DOI: 10.56511/JIPBS.2015.v2.i02.pp182-192

Journal of Innovations in Pharmaceuticals and Biological Sciences
www.jipbs.com

JIPBS

ISSN: 2349-2759

Review Article

Promising Role of *Moringa Oleifera (Lam.)* In Improving Radiotherapy: An Overview

Amrita Singh[1], Renu Dayal[1], Rudra P. Ojha[1], K. P. Mishra*[1]

[1]Division of Life Sciences, Research Centre, Nehru Gram Bharati University, Allahabad- 211002, U.P., India

Abstract

Cancer radiotherapy aims to effectively kill tumor cells but inexorably damages normal tissues which is undesirable. The success of radiotherapy lies in sparing normal tissues from radiation damage. Natural phytochemicals possess attribute which might protect normal cells but enhance tumor cell susceptibility followed by radiotherapy through modulating cellular molecular targets. Previous results of our laboratory and numerous recent studies on herbals have demonstrated significant cytotoxic activity to certain malignant tumors and protection of normal cell after exposure to ionizing radiation. This review describes the radio-therapeutic potential of *Moringa oleifera (Lam.)* that is easily available and common constituent of daily food. *Moringa oleifera* is an indigenous deciduous tree which possesses various therapeutic properties. The mechanisms of radioprotection of normal mammalian cells by alcoholic extracts of leaves and pods of Moringa have been discussed in terms of redox imbalance and oxidative stress. We have focused on the effect of alcoholic bioactive phytoconstituents of plant which displays synergistic cytotoxicity on tumor cells in combination with ionizing radiation. It is concluded that ethanolic extract of Moringa may be useful in efficient killing of tumor cells leading to establishment of improved protocol in cancer radiotherapy of patients.

Key words: *Moringa oleifera,* antioxidants, toxicity, free radical scavenging, extracts.

***Corresponding Author: K. P. Mishra,** Division of Life Sciences, Research Centre, Nehru Gram Bharati University, Allahabad- 211002, U.P., India.

1. Introduction

Cancer is a complex aberrated biochemical disease that acquires characteristic alterations in physical, environmental, metabolic, chemical and genetic factors. It is third leading cause of morbidity and mortality worldwide with an estimated 12 million new cases and 7.6 million deaths [1]. Latest treatment modality involves radical surgery, radiotherapy, γ -radiation and chemotherapy that inevitably leads to treatment complications[2]. Radiotherapy

©JIPBS, All rights reserved

is one of the prominent conventional treatment strategies where cancer cell are treated in the presence of adequate oxygen level; whereas low oxygen environment makes cancer cells more resistant to radiation and chemotherapy [3].

In chemotherapy and/or surgery, high doses of ionizing radiation are employed to treat solid malignant cells which affect normal cells and exert severe side effects including, hair loss, fibrosis, xerostomia, lung and kidney-dysfunction. Considering above points in the view, use of radioprotector is highly recommended in-order to protect normal cells from harmful effects of ionizing radiation. Several synthetic radioprotectors were found to effective on normal cells and tissues, however, most of them exert severe side effects. Therefore, except amifostine and aminothiol no other radioprotector is approved for clinical application [4, 5]. Till date, safe synthetic radioprotectors are not available. Thus, there is an imperative need to identify novel, nontoxic, effective natural bioactive compounds that sensitize tumor cells and protect normal cells in radiotherapy.

Pertinent to it, the herbals mentioned in Ayurveda are used as folklore medicine for the treatment of various diseases since time immemorial. In search of potential radioprotectors to be used in cancer radiotherapy, a number of herbals and traditional compounds are under investigation. Several indigenous medicinal plants have been reported to render protection against radiation damage through improved targeting, selectively sensitizing malignant cells or protecting normal tissues by the use of natural antioxidants as a therapeutic option.

