Molecular activities in *Moringa oleifera* Linn - Review

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**Abstract:**

The terrific increase by the word “modernization” in various fields in the world without boundaries affects the total environmental system, which leads to the emergence of various new diseases in various forms. In that case, cancer is considered as one of such a dreadful disease which is also measured as a leading cause for the death of the people. Even with the advanced treatment of modern medicine in treating cancer and reduce the rate of cancer recurrence using advanced technologies such as immunotherapy, targeted therapy, robotic radiosurgery are still very subjective to the individual, and it causes tremendous side effects to the patient. Alternative medicine plays a vital role in the treatment and management of diseases even before centuries. Many pharmaceutical companies involved in the research development of anticancer properties as a holistic approach in the treatment and management of cancer. *Moringa oleifera*, traditionally used as food sources, has attracted many researchers to evaluate the biochemical properties of Medicinal, antioxidant, as an antiulcer, antimicrobial, antitumour and anticancer. Each part of the tree is nutritive and personalized selective on phytochemicals as an anticancer drug are essential in treating the cancer cells. Limited knowledge on the cytotoxic activity and therapeutic index of *M. oleifera* in treating specific types of cancers are still under study by many researchers. However, the molecular analysis of anticancer properties in *Moringa oleifera* as sustainable preventive and management of cancer therapy still lacking in Malaysia.

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**INTRODUCTION**

*Moringa oleifera* is commonly called as drumstick tree or horse radish tree which belongs to the family of Moringaceae (Anwar and Bhanger, 2003).

*M. oleifera* is native to the sub Himalayan tracts of Northern India. It ranges from tiny herbs to large trees which grow up to 5-10m height (Morton, 1991). *M. oleifera* is rich in nutrition with high iron content and minerals. Though it is common in all countries, the leaves, flowers and fruits were highly considered as a nutritive vegetable in India (Anwar and Bhanger, 2003; Anwar et al., 2005). The species has been cultivated throughout the world, specifically in Asia, Latin America, Florida, the Caribbean, and the Pacific Islands as an eye-opener in the research field.

The leaves of *M. oleifera* is enriched with \(\beta\) - carotene, protein, vitamin C, calcium and potassium and also acts as a good source of more antioxidant compounds (Dillard and German, 2000; Siddhuraju
and Becker, 2003). It is also known as ‘Mother’s best friend’ in the Philippines as it enhances the woman’s milk production (Estrella et al., 2000). Apart from these activities, M. oleifera is considered as an important medicinal plant for treating many prolonged diseases including cancer.

Medicinal Properties of M. oleifera

M. oleifera is highly recognized for its medicinal value. As various parts of the plant possess variety of activities like antitumour, antiulcer, antioxidant, antibacterial, antifungal, anti-diabetic, antiplasmodic, anti-pyretic, anti-inflammatory, antihypertensive, antiepileptic, hepatoprotective (Anwar et al., 2007). The leaves and buds of Moringa can be used to treat headache and the roots can be used as a counterirritant, whereas the leaf juice when mixed with honey is used in treating the eye infections (Ezeamuzie et al., 1996; Rathi et al., 2006). The various medicinal properties of different parts of Moringa oleifera include the leaves involved in lowering of blood pressure level also used to cure fever, bronchitis, inflammation of mucous membrane and it also possess a high antioxidant activity (Morton, 1991). The flowers are used to cure inflammation, muscle diseases, tumours, and it also has the capability to reduce the serum cholesterol level. It also acts as a good abortifacient (Mehta et al., 2003). The gum of the Moringa is used as a good dental carrier and also used to treat Asthma, dysentery and intestinal complaints. The stem bark can be used to treat eye diseases, ulcers and its juice can be used as a pain reliever (Bhatnagar et al., 1961; Sidduraju and Becker, 2003). Even though Moringa possess these types of medicinal properties, it can also possess some pharmacological properties which are useful in curing many ailments. Some of the medicinal properties of this valuable plant have been listed below.

