A Review on the effect of *Moringa oleifera* in the treatment of Hypertension

By

Md. Abidur Rahman Nabil
20146085

A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

School of Pharmacy
Brac University
April, 2024

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Md. Abidur Rahman Nabil
20146085

Approval

The project titled "A review on the effect of *Moringa oleifera* in the treatment of Hypertension" submitted by Md. Abidur Rahman Nabil (20146085) of Spring 2020, has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons) on ……

Supervised By:

_____

Professor Dr. Hasina Yasmin
Program director and Assistant Dean
School of Pharmacy
BRAC University

Approved By:

Program Director:

_____

Professor Dr. Hasina Yasmin
Program Director and Assistant Dean
School of Pharmacy
BRAC University

Dean:

_____

Professor Dr. Eva Rahman Kabir
Dean
School of Pharmacy
BRAC University

Ethics Statement

This study does not use any human or animal trial.

Abstract

The multipurpose plant *Moringa oleifera* contains varieties of biologically active phytochemicals in different parts of the plant that show therapeutic effects on various diseases like diabetes, cancer, and hypertension etc. The study reviewed the clinical trials data of *Moringa oleifera* on the disease hypertension. For reviewing the clinical trials data, our only focus on the trials that are not reviewed before and not include in any meta-analysis which result two relevant articles on clinical trials data of hypertension. From those two articles, one shows positive effect on blood pressure and other article data don't show any changes in blood pressure while reducing Low density lipoprotein and total blood cholesterol. Though the clinical trial data is very less, further research is necessary to determine the plant's effectiveness on hypertension and declare it's potential as an alternative resource for incorporating it into people's lifestyles as we can see the beneficial effects of the plant.

Keywords: *Moringa oleifera*, Medicinal uses, Phytochemicals, Hypertension

Dedication

Dedicated to my parents and my respectable Supervisor of this project Professor Dr. Hasina Yasmin, Program Director and Assistant Dean, School of Pharmacy, BRAC University for their continuous support till the end.

Acknowledgement

Alhamdulillah, all the praises belong to Allah S.W.T. for giving me the strength to finish the project paper without facing much more difficulties. I would like to show my gratefulness to Almighty Allah for blessing me with strength, patience to cop-up with all the difficulties during my Under-graduation period and for allowing me the reach at the very end of Bachelor life.

Project work is not an individual task as it requires continuous guidance full of ideas, suggestion, reviews of the work on a continuous basis. I am very grateful and fortunate to having the opportunity of doing my project with the supervision of Professor Dr. Hasina Yasmin, Program director and Assistant Dean, School of Pharmacy, BRAC University. Her continuous assistance, guidance and supervision had led me to complete me project work accurately. Whenever there were any problem or confusion rise, Ma'am always manages sufficient time to solve my confusion with her immense experience and knowledge.

My ardent thanks go out to our Dean Professor Dr. Eva Rahman Kabir Madam, School of Pharmacy for making a competitive environment for attaining our potential. Her commitment and leadership towards the School of Pharmacy being a motivation for us. I would like to thank all the faculty members of School of Pharmacy for their enormous hard work to make us understand hard topic in easier manner.

Finally, I would like acknowledged my parents for their continuous motivation and prayer for me. I would like to thank my elder sisters for always encouraging me for getting out my best output.

Table of Contents

Declaration ……ii

Approval …….....iii

Ethics Statement ……...iv

Abstract…….……..…….v

Dedication …….……vi

Acknowledgement…..……...vii

Table of Contents ..……...viii

List of Tables ….…….... x

List of Figures ……...xi

List of Acronyms…….…….….xii

Chapter 1- Introduction ……....1

1.1 *Moringa oleifera* ……..…..……1

1.2 Habitat ……..…….…..2

1.3 Phytochemistry ……..…….…….....3

1.4 Medicinal use of *Moringa oleifera* ……...……...….... 6

1.5 Aim of the Study …..……..11

1.6 Objectives of the Study ……..……....11

Chapter 2- Hypertension……...……..…….. 12

2.1 Hypertension ……..……...……...…….12

2.2 Pathophysiology …….…….....…..…….……...……..13

2.3 Prevalence of Hypertension …..……...……..…..….……... 15

Chapter 3- Methodology …….…….…..…...17

Chapter 4- Result and Discussion……...……..….....21

4.1 Effect of *M. oleifera* on healthy participants ….…...……..…...21

4.2 Effect of *M. oleifera* on Pre-diabetes participants ….……...…….22

Chapter 5- Conclusion .……...…….……..29

References …...…….……...30

List of Tables

Table 1: Medicinal uses of *Moringa oleifera*…….. 10

Table 2: Effect of *Moringa oleifera* on blood pressure on healthy patients……. 22

Table 3: Effect of *Moringa oleifera on* lipid profile and blood pressure on prediabetic patients…….……. 24

Table 4: Summary of clinical trials of *Moringa oleifera* on hypertension…….….. 27

List of Figures

Figure 1: *Moringa oleifera* and it's classification…….2

Figure 2: Chemical structures of the major constituents of *Moringa oleifera* ……5

Figure 3: Mechanism of blood pressure control……..…… 14

List of Acronyms

TNF-α	Tumor Necrosis Factor alpha
IL-6	Interleukin 6
Inos	Inducible NO synthase
COX-2	Cyclooxygenase 2
PGE	Prostaglandin E
SOD	Superoxide dismutase
CKD	Chronic kidney disease
RAAS	Renin angiotensin aldosterone system
PWV	Pulse Wave Velocity
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
LDL	Low density Lipoprotein
BMI	Body Mass Index

Chapter 1- Introduction

1.1 *Moringa oleifera*

The *moringa oleifera* tree is a multipurpose plant also known as "drumstick trees'' in some parts of the world; belonging to the Moringaceae family. Among the monogeneric family Moringaceae, *Moringa oleifera* Lam. (syn. M. ptreygosperma Gaertn.) is one of the most well-known, extensively distributed, and naturally occurring species(Anwar et al., 2007). There are 13 species of Moringaceae family from which *Moringa oleifera* is widely used and mostly known. The climate of tropical and subtropical regions are most friendly for the cultivation of this trees (Gayatri et al., 2023).The height of the trees ranges from 5-10 meters (Liu et al., 2018). The usable parts of this *M. oleifera* plant are leaves, seeds and pods; mainly the leaves both in dry and leaf extract form that contains the substance like fibers, proteins, magnesium, calcium, beta carotene and alpha tocopherol (Taher et al., 2017).