Previous research findings from our laboratory and others suggested differential role of triphala, nigella sativa, curcumin to induce apoptosis in tumor cells simultaneously protect normal cells [6, 7, 8]. The mechanism of action includes cell cycle arrest, alterations in survival signaling and up or down regulation of detoxifying enzymes. Recent investigations from our laboratory showed that combined treatment of biochanin A (a major isoflavone), was capable enough to sensitize radioresistant colon cells [9]. The mechanism was reported to involve additive increase of caspase-3 radioresistant cells alongwith substantial increase of ROS, lipid peroxidation and mitochondrial membrane potential. The present review is an attempt to discuss the radioprotection offered by alcoholic extract of *Moringa oleifera in vitro* and *in vivo.*

2. Brief Description of *Moringa Oleifera*

Moringa oleifera Lam. (MO) from the Moringaceae family is a native plant/of the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. It is also known as the drumstick tree, benzolive tree, kelor, saijhan, and sajna or Ben oil tree [10]. Various parts of *M. oleifera* have long been used in habitual diets and traditional remedy in most of the tropical regions. Generation of reactive oxygen species (ROS) and other reactive radicals were found to be significantly reduced along with restored activities of antioxidant enzymes in *M. oleifera.* We have attempted to give a brief account of the progress in our understanding of the mechanisms of radioprotection of normal living cells by some major bioactive compounds of the plant such as quercetin, coumarin, and kaempherol.

MO is a fast growing soft deciduous tree about 10 to 12 m long and 30 cm in diameter. Leaves are alternate bi or tripinnate compounds, feathery, 3-5 cm

long and dark green in colour (Figure 1) White to cream colour flowers are lightly fragrant and straight stems are poorly formed. Barks are white thick corky and sticky [11]. Fruits are rounded green in colour, 15-45 cm long with 5 - 20 rounded or trilobed capsule shaped seeds [12].

3. The Phytoconstituents of *Moringa Oleifera*

The alcoholic, hydroalcoholic and aqueous extracts of various parts of MO have shown the highest antioxidant activity due to the high concentration of bioactive compounds which have defensive and curative properties. Table 1 gives a detailed account of various bioactive fractions available in different parts of the *M.oleifera.*

4. Medicinal and Nutritional Usages

Most parts of the Moringa tree e.g. leaves, fruits (pods), stem, barks, and flowers are consumed by humans in many countries. Bioactive compounds from Moringa are known to be immune boosting, hypotensive, anticancer, antibacterial alongwith antioxidant activities and involve induction of tumor suppressive effects [24, 25, 26].

Different parts of the plant have phyto-pharmaceutical components which have traditional, medicinal and industrial usages (Figure 1) [27]. Ethanolic extract of seeds have shown antipyretic, antiasthmatic and analgesic properties [28,29,30] hypocholesterolemic, wound healing, antithyroid., hypotensive, hepatoprotective, antitumorogenic, antiulcer, antimicrobial activities were shown by extracts of leaf, flower, stem and seed [24,31,32,17,23,19] . Extracts of stem have shown capacity to prevent cardiovascular diseases and reduce high blood pressure [33].

5. Mechanism of Action of *Moringa Oleifera*

As described earlier, radiation affects the biological systems in more than one ways. Herbals have been reported to act as a radioprotector under *in vivo* and *in vitro* conditions. The properties of bioactive compounds can facilitate therapeutic drugs to act differentially towards tumour and normal tissues, thus displaying selective metabolic effects. The alkaloids and flavonoids are among naturally occurring phytochemicals helpful in radioprotection and radiosenstization. They exhibit antimutagenic and anticarcinogenic properties, and prevent cancer [34, 35] as they are an ingredient of human diets.

5.1 Chemopreventive Potential:

Upregulation of antioxidant inhibits tumor progression and protect against damage of normal cells. Under chemo-preventive strategy, antioxidants act as bifunctional inducer that maintains balance of xenobiotic metabolism towards detoxification. Hydroalcoholic extract considerably increased antioxidant activity of pod by significant upregulation of GPx, GR, SOD, GSH, cytochrome p450 and CAT. Moreover, it slightly decreased hepatic MDA level by eliminating free radical in Skin papillomagenesis mice [23]. Sreelatha, et al (2011) reported anti-proliferation and chemoprevention in human tumor (KB) cell line. Leaf extract induced apoptosis as determined by morphological changes and DNA fragmentation. Sometimes, redox-sensitive mechanisms are known to modulate upregulation of ROS [36]. In a report, hydroalcoholic extract of *M. oleifera* leaves was found to show cytotoxic activity against HeLa cell line [37].

