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Review Article

Moringa oleifera as a Herbal Treatment for Oral Cancer : A Systematic Review

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ABSTRACT

Introduction: Oral cancer as a malignancy ranks the fifth most common cause of death in Indonesia and is one of the six incidents in the Asian continent with 274,300 new cases each year. Oral cancer is the second largest in the world with an incidence of 7.6 million deaths in 2014. One of the herbal ingredients is Moringa oleifera which has high nutritional content in all parts. This material makes them effective as a treatment for cancer, including oral cancer. **Objective:** To explore the benefits of Moringa oleifera as a herbal treatment for oral cancer. **Methods:** In this systematic review, the articles search was performed on Google Search and Pubmed. Studies published on 2010-2020. 130 were articles assessed, including 15 articles from the electronic databases, 0 from the manual hand search. 60 records screened, 50 records excluded, 40 full-text articles assessed for eligibility and 15 full text articles included. **Result:** There are 15 articles about Moringa oleifera as a herbal treatment for oral cancer. **Conclusion:** Based on 15 articles show that Moringa oleifera has potential as herbal treatment for oral cancer.

Keywords: Moringa oleifera, Herbal treatment, Oral Cancer

INTRODUCTION

Oral cancer as a malignancy ranks the fifth most common cause of death in Indonesia and is one of the six incidents in the Asian continent with 274,300 new cases each year. Oral cancer is the second largest in the world with an incidence of 7.6 million deaths in 2014.¹ Several studies have shown that vascular endothelial growth factor is the main causative factor involved in angiogenesis.

The choice of cancer treatment with chemotherapy has several limitations, namely, it is expensive and causes several side effects such as mucositis, dizziness, nausea, fatigue, sleep disturbances, loss of appetite, and secondary infections.^{2,3} This is because chemotherapy is not selective, can destroy cancer cells and normal cells around it. There are several other dangerous opportunities from this treatment are cancer second to chemotherapy, hormonal problems, reproduction, effects on the gastrointestinal organs, immunological system, and neurology.⁴ For these reasons, herbal medicines tend to be

used as a cancer treatment. Affordable price and minimal side effects.^{5,6}

One of the herbal ingredients is Moringa oleifera which has high nutritional content in all parts. According to Gupta et al, Moringa leaves contain isothiocyanates which have anticancer properties.⁷ This material makes them effective as a treatment for cancer, including oral cancer. Therefore, the authors are interested in making a systematic review of Moringa oleifera as an herbal ingredient for the treatment of oral cancer.

METHODS

Search Strategy

A search was performed on Google Search and Pubmed. Studies published from 2010-2020. Pubmed terms and keywords used for the search included various combinations of the following: "Moringa oleifera", "Herbal treatment", "Oral cancer", or each of the searches, the titles and abstracts were screened and the full text versions of articles that met criteria were downloaded.

The flowchart in Figure 1 identifies the included and excluded articles at each stage. 130 were assessed, including 115 articles from the electronic databases, 0 from the manual hand

search. 65 records screened, 50 records excluded, 40 full-text articles assessed for eligibility and 15 full text articles included.

