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A Short Review on Cancer and Moringa Oleifera Leaves Treatment

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Abstract

Cancer remains a significant global health burden, particularly in low- and middle-income countries (LMICs) where access to comprehensive treatment is limited. This review explores the potential of Moringa oleifera (MO) as a complementary therapeutic option in cancer care. Known for its rich composition of bioactive compounds, including isothiocyanates and glucosinolates, MO demonstrates promising anticancer properties, notably in inhibiting cell proliferation and inducing apoptosis in various cancer cell types. Studies reveal that MO leaf extracts can inhibit tumor growth and support immune modulation, offering a natural, cost-effective alternative to conventional treatments. This review aims to summarize existing research on MO's anticancer efficacy, assess its potential for integration into treatment regimens, and highlight its implications for expanding accessible cancer therapies worldwide.

Keywords: Moringa Oleifera, Cancer Treatment, Antibody properties, alternative medicine, lower and middle income country.

Introduction

The rise of early deaths and related disabilities due to cancer as well as other Non-Communicable Diseases (NCD) is a case of concern. Most cases at one point where centered on low and middle-income countries (LMIC). This scenario is changing in recent times. During the 1990s, NCDs were responsible

for 57% of all deaths worldwide. Fast forward two decades later and the whole picture changed as in 2013, the NCDs were responsible for 70% of the deaths [1]. Of these deaths, 4/5th of them occurred in LMICs [2]. On the basis of estimates in recent times surrounding the topic of global mortality rates, NCDs are playing a strong role. The numbers from as recent as 2019 show that of the 20.4 million early deaths, three-quarters were caused by NCDs.

Another recent study highlighted that for every 10 death caused by NCDs, cancer is responsible for 3 of them. Cancer is the leader among all NCD-related deaths in at least 57 countries and that list also includes China. On the other side that is, in the sub-Saharan countries, cancer is a leading cause of premature death as well as cardiovascular diseases. Experts opine that the situation developed due largely to a later phase of being an epidemiologic transition. The transition took place during the latter half of the twentieth century as well as the first decade of the current century.

At one point in time, infectious disease were the most difficult to tackle. Nowadays, their dominance is being affected by the rise in NCDs. If there is one thing that can be stated with precision, it is that a correlation exists between the NCDs and Human Development Index (HDI). When it comes to countries that score very highly on HDI, cancer is the number one disease causing premature death [3]. The numbers differ ever so slightly for countries with a high-to-medium HDI score. In those countries, cardiovascular diseases are a slightly bigger threat [4].

If we take a look at past history, there is an indication that cancer mostly affected the rich countries with an elderly population [5]. For this reason, the LMICs were not concerned with developing a system early on to tackle cancer. When coupled with the limited resources for research, it becomes clear why some LMICs may struggle a lot to cope with cancer treatment. It is well known in a large number of countries that cancer is responsible for the unusual growth of cells. In recent times, the global incidence of cancer has risen to a staggering 18.1 million cases.

So far, there are two factors to take into consideration. One is a modifiable factor with the other being a non-modifiable one. The modifiable factors are represented by an individual's behaviors as well as exposures that increase or decrease the probability of having cancer. To clarify further, the behavioral risk factors can be divided into diet and smoking as well as the risk factors associated with environment. On the other hand, biological factors have been placed under the non-modifiable risk factors. The biological factors are genetic disposition as well as aging [6].

Epidemiology of Cancer

With accuracy regarding cancer epidemiology, it is possible to gather vital information about probable causes. Once the causes are known, steps can be developed as a preventive measure as well as necessary healthcare interventions. For cancer, it is becoming more and more important to develop proper screening and diagnosis procedures [7]. The objective of cancer epidemiology is to acquire high quality information about the onset and different causes attributing to its spread.

A report prepared by WHO has declared cancer as the biggest burden. In 2016, the global organization had reported 244.6 million Disability Adjusted Life Years (DALYs) for both men and women [8].

Table 1 World Health Organization (WHO) Global Health Estimates 2016 on the 20 leading causes of disease burden, estimated as cause-specific DALYs