One of the advantageous characteristics of this tree is that it is a really fast-growing plant that makes it able to spread to other regions such as mountainous regions situated in Europe known Iberian Peninsula from their origins (Leone et al., 2015). The plant is well tolerable and able to grow in hot humid dry lands; even in a land little affected by drought. The plant can grow up to an annual rainfall of maximum and the Ph of 6.3-7.0 can be tolerated by the plant (Anwar et al., 2007).

Figure 1 shows different parts of the plant *Moringa oleifera* with their scientific classification, origin, usable parts and their medicinal uses.

<table>
<tr><td>  </td><td>Scientific classification of Moringa Oleifera:
Kingdom: Plantae
Division: Magnoliopsida
Class: Magnoliopsida
Order: Brassicales
Family: Moringaceae
Genus: Moringa
Species: Moringa oleifera</td></tr>
<tr><td>Biological Name: Moringa oleifera</td><td>Origin: Western and sub-Himalayan tracts, India, Pakistan, Asia Minor, Africa and Arabia</td></tr>
<tr><td>Usable parts: Leaves, stem bark, gum, seed, root</td><td>Medicinal Use: Anti-inflammatory, Anti-diabetic, Anti-cancer, Anti-oxidant, Antimicrobial</td></tr>
</table>

Figure 1: Moringa oleifera and it's classification (Anzano et al., 2021; Paikra et al., 2017)

1.2 Habitat

The native of *M. oleifera* are the western and sub-Himalayan tracts, India, Pakistan, Asia Minor, Africa and Arabia but now it spread in the Philippines, Cambodia, Central America, North and South America and the Caribbean Islands (Thapa et al., 2019).As the plant is found in most of the regions of the world, it is known to those region peoples by different local names like "drumstick tree, horse radish tree, kelor tree" and locally known by the name 'Sohanjna' that is found and cultivated all over the countries. It is widely distributed along the sandy banks of rivers and streams, grows best in tropically isolated climates, and can be found both wild and farmed across the plains, particularly in hedges and home yards (Anwar et al., 2007).

1.3. Phytochemistry:

Different chemical constituents exist in various parts of the plant that result in different therapeutic properties. For specific diseases to get cured, different parts of the plant are extracted by using specific methods to isolate target chemical compounds. Different parts of *M. oleifera* trees are rich in two common chemical molecules. The main chemical quantities found in *M. oleifera* are simple sugar called rhamnose and a group that is fairly unique in nature named glucosinolates and isothiocyanates. According to Anwar et al., 2007, the alkaloids named moringine and moringinine were found to be present in the extracted stem bark sample of *M. oleifera*. Other compounds that were also found in stem bark extracted samples were Vanillin, 4-hydroxymellin, octacosanosic acid and β-sitosterol. The extraction of stem bark was done by subjecting the powdered dry sample with 95% ethanol in a glass container which has flat bottom; agitation and shaking were applied occasionally. Then the solution is filtered to get the extract using a vacuum pump with rotary evaporator (Parvin et al., 2014).

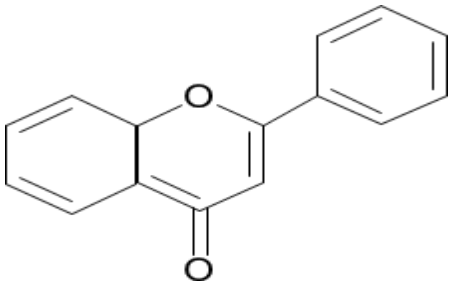
As the leaves of *M. oleifera* contain majorly two constituent's flavonoid and phenolics in a major portion that enable them to provide the antioxidant property(Anwar et al., 2007). Other main constituents present in the leaves are chlorogenic acid, gallic acid, kaempferol, quercetin glycosides, iron, calcium, phosphorus, copper, vitamin A, B and C, pyridoxine and nicotinic acid. The extraction process was done by drying and smashing the *M. oleifera* leaves into the filter basket that is placed in an extraction kettle. Then solvent or water were used according to the demand of the procedure. In case of selection of procedure, the process result maximizes yield value has to be selected. Two simplest methods used in the extraction of *M. oleifera* leaves were squeezing and maceration which used water and 70%

ethanol consecutively.

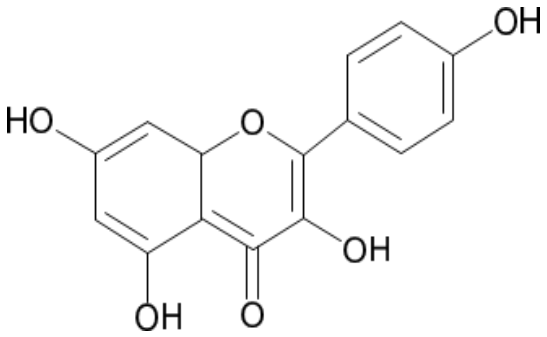
There are two forms of gums that can be extracted from *M. oleifera* plant; one is whole-gum that contains L- arabinose, galactose, glucuronic acid, mannose and xylose as major constituents. Another one is degraded gums which hydrolyze the whole gum by using acid that contains L- galactose, glucuronic acid, L-mannose. Another usable part of the plant is Flowers which used to lower lipid content from the body contains the constituents nine amino acids, alkaloids, wax, quercetin, potassium, calcium, kaempferol (Anwar et al., 2007).

