mostly studied because of their availability and multifunctional properties [2]. *Moringa* is distributed in India, Africa, America, and Madagascar. They are drought-resistant, fast grower (propagated through seeds/cuttings), and can withstand wide range of soil with minimum nutrient requirement [3]. Being a tropical deciduous tree, *Moringa oleifera* possesses bipinnate/tripinnate leaves on grayish white stem with drooping branches. It also bears pendulous 25–35 cm long pods with isodiametric/ovate seeds (Fig. 1) [4].

Leaves and seeds are known to have wide range of amino acids, minerals, protein, carbohydrates, and vitamins. In addition to that, they are also known to have important plant secondary metabolites such as polyphenols, flavonoids, moringin, alkaloids, and tannins [5, 6]. Traditionally, *Moringa* was used by warriors to gain energy and also by queens and king to maintain healthy skin and bones [7]. Medicinal, aromatic, or horticultural plants in general have nutraceutical value as these plants are preferred as tonic or in maintaining vitality and sometimes aphrodiasic. They are medicinally used and exploited for commercial purpose by plant-based industries. For instance, *Gymnema sylvestre* is having gymnemic acid

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Fig. 1 *Moringa oleifera* field

recommended for antidiabetic potential [8, 9].There has been an unprecedented growth in use of plants with nutraceutical and phytomedicinal value because of the non-toxic effect of plants with great medicinal value. Currently, studies are going on to boost the nutraceutical value of less nutritious food and *Moringa,* being an important food and medicinal plant, plays a vital role in increasing the health promoting effects of food via food fortification. Hence, the present book chapter deals with phytomedicinal, functional, nutraceutical, and cosmo-nutraceutical property of *Moringa oleifera* with a view to enhance the use of *Moringa* in developed and emerging nations in combating malnutrition and protein deficiency to harmonize cultural and modern medicine system with minimal side effects.

2 Ethnobotany and Phytochemistry of *Moringa oleifera*

The application of phytocompounds as medicine/ drug is well known since time immemorial when the willow tree leaves were prescribed by Hippocrates to treat fever. Since then, different parts of plants are used in classical and modern medicine system. Phytochemicals are the plant secondary metabolites which are present in abundance with no relation to plant health and development [3, 10]. There are certain classes of phytochemicals (Fig. 2) classified into alkaloids, polyphenols, triterpenoids, sulphur-based compounds, and terpenoids [11, 12]. Almost all the classes of phytochemicals are present in *Moringa* which confers disease resistance potential. Alkaloids are the main group of phytochemical present in form of phenylacetonitrile pyrrolemarumine, 4′-hydroxyphenylethanamide-α-l-rhamnopyranoside – its glucopyranosyl derivative and *N*,α-l-rhamnopyranosyl vincosamide.These alkaloids are organic nitrogen-containing compounds generated from amino acids.

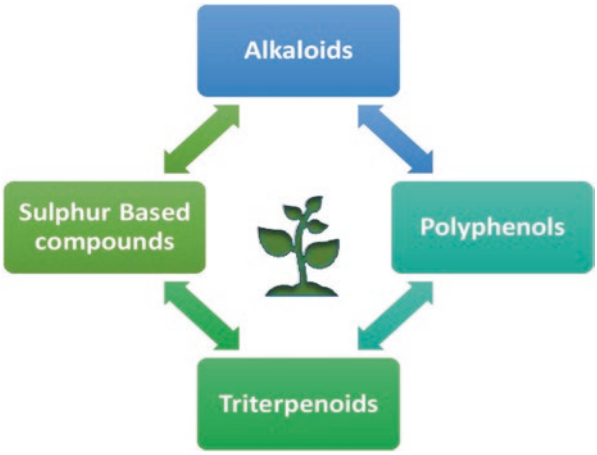

Fig. 2 Classes of phytochemicals in *Moringa oleifera*

Efforts were made to isolate and identify the potentiality of alkaloids from *Moringa* leaves which indicated that they possess cardioprotective activity along with the antihypertensive property [13].

