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EFFECT OF MORINGA LEAVES ORAL SUPPLEMENTATION ON PRO-INFLAMMATORY CYTOKINES IN PEM CONDITIONS

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ABSTRACT
Protein-Energy Malnutrition (PEM) is a nutritional problem resulting from protein or energy deficiency, often associated with the occurrence of infections. Infections due to weakened immune systems caused by protein deficiency can lead to inflammation. The flavonoid content in moringa oleifera leaf (MOL) has anti-inflammatory that can be utilized as an alternative treatment for PEM. Objective: To identified the potential of MOL as an anti-inflammatory in PEM conditions. Method: This study is a systematic literature review that were obtained through Google Scholar, ScienceDirect and PubMed databases for the last 10 years from 2012 to 2022 with a total 80 articles found based on keyword searches. References then re-selected using PICOS method, resulting in 9 articles be reviewed. The review process involves gathering pertinent information that is applicable to the study objectives and analyzing it based on population/problems, intervention or management to the case, comparating the similarities and differences, study the outcome and study design of the previous articles. Then the information will be synthesized to conclude the review. Results: The findings indicate that MOL can be used effectively for patient with PEM as an anti-inflammatory agent by reducing the secretion of pro-inflammatory cytokines such as IL-1, IL-6 and TNF-α Conclusions: Administration of oral supplementation of MOL has a positive impact as an anti-inflamatory in PEM condition.

Keywords: cytokines; il-6; moringa oleifera leaf; pro-inflammatory; PEM

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INTRODUCTION

A relatively large percentage of people continue to suffer from malnutrition, which is a widespread health problem. Protein Energy Deficiency (PEM) is a type of nutritional issue. PEM, or protein-energy malnutrition, is a disorder characterized by insufficient intake of protein and energy (calories) in one's diet. The presence of infection is usually shown to be associated with this condition. Perinatal endometrial malformation (PEM) problems may manifest during prenatal development and persist postnatally as a result of suboptimal nursing techniques, insufficient supplemental nutrition, and inadequate infection management and vitamin deficiencies.(UNICEF Indonesia, 2022)(Victoria et al., 2010) Clinical significance of PEM can be assessed by using various indicators, including stunting, wasting, and underweight. According to data from UNICEF in 2022, 30% of children worldwide would encounter stunting. A total of around 162 million children below the age of 5 encounter this dietary issue.(UNICEF Indonesia, 2022)(UNICEF, 2013) According to the 2018 Basic Health Research Data (RISKESDAS), Indonesia has the second highest prevalence of stunting in Southeast Asia.(Depkes RI, 2018) The 2022 Indonesian Nutrition Status Survey (SSGI)

released by the Ministry of Health reveals that the prevalence of stunting in Indonesia is 21.6%, which is a drop from the previous year's figure of 24.4%. The prevalence of wasting and underweight has exhibited an upward trend, with rates rising from 7.1% and 17% respectively in 2021 to 7.7% for wasting and 17.1% for underweight in 2022.(Kemenkes RI, 2023)

Malnutrition and infection have a complex association that is intricately braided with a myriad of elements that are interconnected with one another. Malnutrition is becoming more recognized as an important etiological factor that contributes to immune illnesses all over the world.(Weckman et al., 2023) When it comes to children in particular, malnutrition increases the likelihood of contracting illnesses, makes diseases more severe, and raises the mortality rate. (WHO, 2012) This intricate interaction highlights the vital relevance of tackling malnutrition as a cornerstone in the battle against infectious diseases like the flu and other infectious diseases. There exists compelling evidence indicating a significant correlation between malnutrition, infection, and heightened mortality risk in newborns and young children. PEM, an acute condition caused by malnutrition, can heighten the susceptibility to infection by impairing the integrity of the intestinal barrier, altering the composition of the intestinal microbiota, disrupting the regulation of inflammatory adipose-cytokines, and reducing the absorption of micronutrients and macronutrients.(Alaaraj et al., 2021)