The seed of *M. oleifera* contains 4(αL-rhamnosyloxy)-benzyl isothiocyanate, niazimicin,3-O-(6′-O-oleoyl-β-D-glucopyranosyl)-β-sitosterol, β-sitosterol-3-O-β-D-glucopyranoside, niazirin, β-sitosterol and glycerol-1-(9-octadecanoate). The chemical constituents were isolated by using ethanol as a solvent and extracted from the ethanol extract of the Moringa seed(Anwar et al., 2007). The root of *M. oleifera* contains potassium, sodium, magnesium, phosphorus, and calcium that are used in water treatment. The roots are collected from a seven-month-old plant, then it is washed, dried and crushed into the powder to use.

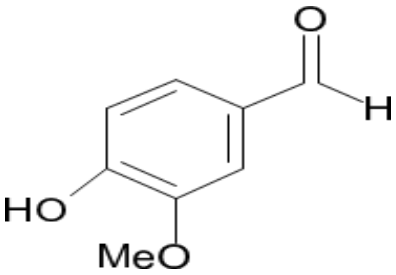
Figure 2 shows the chemical structure of the major constituents like flavonoid, kaempferol, Vanillin, Chlorogenic acid etc. found in different parts like leaves, root, gum, seed etc. of the plant *Moringa oleifera.*



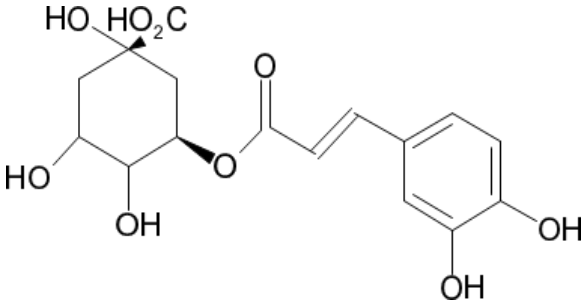
Flavonoid



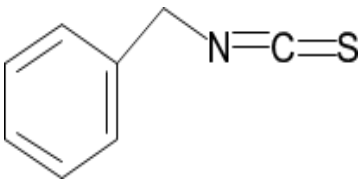
Kaempherol



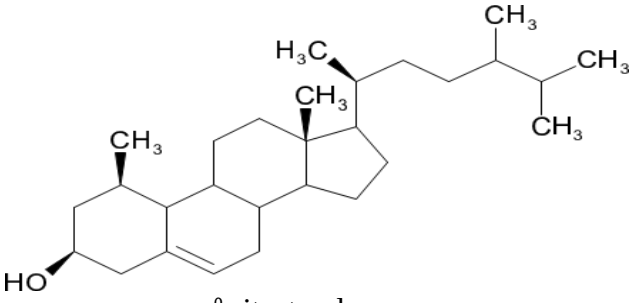
Vanillin



Chlorogenic acid



Benzyl isothiocyanate



β-sitosterol

Figure 2: Chemical structures the major constituents of Moringa oleifera

1.4. Medicinal Uses

M. oleifera shows varieties of therapeutic properties and different parts of the plant generate different properties in curing different diseases related to heart, gastrointestinal tract, hematological system, and liver; in addition to viral illnesses and inflammation. *M. oleifera* is not only just consumed for nutritional value but also it provides a lot of medicinal benefits. The antioxidant property presents in *M. oleifera* due to the availability of beta carotene, polyphenols and vitamins in rich amounts. There are multiple other properties that can be shown by the use of the plant like anti-cancer, anti-inflammatory, hepatoprotective, neuroprotective (Razis et al., 2014). Recent studies have shown, using the plant for medicinal purposes can demonstrate a number of additional benefits; as it prevents diseases like diabetes, rheumatoid arthritis, atherosclerosis, infertility and also relieves the patient from pain, depression (Banji et al, 2012) . For the part of this writing purposes, the major and revolutionary uses of the plant with the mechanism will be focused.

1. Anti-inflammatory agents: Inflammation is the normal physiological response of the body against the infection to remove noxious agents and to restore the damage of the tissue(Chen et al., 2018). But long-term inflammation led to development of many other diseases like diabetes, heart disease, autoimmune disorder and cancer. Macrophage and lymphocyte get activated during inflammation and as a result it releases tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6) which initiates the production of nitrous oxide and prostaglandin E2 (Kou et al., 2018).

The leaves extract of *M. oleifera* significantly reduced the production of PGE2 which is one of the inflammatory mediators that leads to the sign of inflammation like pain, redness. The overall process done by blocking the COX-2 enzyme which leads to the suppression

of PGE2 as prostaglandin is produced through the COX-2 pathway which prevents the inducible NO synthase(iNOS) from getting expressed. So, the dual inhibitory nature of the active ingredients of the plant leads to a path of healing both acute and chronic inflammation remarkably (Fard et al., 2015).

2.Antimicrobial agents: Number of studies were done by extracting various parts of the plant that shows a significant result of presence of antimicrobial property. For example, the growth, survival and cell permeability of some pathological bacteria were inhibited through isolating water-soluble lectin by the seed extract of *M. oleifera*(Moura et al., 2015). Apart from that, the root extract of the plant contains pterygospermin and deoxy-niazimicin which are the active antibiotic against bacteria and fungus (Kou et al., 2018).

3.Anticancer Properties: Cancer is one of the leading diseases that spread all over the world. Though the cancer is treated with some new effective approaches, the resistance makes the scenario a little bit complicated for the drug to work. Studies show that the leaf and bark extract of *M. oleifera* can effectively prevent the growth of cancers. According to Al-Asmeri (2015), out of 12 compounds found in the extract of *M. oleifera* 3 compounds have specific anti-cancer properties. According to Kou et al. (2018), one of the major components of *M. oleifera* plant extract, isothiocyanates have anticancer properties as it prevents the growth of both androgen dependent and independent prostate cancer in the human body. The prevention of cancer cell growth done using multiple pathway

3.1. Regulate cell multiplication: *M. oleifera* can effectively target different cell lines of different cancer types. For example, the plant extract able to target A549 cell line for lung cancer, MDA-MB-231 for breast cancer and HCT-8 cells for colon cancer (Al-Asmari et al., 2015). The leaf extract has antiproliferative effect on KB cells and in case of

neuroblastoma the inhibitory rate of the cancer cell growth is about 95%. (Sreelatha et al., 2011)

3.2. Programmed cell death: The leaf extract of the plant contains isothiocyanates that are able to destroy the cancer cell in a programmed way (Sreelatha et al., 2011).In cancer patients, the genetic mutation occurs due to the deformities of the cell division checkpoints. In some studies, it is shown that the anticancer agents arrest the checkpoint to enable the cell to undergo apoptosis (Khan et al., 2012).