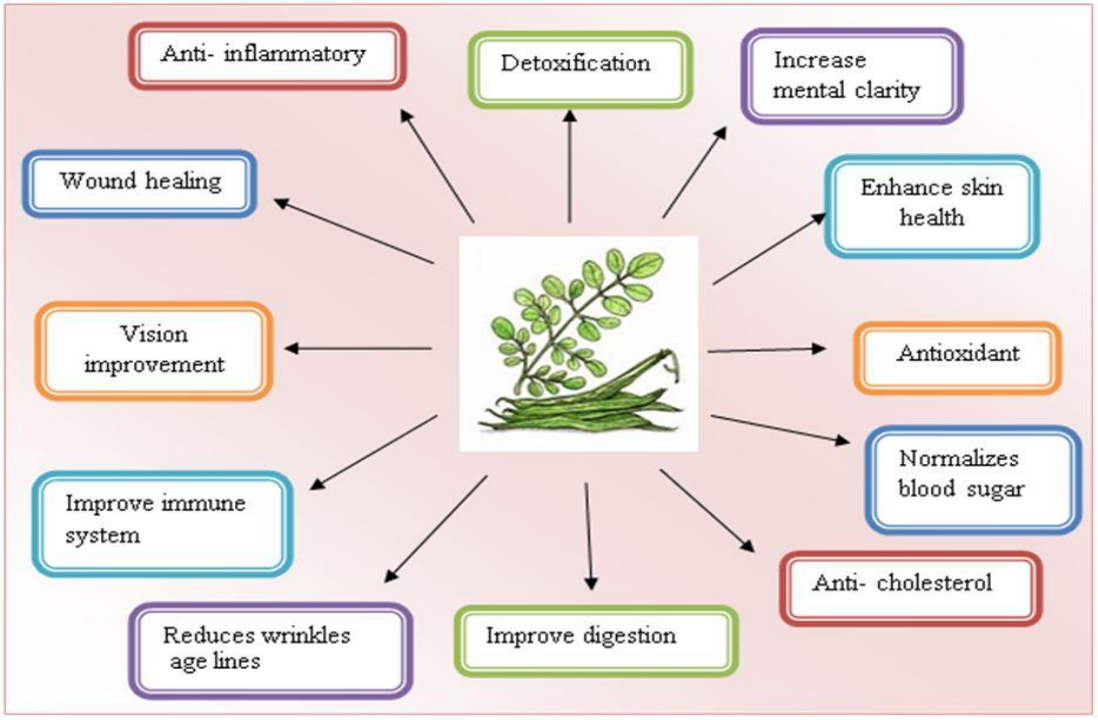


Figure 1: Schematic diagram showing various medicinal uses of edible parts (leaves & fruits) of *M.oleifera*

Sr. No.	Part Used	Bioactive Compounds	Reference
1	Leaves	Gallic acid, chlorogenic acid, ellagic acid, ferullic acid, flavanoid like 5 kaempherol glycosides, quercetin glycosides, rutin, vanillin syringic acid caffeoylquinic acid glycosides, thiocarbonate, carbomate, niazirin, niaziridin, niazirinin, benzyl isothiocyanate, niaziminin A, niaziminin, ascorbic acid, carotenoids, β-sitosterol	[13,14,15, 16,17]
2	Fruits/ Pods	Gallic acid chlorogenic acid, ellagic acid, ferullic acid kaempherol, quercetin vanillin niazirin, niaziridin, glactose, arabinise, rhamnose	[13,14,18]
3	Roots	Benzyl glucosionolate, niazimicin, aurentiamide acetate 4, 1,3-dibenzylurea	[16,19,20]
4	Seeds	Benzyl isothiocyanate, moringyne, several amino acid, sterols, tocopherol, fatty acid, niazimicin, niazirin, β-sitosterol glycosides, glucomoringin	[21,22,23]
5	Bark	Benzyl glucosinolate, niaziridin niazirin	[14,16]
6	Flower	Octadecen, oleol, satol, sipo, deconoic acid, dodecanal	[16]

Table 1: Phytoconstituents present in the parts of *M.oleifera*

5.2 Cytotoxic and Antiproliferative Mechanisms:

Charoensin et al. (2014) demonstrated that bioactive metabolite enhanced free radical scavenging activity in various cancer cell lines [38]. The free radical scavenging mechanism of ethanolic extract was found to be protective against leukemia and hepatocarcinoma cells [39]. Nair et al., (2011) have reported that aqueous extract of leaves possesses anticancerous and cytotoxic properties. Additionally, it displayed non-toxic and proliferative action on normal healthy lymphocytes. Furthermore, increase in extract concentration simultaneously decreased survival of HeLa cell line [40]. Bioactive compounds present in ethanolic seed extract are potent antioxidants that show antitumor promoting activities. Moreover, *in vitro* results showed that benzyl isothiocynates, niazimicin and isolates of β-sitosterol possess ability to inhibit TPA-induced Epstein-Barr virus. Furthermore, Guevera et al. (1999) has reported that niazimicin, hindered antitumor promoting activity in *vivo* [22]. According to Brunelli et al. (2010), in *vitro* and *in vivo* activities of glucomoringin derived isothiocynates (GMG-ITC) prevented damage in various cancer cell lines. The latter is reported to induce apoptosis, cell cycle perturbations and reduced the level of NF-κB activity by modulating GST/GSH pathway [41].