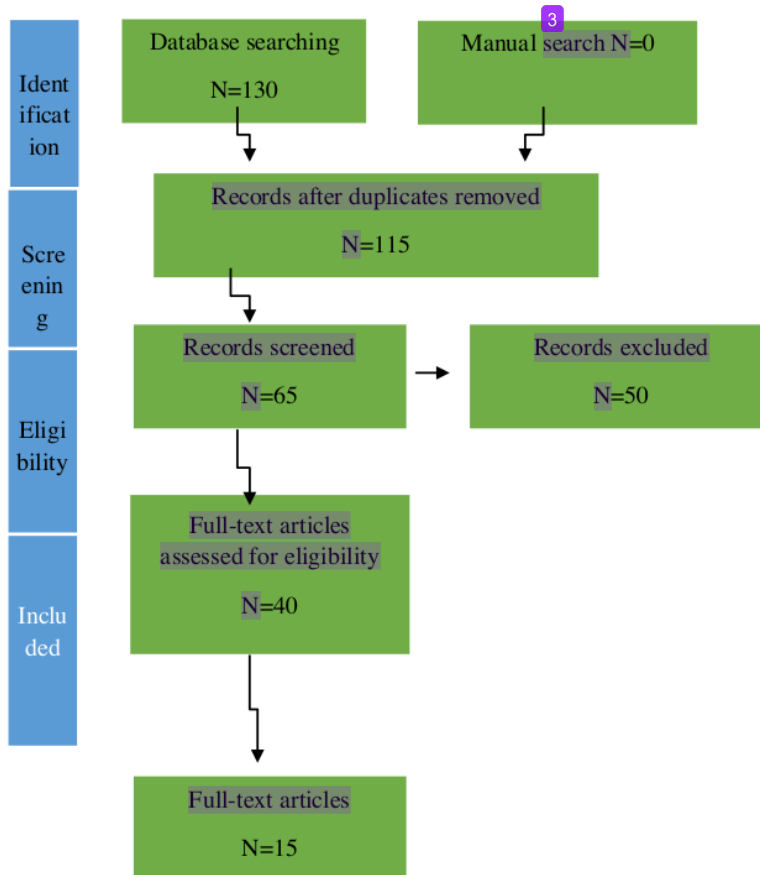


Fig.1:A flow chart describing the search methodology and numbers of articles included/excluded at each stage

RESULTS

In this systematic review there are study selection: inclusion criteria for this review were: 1) Article 2010-2020 year, 2) English Language, 3) All

study designs and publication types were considered. Exclusion criteria were, studies that is not about the Moringa oleifera as a herbal treatment for oral cancer.

Table 1. Article about Moringa oleifera as a herbal treatment for oral cancer

No.	Author	Year	Title	Conclusion
1.	Ismail Abiola Adebayo, Wasiu Gbolahan Balogun dan Hasni Arsad ⁸	2017	Moringa oleifera: An apoptosis inducer in cancer cells	Further research on apoptosis in cancer cells states that disruption along the apoptotic pathway is an important cause of the proliferation and metastatic processes in tumor cells. Thus, the target of cure is

				for normal apoptosis in cells with drugs capable of curing cancer. Many studies support that Moringa oleifera be an herbal medicine that has many benefits with strong compounds that are not harmful to normal body cells and are effective in killing cancer cells.
2.	10 Sonika Jain, Jaya Dwivedi, Pankaj Kumar Jain, Swaha Satpathy, Arjun Patra. ⁹	2016	Medicinal Plants for Treatment of Cancer: A Brief Review	Currently, herbal medicine is an interesting topic to be used as a source of research because it has a lot of potential as an anti-cancer agent and is widely obtained from nature, at a relatively low cost and having few or no side effects. Because of this, the World Health Organization (WHO) supports the use of nutritious and non-toxic traditional medicines in the body.
3.	31 Rani NZA, Husain K, Kumolosasi E. ¹⁰	2018	Moringa Genus: A Review of Phytochemistry and Pharmacology	6 Moringa oleifera extract exerts a suppressive effect on sodium sulfate- and azoxymethane-induced dextran carcinogenesis in mice. Moringa oleifera extract reduces COX-2 and iNOS expression to reduce the PCNA index in mice as well as reduce the multiplicity and incidence of tumors. Various studies show that the omega-9 oleic fat content is high acid in Moringa oleifera extract which has anti-inflammatory activity is able to modulate this cell proliferation.
4.	Ali EN, Chatterton CC ¹¹	2018	Anticancer activity of Moringa oleifera leaves extract	Cancer cell resistance decreased with increasing concentration of sample fractions in Moringa oleifera extract used in the experiment.
5.	5 María Del Mar Zayas-Viera Pablo E. Vivas-Mejía, Jeyshka Reyes ¹²	2016	Anticancer Effect of Moringa oleifera Leaf Extract in Human Cancer Cell Lines	17 Moringa oleifera extract has been tested on cancer cells. Seventy-two hours post-treatment, cell resistance was measured by