Antioxidant properties

Moringa a multipurpose tree which is enhanced with a wide range of pharmacological properties in which the leaves are considered to possess a rich source of antioxidant compounds (Chumark et al., 2008; Leone et al., 2015). The researchers concluded that the Methanolic and the Ethanolic solvents were considered as the best solvents for the extraction of the antioxidant compounds (Vongskak et al., 2013). The crude extract of M. oleifera was shown to have stronger antiradical scavenging activity against the DPPH radical. The phenolic acids present in the leaves were considered as a predominant phenolic constituent for its antioxidant property (Pari et al., 2007). The antioxidant activity of leaf extract of M. oleifera was studied for the stabilization of butter at a cool temperature. LEMO (leaf extract of M.oleifera) was obtained with 80% ethanol at room temperature for 48 hours. It was added to the butter at three various Concentrations, but failed to show any immediate response. After 90 days of incubation, it was concluded that the LEMO at 600 ppm concentration was best to store the butter at the cool temperature (Nadeem et al., 2013).

Antispasmodic activity and Hepatoprotective Activity

The roots of M. oleifera possess antispasmodic activity (Cáceres et al., 1992). As the Ethanolic extract of the M. oleifera leaf consists of calcium block, it shows the antispasmodic activity (Dangi et al., 2002). As this nutritious plant exhibit antispasmodic activity due to the presence of different biological compounds, it can also helpful in curing the gastrointestinal disorders (Rani et al., 2018). Methanolic extract and the aqueous extract of Moringa reduce the induction of gastric lesions and caused various changes in the experimental rats. Although it exhibits the antulcer activity, results also shown that they improve the healing of gastric lesions induced by acid (Pal et al., 1995; Deb-nath and Guha, 2007).

Antimicrobial and Antifungal activity

The roots of Moringa are rich in antimicrobial agents. Due to the presence of antimicrobial agents, the roots have the ability to act against the microorganisms with an eminent antibacterial activity. (Rao et al., 2001). The biochemical compound named pterygospermin, which exist in the roots and flowers of Moringa possess high antibiotic principle such that it acquires a dominant antibacterial and fungicidal activities (Ruckmani et al., 1998; Das et al., 1957). The crude Methanolic extract of the root is enriched with 4-o-L-rhamnosylxyl benzyl isothiocyanate, which also shows high antibacterial activity (Eilert et al., 1981). The chloroform fraction of the Ethanolic extract of the root showed immense antibacterial and antifungal activity (Nikkon et al., 2003). The juice extracted from the bark was reported to show high antibacterial activity against the pathogenic organism Staphylococcus aureus whereas, the leaf juice was found to inhibit the growth of Pseudomonas aeruginosa and Staphylococcus aureus (Mehta et al., 2003).

Antitumor and Anticancer activities

There are many plant derived anticancer agents quantified from different types of medicinal plants. Some plant showed anticancer activity against all tested cancer cell lines, whereas others showed anti-
cancer activity against selected cancer cell lines. Among the various types of medicinal plants, *M. oleifera* is reported by many researchers about its anticancer property. The in vivo study was performed on the Swiss albino mice to analyze the anticancer activity for the leaves and fruits of the *M. oleifera*. It was confirmed that the tumour growth rate was controlled so that the life span of the patients can be increased (Purwal et al., 2010).

The Methanolic extract of the seeds of *Moringa* exhibits anticancer activity against diverse cancer cell lines like colon, lung, liver and neuroblastoma. The extract was treated with these cancer cell lines at different concentrations. The sulforhodamine B dye assay was performed with the concentration of 100 µg/ml on the liver and neuroblastoma cell lines showed 95% and 93% of inhibition whereas the lung cancer cell line showed 80% of inhibition (Shaban et al., 2012). The biochemical compounds named benzyl carbamate, benzyl isothiocyanate, niacinimicin and β - sitosterol present in the leaf extract of *Moringa* were analysed for probable antitumor activity which showed high inhibitory activity against the Epstein Barr virus when tested in the in vitro conditions. Niacinimicin acts as an effective chemo defensive agent in the chemical carcinogenesis (Guevara et al., 1999). The seed extracts showed dominant inhibition against skin papillomagenesis in mice (Bharali et al., 2003).