5.3 Radioprotective Properties:

Rao et al. (2001) demonstrated that pre administration of ethanolic leaf extract was found to be supportive in protection against γ irradiation by inhibiting free radical generation [42]. *In vitro* study by Berkovich et al. (2013) depicted that aqueous extract of leaf is antiproliferative and cytotoxic for pancreatic cancer cells (Panc-1, COLO 357 and p34). The mechanism was mediated by inhibition of

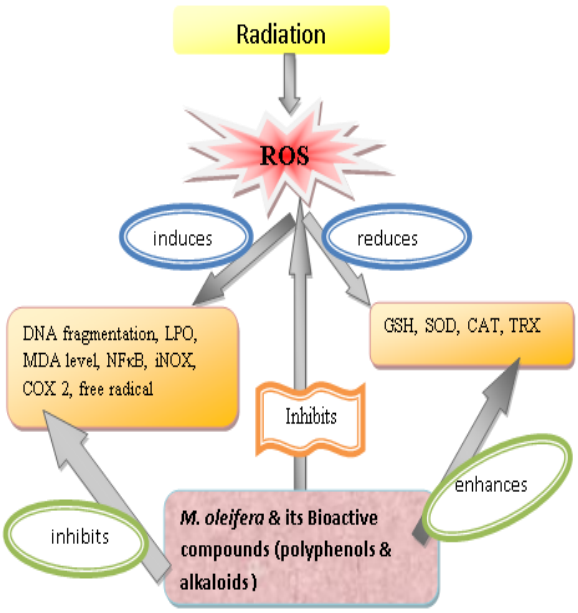


Figure 2: Flowchart depicting various targets of radiation induced damage and mechanism of action of *M.oleifera*

NF-κB signaling cascade and reduces the expression of p65, p-IkBα and IkBα proteins [43]. Moreover, hydro-alcoholic extract of leaf significantly decreased radiation induced oxidative stress that causes lipid peroxidation and hinders the translocation of nuclear factor kappa B (NF-κB) in mice model. In Consequence, endogenous antioxidant such as superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), was upregulated [44, 45].

5.4 Anti-inflammatory Activities:

The boiled pod extract showed anti-inflammatory activity by inhibiting upregulation of mRNA, protein level of interleukine-6, tumor necrosis factor-alpha, inducible nitric oxide synthase, and cyclooxygenease-2 [46]. According to Sashidhara et al. (2009) demonstrated that aurantiamide acetate and 1, 3 dibenzyl urea isolated from roots produced anti-inflammatory and analgesic activities by inhibiting TNF-alpha, IL-2 cytokines [20, 47].

Part Used	Properties	Extract	Cell line	Mechanism	Ref
LEAVES	Chemopreventive	Phenolics	Human tumor (KB) cell line	Induction of apoptosis inhibition of free radical	[36]
	Antitumor	Ethanolic	Leukaemia and Hepatocarcinoma cell line	Inhibition of radical formation	[39]
	Cytotoxic& Anticancer	Aqueous	HeLa cell line & Lymphocytes	Induces DNA fragmentation & Apoptosis	[40]
	Cytotoxic	Hydroalcoholic	HeLa Cell line	Cytotoxic towards cancer cells	[37]
	Anticancer	Methanolic	HepG2, Caco-2 and MCF-7 cancer cell line.	Antiproliferation of cancer cell	[38]
		Methanolic	Swiss albino mice	Inhibition of micronucleus in erythrocytes& aberrations in metaphase chromosomes	[42]
	Radioprotective	Hydro-alcoholic	Swiss albino mice	Inhibition of NF-κB translocation and Lipid peroxidation; increases SOD, CAT, GSH	[44]
		Ethanolic	Swiss albino mice	Inhibit radiation induced lipid peroxidation, increases GSH	[45]
	Hepatoprotective effect	Methanolic	Rat model	Increase GSH, GSH-R, GPx & CAT levels in RBCs and decrease lipid peroxidation in liver	[50]
	Antioxidative properties	Ethanolic /Aqueous extract	Swiss albino mice/ mice erythrocytes	Inhibit free radical	[49]
	Antiproliferative	Aqueous	Pancreatic cancer cell lines (Panc-1 and COLO-357)	Inhibits the NF-κB signalling Pathway	[43]