3.3. Synergistic effects on Anticancer drug: For the treatment of the cancer patient, chemotherapy is given with multiple drugs and one of the major drawbacks of this treatment process is multidrug resistance that leads to the reduction of treatment efficiency. The phytochemical compounds with less side effects, low toxicity, multiple target and tumor resistance are more effective to prevent the cancer growth that raise the scope of natural compounds to be used with the traditional therapy. Although it is in experiment phase that shown the leaf extract of the plant effectively inhibits the growth of HeLa cells when taken with the traditional drug Doxorubicin that ultimately leads to cell death (Jafarain et al., 2014).

4. Anti-diabetic agents: Diabetes mellitus is one of the widespread metabolic disorders which is not possible to cure permanently. Plants have various mechanisms of action to prevent diabetes including stimulating insulin production, inhibiting α-amylase and α glucosidase activity, decreasing gluconeogenesis in the liver, increasing the absorption of glucose in the muscles and liver, blocking intestine glucose uptake, and inhibiting antioxidative properties. The plant leaf exhibits antidiabetic activity due to the presence of certain chemical components, including phenolics and flavonoids like rutin and gallic acid, as well as 4-hydroxyphenyl acetonitrile, vanillin, 4-α-L-rhamnopyranosyl benzyl isothiocyanate, and 3,4-dihydroxy benzonitrile (Krawczyk et al., 2022).

4.Antihypertensive agents: *M. oleifera* extract shows positive effects on cardiovascular disease by controlling blood lipid, the prevention of arteries plaque formation and lowering the blood cholesterol level (Thapa et al., 2019). The plant extract functions as combination of diuretics along with lipid and blood pressure lowering agents. Moringa leaves contain very rare compounds like nitrile, mustard oil glycosides and thiocarbonate glycosides which provide stabilizing effects on blood pressure reduction (Kou et al., 2018).

Table 1: Medicinal uses of Moringa oleifera

Disease	Constituents	Mechanism	Reference
Diabetes Mellitus type 2	*M. oleifera* leaf	1. Reduced blood glucose level, insulin,TNF-α and follicle count in PCOS diabetic model	(Siahaan et al., 2022)
	M. oleifera seed	1.Improved insulin resistance 2. Altered the inflammatory response, insulin-a-related pathway by influencing CASP3, tyrosine-PTPN1, and proto-oncogene SRC	(Huang et al., 2020)
Cancer	Active compounds of *M. oleifera* (4-α-L-rhamnopyranosy l benzyl isothiocyanate)	1. Inhibit the development of five different forms of renal cell cancer. 2. Inhibit cell migration and inhibition Induce cell cycle arrest and apoptosis	(Xie et al., 2021)
	M. oleifera seed	1. Decrease lipid peroxidation and myeloperoxidase activity 2. Reduced pro-inflammatory cytokines TNF-α and IL-2	(Cuellar-Núñez et al., 2021)
Cardiovascular disease	*M. oleifera* seed	1. Decrease lipid peroxidation 2. Improved cardiac diastolic function 3. Reduce interseptal thickness during diastole, decreased anterior wall thickness and decrease fibrosis in the left ventricles of heart. 4. Reduced the level of circulating CRP and Nitrites.	(Randriamboavonjy et al., 2016)
	M. oleifera leaf extract	1.Improved insulin level in plasma, superoxide dismutases(SOD), CAT and glutathione reductase 2. Reduced GSH, serum glucose, glycated hemoglobin	(Aju et al., 2019)

Table 1 manifests the potential activity of plant *Moringa oleifera* on the diseases like diabetes mellitus type 2, Cancer and cardiovascular diseases with their mechanism how the plant constituents improve the disease conditions.

1.5. Aim of the study:

The aim of the study is to review the clinical trial data to investigate the effect of *M. oleifera* plant in the treatment of hypertension.

1.6. Objective of the study:

The main objectives of the study are-

1.To provide the information on the use of the plant including chemical constituents, local uses etc. to the mass audience.

2.Analyzing the clinical trial data of the plant extract in the treatment of hypertension.

Chapter 2- Hypertension

2.1. Hypertension

Hypertension is one of the major causes of premature death worldwide as hypertension promotes the risk of other cardiovascular diseases like coronary heart disease, heart failure, stroke, myocardial infarction, atrial fibrillation and peripheral artery disease, chronic kidney disease (CKD) and cognitive impairment (Ma & Chen, 2022). Hypertension generally refers to the increase in systolic and diastolic pressure than the normal range. But it will be considered as hypertension when a person's following blood pressure examination results in SBP is ≥140 mmHg and/or DBP is ≥90 mmHg. (Unger et al., 2020) On the basis of cause hypertension can be classified into two major categories- (i) Primary Hypertension (without a definite cause) and (ii) Secondary hypertension (with definite cause). (Ma & Chen, 2022) Among all the patients suffering from hypertension, 90% of them fall into the primary hypertension categories who don't know the specific cause for hypertension (Unger et al., 2020). As they don't familiar with the cause of hypertension, they have to go for the treatment that controls blood pressure on a long-term basis but not being able to cure the disease permanently. That will lead to the wastage of high amounts of money and as they are not being recovered from the disease, they lose faith in the treatment (Fang et al., 2020). If they stop taking medication as a result of losing adherence in treatment, it will lead to more critical life-threatening cardiovascular disease. That's why investigation must be required to find out the causative symptoms of primary hypertension. Vasodilation capacity and intravascular fluid volume are the two factors that affect the blood pressure from which vasodilation depends on a vessel's elasticity, caliber and reactivity; and intravascular fluid volume depends on the amount of fluid intake and

amount of fluid excretion. The amount of fluid in the vessel is usually constant unlike excess amounts of fluid intake or excretion.