It was also confirmed by many researchers that the effective compounds like niazinin and thiocarbamate from the leave extract involved in the inhibition of tumor promoter Epstein Barr virus. The anticancer activities of *Moringa* leaves, bark and seed extracts were studied against two types of cancer cell lines like Breast and colorectal cancers.

It was reported that the anticancer compounds like eugenol, D – allose, and hexadecanoic acid present in those extracts showed a high percentage of inhibition against the breast and Colorectal cancers (Al-Asmari et al., 2015). The Methanolic extract of Moringa oleifera showed eminent anti-proliferativeve activity against the liver cancer cell lines due to the presence of the phenolic Compounds (Khalafalla et al., 2010). The dichloromethane extract of the *M. oleifera* shows various properties like antioxidant property, antiproliferative property, and it can also have the ability of inducing the quinone reductase enzyme (Suphachai, 2014).

Hence, from the above literatures, it was clear that the biochemical compounds present in the different solvents of the *M. oleifera* possess the antiproliferative activity and antitumour activity. From the above review, it was understandable that the highly nutritious tree can be used as the best chemo preventive agent for curing many types of cancers. The pharmacological properties of this medicinal plant was used to cure many prolonged ailments, even though it cannot be eradicated completely it can be controlled by these types of medicinal herbs which is also called as nature’s gift to the world as it saves the life of many different types of disease-infected patients.

**Secondary Metabolites in *M. oleifera* and its activities**

The secondary metabolites are the group of biochemical compounds which are derived from the primary metabolites that can not directly involve in the growth of the plants. These are plant-derived compounds with different chemical and molecular structure which plays a major role in the defense and survival of the plant. Though it has this much of properties, it can be extracted in different forms from the plants and used as a medicine and flavouring agents. The plant-derived secondary metabolites includes the alkaloids, flavonoids, terpenoids, phenols, vitamins, tannins, saponins and phenolic acids were also used in the treatment of many diseases in various forms.

**Vitamins**

Vitamins are the organic compounds present in many natural sources with multiple functions. The leaf of *M. oleifera* is highly rich in vitamin A, which plays a vital role in cell differentiation, proliferation of the cell, apoptosis etc. (Ramachandran et al., 1980). The fresh leaves are rich in carotenoids. They contain a high amount of β – carotene; in one gram of leaves which is considerably high when compared with carrots, pumpkin and apricots (Salvini, 1997). β – carotene is highly rich in dried leaves when compared with the fresh leaves, and it may varies with the environmental conditions from which it grows, the origin of the plant and also with the method of drying (Joshi and Mehta, 2010; Busani et al., 2011).

The fresh leaf of *M. oleifera* contains Vitamin C, which is greater than that of orange (Salvini, 1997). These are involved in the metabolism of tyrosine, folic acid, and tryptophan and also have other actions like the modification of cholesterol into bile acids, lowering of blood cholesterol level. It also has good antioxidant activity (Chambial et al., 2013). The vitamin C content may varies based on their plant origin, method of drying and also with the method of extraction. The lyophilization method is the best method to preserve Vitamin C from oxidation (Joshi and Mehta, 2010; Zhang, 2011; Siddharaju and Becker, 2003). The fresh leaves of M.
oleifera is rich in a particular compound named $\alpha$-tocopherol, which is equal to that of the compound present in the nuts (Ching and Mohamed, 2001). Vitamin E undergoes many biochemical metabolisms like it modulate the gene expression level, prohibits the cell proliferation and regulates the bone mass (Borel et al., 2013).