SEED	Antioxidative	Aqueous extract	Female rat	Induced hepatic toxicity	[48]
	Antitumor	Ethanolic	Raji cells/ mouse	Inhibited induction of EBV-EA	[39]
	Anticancerous	Ethanolic	MCF cell line	Cell cycle, Perturbations induces apoptosis, NF-κB inhibition	[41]
	Antitumoral activity	Ethanolic	myeloma mice model	Cytotoxicity in cancer cells	[41]
FRUITS (POD)	Anti-inflammatory activities	Boiled extract	RAW 264.7 murine macrophage cell lines.	Inhibited mRNA elevation, tumor necrosis factor-alpha, iNOS, and COX-2	[46]
	Antioxidative properties	Ethanolic /Aqueous extract	Swiss albino mice/ mice erythrocytes	Free radical scavenging capacity	[49]
	Chemopreventive potential	Hydro-alcoholic	Mice	CAT, GSH, GSH-r,& decrease in MDA level	[23]
	Chemopreventive effect	Dried boiled *M.oleifera*	Colon carcinogenesis	Inhibits iNOS and COX-2 expression .	[51]

Table : 2 Various bioactive fractions available in different parts of the *M. Oleifera*

5.5 Antioxidative Properties: Aqueous extract of seeds are reported to efficiently inhibit arsenic induced alteration in hepatic function. Additionally, Chattopadhyay et al. (2011) demonstrated that the extract prevented DNA fragmentation, ROS initiation, oxidative stress and free radical in female albino rats [48]. Ethanolic and aqueous extract of leaves and pod possesses strong reducing power, good anti-stresser and free radical scavenging activity because of its antioxidant properties. Moreover, it is shown that dose dependent concentration increased the level of endogenous antioxidant with decrease in MDA level [49]. These studies have put forward leaves and pods of *Moringa oleifera* as potent candidate to regulate redox balance.

5.6 Experimental Evidences of Medicinal Properties:

Table 2 gives a detailed account of various bioactive fractions available in different parts of the *M.oleifera*.

6. Discussion

It is evident from above discussed mechanism that various parts of MO contain polyphenols, alkaloids and flavonoids that display antioxidant activity. At present numerous bioactive compounds isolated from *M. oleifera* such as quercetin, rutin, kaempherol, niazimicin, gallic acid are under preclinical or clinical trials. Based on this information as provided in Table 2, it has been presumed that among all studied parts of MO, leaves and pod displayed more potent antioxidant activity as compared to other parts. They were reported to down regulate cytokines, tumor necrosis factor-alpha, inducible nitric oxide synthase, and cyclooxygenease-2 that mediates radiation induced cancer cell death [46]. Various studies from different laboratories are in agreement that bioactive compounds present in the leaves and pod of MO protect from harmful effects of ionizing radiation. Recently, Charoensin and Wongpoomchai (2012) demonstrated free radical scavenging activity of MO leaf extract that contains polyphenols [38]. Moreover, pretreatment of leaf extract before irradiation was reported to initiate senescence and apoptosis in cancer cells by free radicals inhibition and up-regulation of endogenous antioxidants such as GSH, TRX, and CAT [39]. Berkovich et al. (2013) showed hepatoprotective effect from leaf extract through scavenging free radical and down-regulation of NF-κB and LPO [43].

7. Conclusion

Recent investigations have suggested that ethanolic extracts of *M. Oleifera* mainly containing alkaloids, flavonoids and polyphenolic compounds possess antioxidant and anti-inflammatory properties. These bioactive compounds are known to suppress cancer cell proliferation by inhibiting factors such as iNOS, COX-2, NFκB which are upregulated in majority of tumor cells. The components of extracts offer protection to normal cells against radiation by free radical scavenging and enhancing endogenous enzymes. The extract appears to have potential to modulate cell signaling pathways exhibited in therapeutic outcome. It is suggested that leaves and fruits offer greater radioprotection as compared to other parts of Moringa.