In addition, the presence of harmful microorganisms in food might potentially contribute to the development of PEM. The processing of contaminated food by the human body can lead to the disturbance of microbial equilibrium inside the digestive tract, alteration of the composition and functionality of the intestinal microbiota, and hindrance of intestinal cell regeneration. If these effects persist, inflammation may ensue. The processing of contaminated food by the human body has the potential to initiate a series of disturbances within the intricate microbial equilibrium present in the digestive system. The aforementioned disruption frequently presents itself through modifications to the structure and operation of the intestinal microbiota, which plays a vital role in preserving digestive health and overall welfare. Moreover, the consumption of food that is contaminated might hinder the inherent process of intestinal cell regeneration, so exacerbating the compromised state of the digestive system. If left unaddressed, these consequences can gradually lead to the development of chronic inflammation, which not only worsens pre-existing digestive problems but also presents substantial hazards to one's entire well-being. Therefore, ensuring the protection of food safety is of utmost importance, as it serves the dual purpose of preventing immediate disease and maintaining the long-term well-being and functionality of the gastrointestinal system.(Gwela et al., 2019)

During the acute infection phase, the body initiates an inflammatory response by releasing a range of pro-inflammatory cytokines. The production of this cytokine will induce the activation of macrophages and neutrophil cells by the action of inflammatory mediators, including prostaglandins, Reactive Oxygen Species (ROS), and oxidative stress resulting from cellular damage. In the acute phase of infection, elevated levels of pro-inflammatory cytokines, including IL-1, IL-6, and TNF-κ, can serve as biomarkers for reference purposes.(Rose-John, 2012), (Hojjatoleslami & Jamshidi, 2016) The activation of inflammatory cells within the immune system is a prerequisite for the inflammatory response, encompassing both innate and adaptive immune responses. Throughout this process, the generation of C-Reactive Protein will take place, leading to disruptions in cell perfusion. This illness is characterized by hypermetabolic events that deplete a significant amount of energy during the body's metabolic processes, leading to an energy deficit. In response to this

incidence, the body employs a mechanism called gluconeogenesis from protein catabolism to compensate for the energy shortfall, which is a non-physiological state.(Moenadjat, 2023) Nevertheless, there will persist an inequilibrium in both protein and energy levels due to the insufficient influx of supply compared to the demand. necessary. A deficiency in both protein and energy might be a contributing factor in the development of metabolic illnesses such Protein-Energy Malnutrition (PEM).

Presently, there is extensive utilization of botanical plants as an alternative therapeutic approach for health concerns. The Moringa oleifera plant is readily available and has numerous advantages. The Moringa plant is recognized for its abundant presence of nutrients, vitamins, minerals, and bioactive compounds, making it a valuable resource in the realm of health science, particularly in relation to its leaves. Currently, the Moringa plant is employed as a substitute remedy for several ailments. Moringa leaves possess significant quantities of flavonoids and protein, which have a crucial role in the prevention of PEM. Moringa leaves contain flavonoids, specifically flavonols and phenolics, which possess anti-inflammatory and antioxidant properties.(Putra et al., 2021) Protein serves as a crucial substance that facilitates tissue growth and maintenance. It is the primary constituent of body cells and serves as the main energy source, alongside carbohydrates and fat.

Furthermore, protein functions as an essential metabolic regulator through its facilitation of enzyme and hormone activities, thus establishing a protective barrier against potentially detrimental substances that may infiltrate the body. In addition to their metabolic roles, proteins play a substantial role in storage and inheritance processes within living organisms. The presence of genes, which are the fundamental units of heredity, is supported by the existence of chromosomes, intricate structures consisting of DNA and proteins. Protein serves multiple functions within the human body, encompassing both the maintenance of key physiological processes and the facilitation of genetic information transfer over successive generations. This process significantly influences the trajectory of evolution and the overall diversity of biological organisms.(Okinarum & Zakiyah, 2019) Based on the backgrounds written above, the researchers aim to conduct study the study was to synthesize existing research findings and evidence regarding the potential therapeutic benefits of Moringa leaf extract in managing inflammation, especially in individuals suffering from PEM. This is crucial for expanding our understanding of alternative treatment options for inflammation and could potentially contribute to the development of novel therapeutic interventions for individuals with PEM related inflammatory disorders.