2.2. Pathophysiology

The pathophysiology of hypertension is not fully clear yet. Only 2-5 % of patients who suffer from renal or adrenal disease would be able to know if their disease influences the increase in the blood pressure. Other 95% hypertension patients fall in the primary categories (Beevers et al., n.d.). As the maintenance of blood pressure is mainly dependent on cardiac output and peripheral resistance. On the basis of these two factors, there are some hypothetical process or mechanism developed which will be covered below-

Renin-angiotensin-aldosterone system: Blood pressure regulated by Renin angiotensin aldosterone system (RAAS) by constricting arteries and retaining water, sodium into the body. In response to renal under perfusion or reduction in salt intake, juxtaglomerular apparatus in kidney release renin which responsible for converting angiotensinogen to angiotensin I (Inactive form) that activated to angiotensin II with the help of angiotensinogen converting enzyme (Roush & Sica, 2016). Angiotensin II; itself acts as a vasoconstrictor and it further helps to release aldosterone which helps this to increase the blood pressure. Although the renin angiotensin aldosterone system does not directly raise the blood pressure as many hypertensive patients have low amounts of renin angiotensin II (Beevers et al., n.d.).

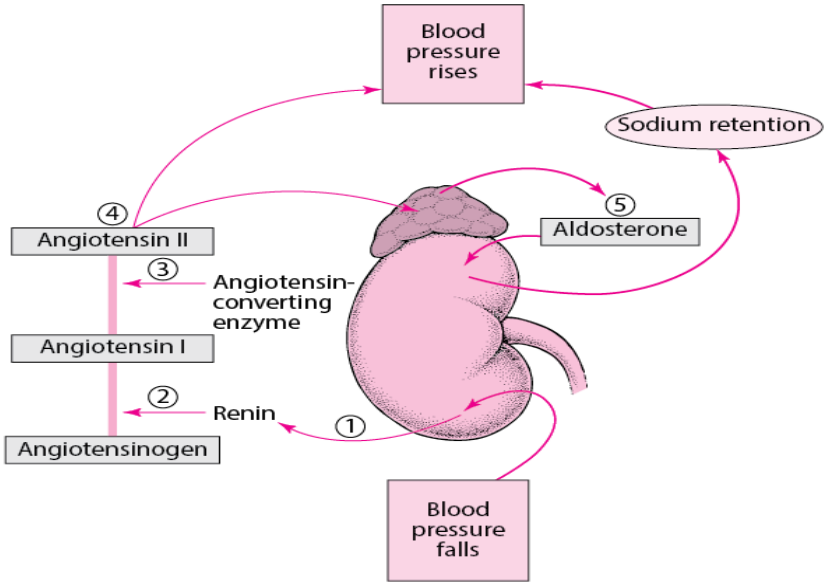


Figure 3: Mechanism of blood pressure control (Roush & Sica, 2016)

Figure 3 shows the controlling mechanism of blood pressure by angiotensin-aldosterone pathway. It shows when the blood pressure falls, kidney release an enzyme renin that splits angiotensinogen to angiotensin I (Inactive) that convert to angiotensin II by Angiotensin Converting enzyme which rises the blood pressure.

Water-sodium retention and salt-sensitive: Water sodium retention plays a vital role of increase in intravascular fluid retention at an abnormal label. Blood pressure caused by water sodium retention was controlled by diuretics, especially thiazide diuretics (Roush & Sica, 2016). Apart from secondary hypertension caused by renal dysfunction, there is another category of hypertensive patients with the sensitivity of salt as salt intake in high amounts for those categories of patients lead to hypertension. But here also two types of patients found- one is salt sensitive and other one is salt resistant (Hall, 2016). The types of this sensitivity and resistance could depend on some other factors like age, obesity,

genetic background and maternal condition. Although the full mechanism of water sodium retention-based hypertension is clear yet (Fang et al., 2020).

Arterial stiffness: A decrease in the elasticity and densibility of arteries is referred to as arterial stiffness, and the degree of stiffness in major arteries is commonly represented by pulse wave velocity (PWV). Arterial stiffness and arterial dilation capacity are often expressed by the value of pulse wave velocity (Segers et al., 2020). Arterial stiffness has a close relationship with blood pressure but there is a burning question of that which arises first in the body hypertension or arterial stiffness. As we can see with arterial stiffness, the dilation capacity of the vessel is lesser which leads to blood pressure to rise higher result hypertension (Fang et al., 2020).

2.3- Prevalence of Hypertension

Hypertension and other complications that arise from elevated blood pressure is responsible for the death of 8.5 million people each year. (Olsen et al., 2016; Zhou, Perel, et al., 2021) About 1.39 billion adults were affected by hypertension worldwide in 2010 (Mills K, 2020). The prevalence of hypertension is rising globally every year due to the increased exposure of the people with some risk factors like adhering to an unhealthy diet, leaving off doing physical exercise. But the consistency of rising hypertension is not the same in every region of the world. As we can see from the data of the previous two decades, there is a slight decrease in the number of hypertension patients in modern countries with high income whereas for middle- and low-income countries there is significant increase in the number of hypertension patients (Mills et al., 2016). Overall, the number of

hypertension patients increase as we can see the number of people with hypertension aged from 30-79 rising double from the year 1990 to 2019. In 1990, the total number of hypertension patients were 648 million (331 million women and 317 million men) whereas in the year 2019 the total number was about 1278 million (626 million women and 652 million women (Zhou, Carrillo-Larco, et al., 2021).

Due to the transition from the traditional foods to the fast foods, Bangladesh is one of the countries from the middle- and low-income countries group which has seen a significant rise in the number of new hypertension patients (M. Z. I. Chowdhury et al., 2020).As we can see from the year 2011 to 2018, the prevalence of hypertension increased from 25.84% to 39.40% ($p<0.001$). The prevalence of hypertension for the adults aged above 35 was 26.4 % in the year 2011 which is 25 times higher than the year 1976 that clearly shows how rapidly the number of hypertension patients increased in Bangladesh (M. A. B. Chowdhury et al., 2016). There is the highest amount of increase shown in obese people. The prevalence of hypertension is higher in women compared to men in Bangladesh but the relative value of hypertension is high among the men (75%) which 39% for the women (M. A. B. Chowdhury et al., 2021).