Disease	Overall			Men			Women		
	DALYs†	Percentage (%)	Rank	DALYs†	Percentage (%)	Rank	DALYs†	Percentage (%)	Rank
Total	2668.475	100	–	1429.691	100	–	1238.785	100	–
Cancers	244.574	9.2	1	137.439	9.6	1	107.135	8.6	1
Ischemic heart disease	203.700	7.6	2	119.756	8.4	2	83.945	6.8	2
Stroke	137.941	5.2	3	72.910	5.1	3	65.031	5.2	3
Lower respiratory infections	129.690	4.9	4	67.542	4.7	4	62.148	5.0	4
Preterm birth complications	101.397	3.8	5	55.618	3.9	6	45.779	3.7	5
Road injury	82.538	3.1	6	60.616	4.2	5	21.922	1.8	13
Diarrheal diseases	81.743	3.1	7	41.412	2.9	7	40.331	3.3	6
COPD	72.512	2.7	8	41.411	2.9	8	31.101	2.5	7
Birth asphyxia and birth trauma	63.928	2.4	9	35.844	2.5	9	28.084	2.3	8
HIV/AIDS	59.951	2.2	10	33.995	2.4	10	25.956	2.1	11
Parasitic and vector diseases	51.838	1.9	11	26.244	1.8	13	25.594	2.1	12
Tuberculosis	51.643	1.9	12	33.020	2.3	11	18.622	1.5	15
Back and neck pain	47.515	1.8	13	21.089	1.5	18	26.427	2.1	10
Cirrhosis of the liver	45.287	1.7	14	31.107	2.2	12	14.179	1.1	18
Depressive disorders	44.175	1.7	15	17.453	1.2	20	26.722	2.2	9
Kidney diseases	39.079	1.5	16	21.353	1.5	17	17.726	1.4	16
Neonatal sepsis and infections	39.009	1.5	17	20.095	1.4	19	18.913	1.5	14
Falls	38.162	1.4	18	22.210	1.6	16	15.953	1.3	17
Self-harm	37.564	1.4	19	23.801	1.7	15	13.763	1.1	19
Interpersonal violence	31.237	1.2	20	24.322	1.7	14	6.914	0.9	20

Figure 1: Table representing the top 20 leading causes of disease burden, image sourced from SPRINGER NATURE Link

The study shows that cancer burden is higher in men than women but the margin is slim. In addition, the highest amount of DALYs occur after people cross 60 years of age. Another study was conducted regarding the types of cancers affecting both men and women which is shown below:

Table 2 List of the most frequent cancers from the World Health Organization (WHO) Global Cancer Observatory (GLOBOCAN) 2018

Cancer	Incidence (million)					Risk 0–74 years (%)		
	Total	Men	Women	Ratio	Age-standardized	Total	Men	Women
All cancers	18.079	9.456	8.623	1.10	197.9	20.2	22.41	18.25
Lung (and trachea and bronchus)	2.094	1.369	0.725	1.89	22.5	2.75	3.8	1.77
Breast	2.088	–	2.088	–	46.3	–	–	5.03
Prostate	1.276	1.276	–	–	29.3	–	3.73	–
Colon	1.097	0.576	0.521	1.11	11.5	1.31	1.51	1.12
Stomach	1.034	0.684	0.350	1.95	11.1	1.31	1.87	0.79
Liver (and intrahepatic bile ducts)	0.841	0.597	0.245	2.44	9.3	1.08	1.61	0.57
Rectum	0.704	0.430	0.274	1.57	7.7	0.91	1.2	0.65
Esophagus	0.572	0.400	0.172	2.32	6.3	0.78	1.15	0.43
Cervix uteri	0.570	–	0.570	–	13.1	–	–	1.36
Thyroid	0.567	0.131	0.436	0.30	6.7	0.68	0.33	1.03
Bladder	0.549	0.424	0.125	3.38	5.7	0.65	1.08	0.27
Non-Hodgkin's lymphoma	0.510	0.285	0.225	1.27	5.7	0.61	0.72	0.51
Pancreas	0.459	0.243	0.216	1.13	4.8	0.55	0.65	0.45
Leukemia	0.437	0.249	0.188	1.33	5.2	0.48	0.57	0.4
Kidney	0.403	0.255	0.149	1.71	4.5	0.52	0.69	0.35

Figure 2: List of most frequent cancers affecting men and women, image sourced from SPRINGER NATURE Link

By 2018, a total of 18.08 million cases had been diagnosed. The study shows lung cancer to have the most adverse effect on people, followed closely by breast cancer. There are other types of cancers as

well which is represented in the image above.

In the normal scenario, genes are in charge of telling the cells in the body about the proper time to grow and then divide. So, the cells are able to make copies of themselves with the same characteristics. When a human being becomes an adult, the cell division only occurs as per the body's need. Generally, the cell division occurs to replace the aging cells or the damaged ones. There are quite a few differences between cancer cells and the normal ones. Cancer cells are also capable of mutating and it is this ability that turns normal cells into cancer cells [9].

The cancer progression has to be viewed at a cellular level to get a thorough understanding. At this level, cancer consists of multistep procedure that includes mutations. In addition, cells that have a inherent capacity to keep proliferating, surviving, and metastasis are primarily selected. At first, tumor is initiated by means of genetic altering which ties into the unusual proliferation of one cell. With proliferation underway, the clonally derived tumor cells keep increasing in number. In the meantime, the tumor population grows due to multiple mutations of those cells. All of these activities have been termed as clonal selection. It is named in this way as the new clones of tumor cells evolve on the back of an increased growth rate. The clonal selection as a process will continue as long as the tumor develops. For this reason, tumors are allowed to become so malignant.

