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Anticancer Potential of *moringa oleifera* Lam: a Systematic Review

Abdulrahman Mahmoud Dogara[1], Ahmad Thamer Kamil Al-Sultani[2], Safa Mahdi Abdul Kadium[3], Huda Amer Mohammed[4], Duraid K. A. AL-Taey[5] , Marwa Fadhil Alsaffar[6] , Zahraa J. M. Al-Musawi[7] and Saber W. Hamad[8]

[1]Biology Education Department, Tishk International University, Erbil, Iraq.
[2,5,7] Department of Horticulture, Faculty of Agriculture, Al-Qasim Green University, Babylon 51013, Iraq.
[3,4] Department of Soil and Water Resources, Faculty of Agriculture, Al-Qasim Green University, Babylon 51013, Iraq.
[6] Medical Laboratories Techniques Department, Al-Mustaqbal University, 51001 Hillah, Babil, Iraq.
[8] Department of Field Crops and Medicinal Plants, College of Agricultural Engineering Sciences, Salahaddin University-Erbil, Kurdistan Region, Iraq.

[1]E-mail : abdulrahman.mahmud@tiu.edu.iq
[2]E-mail : ahmad.tha@agre.uoqasim.edu.iq
[3]E-mail: safa@agre.uoqasim.edu.iq
[4]E-mail: huda.ameir@agre.uoqasim.edu.iq
[5]E-mail: duraidaltaey@gmail.com
[6]E-mail: marwaalsaffar@uomus.edu.iq
[7]E-mail: zahraa@agre.uoqasim.edu.iq
[8]E-mail: saber.hamad@su.edu.krd

Abstract. *Moringa oleifera* is highly esteemed as a therapeutic plant in the realm of traditional folk medicine. This plant has been demonstrated in numerous pharmacological tests to possess anticancer properties. *Moringa oleifera*, a versatile medicinal plant, has garnered significant academic focus and economic appeal due to its pharmacological attributes. The inefficiency of cancer treatment is mostly due to the resistance of cancer cells to chemotherapy. Treatments for cancer are in greater demand. Finding novel compounds with the potential to treat various forms of cancer is therefore essential and indispensable. The review presented a contemporary analysis of the effectiveness of Moringa oliefera in the treatment of cancer. Research publications have been searched utilising the following platforms: Elsevier, Springer, Google Scholar, Taylor & Francis, Pub med, and Scopus. Research the plant species "Moringa oleifera" and its chemical composition, specifically focusing on its potential anticancer properties. The results of the anticancer test demonstrated that Moringa oliefera shown substantial potential as an anticancer agent against many cancer cell lines. The significance of the plant is emphasized in the quest for novel bioactive substances to investigate its therapeutic capabilities in the field of cancer treatment, with the aim of discovering and developing new drugs.

Keywords. Novel compounds, Chemical composition, Anti-cancer.

1. Introduction

Cancer is a collection of disorders characterized by uncontrolled proliferation and dissemination of cells. Cancer is a significant global cause of death. In 2008, cancer caused 7.6 million fatalities globally, with the bulk of them occurring in low-income areas [1]. The projected increase in this number can be attributed to demographic changes and the widespread adoption of high-risk behaviors. Although there is abundant scientific data, a significant number of individuals remain unaware that unhealthy eating habits are a primary contributor to the development of cancer[2]. The lack of selectivity of anticancer drugs in distinguishing between cancerous and healthy cells, along with the resilience of cancer cells to chemotherapy, are significant contributors to the ineffectiveness of cancer treatment [3]. There is an increasing demand for cancer treatments. Therefore, it is imperative and indispensable to seek out innovative molecules that have the potential to treat many types of cancer. Natural products remain integral to the process of drug discovery, with around 50% of approved medications during the past three decades originating from natural sources [1]. Emerging reservoirs of bioactive compounds in medicinal plants that show great promise in the fight against cancer. *Moringa oleifera*, sometimes known as the drumstick tree, is indigenous to South Asia, namely the lower regions of the Himalayas in India. The plant has been intentionally introduced and has also spontaneously established itself in several other countries. The plant is compact, low-maintenance, fast-growing, and has evergreen foliage even in arid conditions. The leaves of this plant are highly nutritious, including a rich supply of vitamins, minerals, amino acids, and naturally occurring antioxidants. The review aims to provide a current analysis of the efficacy of *Moringa oliefera* in treating cancer. This systematic research thoroughly examines the significant possibility of extracting the primary medicine for anticancer purposes from the chemical components found in different parts of *M. oliefera*.