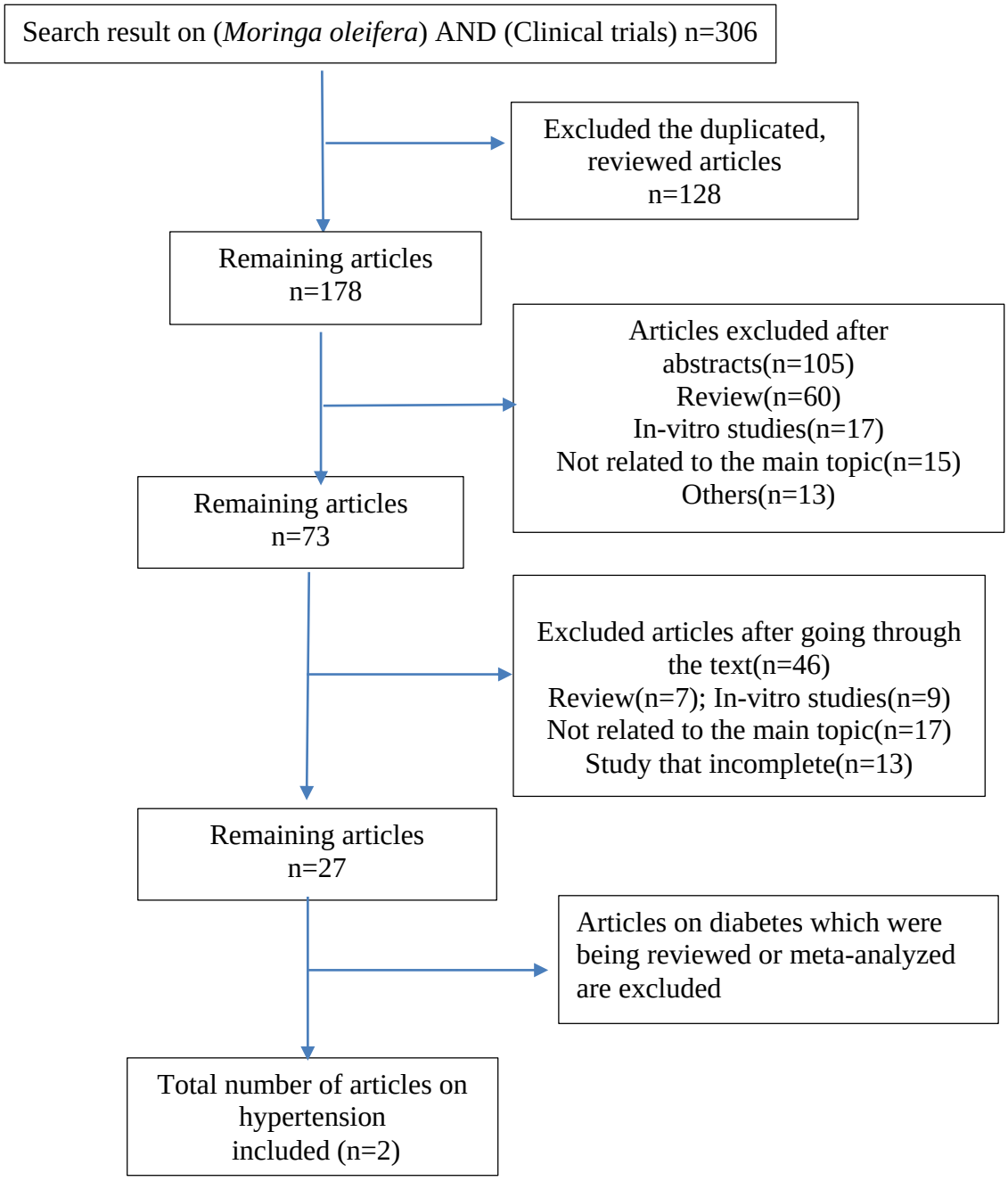
Chapter 3- Methodology

For our study on clinical trials data analysis of *M. oleifera* plant parts, we mainly go through the published articles related to *M. oleifera* in three major online databases called PubMed, Google scholar and Elsevier. The search was done on 13 February, 2024 which indicates all the articles published before the date were considered and gone through for this study. Then all the relatable articles were extracted from the database and then filtering the article to get relevant data related to clinical trials to fit it into our study to analyze the data easily. There are some criteria that we followed to exclude the articles from the total number of articles and it will be covered in the methodology part later.

Searching method: The majority of articles were extracted from two databases PubMed and google scholar. The searching technique and desired data were totally different for introduction and analysis part data. For introduction part, we searched writing "*Moringa oleifera* description", *Moringa oleifera* habitat", "*Moringa oleifera* Scientific classification", "*Moringa oleifera* different usable parts", "*Moringa oleifera* phytochemistry", "*Moringa oleifera* pharmacological properties".

As our main focus of the study is to analyze the clinical trials data of the plant *Moringa oleifera*, the search methods of the data related to clinical trials were described in more detail. In case of PubMed database, we search "(*Moringa oleifera*) AND (Clinical trials)", "(*Moringa oleifera*) AND (Pre-clinical trials)" and then more specifically we search for the disease like diabetes, hypertension, HIV, cancer separately as "(*Moringa oleifera*) AND (Diabetes) AND (Hypertension) AND (Cancer) AND (HIV) AND (Clinical trials) AND (Pre-clinical trials)". But in case of searching articles from google scholar, more

specific search for any disease related clinical trials for the plant extract would result in a very a smaller number of articles than the total number of relatable articles present in the database. To solve this problem, we search for "*Moringa oleifera* clinical trials" and then go through the articles one by one. Then those articles being relatable with the topic were extracted and included for the analysis. Then to look into the articles not included or work for meta-analysis purposes, then we see the articles of diabetic clinical trials from 2000-2023 were included in previously done meta-analysis. That's why, we exclude the diabetic clinical trials articles and further we look forward for the articles on some other diseases. Although in the first view there were much higher numbers of articles, the number of articles being lesser as we removed the articles by filtering duplication, review articles, not related to the disease and for being incomplete studies. At last, we checked the articles of our interest being indexed or not. If it is not indexed then the articles being excluded, as we proceed with the articles being indexed.


