Trop J Nat Prod Res, December 2022; 6(12): ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Review Article

A Review of the Phytochemical, Usability Component, and Molecular Mechanisms of *Moringa oleifera*

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ARTICLE INFO

Article history:
Received 06 June 2022
Revised 16 November 2022
Accepted 02 December 2022
Published online ****

ABSTRACT

Moringa oleifera (*M. oleifera*) or kelor is a well-known herbal plant. *M. oleifera* is believed to be a magical tree because it provides tremendous benefits and is a rich source of nutrients for all living things. The potential value of *M. oleifera* in preventing or treating various chronic diseases is enhanced. There are still scattered details about phytochemical and usability components and their molecular mechanisms. The purpose of this article is to collect the various scattered data to make it easier for readers to get the information. Thus, in this study, we discussed information comprehensively for the phytochemical components of *M. oleifera* and the potential benefits of biological activities. This review will give information to open the possible utilization of *M. oleifera,* especially for the patient's medication and/or supplementation.

Keywords: Biological activities, Molecular mechanisms, *Moringa oleifera,* Phytochemical Components, Plant.

Introduction

Moringa oleifera, also called Kelor, is one of the most well-known herbal plants. *Moringa oleifera* is one of the most commonly used medicinal herbs in the *Moringa* genus. The *Moringa* plant is native to India's southern Himalayan foothills and has been cultivated in almost every tropical area under different names depending on the region. *Moringa* is known as the Drumstick Tree in English because of its drumstick-shaped pods, but it is also known as the Miracle Tree or Magic Tree[1] due to its various health benefits. It has a wide variety of medicinal properties, and a high nutritional value,[2,3] a source of nutrients that can prevent malnutrition,[4] such as protein, vitamins, minerals, and amino acids, [2,5] and it cures various diseases.[6]

Moringa plants are relatively easy to grow and disseminate, both sexually and asexually, and do not need a lot of nutrients or water, making it simple to manage production on a large or household scale. It can also help to improve environmental soil conditions. *Moringa* is a plant that can withstand a wide range of environmental conditions, including diverse climates, lousy soil conditions, and average dryness.[7] This plant grows well in areas with adequate lighting or sunlight exposure and thrives at an altitude of 600m - 2000m a.s.l, reaching a height of 152.40 cm in 5-6 months. The *Moringa* plant is a tree with a height of up to 10-12 m,[8] woody roots, and thin skins that can thrive in highland and lowland environments, with a generative (seed) or vegetative (stem cuttings) distribution. In sandy or loamy soils, the temperature for growth varies from 25 to 35°C (77-95 °F), and it is very tolerant of clay soils.[7]

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Citation: Ade FY, Supratman U, Sianipar NF, Gunadi JW, Radhiyanti PT, Lesmana R. A Review of the Phytochemical, Usability Component, and Molecular Mechanisms of *Moringa oleifera*. Trop J Nat Prod Res. 2022; 6(12):

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

Plant growth is affected by variations in environmental factors such as geographic location, altitude, and temperature/climate where it grows. Furthermore, genetic variation in a plant affects the nutritional content and phytochemical composition of each part of the plant, Cultivar conservation and growth of breeding programs to grow superior cultivars,[9] genetic explorations, as well as genetic improvement initiatives,[10] and the future selection and breeding programs aimed at tree improvement[11], can all benefit from genetic diversity studies. *Moringa* has a wide range of characteristics and morphological variability, which can be used to conserve and identify *M. oleifera* germplasm.[7]