Polyphenols are the second group of phytocompound found in both fresh and dry leaves of *Moringa* conferring them antimicrobial and antioxidant properties. Chemically, polyphenols are either in form of phenolic acid with one phenol ring or in form of flavonoids with more than one phenol ring and they are often quantified as tannic acid equivalent and gallic acid equivalent, respectively [12, 14, 15]. Several researchers have identified presence of quercetin, myrecytin, and kaempferol along with 11 more compounds through GC-MS profiling of leaves except roots, seeds, and flowers [16, 17]. Chemical and agronomical variations were observed in accessions collected and identified from India, Pakistan, and Africa which shows that there is higher possibility of genetic variation among them regulating their metabolic pathway [16, 18, 19]. Geographical and environmental variations were also observed in some accessions of *Moringa* with predominant difference in tannins, flavonoids, and polyphenols including major quantities of ellagic acid, coumaric acid, and caffeic acid [20–22].

Another group of phytochemical known as carotenoids are coloured molecules found in *Moringa oleifera* leaves as provitamin A or β-carotene which implicate vitamin A deficiency. Carotenoids are generally characterized by their colour either in form of yellow, red, or orange and are mostly present in vegetables and fruits imparting their coloured complexity. Several compounds such as lutein, luteoxanthin, and zeaxanthin were isolated and purified from *Moringa* exploring their health benefits [23]. Apart from polyphenols, flavonoids, and pigmented compounds, *Moringa* leaves, pods, and seeds are known to have isothicyanate and glucosinolate compounds. Basically, these compounds are synthesized from amino acid moieties. A group of researchers have identified glucosinolate from wild and cultivated source

of *Moringa* as glcomoringin and glucosoonjnain, suggesting that they may differ in taste but not in their myrosinase activity or protein content [24, 25]. Recently, denovo computational biology studies have suggested the probability of using compounds from *Moringa* against SARS CoV- 2 M-Pro [26]. A total of 35 compounds were identified from *Moringa* leaves, peduncle, roots, and flowers which include tetradecanoic acid, n- hexadecenoic acid, gamma sitosterol, anthonin, siphorochin, vanillin and β-sitosterol, isoquercitrin, rhamnetin, and kaempferitrin [27–29]. Whole gum exudates of *Moringa* revealed the presence of sugars such as rhamnose, l-arabinose, d-glucuronic acid, d-mannose, d-xylose, d-galactose, and leucodelphinidin-3-O-B-D-galactopuranosy (1 -> 4)-O-B-D-glucopyranoside [30]. Furthermore, tannins are also present in *Moringa*. They are hydrophilic compounds which aid in precipitation of gelatin, alkaloids, and other proteinaceous compounds and hence they are not desirable for human or animal consumption. However, it can be removed by proper processing techniques [31]. Isoprenoidal aglycone also known as saponins is also found in *Moringa* in appreciable amounts, which exhibits anticancer effects [32].

Each and every tribal or local culture has different perspectives on utilization of medicinal plant and hence, it is imperative to study their geographical and ethnobotanical variation to expand the knowledge regarding drug designing, value addition, and genotypic variation. This information helps in expanding the economic importance of medicinal plant exponentially. Information and knowledge about geographical diversity of plant is a pivotal part of diversity study to ascertain the superior and high yielding accession for commercialization [33]. Ethnomedicinally, different parts of *Moringa* such as seeds, stem, leaves, fruits, flowers, bark, and gum exudates are used in treatment of malaria, fever, stomach pain, wound healing, diabetes, sores, piles, tooth ache, anaemia, dropsy, and hysteria [34, 35].

3 Phytomedicinal Property of *Moringa oleifera*

Over the past years, utilization of plants with medicinal properties has increased rapidly. Current research is focused on medicinal and nutritional property of plants covering phytochemistry, horticulture, pharmacology, and nutraceuticals. However, the potent phytomedicinal action often results from consortia of plant secondary metabolites/bioactives [36]. Studies have revealed the incidence of various diseases associated with different age groups. It was observed that the key factor responsible for this situation is generally the weakened immune system, autoimmune diseases, or immunosenescence [37]. Phytomedicines are termed as use of plant or plant parts in treatment and improvement of human health. It was first coined by Henry Leclerc in 1913. Phytomedicines are advantageous in terms of minimum side effects caused by synthetic drugs. *Moringa* being a food plant has many phytomedicinal properties (Fig. 3).