2. Methods

2.1. Inclusion Criteria

Elsevier, Springer, ScienceDirect Elsevier, Google Scholar, Taylor & Francis, Pub med, and the Scopus database were searched using the terms chemical composition, *Moringa oliefera*, anticancer, anti-cancer, cancer, within 2020 to 2024.

2.2. Exclusion Criteria

Research papers not published in English, review papers, conference proceedings, abstracts, thesis, and preprint **:** research papers published prior to 2020 were excluded.

3. Results and Discussion

Moringa oleifera exhibited significant anti-cancer activity against multiple types of cancer (Fig.1). Aqueous leaves extract administration caused dose- and time-dependent damage in both cell lines, according to in vitro cytotoxicity tests [4]. Administered aqueous leaves extract to tumor-bearing mice increased their lifespan while decreasing tumor volume and tumor weight. Examining the ehrlich acites cancer cell line via the lens of flow cytometry, we found that altering the mitochondrial membrane potential significantly induced apoptotic cells [4]. At 416 μg mL−1, the n-hexane fraction reduced the viability of Hela carcinoma cells by 50% compared to the control [5]. The *Moringa oliefera* leaves extract mediated gold nanoparticles (MO-AuNPs) were found to be effective anticancer agents with an IC_{50} value of 67.92 μg/mL, according to a cytotoxicity investigation conducted on MCF-7 cell lines [6]. The extracts with the lowest IC_{50} values were crude EtOAc (233.5 μg/mL), crude EtOH (241.1 μg/mL), and crude hexane (342.6 μg/mL), in that order. Cell viability, clonogenic growth, and cell apoptosis were all drastically decreased by the ethyl acetate fraction [7]. There was a dose-dependent inhibition of cell growth in the A549 human cancer cell line by the extracts of leaves. Morphological tests revealed that the moringa leaf extract induced cell death by causing blebbing, nuclear disintegration, chromatin condensation, and cell shrinkage [8]. The cytotoxic effects of ethanolic MLEs on the HepG2 cell line, as determined by the IC_{50} values, followed a specific trend: conventional (1.22 mg/mL) > ODC (0.90 mg/mL) > PKM-2 (0.65 mg/mL) > PKM-1 (0.35 mg/mL) >