METHOD

This study represents a Systematic Literature Review (SLR) that systematically examines articles to gather, analyze, and subsequently present the findings of numerous research trials, with a specific focus on the potential anti-inflammatory properties of Moringa leaf extract in individuals with PEM. The literature collection process was conducted between January to February 2024 thorough collection of secondary data from a range of trustworthy sources. The researchers found and retrieved relevant studies on issues pertinent to the research by utilizing the enormous databases of Google Scholar, ScienceDirect, and PubMed. Specific inclusion criteria were devised to ensure the quality and relevancy of the material. Inclusion criteria were limited to written works in the form of journal articles that were published between the years 2012 and 2022. The collection of literature sources was conducted with the intention of incorporating the latest and most authoritative contributions to the subject, in order to establish a strong basis for the research undertaking. The articles were written in either Indonesian or English and were selected based on the keywords "Moringa leaves,"

"cytokines," "anti-inflammatory," and "protein-energy malnutrition." There were around 80 articles found based on keyword searches and met the inclusion criteria to be re-selected.

The researchers employed the PICOS method to get a total of 9 articles that can be used in the review process. PICOS representing, P (population, problems), I (intervention, prognostic factor, exposure), C (comparisons, control), O (outcome), and S (study design).(Methley et al., 2014) This methodology encompasses several key components: Population/problem (referring to the population or problem under analysis, such as health services), Intervention (referring to a specific action or management of a particular problem, such as the oral supplementation of Moringa leaves as an anti-inflammatory in PEM) conditions, Comparators (referring to the oral use of other Moringa leaves that are not related to PEM conditions), Outcomes (referring to previous research, particularly those involving the provision of Moringa leaf supplementation), and Study design (incorporating articles with true experiment, quasi-experimental, quantitative, and case study research designs). Following the collection of literature sources, the researcher proceeded to identify and evaluate the findings for the purpose of analysis and making conclusions.

RESULTS

Following the examination, a total of 9 (nine) papers were found to be in accordance with the concerns that were being investigated in this research and to have satisfied the inclusion criteria. The publications that were published as a consequence of searches conducted on Google Scholar, ScienceDirect, and PubMed are presented in the table that can be found below:

Table 1.
Data on article characteristics collected (n= 9)

Research Title and Authors	Research Design	Samples	Results
Moringa Leaf Powder Reduces the Degree of Fatty Liver and Interleukin 6 Expression in Rats with Protein Energy Deficiency Agustina Dwi, Tinny Endang H, Hidayat Sujuti (2012)	Experimental research with a post-test only group design approach	24 males Rattus novergicus rats were divided into 6 groups (1 negative control group, 1 positive control group, and 4 treatment groups)	The degree of obese liver and IL-6 expression can be diminished by administering Moringa leaf powder at any dose. At a daily dosage of 720 mg, the level of hepatic steatosis and interleukin-6 (IL-6) expression exhibited a reduction comparable to that observed in the control group.
An Ethyl Acetate Fraction of Moringa oleifera Lam. Inhibits Human Macrophage Cytokine Production Induced by Cigarette Smoke Nateelak Kooltheat, Rungapa Pankla Sranujit, Pilaipark Chumark, Pachuen Potup, Nongnit Laytragoon-Lewin, Kamchana Usuwanthim (2014)	*True experiment*	Monocyte Derived Macrophages (MDM) from human blood obtained from the blood bank of Buddhachinaraj Phitsanulok hospital	Moringa extract's phenolic content suppressed pro-inflammatory cytokines (IL-6, TNF-κ, and IL-8) in macrophages, outperforming cigarette smoke extract in an in-vitro study. Moringa extract may reduce RelA expression, an NF-κB-triggered inflammatory response, according to existing data.
Administration of Moringa Leaf Flour on Blood Transferrin Levels of White Rats with PEM Model	Experimental research with a post-	The samples were divided into 6 groups	An oral dose of 360 mg of NTT variety Moringa leaf flour had the best effect on blood transferrin