				colorimetric analysis with AlamarBlue stain. 50% concentration can inhibit cell growth (IC50) with Moringa oleifera extract.
6.	Nurul Ashikin Abd Karim, Muhammad Din Ibrahim, Saie Brindha Kntayya, Yaya Rukayadi, Hazrulizawati Abd Hamid, Ahmad Faizal Abdull Razis ¹³	2016	Moringa oleifera Lam: Targeting Chemoprevention	Moringa oleifera has a chemopreventive effect on cancer cells. It is estimated that, in the next few years, cancer will increase. Moringa oleifera can be an effective herbal medicine as a chemopreventive agent in curing diseases in the cancer mechanism. ⁴² here have been many in vivo studies on the effects of the process and development of cancer cells.
7.	Ahmed A Abd-Rabou, Aboelfetoh M Abdalla, Naglaa A Ali1, Khairy MA Zoheir ¹⁴	2017	Moringa oleifera Root Induces Cancer Apoptosis more Effectively than Leave Nanocomposites and Its Free Counterpart	Moringa ML, ML ¹⁶ Rc, and Ro extracts acts as an anti-cancer agent by reducing cell proliferation and shows cell death. In addition, cell survival is low and apoptosis is high detected after treatment using the MLn/ML extract and Rc/Ro compared to control cells. Moringa oleifera extract has promising potential in the treatment of cancer. Therefore, moringa extract can be a valuable therapeutic approach in case of carcinoma.
8.	Dina M. Abdel Khalik and Hala A. El-kammar ¹⁵	2017	Possible Synergic Anti-Carcinogenic Effect of Moringa Oleifera And Cisplatin on Human Squamous Cell Carcinoma	Moringa oleifera has an effective anti-carcinogenic role on the HEp2 cell line.
9.	Jacob O. Popoola, Oluwadurotimi S. Aworunse, Olusola L. Oyesola, Olayemi O. Akinnola, Olawole O. Obembe ¹⁶	2020	A systematic review of pharmacological activities and safety of Moringa oleifera	Many Moringa oleifera products sold in the market require a quality assessment for their safety and consumption. Importance Moringa oleifera cannot be overemphasized in its new bioactives which can be harnessed for therapeutic potential and to explore future research options.

			29	engaged in the pharmaceutical sector.
10.	Indres Moodley ¹⁷	2018	Evaluation of Sub Chronic Toxicity of Moringa Oleifera Leaf Powder in Mice	This study shows that oral administration Moringa oleifera dry leaf powder 1000 mg/kg daily showed no change in clinical signs or severe pathology during chronic prolonged 90 days.
11.	Thitiya Luetragoon, Rungnapa Pankla Sranujit, Chanai Noysang, Yordhathai Thongsri, Pachuen Potup, Nungruthai Suphrom, Nitra Nuengchamnong and Kanchana Usuwanthim ¹⁸	2020	Anti-Cancer Effect of 3-Hydroxy Ionone Identified from Moringa oleifera Lam. Leaf on Human Squamous Cell Carcinoma 15 Cell Line	Moringa oleifera extract and its compound, 3-HBI suppresses cell proliferation and induces apoptosis of Bcl-2. In addition, treatment with Moringa oleifera extract and 3-HBI significantly increased the G2/M phase. Our findings showed that MO and 3-HBI extracts have potential as anti-cancer treatments.
12.	Il Lae Jung, Ju Hye Lee and Se Chan Kang ¹⁹	2015	A potential oral anticancer drug candidate, Moringa oleifera leaf extract, induces the apoptosis of human hepatocellular carcinoma cells	Significant cancer inhibition resulted after oral administration of MOL with a high bioavailability of the extract, since the concentrations used in the in vitro cell experiments were similar to those used in mice in vivo. Future preclinical tests, such as pharmacokinetic studies, could reveal this.
13.	Mownica Udikala, Yashodhara Verma, Sushma, Sapna Lal ²⁰	2017	Phytonutrient and Pharmacological Significance of Moringa oleifera	Pharmacological studies have confirmed the therapeutic value of Moringa oleifera as an anticancer agent.
14.	Arijwan A Alsudani, Hussein A Alhamadawi ²¹	2020	The role of Moringa leaf extract to reduce the negative effect of some food additives on gene expression of CYP11A1 gene in male albino rats	The use of Moringa leaf alcohol extract at a concentration of 200 mg / kg was able to increase the expression of the CYP11A1 gene in mice treated with several food additives (Carmoisine, Monosodium Glutamate, Sodium Benzoate), because Moringa leaves contain many phytochemical compounds that act as antioxidants such as flavonoids, vitamins, Minerals, Amino Acids, Phytosterol and others.
15.	Garima Mishra, Pradeep Singh,	2011	Traditional uses, phytochemistry and	Antitumor activity of Moringa oleifera containing