Flavanoids

Flavanoids are commonly called a group of polyphenolic compounds with benzo – pyrone structure. They are highly present in plants as the flavanoids plays a major role in combating against the infections caused by the microbes (Kumar and Pandey, 2013). Many recent researches reported that the huge ingestion of this type of secondary metabolites may showed a preventive effect against many microbial infections, heart diseases and also some other prolonged diseases like cancer (Pandey and Rizvi, 2009). The leaves of Moringa are highly rich in flavonoids like myricetin, quer cetin, kaempferol etc. The concentration of the flavonoids present in the dried leaves is seven times higher in the freeze-dried leaves of M. oleifera (Amaglo et al., 2010). The concentration of flavanoids may varies according to the environmental conditions of the plant, harvesting system, drying method, leaf maturity stage, genetics of the plant and also depends on the various type of methods used for the extraction process.

Phenolic Acids

The phenolic acids are the derivatives of hydroxybenzoic acid and hydroxycinnamic acid, which are also the natural source obtained from the plants. The phenolic acids exhibit some medicinal properties like anti-inflammatory, antimutagenic, antioxidant and also anticancer properties (Verma et al., 2013; Duthie and Wood, 2011). The phenolic acids were found to be high in many fruits and vegetables; in that case, it is also found abundantly in the leaves of Moringa. As like the flavonoids, the environmental conditions of the plant, harvesting system, drying method, leaf maturity stage, genetics of the plant and also depends on the various type of methods used for the extraction process may varies the concentration of the phenolic acids present in the leaves of M. oleifera.

Alkaloids

Alkaloids are commonly defined as a nitrogen-containing organic compound derived from the amino acids which are present in the plants. Plant derived alkaloids are used in the preparation of drugs for many diseases. These are soluble in water and can be extracted easily with the alcohols. As this secondary metabolite possess some pharmacological properties, the alkaloid compounds like vincosamide, phenylacetonitrile etc. were found to present in the leaves of Moringa oleifera (Kasolo et al., 2010). Secondary metabolite compound alkaloid in M. oleifera leaf is one of the largest phytochemical group of compounds which have a variety of medicinal properties, for example, one of the powerful pain killer drugs is developed from this (Kam and Liew, 2002). These compounds also have toxicity against cells of foreign organisms which is useful in the reduction of human cancer cell lines (Nobori et al., 1994) other uses of their derivatives were analgesic, antispasmodic and bactericidal effects (Rani et al., 2018). This study was showed that the alkaloids were higher in leaves followed by bark and pods, and they are the highest in concentration compared to other group of compounds.

Tannins

Tannins are frequently called as water-soluble compounds which can also have the capability to bind and precipitate the other secondary metabolites like alkaloids, proteins and the gelatin. The tannins reveal many biological properties like anti-inflammatory, anticancer, antiheliototoxic and antibacterial activity (Kancheva and Kasaikina, 2013). M. oleifera leaves are an excellent source of tannins, and their concentration of tannins in dried leaves are little greater than the freeze-dried leaves (Makkar and Becker, 1997). The amount of tannins present in the leaves are greater than the concentrations found in nuts and equal to that of the berries but much lower when compared to the concentrations found in different types of medicinal plants (Edeoga et al., 2005).

Saponins

Saponins are the group of compounds derived from the compound isoprenoidal which are connected with one or more sugar molecules (Augustin et al., 2011). As M. oleifera leaves are considered as a good source of Saponins, their concentration may varies between the dried and the freeze-dried leaves (Makkar and Becker, 1997). Saponin precipitates and coagulates red blood cells and forms foams in water, have haemolytic activity, binds with cholesterol with bitterness prevents excessive intestinal absorption of cholesterol and reduces cardiovascualar diseases. It is also reported that total saponins have the antioxidant, antimutagenic and anticancer property (Luo et al., 2002).