Moringa oleifera is rich in various nutrients such as carotenoids, tannins, flavonoids, anthraquinones, steroids, alkaloids, terpenoids, anthocyanins, glycosides, and saponins[12] which are abundant in different parts of the *M. oleifera* plant. Amino acids, flavonoids, phenolic acids, vitamins, glucosinolates, carotenoids, tannins, alkaloids, polyphenols, isothiocyanates, and saponins are available in the plant's leaves.[4,7] The leaves of *M. oleifera* are rich in vitamins, minerals, and various health-promoting secondary metabolites. The high concentration of bioactive compounds in *M. oleifera* leaves accounts for their pharmacological properties.[7] The *Moringa* plant's phytochemicals help prevent diabetes, inflammation, cancer, arthritis, cardiovascular disease, and age-related functional disorders, among other health problems. *M. oleifera* has been shown to have anti-hypertensive, anti-diabetic,[2] anti-inflammatory, anti-cancer,[4] and anti-oxidant potential.[4,5] *M. oleifera's* anticancer, antioxidant, antimicrobial, and anti-diabetic effects are all due to its bioactive compounds.[12] Extracts of the leaves of *Moringa* (*Moringa oleifera*) have different phytochemical content, which showed a significant benefit in herbal medicine, one of them is in the anti-obesity activity.[13] The pathogenesis of obesity involves the accumulation of lipids, the formation of oxidative stress, and inflammatory reactions. As one of the anti-obesity agents, Moringa's leaf extract has antioxidant, anti-inflammatory, and hypolipidemic effects. *Moringa* leaf extract contributes to modifying lipid metabolism in the mevalonate pathway.[13] The mevalonic pathway is one of the pathways that involve

adipogenesis.[14] Adipogenesis inhibition is crucial for developing anti-obesity drugs, and it is a significant field of research. Astragalin *m. oleifera* increases lipolysis and suppresses adipogenesis in 3T3-L1 adipocytes, making it a promising candidate for obesity treatment.[15]

Methods

The review was based on studies discovered using the keywords *Moringa oleifera*, phytochemical component, the usefulness of Moringa oleifera, genetic diversity, Moringa molecular mechanism, and other similar terms in electronic databases such as Google Scholar, Elsevier, PubMed, and Mendeley. Unrelated studies were excluded. We gathered all of the relevant research papers. The literature method diagram is shown in Figure 1.