Search result on (*Moringa oleifera*) AND (Clinical trials) n=306
Excluded the duplicated, reviewed articles n=128
Remaining articles n=178
Articles excluded after abstracts(n=105)
Review(n=60)
In-vitro studies(n=17)
Not related to the main topic(n=15)
Others(n=13)
Remaining articles n=73
Excluded articles after going through the text(n=46)
Review(n=7); In-vitro studies(n=9)
Not related to the main topic(n=17)
Study that incomplete(n=13)
Remaining articles n=27
Articles on diabetes which were being reviewed or meta-analyzed are excluded
Total number of articles on hypertension included (n=2)

Inclusion criteria:

- Literature published in English.
- Literature published at least 10 years.
- Literature that done in-vivo clinical trials.

Exclusion criteria:

- Review articles not included
- Articles that are not indexed

Chapter 4- Result and Discussion

4.1. Effect of *M. oleifera* on healthy participants

The study to see the effect of *M. oleifera* on blood pressure was done with a random sample of 41 healthy participants (Male: n=14 and Female: n=27). Participants that are treated for hypertension or usually have low blood pressure were excluded. Participants were divided into two groups, one group consisting of 23 participants were taken 120g of *M. oleifera* leaves and other 18 participants were taken equivalent amounts of placebo. Data is collected by questionnaire of the food intake and by measurements of baseline mean Systolic and diastolic blood pressure and also 24 hours (on different time intervals; T2, T4, T6, T10, T20, T24) postprandial follow up for both groups. After measuring the blood pressure, there was a significant difference in case group mean DBP in between baseline and T2 ($p=0.013$) whereas in case of controlled group it was $p=0.326$ which indicates consumption of *M. oleifera* significantly lowering the blood pressure. We know, salt intake plays a huge role in raising blood pressure. But in case of *M. oleifera* intake, it showed that the DBP and SBP were decreased significantly within the group of people who consumed high amounts of salt whereas for the control group, the DBP and SBP were significantly increased with the intake of salt. There shows other relation in the article using the angle of obesity or high BMI with the blood pressure as the participants with the high BMI result elevated blood pressure.

Table 3 shows the effect of moringa supplements on blood pressure of healthy participants. The table contains both systolic and diastolic pressure on different time intervals of the participants taking moringa supplements and for the participants taking placebo.

Table 2: Effect of Moringa oleifera on blood pressure on healthy patients (Chan Sun et al., 2020)

Time interval	Mean Systolic blood Pressure (mm Hg)		Mean Diastolic blood pressure (mm Hg)	
	Case	Control	Case	Control
Baseline level (T0)	124.33 ± 4.14	123.93 ± 6.06	78.25 ± 2.48	80.98 ± 4.12
2 hours postprandial (T2)	119.86 ± 4.66	118.74 ± 6.26	71.64 ± 2.84	73.90 ± 4.78
4 hours postprandial (T2)	125.37 ± 4.16	121.13 ± 6.34	77.39 ± 3.36	79.33 ± 5.28
6 hours postprandial(T2)	122.82 ± 4.18	120.03 ± 5.68	77.22 ± 3.04	80.84 ± 4.42
10 hours postprandial (T10)	120.29 ± 4.50	123.64 ± 5.80	74.37 ± 3.32	77.60 ± 4.90
20 hours postprandial (T20)	120.98 ± 4.34	119.93 ± 6.40	77.92 ± 3.44	77.95 ± 4.90
24 hours postprandial (T24)	124.48 ± 3.82	121.78 ± 6.56	78.88 ± 3.08	76.24 ± 4.18

4.2. Effect of *M. oleifera* on prediabetic participants

The study was done to the participants who had never taken any medication for controlling blood glucose and the participants within age range between 40 to 70 years were included. The participants being considered as prediabetic by following the criteria of American Diabetic Association (ADA): HbA1C: 5.7-6.4% or fasting glucose level in between 100-125 mg/dL or 2-hour glucose tolerance test result must be within the range 140-199 mg/dL. (Díaz-Prieto et al., 2022) Total 73 participants enrolled for a parallel group trial that was randomized, double-blind, and placebo-controlled was carried out. who were divided into

two groups; one group were taken 6 capsule containing *M. oleifera* dry leaf powder of 400 mg and other group were taken placebo. The trials were carried out for 12 weeks. From the total number of participants (73), thirty-five participants taken placebo (n=35) and thirty-eight participants taken Moringa capsule (n=38) with the instruction of taking 2 capsules before each main meal for 12 weeks. They were told not to change their diet or lifestyle and the sample was collected from them 3 times, 0 weeks (Baseline), 6 weeks and 12 weeks. Multiple markers of the body were checked in these clinical trials. But we only focus on the parameters like blood lipid profile with the help of cholesterol contain and the blood pressure of the participants. For lipid profile, blood sample was collected and centrifuged within two hours of collection. For taking blood pressure data, it was measured with an OMRON M6 device and taken two times in each visit from which lowest value were taken for the analysis.

Table 4 shows the effect of moringa supplements on blood pressure, total cholesterol, High density lipoprotein and Low-density lipoprotein of prediabetic participants. The table contains both systolic and diastolic pressure on different time intervals (0 weeks, 6 weeks and 12 weeks) of the participants taking moringa supplements and for the participants taking placebo.