Research Title and Authors	Research Design	Samples	Results
Etik Sulistyowati, Arlik Rio Julia, Dhaniar Mudita (2015)	test only control group design approach	with 1 negative control group, 1 positive control group and 4 treatment groups	levels (0.23 ± 0.17 g/dl) in PEM mice fed a normal diet. The blood transferrin levels of the non-PEM/negative control group (0.22 ± 0.01 g/dl) were similar to this level (p= 0.000).
Effectiveness of Moringa Leaf Extract (Moringa oleifera) on Reducing Total Cholesterol Levels in White Rats (Rattus novergicus) Sri Wahyu, Andi Sitti Fahirah Arsal, Indah Chintya Maharani (2019)	Pre-experimental designs with a one group pre-test post-test approach	Fifteen males Rattus novergicus rats were separated into three groups, consisting of two control groups and one treatment group.	The average cholesterol before Moringa leaf extract treatment was 307.40 mg/dl; after, 209.00 mg/dl. A substantial difference in mean cholesterol levels was found before and after medication (p value = 0.004 (<0.05). Before and after simvastatin, the average cholesterol was 271.20 mg/dl and 127.40. The study found a significant difference in average cholesterol levels before and after treatment (p= 0.009, <0.05).
Polyphenol Extract of *MoringaOleifera* Leaves Alleviates Colonic Inflammation in Dextran Sulfate Sodium-Treated Mice Yunjuan Zhang, Lei Peng, Wenyun Li, Tianyi Dai, Long Nie, Jing Xie, Yu Ai, Lingfei Li, Yang Tian, Jun Sheng (2020)	Experimental research	30 male mice were divided into 5 groups, with 1 control group and 4 treatment groups	In mice with dextran sulfate sodium (DSS)-induced colitis, the administration of Moringa leaf polyphenol extract resulted in a decrease in body weight, alterations in intestinal length, release of pro-inflammatory cytokines (IL-6, TNF-κ), intestinal tissue damage, and infiltration of inflammatory cells.
Ethanolic Extract of Moringa oleifera Leaves Influences NF-κB Signaling Pathway to Restore Kidney Tissue from Cobalt-Mediated Oxidative Injury and Inflammation in Rats Mohammed M. Abdel-Daim, Samah R. Khalil, Ashraf Awad, Ehsan H. Abu-Zeid, Reda Abd El-Aziz, Hamed A. El-Serehy (2020)	The experimental research designs	50 Sprague-Dawley rats were divided into 5 groups, with 1 control group and 4 treatment groups	The administration of Moringa ethanol extract can serve as a preventive measure for rat kidney injury caused by CoCl2. It achieves this by minimizing oxidative damage to the kidneys and regulating the action of mRNA, hence reducing inflammatory consequences.
Benefits of Giving Moringa Leaf Flour (Moringa oleifera) on IL-6 and LDL Cholesterol Levels in Sprague Dawley Dyslipidemia Rats Welresna J.P Rupiasa, Siti Fatimah-Musi, Ahmad Syauqy, Kusmiyati Tjahjono, Gemala Anjani (2021)	A Completely Randomized Design (CRD) with a pre- and post-test control group design was used in the investigation.	24 male Sprague Dawley rats were divided into 4 groups with 1 negative and positive control group each and 2 treatment groups.	Moringa leaf powder at 0.1 and 0.2 g/BW/day reduces IL-6 and LDL cholesterol in dyslipidemic Sprague Dawley rats. Doses 1 and 2 had similar effects on IL-6 levels, as there was no significant difference.
Moringa oleifera Ethanolic Extract Attenuates Tilmicosin-induce Renal Damage in Male Rats via Suppression of	Experimental with a post-test	60 male Sprague-Dawley rats	In mice with Tilmicosin-induced kidney injury, TNF-α, IL-1β, and mRNA secretion increased,

Research Title and Authors	Research Design	Samples	Results
Oxidative Stress, Inflammatory Injury, and Intermediate Filament Proteins mRNA Expression Shimaa M. Abou-Zeid, Amany I. Ahmed, Ashraf Awad, Wafaa A. Mohammed, Mohammed M.M. Metwally, Rafa Almeer, Mohamed M. Abdel-Daim, Samah R. Khalil (2021)	only control group approach	weighing 180-190 grams. Divided into 1 control group and 5 treatment groups.	leading to problems such H202 and MDA levels in kidney tissue. Tilmicosin adverse effects can be prevented by giving 800 mg/kgBW Moringa leaf extract, an antioxidant and anti-inflammatory.
Moringa oleifera *Leaf* Polysaccharide Alleviates Experimental Colitis by Inhibiting Inflammation and Maintaining Intestinal Barrier Hosameldeen Mohammed Husien, Weilong Peng, Hongrui Sui, RuiGang Zhou, Ya Tao, JunJie Huang, MingJiang Liu, RuoNan Bo, JinGui Li (2022)	*True experiment al*	40 male mice were divided into 5 groups, with 1 control group and 4 treatment groups	Moringa leaf extract exhibits a prophylactic effect against DSS-induced ulcerative colitis in mice, as evidenced by its polysaccharide content. This effect is achieved through the reduction of damage to the intestines, goblet cells, and crypts, as well as the suppression of TLR4/MyD88/NF-κB signaling activation and the expression of pro-inflammatory cytokines, namely TNF-α, IL-1β, and IL-10.