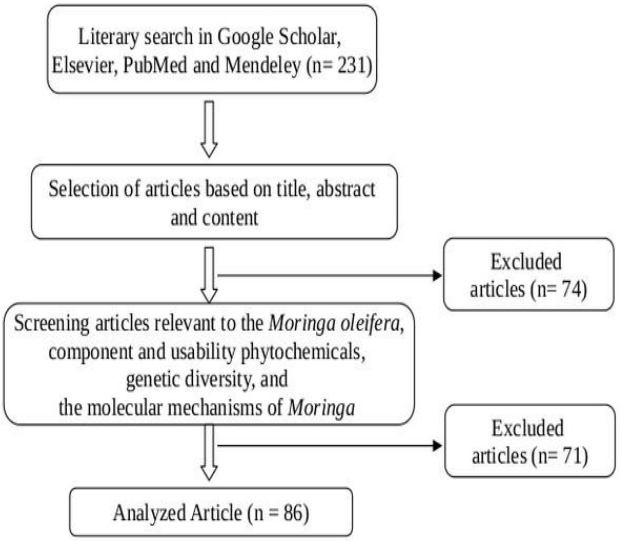

Figure 1: Method diagram of literature review

Results and Discussion

Moringa oleifera Phytochemical Material

Research on the phytochemical content of each part of the *Moringa* plant has also been carried out and is presented in Table 1. The leaves contain amino acids (arginine, histidine, methionine, cystine, tryptophan, and lysine),[5,25] vitamins (A, B, B1, B2, B3, C),[5,25,26] minerals (Mg, Ca, K, phosphorus, sodium, sulfur, zinc, copper, manganese, iron, selenium),[5,21,25] alkaloids,[18] phenolic acids,[5,16,18,21,25,27,28,29] flavonoids,[5,16,18,24,27,28,29] terpenoids,[17] polyphenols,[19,24,25] ascorbic acid,[21] protein, folic acid, β-sitosterol, iron, α-tocopherol, oestrogenic substances, riboflavin, β-carotene, nicotinic acid, pyridoxine,[25,26,38] thiocarbamate glycosides, nitrile, and mustard oil glycosides.[20,22,23] Those components have antioxidant activity,[5,16,18,19,24,28,29,36] antiinflammatories,[5,16] antibacterial,[5,16] antimicrobials,[30,36] anticancer,[5] antidiabetic,[5,24] and antihyperglycemic effects,[17] The leaves virtually are ideal for dietary supplements[26] and responsible in lowering the blood pressure.[20,22,23]*Moringa* leaves contain mainly phenolic compounds, which are natural plant-based micronutrients. Flavonoids and tannins are among the several forms of polyphenols. Kaempferol and quercetin derivatives are primarily composed of flavonoids.[13] The presence of β-sitosterol, 4-hydroxymellin, β-citostenone, vanillin, octacosanoic acid,[20] phenolic, alkaloids,[31] which have potential antimicrobial activity,[30,36] antioxidant.[31,36] are found in the bark of moringa. Meanwhile, in the *Moringa* seeds, there are ash, fat, seven bioactive compounds, carbohydrates, β -sitosterol-3-O- β-D-glucopyranoside, 4 (α -L -rhamnosyloxy)-benzyl isothiocyanate, niazirin, 3-O-(6′-O-oleoyl-β-D-glucopyranosyl)- β-sitosterol, glycerol-1-(9-octadecanoic), β -sitosterol, vitamin,[33] niazimicin,[2] flavonoids,[32] ascorbic acid, protein;[33,38] and has antimicrobial activity,[30] antitumors,[2,33] antioxidants,[32] and anti-obesity.[34] In *Moringa* flowers were found the presence of amino acids, kaempferol, sucrose, wax, D-glucose, alkaloids, quercetin,[35] potassium, calcium, flavonoid pigments (alkaloids, kaempferitrin, rhamnetin, isoquercitrin, kaempferol), vitamin, and ascorbic acid.[20,31] The flower's components were used as antioxidant and diuretic agent.[31] Diuretic activities eventually will stabilize the blood pressure.[31] In the *Moringa* root, alkaloids[36] and protein[38] are found, which have the potential for antimicrobial activity,[30,36] diuretic action, antioxidant,[36] and anti-inflammatory.[37] Isothiocyanate glycosides, thiocarbamate,[39] ascorbic acid, phosphorus, oestrogenic substances, iron, riboflavin, β -sitosterol, pyridoxine, protein, calcium, vitamins, nicotinic acid, β -carotene, α -tocopherol, amino acids (methionine, cystine, tryptophan, and lysine), copper, and folic acid;[32] are found in *Moringa* pods and have potential as an antioxidant [2,40,41] and an antihypertensive.[39] The chemical structure figures of the Moringa's seed, pod, root, bark, leaf, and flower compounds are presented in figure 2.

Uses of Moringa oleifera

Every part of the *Moringa* plant (roots, stems, leaves, flowers, and fruit) has been widely researched and used in medicine, food ingredients, dyes, animal feed, water purification, and renewable energy source for ethanol raw materials. The *Moringa* plant contains many beneficial chemicals.[36] Moringa leaves, roots, and seeds contain essential medicinal and antioxidant components such as alkaloids, phenolic acids, flavonoids, and tannins.[43-49] In addition, research on the nutrients contained in *Moringa* plants has also been carried out, including Bharali et al. (2003) stating that *Moringa* plants contain pro-vitamins A and C, especially β-carotene, which will be converted into vitamins in the body; [50] Saini et al. (2016) found vitamins A, C, calcium, protein in *Moringa* leaves. The presence of gluconate and isothiocyanate compounds found in *Moringa* plants can be an anti-cancer agent and inhibit bacterial and fungal activity;[2] Moringa oil contains oleic acid, which can be a raw material for biodiesel.[51]

Research on the medicinal properties of *Moringa* has also been carried out, including the anti-tumor activity,[33,52] antimicrobial,[36] anticancer,[2,53] allergies,[42] antioxidants,[24,28,31,36,40,49,53,54,55] anti-inflammatories,[37,53] anti-obesity,[34] antihyperglycemics (antidiabetic).[24,34] Therefore, *Moringa* is commonly used as a phytotherapeutic agent in Africa and India. [56] Interest in research on *Moringa* and its medicinal properties and health, as well as on the utilization of the environment such as water purification, conservation, breeding, and increasing the variability of the species, are genetical.[7,57,58,59,60,61]