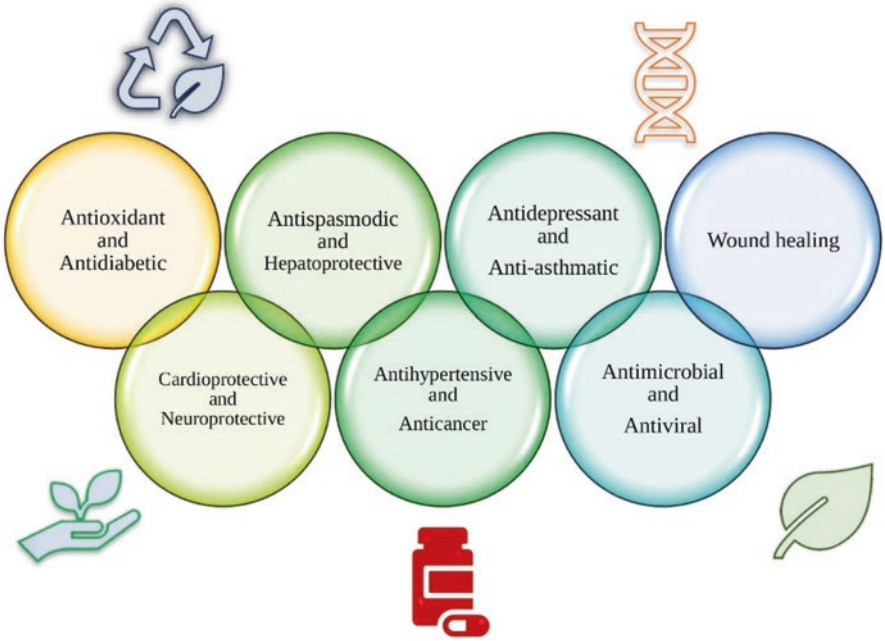

Fig. 3 Phytomedicinal property of *Moringa oleifera*

3.1 Moringa oleifera *as Potent Antioxidant Agent*

Moringa leaf, seeds, flowers, and roots are known to have remarkable DPPH radical scavenging activity. This activity is conferred to any plant/ plat tissue because of high amount of polyphenols in it. They help to scavenge reactive oxygen species (ROS) by reducing oxidative stress. Study on antioxidant capacity of saline and alcoholic extracts revealed that the extracts of flowers, leaf rachis, and leaves were able to react and scavenge free radicals; however, ethanolic seed extract and saline extracts were able to react slowly [38]. A compound myrecitin isolated from seeds showed higher antioxidant activity when compared to BHT and α- tocopherol [39]. Free radicals are generally categorized into hydroperoxyl, hydroxyl, superoxide, halogen, hydrogen, and nitrogen dioxide along with reactive oxygen species (ROS). A study on methanolic extract of *M. oleifera* leaves depicted higher antioxidant activity through in vitro FRAP, DPPH, and metal chelating assay [40]. Hence, the bioactives from plants help them to stabilize/neutralize free radicals enabling them to be used as phytomedicine.

3.2 Moringa oleifera *as Antihypertensive Agent*

Hypertension or high blood pressure is a global health concern affecting around 1.13 million people worldwide. Blood pressure can be lowered by inhibiting ACE enzymes [41]. *Moringa* leaf is known to reduce blood pressure. It was reported that two flavonoid glycosides from ethyl acetate fraction of *Moringa* leaves were able to inhibit ACE enzyme attributing it to antihypertensive property [42]. Apart from this, thiocarbamate glycosides, glycosides, and nitrites isolated from the leaves alleviate vascular dysfunction and promote vasorelaxation [13]. A comparative study of seed and leaf diet conducted by [43] revealed that this supplemented diet could improve the systolic and diastolic blood pressure by increasing nitric oxide and minimizing lipid peroxidation (LPO) in hypertensive state. Secondary bioactives such as α-L- rhamnopyranosyl vincosamide, acetonitrile, glucopyranosyl derivatives, 40- hydroxyphenylethanamide-α-L-rhamnopyranoside, and its derivatives along with β- sitosterol (a cholesterol lowering compound) were identified and isolated from *Moringa* and showed potent antihypertensive activity [44–46].