DISCUSSION

Malnutrition, also known as protein energy deficiency (PEM), is a kind of malnutrition that accounts for 60% of the mortality of babies under the age of five (toddlers) in tropical and subtropical countries. The etiology of PEM can be attributed to underlying dietary inadequacies and protein deficiencies, leading to subsequent difficulties arising from infection. When managing PEM, ensuring that food intake is both of high quality and sufficient in quantity is typically the primary focus. High-quantity food refers to food that adequately satisfies the body's nutritional requirements, whereas high-quality food encompasses a comprehensive array of essential nutrients, including protein, carbs, fats, vitamins, and minerals. In this particular scenario, Moringa leaves, renowned for their nutritional value, vitamin content, and bioactive compounds, present a viable alternative for the treatment of PEM disorders. This study examines the impact of the constituents found in Moringa leaves on addressing nutritional issues, namely post-exposure prophylaxis (PEM) and other conditions associated with the anti-inflammatory capabilities of Moringa leaves.

Dwi et al., studied 24 males Wistar Rattus novergicus rats that had been conditioned with PEM for two months while being fed non-protein chow. Following the modeling process, mice exhibited the clinical manifestation of PEM, characterized by a persistent decline in body weight resulting from reduced hunger, along with an upregulation of IL-6 expression. Following the administration of Moringa leaf powder at different dosages, a noticeable improvement in the condition of the samples was seen. The treatment group 3 (dosage 720 mg) exhibited the most notable disparity, with the lowest degree of fatty liver and a near proximity to normalcy seen. Additionally, there was an optimum drop in IL-6 secretion.(Dwi et al., 2012)

Absence of a protein source that provides amino acids will impede the formation of lipoproteins. Triglycerides and cholesterol are transported from the liver to the tissues by this lipoprotein. The accumulation of lipids in the liver can result in the creation of lipid peroxides, which have the potential to harm DNA and cell membranes, ultimately leading to cellular demise if not well managed.(Koruk et al., 2004) This event will induce the

upregulation of pro-inflammatory cytokines, specifically IL-6, in macrophages and monocyte cells, hence promoting the activation of Reactive Oxygen Species (ROS). Administering appropriate dosages of Moringa leaf powder, which is rich in protein, can effectively meet the body's energy and amino acid requirements. As a consequence, lipoproteins containing approteins B and C undergo re-formation. By adopting this approach, the equilibrium of fat influx and outflow from the day to the tissues will be maintained. Hence, the efficacy of Moringa leaf powder in mitigating fatty liver and decreasing lipid peroxides and free radicals in liver tissue is widely acknowledged. The reduction of free radicals and the mitigation of liver damage will lead to a decrease in the inflammatory process, as seen by a decline in the levels of IL-6, a pro-inflammatory cytokine, in the blood serum.

Kooltheat et al., utilized a macrophage sample acquired from monocyte derivatives formed from human blood cells that were exposed to cigarette smoke.(Kooltheat et al., 2014) This exposure led to an increase in pro-inflammatory cytokines, including TNF-κ, IL-6, and IL-8. Cigarette smoke contains several chemical compounds, including acroleine, nitrosamines, polycyclic aromatic hydrocarbons, and reactive oxygen species (ROS), as well acknowledged.(Marcilla et al., 2012) ROS induce oxidative stress, leading to detrimental effects and exacerbation of diseases, including emphysema and an elevated susceptibility to lung cancer.(Kundu & Surh, 2012)(Tamimi et al., 2012) In essence, this sequence will elicit the activation of immune cells, leading to the generation of macrophages that contribute to the production of pro-inflammatory cytokines. These cytokines are distinguished by an elevation in levels of TNF-κ, IL-6, and IL-8 responses to acute stimuli. The phenolic component of Moringa leaf extract, which functions as an antioxidant and anti-inflammatory agent, has a beneficial impact on enhancing the state of macrophage cells. Extracting Moringa leaves with ethyl acetate yields the most potent phenolics and has potent antioxidant action, thereby effectively suppressing the release of pro-inflammatory cytokines by macrophages.(Purkis et al., 2011)