Molecular Mechanism of Moringa

The plant *Moringa oleifera,* which has benefits and nutritional and medicinal value, has been widely reported in various studies regarding the potential activity and molecular mechanisms of the extract of every part of the *Moringa* plant. *M. oleifera* extracts have been shown to have a variety of nutraceutical and pharmacological properties, including anti-inflammatory properties,[43] anti-oxidant,[52,62] anti-obesity,[62,63] anti-cancer,[43] anti-tumor, hepatoprotective,[52] neuroprotective, hypoglycemic, anti-diabetic, and blood fat reduction.[64,65,66] Some studies in the treatment of diabetes used *M. oleifera* leaves, which have many dissolved compounds involved in glucose homeostasis, including isothiocyanates which can reduce insulin resistance and liver gluconeogenesis.[67] *Moringa* leaves contain many polyphenolic compounds, such as flavonoids and phenolic acid, which may also play a role in glucose homeostasis, which exerts anti-diabetic effects.[43] The glucose homeostatic effect may also be due to anti-oxidants, receptor agonists or antagonistic activity, and enzyme inhibition.[64-66] Although several scientific studies on *Moringa* leaves' hypoglycemic effect have been conducted, more information about age, gender, nutritional status, ethnicity, and dietary habits in humans is required before using the leaves as a herbal medicine for diabetes treatment. Compared to *Moringa stenopetala* leaf, the *Moringa oleifera* leaf has hypolipidemic activity, suggesting that its extract could be used in obesity management.[68] Latest study revealed that *Moringa oleifera* leaf extract could hinder some enzymes, such as pancreatic lipase and pancreatic cholesterol esterase. This study also showed that *Moringa oleifera* leaf extract prevents cholesterol

micellization formation. *Moringa* leaf contains chlorogenic acid, which inhibits lipogenesis and cholesterol production.[69]

Table 1: Phytochemicals and usability components of *Moringa oleifera*

Plant Part	Phytochemical components	Medicinal uses / potential activity
Leaf	amino acid [5,25], vitamin [5,25,26], mineral [5,21,25], phenolic [5,16,18,21,25, 27, 28, 29], flavonoid [5,16,18,24,27,28,29], Terpenoid [17], Polyphenols [19,24,25], alkaloid [18], ascorbic acid [21], folic acid, β-sitosterol, iron, α-tocopherol, oestrogenic substances, riboflavin, β-carotene, nicotinic acid, pyridoxine, protein [25,26,38], thiocarbamate glycosides, Nitrile, and mustard oil glycosides [20,22,23]	Antioxidants [5,16,18,19,24,28,29,36], antimicrobial [30,36], antidiabetic [24], anti-inflammatory [5,16], antibacterial [5, 16], antihyperglycemic [17], virtually ideal dietary supplement [26], responsible for the reduction of blood pressure [20,22,23]
Bark	Alkaloid (moringine,moringinine) [36], β-sitosterol, 4-hydroxymellin, β-citostenone, vanillin, octacosanoic acid [20], phenolic [31]	Antimicrobial [30,36], antioxidant [31,36]
Pods	isothiocyanate glycosides, thiocarbamate [3], ascorbic acid, phosphorus, estrogenic substances, iron, riboflavin, β -sitosterol, pyridoxine, protein, calcium, vitamins, nicotinic acid, β -carotene, α -tocopherol, amino acids (methionine, cystine, tryptophan and lysine), copper, folic acid [32]	Antioxidant [2,40,41], Antihypertensive [39]
Seed	Flavonoid [32], β -sitosterol-3-*O*- β- D-glucopyranoside, 4 (α-L-rhamnosyloxy)-benzyl isothiocyanate, niazirin, 3-*O*-(6′-O-oleoyl- β- D-glucopyranosyl)- *β*-sitosterol, glycerol-1-(9-octadecanoic), *β*-sitosterol,[33] niazimicin [2,33], vitamin, ascorbic acid, protein [38]	Antimicrobial [30], antitumor [2,33], antioxidant [32], stabilizing effect on blood pressure, anti-obesity [34]
Flower	nine amino acids, kaempferol, sucrose, wax, D -glucose, traces of alkaloids, quercetin [35]; potassium and calcium, flavonoid pigments (alkaloids, kaempferitrin, rhamnetin, isoquercitrin, kaempferol), vitamin, ascorbic acid [20, 31]	Diuretic activities, stabilizing effect on blood pressure, antioxidant [31]
Root	Alkaloids [36], protein [38]	Antimicrobial [30,36], diuretic activities, antioxidant [36] anti-inflammatory [37]