References

1. American Cancer Society. Global Cancer Facts and Figures 2007. Atlanta, GA: American Cancer Society
2. Wong R., Sagar C.M. & Sagar S.M. Integration of Chinese Medicine into supportive cancer care: a modern role for an ancient tradition. Cancer Treatment Review, 2001; 27, 235–246.
3. Fyles, A., Milosevic, M., Hedley, D., Pintilie, M., Levin, W., Manchul, L., & Hill, R. P. Tumor hypoxia has independent predictor impact only in patients with node-negative cervix cancer. Journal of Clinical Oncology,2002; 20(3), 680-687.
4. Weiss, J. F. & Landauer, M. R. Protection against ionizing radiation by antioxidant nutrients and phytochemicals. Toxicology, 2003; 189: 1–20.
5. Bensadoun, R.J., Schubert, MM. Lalla RV. Amifostine in the management of radiation-induced and chemo-induced mucositis. Support Care Cancer; 2006; 14:566 –572.
6. Bhosle, S. M., Huilgol, N. G., & Mishra, K. P. Enhancement of radiation-induced oxidative stress and cytotoxicity in tumor cells by ellagic acid. Clinica chimica acta, 2005;359(1), 89-100.
7. Sandhya, T., & Mishra, K. P. Cytotoxic response of breast cancer cell lines, MCF 7 and T 47 D to triphala and its modification by antioxidants. Cancer letters, 2006; 238(2), 304-313

8. Rastogi, L., Feroz, S., Pandey, B. N., Jagtap, A., & Mishra, K. P. Protection against radiation-induced oxidative damage by an ethanolic extract of Nigella sativa L. International Journal of Radiation Biology, 2010;86(9), 719-731.
9. Puthli, A., Tiwari Reeta, Mishra K.P. .Biochanin A Enhances the radiotoxicity in colon tumor cells in vitro, Journal of Environmental Pathology, Toxicology and Oncolgy, 2013; 32(2) :1.
10. Fahey, J. W. Moringa oleifera: A Review of the Medical Evidence for Its Nutritional, Therapeutic, and Prophylactic Properties. Part 1. Phytochemistry, 2005;47, 123-157
11. Mishra, G., Singh, P., Verma R., Kumar S., Srivastav S., Jha, K.K., & Khosa R.L. Traditional uses, phytochemistry and pharmacological properties of Moringa oleifera plant: An overview. Der Pharmacia Lettre, 2011; 3(2): 141-164
12. Hsu R., Midcap S., Arbainsyah, De Witte L. Moringa oleifera; Medicinal and socioeconomic uses. International Course on Economic Botany, National Herbarium Leiden, The Netherlands, 2006; pp. 18.
13. Singh, B. N., Singh, B. R., Singh, R. L., Prakash, D., Dhakarey, R., Upadhyay, G., & Singh, H. B. Oxidative DNA damage protective activity, antioxidant and anti-quorum sensing potentials of Moringa oleifera. Food and Chemical Toxicology, 2009; 47(6), 1109-1116.
14. Shanker, K., Gupta, M. M., Srivastava, S. K., Bawankule, D. U., Pal, A., & Khanuja, S. P. Determination of bioactive nitrile glycoside (s) in drumstick (Moringa oleifera) by reverse phase HPLC. Food Chemistry, 2007; 105(1), 376-382.
15. Manguro, L.O., & Lemmen P. Phenolics of Moringa oleifera leaves. Nat. Prod. Res.2007; 21:56-68.
16. Bennett, R. N., Mellon, F. A., Foidl, N., Pratt, J. H., Dupont, M. S., Perkins, L., & Kroon, P. A. Profiling glucosinolates and phenolics in vegetative and reproductive tissues of the multi-purpose trees Moringa oleifera L.(horseradish tree) and Moringa stenopetala L. Journal of Agricultural and Food Chemistry, 2003; 51(12), 3546-3553.
17. Faizi, S., Siddiqui, B. S., Saleem, R., Siddiqui, S., Aftab, K., & Gilani, A. U. H. Isolation and structure elucidation of new nitrile and mustard oil glycosides from Moringa oleifera and their effect on blood pressure. Journal of Natural Products, 1994; 57(9), 1256-1261.
18. Roy, S. K., Chandra, K., Ghosh, K., Mondal, S., Maiti, D., Ojha, A. K., & Islam, S. S. Structural investigation of a heteropolysaccharide isolated from the pods (fruits) of Moringa oleifera (Sajina). Carbohydrate research, 2007; 342(16), 2380-2389.
19. Nikkon F, Saud ZA, Reedman MH, Haque ME. In vitro antimicrobial activity of the compound isolated from chloroform extract of Moringa oleifera Lam. Pak J Biol Sci ,2003; 22: 1888-1890.
20. Sashidhara, K. V., Rosaiah, J. N., Tyagi, E., Shukla, R., Raghubir, R., & Rajendran, S. M. Rare dipeptide and urea derivatives from roots of Moringa oleifera as potential anti-inflammatory and antinociceptive agents. European journal of medicinal chemistry, 2009; 44(1), 432-436.
21. Anwar, F., & Rashid, U. Physico-chemical characteristics of Moringa oleifera seeds and seed oil from a wild provenance of Pakistan. Pak. J. Bot, 2007; 39(5), 1443-1453.
22. Guevara, A. P., Vargas, C., Sakurai, H., Fujiwara, Y., Hashimoto, K., Maoka, T. & Nishino, H. An antitumor promoter from Moringa oleifera Lam. Mutation Research/Genetic Toxicology and Environmental Mutagenesis, 1999; 440(2), 181-188.
23. Bharali, R., Tabassum, J., & Azad, M. R. H. Chemomodulatory effect of Moringa oleifera, Lam, on hepatic carcinogen metabolising enzymes, antioxidant parameters and skin papillomagenesis in mice. Asian Pacific Journal of Cancer Prevention, 2003; 4(2), 131-140.
24. Chumark P, Khunawat P, Sanvarinda Y, Phornchirasilp S, Morales NP, et al. The in vitro and ex vivo antioxidant properties, hypolipidaemic and antiatherosclerotic activities of water extract of Moringa