Additionally, a study conducted by Sulistyowati et al. provides an account of the state of PEM in male white rodents subsequent to a 56-day administration of a non-protein diet. The PEM condition leads to a reduction in body weight by 8.56 grams, a decrease in appetite, yellowish fur that falls out, decreased activity in the sample, and a decrease in albumin level to 2.6 grams/dL (out of the normal range of 3.8-4, 8 grams/dL) and blood transferrin. The serum protein known as blood transferrin is formed by the use of amino acids.(Sulistyowati et al., 2015) However, in the presence of PEM, the quantity of amino acids diminishes and fails to meet the body's daily requirements, resulting in disruptions to metabolic processes, including the production of blood transferrin. The administration of Moringa leaf flour, which is abundant in protein and contains 10 necessary amino acids, has the potential to enhance the formation of blood transferrin, hence facilitating gradual improvements in various bodily processes.(Cheng et al., 2004)

According to a further study in 2020 conducted by Zhang et al., it was found that the oral administration of Moringa leaf polyphenolic extract had the potential to mitigate the adverse effects of colitis in mice that were produced by Dextran Sulfate Sodium (DSS).(Y. Zhang et al., 2020) Moringa extract possesses anti-inflammatory properties that can effectively decrease the presence of CD3+ T cells, CD177+ in neutrophils, and F4/80+ in macrophages. Additionally, it can significantly suppress the release of IL-6 and TNF-α, while also regulating the activity of NF-κB p65 and p-IκBα signals. Specifically, it downregulates NF-κB p65 and upregulates p-IκBα. In mice with colitis induced by DSS, there was a notable reduction in size and an increase in blood volume in the large intestine. Additionally, the

epithelial cells in the lamina propria and surrounding glands were observed to be damaged, and there was an augmentation in the presence of T cells, neutrophils, and macrophages, which were examined in the distal section of the large intestine. Consequently, there will be a significant release of pro-inflammatory cytokines, specifically IL-6 and TNF-κ, which might lead to harm to the colon tissue by activating chemotactic neutrophils. The application of Moringa leaf polyphenol extract, which predominantly possesses anti-inflammatory characteristics, has demonstrated efficacy in the prevention or amelioration of colitis.(Hong et al., 2022)

In 2020, Abdel-Daim et al. conducted a study to investigate the efficacy of Moringa ethanol extract in alleviating the adverse effects of CoCl2 (Cobalt Chloride) exposure on the kidneys of mice. This phenomenon leads to a notable elevation in the levels of oxidative stress and inflammatory reactions. The sample's physical condition deteriorated, characterized by dull fur, reduced body weight, frailty, and inactivity.(Abdel-Daim et al., 2020) A further outcome resulting from exposure to CoCl2 is an augmentation in the activity of the inflammatory signaling pathway mediated by NF-κB, which is implicated in renal inflammation. This leads to a reduction in total protein and albumin levels, as well as a drop in antioxidant levels (specifically SOD, CAT, and GSH) within the kidney tissue.(Zeeshan et al., 2017) As anti-inflammatory agents, the ethanol extract of Moringa leaves contains bisabolol, thymol, caryophyllene, and eugenol, all of which substantially reduce nitric oxide (NO) and inflammation, respectively. Additional components have the potential to impede nephrotoxic responses resulting from the production of CoCl2 by alleviating DNA damage, oxidative stress, and inflammation through the modulation of expression patterns. The efficacy of Moringa leaf ethanol extract supplementation in mitigating renal toxicity and inflammatory reactions has been demonstrated.(Fontinele et al., 2019)