Over the decades, several studies conducting on the reason for cancer's development revealed certain substances responsible for causing cancer. These substances are referred to as *carcinogens*. It is difficult yet to pinpoint the cause of cancer's development as it is a multistep process. There exists a number of factors that may play a major role in the development of cancer. Studies have confirmed the role of radiations, chemicals as well as viruses in the development of cancer in animals alongside human beings.

The DNA is damaged by radiations and a variety of chemical carcinogens; while also inducing mutations. Cancer develops after the carcinogens initiate the mutations. As such, the carcinogens are also referred to as initiating agents and the most notable ones are solar ultraviolet radiations, aflatoxins along with the carcinogenic chemicals available in tobacco [10].

Impact of Cancer

According to a study conducted in 2019 by the WHO, cancer ranks either first or second as the leading cause of death below 70 years of age. This study was conducted by collecting data from 183 countries and the scenario mentioned above is prevalent in at least 112 of those countries. From the rest of the countries, it has been reported that cancer is at least the third or fourth leading cause of death in 23 of those countries.

While cancer is on the rise as a leader among premature deaths, it also is a reminder that fewer deaths are being caused by strokes and heart diseases. This can be attributed to the advancements in healthcare technology. Even so, the burden created by cancer outweighs that of strokes and heart diseases on a global scale. It is a reflection of the primary cancer risk factors. A high number of these risk factors can be linked to the socioeconomic developments in each country.

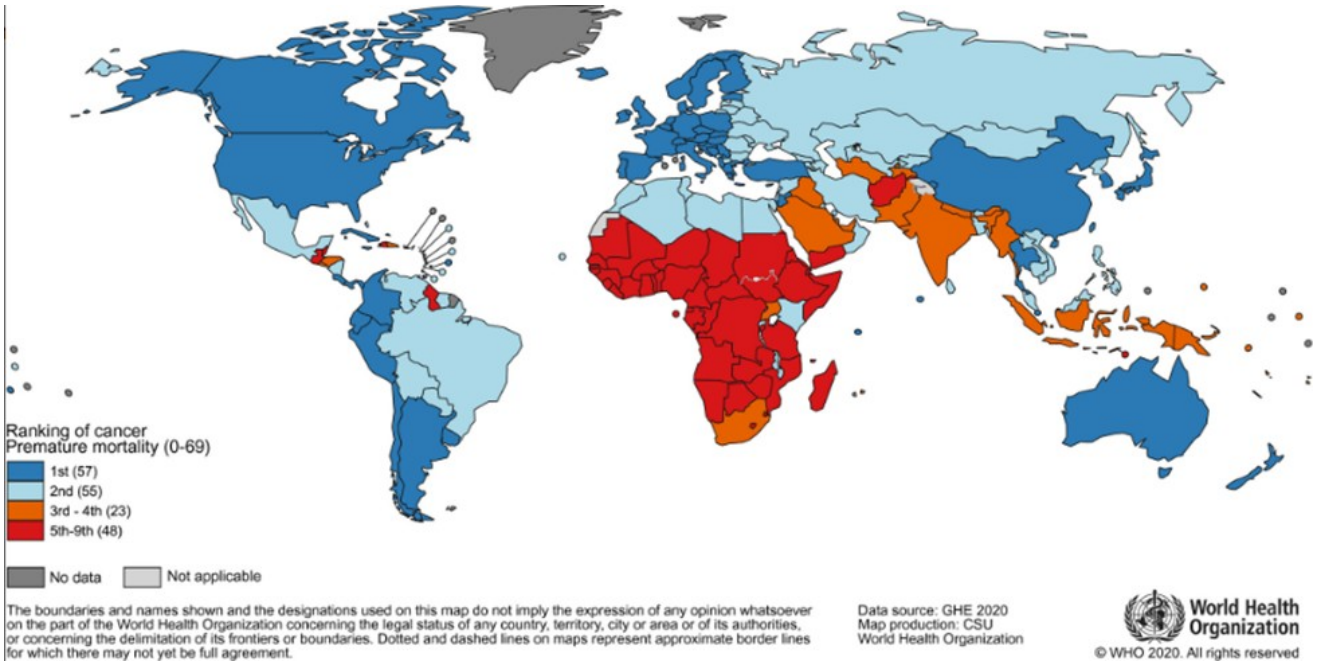

Figure 3: Cancer being a leading cause of death in 183 countries, image sourced from the World Health Organization study

Over the years, cancers has not only caused premature deaths but also is the reason behind financial toxicity (FT). The impact of cancer is always perceived to be negative across countries. This negative impact can be viewed as monetary burden related to a patient's medical treatment. Monetary burden for this case is related to direct medical and nonmedical costs. There are some indirect costs related to it as well [11].

When a patient is diagnosed with cancer, the first order of business is the hospitalization process. This hospitalization falls under direct medical costs and is accompanied by laboratory charges, pharmaceutical expenses as well as expenses related to outpatient treatment. To add to that, the patient's family also has to bear nonmedical costs such as, transportation costs, food and logging expenses to name a few. In many cases, the patient may have to deal with employment loss as well. It can fall under the indirect cost category.