Moringa oleifera leaf extract (MLE) has been shown to inhibit lipogenesis in 3T3-L1 adipocytes via the 5' adenosine monophosphate-activated protein kinase (AMPK) pathway. AMPK is a major glucose and lipid metabolism regulator at the cellular level. AMPK is a major glucose and lipid metabolism regulator at the cellular level.[13] The lipolysis of 3T3-L1 adipocytes was improved by quercetin. Chlorogenic acid's reduction of insulin in MLE indicated that insulin sensitivity was improving positively.[69] Insulin sensitivity was improved by kaempferol. In MLE, quercetin and kaempferol had the most significant potential for binding to α-glucosidase.[70] In 3T3-L1 cells, kaempferol potency, was also found to have anti-adipogenic properties in a previous study.[71] MLE treatment improved lipid profiles in 3T3-L1 adipocytes.[70] In high-lipid rats, astragalin, the 3-O-glucoside form of kaempferol, showed anti-hyperlipidemic activity.[13] In 3T3-L1 adipocytes, these anti-adipogenic effects could reduce leptin gene expression and secretion. The protein pro-lipogenesis sterol regulatory element binding proteins (SREBP) transcription factor had been an inhibitory target of MLE phytochemistry, astragalin.[15] SREBP was essential for activating the SREBP/mevalonate pathway linked to lipid metabolism. Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ) activity, also called YAP/TAZ activity, was promoted by the SREBP-mevalonate axis.[13] MLE has also been shown to block the HMG-CoA reductase enzyme.[72] The presence of SREBP and HMG-CoA reductase in the mevalonate pathway has been a priority of MLE in reducing adipogenic activity.[15] Statins have been shown in vitro to inhibit mevalonate pathways and YAP/TAZ activity.[73] Several studies have implicated the Hippo-YAP / TAZ pathway in organ size regulation, tissue regeneration, organ formation, and self-renewal.[73,74] Thus, the Hippo-YAP / TAZ line is one of the central components in network homeostasis.[74] Quercetin and kaempferol in MLE have been shown to inhibit PPARγ activity in previous studies. YAP/TAZ signaling was also found to control PPARγ.[13] PPARγ continues to express adipogenic genes when carrying out its transcription function.[75] Along with their extraordinary biological properties in growth, cancer, and tissue homeostasis, the transcription regulators Yes-associated Protein (YAP) and Transcriptional Co-activator with PDZ-binding motif (TAZ) are the main focus of attention.[76] The mevalonate pathway regulates YAP / TAZ action.[69] The YAP and TAZ read various mechanical cues, including shear stress, cell structure, and extracellular matrix stiffness, and convert them into cell-specific transcription programs. Mechanotransduction in YAP and TAZ is needed for behavior and stem cell regeneration. They provide new insights into how aberrant cell processes contribute to developing diseases such as inflammation, atherosclerosis, muscular dystrophy, fibrosis, cancer, and pulmonary hypertension.[77] The Hippo pathway, which controls homeostasis and plays a crucial role in carcinogenesis and regenerative processes, is one of the most critical cellular signaling pathways.[78]

YAP/TAZ signaling has been shown to affect lipid metabolism and insulin sensitivity. In adipose-derived human mesenchymal stem cells treated with MLE, the expression of the insulin receptor substrate (IRS1) gene increased.[79] The TAZ protein influenced glucose absorption by GLUT4 by upregulating IRS1.[80] *M. oleifera* Lam. It ultimately uses thermogenic pathways to influence lipid metabolism. In a previous study,[79] uncoupling protein 1 (UCP1) was overexpressed

as a thermogenesis marker during adipose tissue differentiation. UCP1 control is inextricably linked to YAP/TAZ signaling.[81]

YAP and TAZ are Hippo signaling pathway downstream effectors that play a crucial role in cancer growth, including metastasis[82].