3.3 *Antispasmodic and Hepatoprotective Behaviour of* Moringa oleifera

Herbal antispasmodic agents help relieve gastrointestinal muscle spasm by their therapeutic action [47]. *Moringa* seeds, roots, and leaves exhibited antispasmodic activity against acetylcholine-induced contractions. As leaf is the most studied part of *Moringa oleifera,* the ethanolic fraction of leaves exhibited antispasmodic effect by blocking the calcium channel. Hence, this information provides the base for traditional use of *Moringa* [13, 48, 49]. Liver plays an important role in detoxifying certain drugs and xenobiotic compounds. Study on carbon tetrachloride-induced hepatotoxicity revealed that leaves' extract of *Moringa* helps in improvement of hepatic fatty disintegration and balancing their architecture [50]. Several researchers have observed an increase in liver functioning enzymes, but they did not report any histopathological kidney or liver damage which stated that *Moringa* ameliorates the hepatic damage induced by certain chemicals. Recent studies on Thiamethoxam-induced hepatotoxicity also suggested that *Moringa* can inhibit the deleterious effect TMX to normal levels [51]. On the other hand, several chemical compounds, rifampicin, isoniazid, gentamicin pyrazinamide, and acetaminophen, that cause hepatotoxicity also revealed the beneficial role of *Moringa* in treating them [52–55].

3.4 Moringa oleifera *as Antidepressant and Neuroprotective Agent*

Depression is a widely known mental disorder across the globe and almost half of the population is suffering from anxiety and mood swings. The constant state of depression is due to oxidative stress and neurological imbalance [56]. An approach was made to identify the efficacy of *Moringa* as antidepressant agent through in vivo animal model study. It was depicted that ethanolic fraction of *Moringa* leaves along with fluoxetine has potential antidepressant activity [57]. Ethanolic leaf extract of this plant was able to minimize the chronic stress in zebrafish model [58]. Antidepressant study through tail suspension and forced swim test also indicated the potential of n-hexane and ethanolic fraction of *Moringa* in relieving stress and depression [59, 60].

Neurological disorders are also associated with nervous system mostly affecting brain cells and spinal cord along with ganglia and nerves. Dementia (Memory loss) mostly seen in aged people is a form of neurodegenerative disorder. Alzheimer's disease, Parkinson disease, Schizophrenia, and Huntington disease are associated with reactive oxygen species and oxidative stress [61, 62]. Many efforts were made to treat these diseases, but none of them were effective to halt their progression [63]. As the cost production of synthetic drugs is higher, natural phytocompounds were searched and synthesized. *Moringa* leaf extracts (MLE) were proved to have nootropic and antioxidant properties and hence several studies stated that solvent fractions of *Moringa* can be beneficial in terms of colchicine-induced Alzheimer's disease in animal model study [64, 65]. Current in vitro studies using SHSY5Y neuroblastoma cells also noted the neuroprotective effect of *Moringa leaf* extract (MLE) [62].

3.5 Moringa oleifera *as Antimicrobial Agents*

Many studies have been undertaken to determine the role of *Moringa* as antimicrobial agent. The bioactives from *Moringa* leaf, stem, roots, seeds, and bark exert potent antimicrobial property against various pathogens [66, 67]. They show inhibitory activity by altering their cell permeability, growth, and multiplication rate. Various aqueous, hexane, methanolic, and ethanolic extracts have shown potent bioactivity against Enteropathogens, *Salmonella* sp., *Vibrio* sp., *Pseudomonas* sp., *Erwinia* sp., and *Bacillus* sp. [3, 67, 68]. *Moringa roots were also found to have* antibacterial activity against peptic ulcer caused by *Helicobacter pylori.* It was noted in another study that presence of pterygospermin and isothiocyanate molecules in the roots attributed this phytomedicinal property to *Moringa* [69, 70]. Different solvent preparations of *Moringa* showed potent inhibitory activity against various fungal strains such as *Aspergillus* sp., *Fusarium* sp., *Alternaria* sp. and *Candida* sp. [71, 72]. In vitro studies of n-hexane, ethyl acetate, aqueous,

methanolic, and alcoholic fraction of *Moringa* leaves predominantly decreased the fungal strains affecting the productivity of Papaya [73].