The key issue to address with nonmedical and indirect costs is that, there is no coverage for these expenses in the form of insurance. There are some financial aid programs prevalent in certain countries. Even those aid programs cannot cover these costs. So, the patient and their family are on their own when having to deal with these costs. Cancer can be compared with other chronic conditions regarding these out-of-pocket-costs (OOPC). There is strong reason to believe that the OOPC for cancer exceeds that of other chronic conditions. These OOPCs certainly create a huge impact on the level of medical treatment that a patient receives. In addition, it is certain to negatively impact the psychosocial wellbeing of patients [12].

One study in particular declares Breast Cancer to be most related to the high levels of financial toxicity. A large part of that reason is a regular need to screen and diagnose patients along with providing multidisciplinary care. Other than that, the longitudinal follow-up has also been identified as another cost for high FT [13].

Cancer is known to impose a heavy toll on economies as it reduces productivity and capital investments. On another note, cancer can also lead to unemployment as well as labor losses. Every country has to invest on cancer screening and diagnosis as well. The case is even more applicable for LMICs as a proper diagnosis can yield health as well as economic benefits. In these countries, the survival rate is much lower than in developing and developed countries [14]. If the economic costs related to cancer becomes known to policymakers, it will be beneficial to the country's economy. The reasons being that policymakers can enact policies for curbing the rise of cancer-related morbidity [15].

Cancer impacts the psychosocial wellbeing of patients and their family too. The patients in particular are faced with adjustment issues. Here are some of the other issues that cancer patients and survivors may deal with on a daily basis:

- **Anxiety:** Cancer patients have to deal with anxiety. Of the 10 patients, at least 3 of them do.
- **Body image:** There will be scars on the body as well as changes in weight. Certain body parts are likely to have limited function or none whatsoever. For some, it becomes a matter of being too self-conscious about the body [16].
- **Fear of a return:** There is fear and worry in the cancer survivor's mind that a small ache may signal the return of cancer.
- **Survivor's guilt:** There have been many cancer survivors who thought about why they survived cancer while others did not. In fact, it is a feeling of guilt for an incredibly long duration which affects their perception of reality [17].

Studies were also conducted on other aspects of the psychosocial wellbeing of patients. According to those studies, rurality can have a negative impact on survival rate. Another study was conducted on Australian cancer patients and the result was that people living with cancer in rural areas have a higher chance (35%) of dying inside 5 years of first diagnosis than people living in the cities [18].

The geographical location may change but some of the factors contributing to the downfall of psychosocial wellbeing are constant. Some of the factors are delays in diagnosis, low income levels, socioeconomic status as well as geographic isolation [19]. There is also a matter of healthcare facilities' availability to remote areas. As such, people from remote areas may find it difficult to access proper care and need to travel a great distance for it. It will inevitably play a role in their mind to shape the decision to seek further treatment for cancer [20].

Prevalence of Cancer

Each year, there are newly reported cases of cancer in several different countries. In the United States of America alone, there were 313,510 new cases of breast cancer in the year of 2024. The list for new cases as well as deaths in 2024 for cancer is shown below and it does involve slight estimation:

Table 1 Prevalence of Cancer

Cancer Types	Estimated New Case	Estimated Death
Breast (Female – Male)	310,720 – 2,790	42,250 – 530
Bladder	83,190	16,840
Kidney (Renal Cell and Pelvis)	81.610	14,390
Colon and Rectal (Combined)	152,810	53,010
Lung (including Bronchus)	234,580	125,070
Prostate	299,010	35,250
Pancreatic	66,440	51,750
Thyroid	44,020	2,170

In the list, colon and rectal cancers have been combined as they are commonly referred to as "colorectal cancer" [21]. Each year in the USA, at least 2 million people are diagnosed with cancer which is a confirmation of the rapid growth of the disease [22]. In the United Kingdom (UK) a study was conducted around 2017-2019 to find out the most common cancer types. The result is:

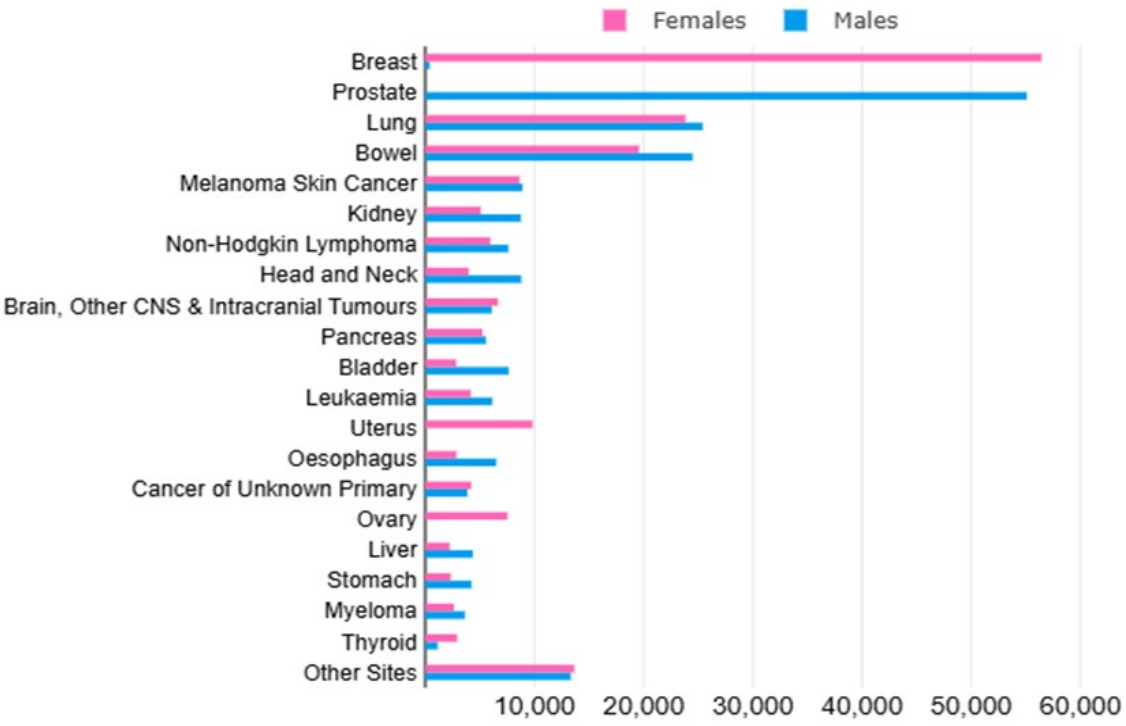

Figure 4: Common cancer types in the UK from 2017-2019, image sourced from Cancer Research UK

As the image highlights, the number of breast cancer cases are on the rise in multiple developed countries [23]. For this reason, more investments are being made to develop better healthcare packages to aid breast cancer patients.

Prognosis of Cancer

The first question any person has after being diagnosed with cancer is about their survival chances. It is normally referred to as prognosis. Naturally, the patient will want to know just how curable the cancer is. There are some factors which will shape the doctor's answer to these questions:

- What type of cancer it is and which body part it affects
- What stage is it in, meaning how big it is and how much area of the body it covers
- What grade the cancer is, referring to the cancer cells' abnormality and how much time it will take to spread
- What traits these cancer cells possess
- What is the age of the patient
- How healthy was the patient before being diagnosed with cancer

All of these are factors that will be used to give a fair idea of how much the cancer has affected one's body. Some people may not want to know but, for others it is an absolute necessity. The prognosis can act as a coping mechanism for patients as they can come to terms with it. For the doctors, it is all about using the statistics collected from several researches on people with a certain kind of cancer. There are statistical measures to deal with for both

doctors and patients in order to provide an estimation.

- **Cancer-specific survival rate:** As previously highlighted, people are diagnosed with different types of cancer each year. So, what this means is to understand the survival rate of patients from a specific type of cancer after diagnosis. There is a time period attached to each case and it can range from 1-2 years. It can also expand to 5 years and in fact, for certain types of cancers, it is the most appropriate time period. Majority of times, the foundation for the cancer-specific survival rate is laid by causes of death documented in medical records.
- **Relative survival:** There is another way to look at survival rate. In this method, instead of looking for confirmed deaths, it is vital to look for cancer survivors for a specific time period since they were first diagnosed with it [24].

With the emergence and recent development trends of Artificial Intelligence (AI), it has also been considered an option for cancer prognosis by experts. As part of this approach, the help of clinical professionals was sought. Clinical professionals are aware of the value of incorporating AI in this field. A research was conducted not too long ago which used AI for predicting metastasis in the brain [25]. There is a challenge for clinical professionals to forecast the cancer's direction. It is due to the fact that the use of regular statistical analysis may not be enough to provide accurate predictions. At present, there is a lot of focus placed on predicting the ways a patient reacts to a particular treatment. In addition, there is use of AI in order to determine the prognosis.

For AI to forecast anything related to cancer, it needs to make an analysis and interpret multi-factor data. The data in question needs to be collected from the assessments of several patients. Only then will AI be able to inform clinical professionals about a patient's prognosis as well as survival rate. In addition, AI can be employed to tell patients about their chance of survival [26].

Current Status of Cancer Treatment and Preventive Activities

In today's new world, there are methods to detect cancer in the early stages and provide advanced therapies. Despite that, cancer is making lives difficult throughout the world due to a high incidence as well as the mortality rate. Here are some of the cancer treatments provided in healthcare facilities:

- **Immunotherapies:** This system uses the patient's immune system in the fight against cancer. There seem to be fewer side effects to this form of treatment when compared with chemotherapy. The therapeutics involved in this form of treatment are the inhibitors of the immune checkpoint, mRNA vaccines as well as monoclonal antibodies. Immunotherapy is divided into two sections: active and passive. The division is done on the basis of the immune response. It is called passive immunotherapy if certain agents are used which boost the pre-existing anti-tumor response. These agents consist of lymphocytes, cytokines, or mAbs. On the other hand, the active form of immunotherapy consists of vaccination and activation of the immune system. The immune system is activated when the antigen receptors are specifically targeted to fight the tumor cells [27].
- **Monoclonal Antibodies for Cancer Treatment:** Experts are preferring this form of treatment in recent years as the monoclonal antibodies do not have a high level of cytotoxic effect [28]. Several studies have been conduct-

ed over the last decade to confirm the positive impact of monoclonal antibodies in the treatment of cancer. With the help of antibody engineering process, it is possible to develop monoclonal antibodies.