Manifestation of cancer

Cancer is defined as the uncontrolled growth of cell division that may affect the immune system. Though lots of treatment facilities were available to cure...
this dreadful disease, it cannot be eradicated completely. The recent studies are focusing on natural products to cure. This type of emerging diseases. In recent years, the medicinal plants act as an outstanding source for drug discovery. Various herbal plants and plant-derived compounds were used for treating the newly emerging diseases in an innovative approach. M. oleifera is one of the plants with various anticancer compounds which can be used to control the cell proliferation in various stages. The study at the molecular level was not keen, and it was needed to study the changes that occur in the DNA and also in the different enzyme changes that occur after the treatment of the compounds quantified from the particular type of plant species.

**Cellular mechanism**

Cyclin-dependent kinases (cdks) are a family of serine/threonine protein kinases whose members are small proteins (~34-40 kDa). Most of the known cyclin–cdk complexes regulate the progression through the cell cycle. Cell cycle defects are often mediated by alterations in cdk activity. In general, cdks play a major role in control cell cycle progression through phosphorylation of proteins that function at specific cell cycle stages. However, some mutations in these proteins interrupt their role in controlling the cell cycle, which can significantly lead to the uncontrolled cellular proliferation or cell death. In humans, mutations in cyclin dependent kinase 2 (CDK 2) is responsible for nearly 50% of cancers. In line with this, blocking the activity of cdk proteins is considered as a treatment strategy to control the over-regulating cell-cycle mechanism (Alshehri and Elsayed, 2012).

**Anticancer agents from M. Oleifera**

The biochemical compounds like benzyl carbamate, niazimicin, Benzyl isothiocyanate and β - sitosterol present in the leaves of M. oleifera shows a potent antitumour activity (Anwar et al., 2007). The compounds present in M. oleifera leaves like benzylisothiocyanide, and niazimicin exhibits a cytotoxicity activity against the cervical cancer cell lines (Varalakshmi and Nair, 2011).

M. oleifera a traditional Indian healer which was used by many practitioners consists of many Phytochemical constituents like isothiocyanate and hexa-deconic acid present in all parts of Moringa arrest the cell cycle growth in G1 phase (Razis et al., 2014). Such that among all the components quantified from the extracts of all the parts of this plant nearly five to six compounds of it showed high docking score when compared to the other biological components.

**Biochemical compounds of M. oleifera**

The recent research on this medicinal plant reported that the Ethanolic extract of M. oleifera contains many secondary metabolites, especially the alkaloids, flavanoids and phenolic compounds. The biological components present in this extract can inhibit cancer cell proliferation by suppressing the tumour growth factors. These compounds may increase the enzyme levels, which is highly responsible for the antioxidant and antiproliferative properties (Singh et al., 2015).

Number of studies reported that the changes in the antioxidant enzyme levels may due to the metabolic changes and its mitochondrial functions of the cell. The increasing levels of SOD and GST were based on the enzyme inactivation (Dursun et al., 2006).

The recent findings suggest that the venom isolated from the stingray Dasyatis sephen enhances the cancer cell death by inhibiting the cancer cell proliferation, antioxidant properties of the target and also the potential of the mitochondrial membrane. It may also increase the ROS system, lipid peroxidation and apoptosis in the cervical cancer cell lines at molecular levels (Rajeshkumar et al., 2015).

M. oleifera contains high amount of zeatin that has been used as a natural plant growth enhancer and helps to increase crop yields. The natural ability of zeatin as aminopurine factor induces cell division. In vitro findings concluded zeatin found in plant extract shows effective regenerative effects on human skin fibroblast. Further, studies on these properties of M. oleifera may be useful for post-treatment of cancer patients.

**CONCLUSIONS**

This review study focused on molecules involved in anticancer activity of Moleifera at different forms. Thus, the phytochemicals were extracted by using different solvents, and it was subjected to GCMS analysis to find out the biochemical compounds found in the extracts. The biochemical compounds were identified and docked with the docking receptor to find out the effective anticancer compound from the other compounds. The effective compounds can be isolated, and it can be treated with the different cell lines at the molecular level for Studying its polymorphic level and enzyme activity levels at different concentrations.

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