Based on a study conducted by Rupiasa et al., the administration of Moringa leaf flour to mice exhibiting dyslipidemia leads to a reduction in low-density lipoprotein (LDL) levels, as well as an inflammatory response defined by reduced levels of interleukin-6 (IL-6).(Rupiasa et al., 2021) The function of moringa content is closely associated with its anti-oxidant and anti-inflammatory properties, which contribute to the smooth functioning of fat metabolism and the prevention of future damage. Dyslipidemia, characterized by an aberrant lipid profile in the blood, leads to elevated LDL levels and reduced HDL due to an unhealthy diet. This, in turn, causes cholesterol deposits on the walls of blood vessels.(Sudargo et al., 2017) Oxidative stress results from the imbalance between the concentrations of free radicals and antioxidants in the body, which is caused by the oxidation of this LDL. As a result, there is an increased likelihood of tissue injury, which can lead to an inflammatory response characterized by the release of IL-6 into the bloodstream. If not properly managed, this disorder has the potential to initiate more significant harm, such as cardiovascular disease. The administration of Moringa flour serves as an antioxidant and anti-inflammatory agent, potentially exerting a direct impact on dyslipidemia. The presence of flavonoids, tannins, saponins, and β-sitosterol in the substance would lower triglyceride levels by enhancing the lipoprotein lipase activity, resulting in a reduction of LDL cholesterol levels and so mitigating the risk of inflammation.(Santosa & Baharuddin, 2020)(Helmy et al., 2017)

Feline Sprague-Dawley rats were subjected to tilmicosin-induced nephrotoxicity conditions in 2021 research by Abou-Zeid et al. The deleterious effects induced by the administration of tilmicosin can be mitigated with the administration of Moringa leaf ethanol extract at a dosage of 800 mg/kgBW. This extract contains antioxidant and anti-inflammatory compounds, which effectively reduce the levels of TNF-κ and IL-6.(Abou-Zeid et al., 2021) The administration

of tilmicosin to the kidneys will cause an elevation in H2O2 and lipid peroxidase levels, resulting in an increase in MDA levels and a decrease in antioxidants (SOD and GPx) in the body.(X. Zhang et al., 2020) The inherent water-like properties of H2O2 facilitate its facile diffusion across various membranes, hence exerting an impact on cellular regulation. Adjacent cells. Elevated concentrations of H2O2 will undergo a Fenton reaction with iron, resulting in the formation of hydroxyl radicals. This, in turn, initiates an escalation in oxidative stress, which subsequently leads to an inflammatory reaction characterized by the release of TNF-κ and IL-6. If not addressed, this condition can lead to alterations in gene expression at the cellular level, necrosis, apoptosis, tissue destruction, and impaired renal function. The efficacy of Moringa leaf extract administration as a prophylactic measure in cases of nephrotoxicity is demonstrated through its ability to decrease the release of pro-inflammatory cytokines and meet the body's antioxidant requirements. This leads to an elevation in the levels of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), subsequently impeding the synthesis of harmful substances. Within the human body.(Ratliff et al., 2016)

In their 2022 study, Husien et al. employed a murine model of ulcerative colitis induced by DSS to investigate the impact of Moringa extract's polysaccharide content on the intestinal protection and inflammatory response. The findings of this study demonstrated that the administration of Moringa extract effectively mitigated the risk of intestinal injury by suppressing the activation of inflammatory signaling pathways and the release of pro-inflammatory cytokines.(Mohamed Husien et al., 2022) The administration of Moringa extract to mice at different dosages resulted in notable enhancements in conditions associated with ulcerative colitis. These improvements included a decrease in the likelihood of intestinal mucosa damage, amelioration of intestinal histopathological conditions (such as reducing damage to epithelial cells, goblet cells, and crypt structures), reduction in inflammatory infiltration within cells (with decreased levels of IL-1β and TNF-α, and increased levels of IL-10), inhibition of the activation of the inflammatory signaling pathway in TLR4/MyD88/NF-κB, and maintenance of equilibrium in goblet cell and tight junction protein expression.(Hong et al., 2022)

CONCLUSION

After doing a comprehensive analysis of several scholarly studies, it becomes apparent that the administration of Moringa leaves orally provides a dual advantage, functioning as both an anti-inflammatory agent and a powerful antioxidant. These characteristics make it highly efficient in treating a range of illnesses, including those connected to malnutrition caused by deficits in energy and protein, as well as infections like Protein-Energy Malnutrition (PEM). The potential therapeutic efficacy of Moringa leaves in addressing PEM disorders is attributed to their abundant nutritional composition, as well as their notable anti-inflammatory and antioxidant characteristics. thereby, it can be deduced that taking Moringa leaves orally shows significant potential in improving the inflammatory elements of PEM, thereby making a good contribution to the management and treatment of this incapacitating condition.

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