Jaffna (0.15 mg/mL) [9]. Comparing the (IC_{50}) values of Doxorubicin, which were 5.25, 4.25, and 4.45 µg/ml, respectively, to those of synthetic AgNPs, the IC_{50} values against the HCT-116, HepG-2, and MCF-7 cell lines were 6.51, 4.75, and 5.54 µg/ml, respectively. The HepG-2 and MCF-7 cell lines showed a greater response to e synthesized silver nanoparticles (AgNPs) treatment compared to the HCT 116 colon cancer cell lines, indicating that AgNPs had a cytotoxic effect comparable to Doxorubicin [10]. In both the groups that received nano-extract returned hematological and biochemical measures, tumor and inflammatory marker levels, and other metrics to normalcy. The histopathological changes were less severe in the group that received treatment simultaneously, and they were entirely prevented in the group that received treatment thereafter [11]. 127.95 ppm and 117.52 ppm, respectively, were the LC_{50} values of the methyl acetate extract of moringa leaves and seeds. In addition, the LC_{50} values for the Moringa seed and leaf ethanol extract were 60.69 and 34.58 ppm, respectively. Results from tests evaluating the anti-cancer effects of extracts from Moringa leaves and seeds indicate that antitumor activity that is strong (<1000 ppm) [12]. The findings indicate that the toxicity of the leaves extract is greater against A549 cell lines, with an IC_{50} of 1062.87 µg/mL, compared to MCF-12A cell lines, which have an IC_{50} of 1424.04 µg/mL [13]. The extracted leaves demonstrated an average inhibition of 87.13% on the MCF-7 cell line at a wavelength of A570nm [14]. Significant decrease (90.1%-97.9%) in tumour weight was seen after treatment with a trypsin inhibitor. There were fewer secondary vessels and smaller primary vessel gauges in the tumours of the treated animals as compared to the control group [15]. The HNC cells showed substantial anti-cancer activity across all extracts. Root, stem, leaf, and seed IC_{50} values in CNE-1 cells were 0.135, 0.298, 1.07, and 1.10 mg/mL, whereas in CAL27 cells they were 0.163, 0.251, 1.19, and 1.22 mg/mL, respectively [16]. The findings showed that in vitro cell viability was 72%, 81%, and 84% when 2.5, 5, and 10 µgml− 1 of ZnO/Ag NPs were used for 24 hours [17]. In both cell lines, the *M. oleifera*-AgNPs reduced CTNNB1 and LRP6 gene expression while increasing LRP5 gene expression. Compared to HTC116, SW480 showed a decrease in APC gene expression after treatment [18]. The extract suppressed the proliferation of A375 cells and A2058 cells in a way that was dependent on the dosage, while having minimal impact on human normal fibroblasts [19]. The results indicate a statistically significant disparity in cell proliferation among the lung cell lines. Low amounts of the substance stimulated cell growth in the healthy lung cells but did not have a notable impact on the malignant lung cells [20]. The dichloromethane extract exhibited preferential cytotoxicity towards MCF7 cells at a concentration of 5 µg/mL, while showing no substantial inhibition of non-cancerous breast cells (MCF 10A). Among the studied extracts, it had the highest selectivity index (SI) value of 9.5 [21]. The viability of tumour cell lines was decreased, and apoptosis levels were enhanced after treatment with an extract. This was accompanied by a drop in the expression of B-cell lymphoma 2 protein and a reduction in mitochondrial membrane potential [22]. A study shown that an extract derived from leaves, containing methanol, effectively decreased the growth of Dalton's Lymphoma cells by reducing the mitochondrial membrane potential ($\Delta\Psi m$) and altering the overall shape of the cells [23]. The hexane fraction of the seeds (HF-CEE) demonstrated an inhibitory effect on the proliferation of breast cancer (MCF7) cells, with an IC_{50} value of 130 µg/mL [24]. The methanolic extract of *M. oleifera* leaves effectively suppresses cell viability and induces concentration-dependent changes in both cellular structure and nuclear characteristics [25]. Following a 72-hour treatment period, the IC_{50} value for the inhibitory effects on Kasumi-1 cells was 10 µg/mL for the moringa leaf absolute ethanol extract, compared to 25 µg/mL for the moringa leaf 50% ethanol extract and >400 µg/mL for the aqueous extract [26]. After being treated with extract, the cell viability of MCF-7 breast cancer cells and PMECs dropped dramatically. By the third week following treatment with a high-dose of extract, solid tumours in MDA-MB-231 xenograft mice had been suppressed by as much as 64.5% [27]. The tumour size was shown to be reduced in the groups that were treated with Moringa Oleifera pod and leaf extract. Histopathology showed cell infiltration and epidermal scarring in the groups treated with the extract, suggesting that tissue repair was more prominent at greater concentrations [28]. By activating caspase-3 and triggering ROS-mediated apoptosis in prostate cancer, the methanolic extract of the leaves demonstrated substantial anticancer potential [29]. The extracts had the lowest IC_{50} in T-84 and HCT-15 (resistant) cells, respectively. Additionally, they exhibited the best amount of inhibition of proliferation in multicellular tumour spheroids of HCT-15