27	Ramesh Verma, Sunil Kumar, Saurabh Srivastav, K. K. Jha and R. L. Khosa ²²	1 pharmacological properties of Moringa oleifera plant: An overview	leaves teleocidin B-4- tumor 11 motor inhibitors induce. ITC-related compounds, naturally occurring 4 - ((4'-O-acetyl-alpha-Lrhamnosyloxy) benzyl] ITC and allyl- and benzyl-ITC were significantly available inhibits the activity of the isothiocyano group as an important structural factor anti-tumor activity.
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DISCUSSION

Moringa oleifera is an herbal plant that has many chemical compounds, one of which is isothiocyanate as a chemopreventive agent in cancer cells. Research according to Cavell et al²³ shows that isothiocyanate has the ability as chemopreventive and chemotherapy in 44 pathway that inhibits the angiogenesis 40 process in vitro and in vivo in various studies. Angiogenesis is the process of forming new blood vessels in the human body and is a sign of tumors.^{24,25,26,27,28}

An important mediator in 39 the development of tumor angiogenesis is Vascular Endothelial Growth Factor (VEGF).^{29,30,31,32} As the tumor mass increases, what happens is that the distance between the cells and the closest blood vessels also increases. Tumor cells will produce 45 endothelial growth factors, one of which is vascular endothelial growth factor. With this pathomechanism, vascular endothelial growth factor will increase in tumors in 15 necrotic areas with low oxygen levels. Therefore, overexpression of vascular endothelial growth factor markers is considered tumor tissue to increase oxygen uptake via endothelial proliferation.^{33,34,35,36}

34 results showed that Moringa leaf extract reduced the expression of vascular endothelial growth factor. Therefore, the use of herbal substances that have the potential to act as antiangiogenic agents can reduce the number of proangiogenic factors such as vascular endothelial growth factors. A balance between pro and antiangiogenic factors will occur which reduces the angiogenesis rate in oral cancer.^{37,38,39,40}

16 Several studies have found the ability of Moringa oleifera leaves, seeds and bark to induce profuse apoptosis in cancer cells as the final cause of death in controlling the activation of cell proliferation in inhibition as 6 biomarker of apoptosis. Moringa oleifera leaf extract has been shown to trigger apoptosis in lung cancer cells through the A549 pathway formed by

mitochondria through activation of pro-caspase 3 to caspase 3.^{41,42,43} According to research 9 induced by Tiloke et al. which proved that the hot water extract of Moringa oleifera leaves was an apoptosis inducer in epithelial cells by regulating the expression of proapoptosis protein, p53, Smac/DIABLO, lowering the anti-apoptotic protein regulatory system for Nrf2 expression, and increased activity of caspases 3,7 and 9 observed in A549 cells who have been tried.^{44,45,46}

The anticancer properties of Moringa oleifera as phytochemicals have the characteristics of moringinine and quercetin in reversing tumorigenesis. Research conducted by Jaafaru et al. Provided more neuroprotective activity of isothiocyanate-based Moringa oleifera against hydrogen peroxide induced oxidative stress.^{47,48}

The isolated co 22 ound, 4- (α-Lrhamnopyranosyloxy) benzyl ITC (moringin) complexed with alpha-cyclodextrin (moringin + α-CD; MAC) has antiproliferative ability on SHSY5Y human neuroblastoma cells. Moringa oleifera is non-toxic in inducing apoptosis and inhibiting cancer cell metastasis in humans. In previous studies, isothiocyanates from Moringa oleifera seeds have been demonstrated to reduce hydrogen peroxide-induced cytotoxicity and maintain human nerve cell morphology.^{26,49}

The beneficial effects of Moringa oleifera root extract were evaluated against oxidative 38 stress in mice. The study revealed that Moringa oleifera with piperine therapy was effective, while the mixture of Moringa oleifera and curcumin was more active and showed better treatment results.^{30,50}

CONCLUSION

Based on a systematic review study, Moringa oleifera has a potential chemopreventive agent in its use as an herbal treatment in cases of oral cancer.

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