3.6 Moringa oleifera *as Anticancer Agents*

Various physical and environmental stress lead to accumulation of reactive oxygen species leading to cell death. Several approaches are made to mitigate the cell death caused by oxidative stress. However, radiotherapy, surgery, and chemotherapy are expensive and toxic to humans [74]. Recent advances in phytomedicine have led to the development of plant-based drugs with minimal side effects. The cold water extract of leaf demonstrated potent antiproliferative effects against A549 lung cancer cell line in an in vitro assay [75]. Mostly, glucosinolates and niazimicin isolated from leaves are known to have chemopreventive property. Fruits and leaves were apparently reported to have anticancer property against B16 F10 melanoma tumor with a sizeable rise in survival rate and lifespan of cancer patients [76].

The in-depth study on apoptotic and cytotoxic property carried out by Sreelatha et al. [77] showed the inhibition of cell proliferation of KB cell line in a dose-dependent manner. Other than that, several *in vitro* studies on acute lymphoblastic leukaemia, acute myeloid leukaemia, and hepatocarcinoma cell line through MTT assay also proved the efficiency of *Moringa* as anticancer agent [78]. Recently, nanotechnology has evolved into great dimension by their enhanced functionality. Green synthesized gold nanoparticles were also found to be effective against MCF-7 breast cancer cell line [79]. Colorectal cancer (CRC) or colorectal carcinoma is considered as the most prevalent type of gastrointestinal cancer affecting both men and women equally. A study on *Moringa*-based silver nanoparticles found that they were able to prevent quantitative and qualitative alteration in colon carcinoma induced by chemicals exploring them to be employed as phytomedicine [80].

3.7 Moringa oleifera *as Antidiabetic Agent*

Diabetes is a common metabolic disorder usually marked by chronic hyperglycaemia often resulting into aberrant insulin action or production with major consequence. Later it develops into macro/micro vascular complications leading to cell death. Several synthetic medications and insulin treatment are mostly detrimental to health. Hence, there is always a need to search non-toxic natural plant-based product to treat diabetes type I and type II with lesser side effects [81, 82]. Many studies were reported on hypoglycaemic property of leaf, roots, and pods of *Moringa* [83]. The presence of polyphenols, alkaloids, flavonoids, and carotenoids is known to attribute antidiabetic property to *Moringa.* The *Moringa leaves* were proven to ameliorate diabetes in Streptozotocin-induced diabetic albino rats STZ [84]. Another

study conducted on antidiabetic property of *Moringa* seed and aqueous leaf extract also showed reduced level of Interleukin 6 in STZ-induced rats [85].

According to International Federation of Diabetes (IDF), about 360 million people are affected by Diabetes mellitus (type 2) globally and it is expected to rise by 552 million by 2040 [86]. In silico study was conducted to identify the targeted therapeutic drug that can bind the protein moiety. It was identified that anthraquinones, anthocyanins, hemlock tannins, and phenolics from *Moringa oleifera* could easily bind the targeted protein molecule which assisted in treatment of diabetes mellitus [87]. Alloxan-induced diabetic rats were treated with hydroalcoholic extract (95%) of *Moringa* leaves by reducing the serum glucose levels at the level of 250 mg/kg [88]. Generally, the mechanistic action of *Moringa* works by inhibiting the activity of glucose transporter proteins- GLU 1 and GLU 4, thereby increasing insulin production and treating damaged pancreatic β-cells [89].

3.8 Moringa oleifera *as Anti-asthmatic Agent*

Asthma is a chronic syndrome caused due to increased responsiveness of bronchi and trachea manifested by chronic and recurrent attacks due to narrowing of airway passage. It is mostly expressed by inflammation of pulmonary airway and hyperresponsiveness of bronchi. Mostly, lymphocytes, cytokines, histamines, and eosinophils are involved in constriction of bronchi leading to asthma [90, 91]. Asthma accounts for more than 90% of population worldwide [92]. Several studies on guinea pigs demonstrated low levels of lung tissues and plasma of the animal [93, 94]. Studies on seed kernel and butanol extracts were carried out against ovalbumin and acetylcholine-induced bronchial constriction which showed potent anti-asthmatic effect [90, 95]. It has been observed from several studies that phytocompounds such as rutin, apigenin, quercetin, and kaempferol are helpful in prevention of asthma and airway inflammatory response [96, 97]. Methanolic (MeOH) leaf extract of *Moringa* was also found effective against bronchospasm, oedema, and mucus secretion confirming its potent anti-asthmatic activity [98].