- **CAR-T-Cell Therapy:** The full form of it is chimeric antigen receptor-T cell therapy. This form of therapy is provided by genetically modifying the T-cells of cancer patients. When the modification is complete, the T-cells are used for targeting the tumors. The advancements in genetic engineering have been beneficial to this cause as the chimeric receptor can be expressed. It allows for cancer cells to be targeted with more accuracy. In recent times, this form of therapy has gained recognition for treating hematological cancers. Furthermore, this form of therapy has been used to great effect in the fight against leukemia, to be precise, B-cell acute lymphoblastic leukemia [29].

Chemotherapy was among the first forms of treatment provided for cancer-affected patients. The main working theory of chemotherapy is to circumvent the growth and division of the cancer cells. In recent years, healthcare practitioners have used promising inhibitor therapies to treat the patients. Some of these inhibitors are angiogenesis inhibitors, histone deacetylase (HDAC) inhibitors and poly polymerase inhibitors to name a few. Nowadays, there are variations of chemotherapy and each are distinct in how they target the cancer cells.

In some forms of chemotherapy, it is possible to bring change to the quality of cellular proteins. As such, these proteins become dysfunctional. Due to this, there is an impact on the physiological pathways on a cellular level [30]. Meanwhile, some drugs have been developed to target the key hormones; which results in them interfering with the human body's overall metabolism [31].

One form of chemotherapy that has gained popularity across multiple continents is Intravenous Chemotherapy. The process of this chemotherapy requires the drug to be infused to the patient's body through the veins. It may take from a few minutes to a couple of hours or even more. When this form of chemotherapy is underway, patients may also be provided with pills or fluids at regular intervals in the form of medication. Of the new approaches to treating cancer, the use of small molecule inhibitors need to be mentioned.

Here is a table that lists some of the widely used chemotherapeutic drugs:

Table 2 Widely used chemotherapeutic drugs

Drugs	Molecular Target	Mechanism of actions
Bendamustine	DNA	Intra and interstrand crosslinking
Busulfan	DNA	Crosslinking
Carmustine	DNA Glutathione reductase, mRNA	Other/unknown inhibitor
Cisplatin	DNA DNA-3-methyladenine glycosylase Alpha-2-macroglobulin Serotransferrin Copper transport protein ATOX1	Crosslinking Not available Not available Not available Not available

All of these drugs and chemotherapies can have varying levels of success. A high number of treatments can yield success if the stability of nucleic acids are compromised as they may momentarily halt the cell cycle. These forms of treatment will be sustainable if they can continually create an impact on the tumor growth [32].

In the LMICs, one of the leading causes of cancer is the massive level of tobacco smoke consumption. Over $4/5^{th}$ of global smokers reside in these countries which can be cause of headache [33]. Some countries have adopted tobacco-control interventions as a preventive measure against cancer. However, many of the LMICs are yet to take up this approach. The cause for concern is validated by the tobacco smokers' change in lifestyle. Meanwhile the aggressive marketing for tobacco smoke does not help matters much to control the intake. In Africa, the rise in smoking prevalence particularly men can be seen as detrimental to the overall cause. As a matter of fact, the LMICs have been host to a high number of infection-related cancer cases [34].

The overall rise in cancer in the last two decades have provided researchers with enough evidence to suggest that at least half of them could have been prevented. For that, it is imperative to impart the knowledge we now have about the onset of cancer. According to many evidence-based studies, it is clear that if people reduce their exposure to the substances causing cancer then they can reduce the risk of contracting cancer. Of course, there are a few more steps to take such as, getting vaccinated against the human papillomavirus (HPV). In addition, maintaining a healthy lifestyle can go a long way to reduce the risks of cancer. There are cancer screening tests which anyone can take for instance, the HPV DNA test. By taking this test, one can be aware about their chances of contracting cervical cancer [35].

Use of Moringa Oleifera in Cancer Treatment

The primary objective for using natural medicinal plants is to reduce the costs related with cancer treatment. Conventional approaches to cancer treatment cannot always be accessed from all corners of the globe. The debt it incurs leaves families with more financial burden than they may initially think. India is the first place anyone may think of when they hear about Moringa oleifera (MO). While the plant has its origins in this part of Asia, it can be found in other corners of the globe as well [36].