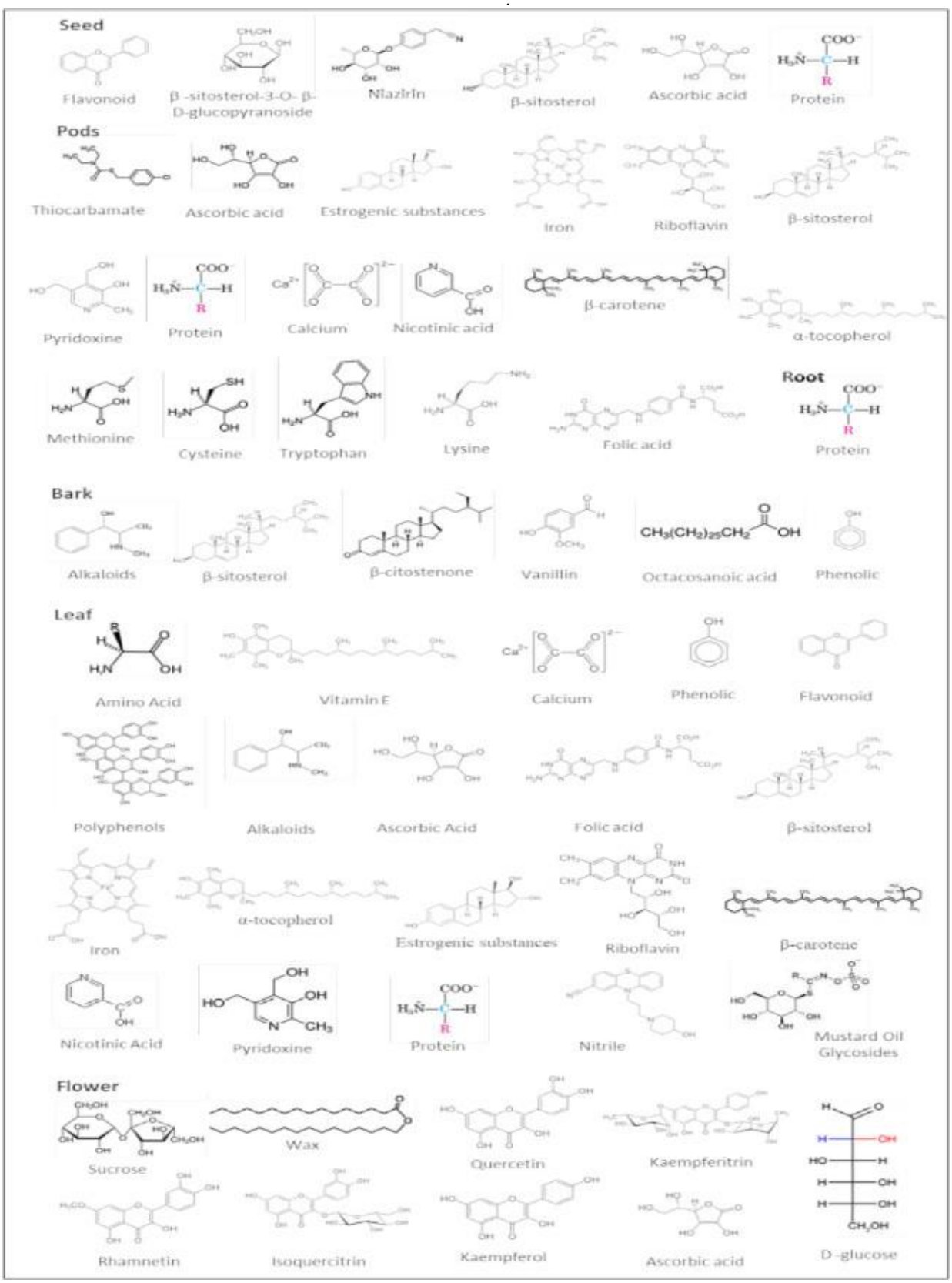

Figure 2: Chemical Structure of Moringa's Compound

Cell adhesion and mechanical signals had received from the network architecture and surrounding extracellular matrix (ECM) is also modulated by YAP/ TAZ activation.[76] The Hippo signaling pathway regulates various physiological processes, and its dysfunction has increased the number of human diseases, including cancer.[83] YAP / TAZ controls cell metabolism in response to phenotypic changes, and recent research has shown that metabolic changes induced by YAP / TAZ lead to metastasis.[82] *M. oleifera* leaves contain various beneficial natural substances such as flavonoids, ascorbic acid, phenolic acids, and carotenoids, making them an excellent antioxidant source.[84] In the variation of antioxidant activity, the primary and lateral roots of *M. oleifera* had higher antioxidant activity than the leaves.[85] Isothiocyanates, glucosinolates, and thiocarbamates were phytochemical constituents with significant antioxidant activity from the *M. oleifera* plant.[86] Antioxidant elements in *M. oleifera*, such as phenolics, flavonoids, ascorbic acid, and carotenoids, have been shown to increase the shelf life of lipid foods.[5] Another research has shown that *M. oleifera* seed oil containing oleic acid has a significant anti-inflammatory effect by interfering with PKC pathways linked to the glucocorticoid response.[87] Flavonoids, phenols, tannins, saponins, vanillin, β-sitosterol, and terpenoid present in MLE were thought to be responsible for all these anti-inflammatory activities.[88] While quercetin and β-sitosterol have been linked to MLE's hypolipidemic activity, they also have anti-inflammatory properties. Due to their pleiotropic effects, both compounds restored normal hepatic morphology and physiology.[89] The molecular mechanism of MLE's effect on autophagy has been approached slowly in research. Autophagy is the degradation of a specific cell component or cytoplasmic substance within the cell.[90] In a study on MLE's antioxidant and anti-inflammatory effects through the autophagic route, isothiocyanates (ITCs) were highlighted. β-sitosterol has similar anti-inflammatory properties in vitro. [91,92] *M. oleifera* is an effective antibacterial agent, as shown by a study that found a significant reduction in the growth of test bacteria. [93] The antibacterial and antifungal activities of the aglycone of deoxy-niazimicin obtained from the chloroform fraction of ethanolic extracts were found in the root bark of *M. oleifera*. [43] Aqueous and ethanol extracts of *M. oleifera* showed strikingly close results in lowering blood pressure in another study.