oleifera Lam. leaves. J Ethnopharmacol, 2008; 116: 439-446.
25. Iqbal, S., & Bhanger, M. I. Effect of season and production location on antioxidant activity of Moringa oleifera leaves grown in Pakistan. Journal of food Composition and Analysis, 2006; 19(6), 544-551.
26. Murakami, A., Kitazono, Y., Jiwajinda, S., Koshimizu, K., & Ohigashi, H. Niaziminin, a thiocarbamate from the leaves of Moringa oleifera, holds a strict structural requirement for inhibition of tumor-promoter-induced Epstein-Barr virus activation. Planta Medica, 2007; 64(04), 319-32.
27. Fuglie LJ. The Miracle Tree: Moringa oleifera: Natural Nutrition for the Tropics. Church World Service, Dakar.Revised in 2001 and published as The Miracle Tree: The Multiple Attributes of Moringa, pp. 1999; 68,172.
28. Mahajan SG, Mali RG, Mehta AA. Effect of Moringa oleifera Lam. Seed extract on toluene diisocyanate –induced immune-mediated inflammatory responses in rats. J Immunotoxicol, 2007; 4: 85-96.
29. Sutar NG, Patil VV, Deshmukh TA, Jawle NM, Patil VR, et al. Evaluation of anti-pyretic potential of seeds of Moringa oleifera Lam. Indian Journal of Green Pharmacy, 2009; 3: 148-150.
30. Sutar N, Bonde CG, Patil VV, Narkhede SB, Patil AP, Kakade RT Analgesic activity of seeds of Moringa oleifera Lam. International Journal of Green Pharmacy 2: 2008; 108-110.
31. Tahiliani P, Kar A. Role of Moringa oleifera leaf extract in the regulation of thyroid hormone status in adult male and female rats. Pharmacol Res, 2000; 41: 319-323.
32. Rathi BS, Bodhankar SL, Baheti AM. Evaluation of aqueous leaves extract of Moringa oleifera Linn. for wound healing in albino rats. Indian J Exp Biol , 2006; 44: 898-901.
33. Ayinde, B. A., Onwukaeme, D. N., & Omogbai, E. K. I. Isolation and characterization of two phenolic compounds from the stem bark of Musanga cecropioides R. Brown (Moraceae). Acta Pol. Pharm, 2007; 64, 183-185.
34. Moridani, M. Y., Pourahmad, J., Bui, H., Siraki, A., & O'Brien, P. J. Dietary flavonoid iron complexes as cytoprotective superoxide radical scavengers. Free Radical Biology and Medicine, 2003; 34(2), 243-253.
35. Selvendiran, K., Banu, S. M., & Sakthisekaran, D. Protective effect of piperine on benzopyrene-induced lung carcinogenesis in Swiss albino mice. Clinica chimica acta, 2004; 350(1), 73-78.
36. Sreelatha, S., Jeyachitra, A., & Padma, P. R. Antiproliferation and induction of apoptosis by Moringa oleifera leaf extract on human cancer cells. Food and Chemical Toxicology, 2011; 49(6), 1270-1275.
37. Ghassami, A., Asghari, G., & S Dehshahri, E. Evaluation of cytotoxicity of Moringa oleifera lams. callus and leaf extracts on HeLa cells. Research in Pharmaceutical Sciences, 2012; 7(5), S104.
38. Charoensin,S. Antioxidant and anticancer activities of Moringa oleifera leaves. J. Med. Plants Res. 2014; Vol. 8(7), pp. 318-325
39. Khalafalla, M. M., Abdellatef, E., Dafalla, H. M., Nassrallah, A. A., Aboul-Enein, K. M., Lightfoot, D. A., & El-Shemy, H. A. Active principle from Moringa oleifera Lam leaves effective against two leukemias and a hepatocarcinoma. Afr J Biotechnol, 2010; 9(49), 8467-8471.
40. Nair, S., & Varalakshmi, K. N. Anticancer, cytotoxic potential of Moringa oleifera extracts on HeLa cell line. Journal of Natural Pharmaceuticals, 2011; 2(3), 138.
41. Brunelli, D., Tavecchio, M., Falcioni, C., Frapolli, R., Erba, E., Iori, R., & D'Incalci, M. The isothiocyanate produced from glucomoringin inhibits NF-κB and reduces myeloma growth in nude mice in vivo. Biochemical pharmacology, 2010; 79(8), 1141-1148.
42. Rao, A. V., Devi, P. U., & Kamath, R. In vivo radioprotective effect of Moringa oleifera leaves. Indian Journal of Experimental Biology, 2001; 39(9), 858.