Every part of this plant may be used as a source of food. The plant has its benefits as do its leaves, flowers, roots, seeds etc. can all be used for medicinal effects. In fact, it has long been used in the treatment of bronchitis as well as some infections. Moringa oleifera has a number of characteristics which will draw researchers to it such as, antibacterial, antidiabetic, antioxidant as well as anti-inflammatory characteristics. With the help of MO, the immune system can be modulated and it has the properties to lower cholesterol activity [37].

There is potential in MO to act as an anticancer agent. Leaf extracts of this plant are known to inhibit cell viability for a number of diseases, namely myeloid leukemia and hepatocellular carcinoma. A study conducted over a decade ago by Berkovich et al., shows that leaves of MO have the potential for inhibiting pancreatic cancer cells growth [38]. The leaf extracts get to work on pancreatic cancer by targeting the cell cycle. This results in cells accumulating at the sub-G_1 phase.

Table 3: Summary of Bioactive Compounds in Moringa oleifera and Their Anticancer Properties

Bioactive Compound	Mechanism of Action	Impact on Cancer Cells	Supporting Research Findings
Isothiocyanates (ITCs)	Inhibit cancer cell growth, induce apoptosis by targeting specific cell cycles	Reduces cell viability in cancers such as pancreatic, leukemia, and hepatocellular carcinoma; inhibits key survival pathways (PI3K/Akt, MAPK)	In vitro and in vivo studies demonstrate reduced tumor size and cell proliferation; MIC-1 shown to inhibit cancer cell development effectively
Glucosinolates	Precursors to isothiocyanates; activated through enzymatic hydrolysis upon tissue damage	Provides a steady supply of ITC precursors; supports prevention of metastasis and detoxification of carcinogens	Evidence suggests reduced cancer incidence with glucosinolate-rich diets, especially in colon and liver cancers
Antioxidants (Quercetin, Kaempferol)	Neutralize free radicals, reducing oxidative stress linked to cancer development	Enhances other treatments, reduces inflammation, and supports immune function	Studies indicate improved tumor response, increased survival rate, and reduced DNA damage in cancer models
Phenolic Compounds (Gallic Acid, Chlorogenic Acid)	Modulate enzymes involved in cancer progression and inhibit cell growth	Induces apoptosis and suppresses angiogenesis, limiting nutrient supply to tumors	Experimental findings show significant reduction in cancer cell viability, particularly in breast and colorectal cancer models when combined with conventional therapies

There are 12 different compounds available in Moringa oleifera. According to a study from 2015, it was revealed that 3 of these compounds contain anticancer properties [39]. These 3 compounds consist of the precursor form for isothiocyanates as well as glucosinolates. Isothiocyanates in particular can be found to occur naturally in the plant and acts as anticancer chemical. Here is a table to support the anticancer claims of MO on the basis of in vitro reports:

Table 4 The anticancer claims of MO on the basis of in vitro reports

Form of Dosage	In vitro model	Dose	Standard	Activity	Reference
Aqueous extract of leaves	Ehrlich ascites carcinoma (EAC) and human laryngeal carcinoma (Hep-2) cell culture	0.05, 0.1, 0.25, 0.5, and 1 mg/ml	Control (No treatment)	Anticancer	Barhoi et al,. (2020)
7-Octeonic Acid	Cell migration assay	1.5mg/ml	Doxorubicin (1.5 µM)	Decrease of migratory cell number across the wound which reflects the antimigratory effect	
Oleamide		40 µg/ml	Doxorubicin (1.5 µM)	Decrease of migratory cell number across the wound which reflects the antimigratory effect	
7-Octeonic Acid	Hoechst staining	2.5 mg/ml	Control (No treatment)	Apoptosis	
Ethanol extract of leaves, barks and seeds	HCT-8 and MDA-MB-231 cell line	250 and 500 µg/ml	Control (No treatment)	Leaves and bark inhibit cell survival	Al-Asmari et,al. (2015)

Moringa oleifera contains antioxidant potential that should not go unnoticed. Carcinogenesis is a multi-stage procedure in which oxidative stress is vital for tying up environmental toxicities with carcinogenesis. There have been multiple studies to exhibit antioxidant supplementation by the plant which results in prolonged survival. In addition, it is shown to improve tumor response [40].

Moringa oleifera's biological attributes have much to reveal according to experts. As such, there needs to be a number of experiments conducted to understand these biological attributes. Isothiocyanates (ITC) can be found inside Moringa oleifera (MO) and it has been used in studies for treating mice. For this treatment, ITCs were used with varied concentrations. During one experiment in particular, it was discovered that Moringa Isothiocyanate (MIC-1) consists of less toxic components than rest of the ITCs [41]. Here are some of the possibilities regarding the attributes of MIC-1:

- **Anti-Cancer:** MIC-1 is known to possess the ability as cancer cell proliferation inhibitor and it also inhibits metastasis. Meanwhile, MIC-1 also works as a promoter of apoptosis in the cancer cells. There were signs of selective cytotoxic as well as apoptotic activity in human cells when MIC-1 had been used experimentally for HepG2, HEK293 alongside Caco-2 [42]. In addition, MIC-1 is known to downregulate the signaling pathways that are in connection with the proliferation of cancer cells. The result of which is the inhibition of cancer cell development.
- **Neuroblastoma:** After leukemia and brain tumor, neuroblastoma (NBL) takes the third place as a common malignancy. At the same time, it is such a common type of cancer that can be used for studying anti-cancer properties of Moringa Isothiocyanate (MIC-1). The way it works is by taking the NBL cell line of SH-SY5Y human and testing to check if it can activate apoptosis. One particular study went far in its cause to show that MIC-1 can downregulate the amount of p-PI3K, p-mTOR as well as p-Akt if the MIC-1 gets complexed with α-cyclodextrin. It is well known that MIC-1 inhibits the pathway for mitogen-activated protein kinase (MAPK). At the same time, it is going to trigger the signaling of the p13Akt to signal the pathway. In addition, p13Akt is in charge of regulating for the cells. For this reason, MO is lethal against the proliferation of cancer cells.
- **Hepatocarcinoma:** There are two pathways in possession of the control of apoptosis. The first one is known as an extrinsic pathway and becomes active following the interactions of death ligands with the death receptor. From this interaction, it becomes possible to activate the initiator caspase 8 as well as effector caspase 3. Meanwhile, the other pathway being an intrinsic one, it becomes regulated with the help of initiator caspases 2 as well as 9. A study was conducted regarding the use of MIC-1 with avenanthramide 2f also known as AVN 2f in the treatment of hepatocarcinoma cells. There were positive results as the combination of these two worked in favor of inhibiting the proliferation. It was achieved through the activities of caspases 2, 8, 9 and 3 being increased [43].
- **Skin Carcinoma:** There are tumor accelerators that also induce inflammation and one such component is TPA. It is known to promote the formation of skin cancer. TPA has been found in the epidermal JB6 cells in mice. One study conducted on mice with this TPA promoter and the MIC-1 presence can alter the gene expres-

sion. There are 76 pathways and TPA can activate them all. At the same time, MIC-1 can inhibit the pathways [44]. A high portion of the signaling pathways consist of inflammatory responses and cancer. In addition, the signaling pathways consist of oxidative stress-related pathways. Further experiments have also shown that MIC-1 can inhibit factors that are tied to proliferation as well as inflammation. In the case of tumorigenic transformation of the mouse epidermal JB6 cells, MIC-1 can work as chemoprophylactic [45].

There have been multiple studies over the years to confirm the active role of Moringa oleifera in inducing the cell cycle arrest inside a number of tumor cells. Every part of the plant can be used for therapeutic purpose. In that regard, the moringa leaf extracts were studied for their impact on the B-lymphocyte plasmacytoma-U266B1 cell line of human body [46]. These cells had to be treated with the serial dilutions from the moringa leaf's methanol, ethanol, chloroform as well as ethyl acetate extracts. In the meantime, the cytotoxicity had to be measured with the use of a neutral red dye uptake assays. On the basis of the cytotoxicity activity, the methanol extracts created the highest impact against the U266B1 cells. This can be interpreted as the extracts being capable of inhibiting the proliferation of the aforementioned cells.

Another significant study regarding the anticancer impact of Moringa oleifera leaf extracts focused on the leukemia cells. These cells had been harvested from a total of 15 patients suffering from acute myeloid leukemia (AML). On top of that, the researchers took more leukemia cells from 10 patients suffering from acute lymphoblastic leukemia (ALL). Initially, the leaf extracts had been tested for the antioxidant activities with the use of DPPH assay. As part of the test, they used hot water alongside 80% ethanol extracts and the results highlighted a high level of antioxidant activity [47]. It can be stated that the moringa leaf extracts showed a strong performance regarding anticancer activity in vitro going up against AML and ALL cells.

Moving onto the in vivo section, a particular study had been conducted taking on the human hepatocellular carcinoma (HepG2) cells for anticancer activities. The extraction process involved cold water for the extracts. After that, the HepG2 cells had been treated with the leaf extracts and then tested by using flow cytometry. It was done so that the extracts' impact on the DNA content alongside the cell cycle stage could be understood. With the help of the MTT assay, the outcome was the inhibition of the cell proliferation with the extract's concentration on the rise [48].

Conclusion

Cancer's rising incidence and the high costs of conventional treatments emphasize the need for accessible, affordable alternatives, especially in resource-constrained settings. *Moringa oleifera*, with its unique profile of bioactive compounds, presents a promising natural option. Research demonstrates MO's efficacy in reducing cancer cell viability, promoting apoptosis, and modulating immune responses. While these findings are encouraging, further clinical trials are essential to validate MO's therapeutic potential and safety. Expanding research on MO can pave the way for developing affordable, plant-based treatments that mitigate financial burdens on patients and healthcare systems alike, ultimately enhancing global cancer care accessibility.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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