cells [30]. Ten phenolic chemicals were found in the solvent-fraction extracts: quercetin, gallic acid, sinapic acid, vanillic acid, p-coumaric acid, m-coumaric acid, 4-hydroxy-3-methoxy cinnamic acid, caffeic acid, and syringic acid [5]. Reduced Bcl-2 expression induces cell cycle arrest and initiates apoptosis, which enhances activation of caspase 3, markers for the apoptosis pathway, 7-octenoic acid, oleamide, and 1-phenyl-2-pentanol extracted from the leaves' ethyl acetate extract demonstrated anticancer effects[7]. The suppression of cell development was caused by apoptosis, which was manifested through chromatin condensation and externalisation of phosphatidylserine (PS)[19]. MOE caused a reduction in mitochondrial membrane potential. In addition, MOE augmented the Bax/Bcl-2 ratio, triggered the activation of Caspase-3/7, Caspase-9, PARP, and facilitated the transfer of AIF, resulting in apoptotic cell death[19]. Ultimately, the *M. oliefera* has significant prospects for future development as an anticancer drug. This investigation has unveiled the latent possibilities of the species. Given these promising results, it is apparent that a natural chemical has the potential to play a pivotal role in the future of cancer treatments. In order to efficiently address cancer cells, we suggest conducting more research that encompasses multiple disciplines.

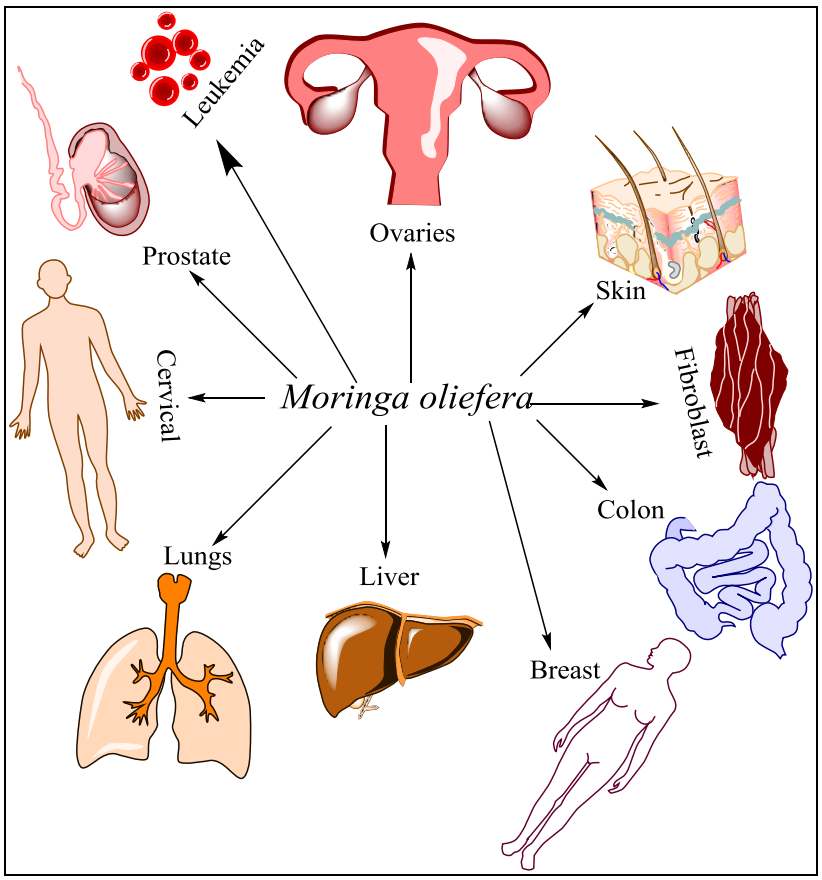

Figure 1. Cancer treated with different parts of *Moringa oleifera*.

Conclusion

Therapeutic plants, particularly natural products, play a crucial role in the process of discovering new drugs and developing therapeutic medicine. *Moringa oleifera* possesses a broad range of secondary metabolites that exhibit various biological or pharmacological impacts. Information was collected and analysed from the research articles. It has been discovered that *M. oliefera* has a history of being used to treat cancer, and it has been found to be effective in doing so based on laboratory tests as well as a small number of studies conducted on living organisms. This comprehensive investigation indicates that the species does not impact regular cells and predominantly inhibits the growth of all tested forms of cancer cells. Therefore, with regards to clinical trials, the appropriate dosage, potential harm, and the actual mechanism of action of the plant extract or isolated compounds, the systematic review

recommends further investigation on the following species. Interdisciplinary scientific inquiry is necessary for the development and discovery of pharmaceuticals related to the *M. oleifera* plant.

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