[84] *M. oleifera* saponin has been reported as having antihypertensive properties.[94] The substance responsible for these effects, like thiocarbamate, and isothiocyanate glycosides, was successfully separated from the acetate stage of the ethanol extract of *M. oleifera* pods in a study that further supports the antihypertensive behavior of *M. oleifera* pods.[84] In many studies, *Moringa oleifera* leaves have been shown to have anticancer properties.[94] Isothiocyanate and thiocarbamate are two related bioactive compounds that have been isolated and have an inhibitory effect on the tumor promoter.[42] Another research[95] found that *M. oleifera* leaf extract in an aqueous medium decreased the presence of cancer cells in the pancreas, tumor formation, and metastatic activity. *M. oleifera* exhibited cell death via the induction of apoptosis and necrosis mechanisms.[96] *Moringa oleifera* can also improve the killing of cervical cancer cells.[97] Another study[98] found that *Moringa* leaves suppressed AOM/DSS-induced colorectal carcinogenesis in a vivo model, suggesting that Moringa's phenolics and complete dietary fiber may have chemopreventive potential. All the results presented in this review can ideally serve as a foundation for future research into the molecular mechanism of *M. oleifera*.

Conclusion

Moringa oleifera is a rich source of nutrition and has the potential value in preventing or treating several chronic diseases in the last few years. Many literature reviews had shown the utilization of various parts of Moringa oleifera in biology medicine and pharmacology. Although many studies in *Moringa oleifera*, unfortunately, details investigation and analysis into this plant are not well reported. There is an expectation to provide protocols and medicinal properties or supplementation for patients' treatment.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgments

This work was supported by funding from Hibah Post-Doctoral Universitas Padjadjaran (3570/UN6.3.1/LT/2020) to FYA.

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