43. Berkovich L, Earon G, Ron I, Rimmon A, Vexler A, Lev-Ari S. Moringa oleifera aqueous leaf extract down-regulates nuclear factor-kappaB and increases cytotoxic effect of chemotherapy in pancreatic cancer cells BMC Complementary and Alternative Medicine 2013, 13:212.
44. Sinha, M., Das, D. K., Bhattacharjee, S., Majumdar, S., & Dey, S. Leaf extract of Moringa oleifera prevents ionizing radiation-induced oxidative stress in mice. Journal of Medicinal Food, 2011; 14(10), 1167-1172.
45. Sinha, M., Das, D. K., Datta, S., Ghosh, S., & Dey, S. Amelioration of ionizing radiation induced lipid peroxidation in mouse liver by Moringa oleifera Lam. leaf extract. National Journal of Medicinal Food,2012; vol 50,209-215
46. Muangnoi, C., Chingsuwanrote, P., Praengamthanachoti, P., Svasti, S., & Tuntipopipat, S. Moringa oleifera pod inhibits inflammatory mediator production by lipopolysaccharide-stimulated RAW 264.7 murine macrophage cell lines. Inflammation, 2012; 35(2), 445-455
47. Cheenpracha S, Park EJ, Yoshida WY, et al. Potential antiinflammatory phenolic glycosided from the medicinal plant Moringa oleifera fruits. Bioorg Med Chem Lett, 2010; 8, 6598-602.
48. Chattopadhyay, S., Maiti, S., Maji, G., Deb, B., Pan, B., & Ghosh, D. Protective role of Moringa oleifera (sajina) seed on arsenic-induced hepatocellular degeneration in female albino rats. Biological trace element research, 2011; 142(2), 200-212.
49. Luqman, S., Srivastava, S., Kumar, R., Maurya, A. K., & Chanda, D. Experimental assessment of Moringa oleifera leaf and fruit for its antistress, antioxidant, and scavenging potential using in vitro and in vivo assays. Evidence-Based Complementary and Alternative Medicine, 2012.
50. Babu, B.P., Kumar, R., Bharavi, R., Venkateswarlu, U., Devi, V. R,. & Srilatha, Ch. Protective Effect of Moringa oliefera Lam Leaf Extract in Paracetamol Induced Hepatotoxic Rat. IJPI's Journal of Pharmacology and Toxicology. 2011; Vol 1:5.
51. Budda, S., Butryee,C., Tuntipopipat, S., Rungsipipat, A., Wangnaithum ,S., Lee,J., Kupradinun,P. Suppressive Effects of Moringa oleifera Lam Pod Against Mouse Colon Carcinogenesis Induced by Azoxymethane and Dextran Sodium Sulfate. Asian Pacific J Cancer Prev, 2011; 12, 3221-3228.