3.9 Moringa oleifera *as Antiviral Agents*

Therapeutic potential of *Moringa* has been traced long time back in yielding potent antiviral activity owing to the profound activity against HIV, EBV, HBV, HSV, NDV, and FMDV [99–103]. The flowers, seeds, gum, root bark, and leaves were reported to be used as immunobooster and antiviral drugs. However, evidence-based reports were revealed to be scanty on the use of *Moringa* against small pox virus/ Chicken pox as world health organization has declared countries to be free from small pox virus since May-1980 (World Health Organization, 1980) [123]. Recently, baseline study carried out against Influenza virus depicted that *Moringa* A isolated

from seed material was able to decrease the expression of transcription factor EB and weaken the autophagy in virus-infected cells [104].

3.10 Moringa oleifera *as Wound-Healing Agent*

Skin is one of the important protective barriers and first defence system towards the noxious pathogenic micro-organisms. As result of wound or injury, this barrier gets disrupted which results into impairment into the connectivity of epithelial tissues. It represents significant burden on patients affecting their mental state [105]. Generally, the tissue regeneration/wound healing process involves hemostasis, inflammation, proliferation, and remodelling of tissues [106]. Study on bioguided solvent fractions of leaf was carried to ascertain the cell viability, proliferation, and wound scratch test which depicted enhanced wound healing property. This property was known to be attributed by vicenin-2compound isolated from methanolic fraction [107]. Recently, the intervention of nanotechnology has paved an effective way in phyto-medicine through green synthesis. The polysaccharide extracted from *Moringa* seed and its nanocomposite prepared from silver were found to be better candidate as optimal wound dressing material [108].

4 Nutraceutical/Cosmo-Nutraceutical Value of *Moringa oleifera*

The cruciferous plant *Moringa oleifera (Drumstick tree)* is a staple food in majority of the countries across the globe. Due to its versatile nutritional and medicinal property, *Moringa* is known as "Miracle Tree". During ancient period, both leaves and fruits were known to maintain skin and health of Queens and King [109]. Leaves of this tree are worthy and precious in terms of providing nourishment to the malnourished and pregnant woman. The drumstick leaves are highly packed with minerals, vital amino acids, fatty acids, protein, and carbohydrates [110]. Most of the studies on leaves have suggested its efficacy for combating malnutrition and also for pregnant women and infants [111, 112]. Moreover, *Moringa oleifera* is known to provide 7 × more of Vitamin C, 17 × more of Calcium, 10 × more of Vitamin A, and 25 × more of iron [113]. In emerging and underdeveloped countries where food security is a major concern, *Moringa* is a great healthy diet for them. Apart from this, immature pods are good source of fibres, minerals, and proximates [114].

As per the report suggested by Moyo and his coworkers, dietary polysaturated fatty acid and unsaturated fatty acids were identified in dehydrated leaves of *Moringa* where linolenic acid, α-linolenic acid, and linolenic acid were present in considerate amount [115]. The culinary usage of this plant ranges from soup, salads, to main dishes. The seed portion of this plant is well-known for highly valued ben

oil used as cosmeceutical, cooking, and perfume industry. The specific protein peptides are also used for premature skin ageing and maintaining skin health [116]. The inflorescence/ flowers of this miracle tree are also used in brewing infused tea and chutney preparation due to high mineral content in them [117]. The oil separated from *Moringa* seeds is also used in aromatherapy process [118]. Furthermore, the sunscreen prepared from different herbs along with kernel oil of *Moringa* effectively reduced UV radiation associated with conjugation system [119]. Additionally, the facial mask prepared from leaves extracts was also demonstrated to be efficient as cosmeceutical agent [120]. It was also observed by several researchers that the protein and nutritional content of accessions vary from cultivar to source with substantial difference among mineral content (approx.270–271 mg/100 g Vit C;17–27% leaf protein and 36–38% seed protein) [121, 122].

5 Conclusion

People's accessibility to food has three dimensions including physical, social, and pecuniary and the condition of life in the contemporary world is often alternating in which poverty and malnutrition are the major factors. The increasing comorbidities, malnutrition, and viral infection have become a major concern for all the age groups and use of synthetic drug has increased the complications through their side effects. The multipurpose phytomedicinal and nutraceutical plant *Moringa* could help in maintaining food security by providing vital micronutrients, antioxidants, and protein at an economical cost. Therefore, it can be concluded that *Moringa*-based phytomedicine can be a great paradigm for the future.

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