Table 3: Effect of Moringa oleifera on lipid profile and blood pressure on prediabetic patients (Díaz-Prieto et al., 2022)

		O Week	6 Weeks	12 Weeks
HDL-C (mg/dL)	PLC	57.8 ± 12.0	59.6 ± 13.4	61.8 ± 15.0
	MO	57.8 ± 14.3	59.1 ± 14.7	58.9 ± 14.9
LDL-C (mg/dL)	PLC	128.1 ± 34.4	126.8 ± 33.2	126.7 ± 34.5
	MO	118.1 ± 27.9	126.4 ± 27.4	119.8 ± 30.0
Total Cholesterol (mg/dL)	PLC	206.4 ± 36.4	207.7 ± 36.0	211.2 ± 34.6
	MO	197.9 ± 31.5	208.6 ± 29.1	203.1 ± 35.0
SBP (mm Hg)	PLC	129 ± 15	127 ± 187	128 ± 16
	MO	129 ± 15	125 ± 11	126 ± 11
DBP (mm Hg)	PLC	79 ± 9	78 ± 11	81 ± 11
	MO	80 ± 9	76 ± 8	77 ± 8

According to Chan Sun et al. (2020), *M. oleifera* shows a significant blood pressure lowering effect as we have seen after 2 hours from consumption of Moringa, the diastolic blood pressure reduces from 78.25 ± 2.48 mmHg to 71.64 ± 2.84 mmHg which is much lower compare to the participants taking placebo. The blood pressure of the participants taking Moringa being gradually increased with the time pass from the intake of the capsule. During the postprandial follow-up (T2-T24), both systolic and diastolic pressure were recorded in case of case and control group. It clearly shows that there is no significant difference in systolic blood pressure between case and control group in various time interval from baseline to T24. Whereas there is slight difference in diastolic blood pressure of case and control participants over the time interval (T2-T24) from initial intake. The highest amount of difference observes in diastolic blood pressure (DBP) in the time interval

T2 when the difference in mean DBP from baseline to T2 were 0.013 whereas for control group it was observed 0.326 which indicates the lowering effect of blood pressure from *M. oleifera* on initial intake.

There is another health condition taken for analysis the blood pressure reducing effect of *M. oleifera* which is salt intake by the participants. For knowing the salt intake of every person, a questionnaire is served before starting the clinical trials to the participants on which all the food and lifestyle habits were mentioned. Participants after filling the form being ready for taking the Moringa and placebo. As we know, salt has the tendency to increase the blood pressure by itself. So, the participants with high amount of salt intake (8gram/day) must be in consideration as their data could be misleading if their blood pressure being compare with other participants taking low amount salt in their diet. According to clinical trial data of Chan Sun et al. (2020), Moringa also being able to lower the blood pressure (both SBP and DBP) of the participants (Case group) taking high amount of salt in their diet whereas control group shows higher SBP and DBP. Some other considerations taken for clinical trial data analysis were obesity and age.

According to Díaz-Prieto et al. (2022), intake of *M. oleifera* effectively reduce the amount of Low-Density Lipoprotein and total cholesterol in the blood of the participants. As we can see, the blood sample taken at the time 0 week and 12 weeks shows difference in case and control group test result data. At 0 week, the LDL of the participants taking Moringa was about 118.1 ± 27.9 whereas the participants taking placebo shows 128.1 ± 34.4 which indicates the effect of Moringa in reducing Low-density cholesterol that is bad if remain high amount in the body. Likewise at 12 weeks the amount of LDL in the blood of the participants taking Moringa and Placebo were 119.8 ± 30.0 and 126.7 ± 34.5 whereas in 6

weeks Moringa and placebo intake participants result similar LDL data. The amount of Total cholesterol were also decreasing with the intake of Moringa as we can see at 0 week the group taking Placebo and Moringa shows total cholesterol of 206.4 ± 36.4 and 197.9 ± 31.5 whereas at 12 weeks the control and case group blood cholesterol amount were 211.2 ± 34.6 and 203.1 ± 35.0 which shows the effect of cholesterol reduction of the blood of the participants. But in case of reduction of blood pressure level of the participants, this study clinical trial data doesn't prove any significant changes.

Table 5 summarize the overall study to determine the effect of moringa supplements on blood pressure of both healthy and prediabetic participants. The table describes about the design of the study with the details of the participants and the response shown on them after taking moringa.

Table 4: Summary of clinical trials of Moringa oleifera on hypertension

Study design	Participants	Study Group	Response	Result	Reference
A placebo-controlled study was conducted	Total 41 healthy participants who were not suffering from any chronic disease, not taken any medication for controlling hypertension age between 18-65	Control group: 18 participants taken 120g amount of placebo Case group: 23 participants were taken 120g amount of *M. oleifera* leaves	Moringa tends to reduce the diastolic blood pressure from baseline to postprandial 2 hours compare to the participants taking placebo.	Notable change in diastolic blood pressure from baseline after two hours.	(Chan Sun et al., 2020)
Randomiz-ed double-blind, placebo controlled, parallel group study was conducted	Total 73 participants were conducted the study who were aged in between 40-70 years and they were prediabetic; HbA1C: 5.7-6.4%; not taken any medication for reducing blood glucose.	Control group:35 participants were taken 6 capsule containing Placebo of 400mg. Case group: Six capsules containing 400 mg of placebo were given to 38 participants.	Moringa tends to lower the amount of LDL and Total cholesterol significantly at baseline and after 12 weeks consumption. But no significant change occurs in case of blood pressure.	In the participa-nts under supervis ion, there was not a notice--able change in blood pressure	(Díaz-Prieto et al., 2022)

The possible mechanism of reducing blood pressure could be the present of nitrile, thiocarbonate and isothiocyanate glycosides in *M. oleifera* leaves(Kumar Biswas et al., 2012). The other constituents in *M. oleifera* leaves called antioxidant that help in reducing oxidative stress which may leads to the decrease of blood pressure(Mbikay, 2012; Vergara-Jimenez et al., 2017). The phenolic extract from *M. oleifera* shows inhibitory activity to Angiotensin Converting Enzyme. It is done by interacting the disulfide bridges found in Angiotensin Converting enzyme that leads to the alteration of the enzyme structure that eventually led to lower the blood pressure. Some other constituents like tannins and flavonoid in a high amount result inhibitory activity on enzyme elastase, decarboxylase and Angiotensin converting enzyme which also result reduce in blood pressure(Chan Sun et al., 2020).

Chapter 5- Conclusion

There are some misconceptions regarding the use of plant-based medication of causing adverse side effects as the study done by (Neergheen-Bhujun et al., 2020) shows about 15.1% population of Mauitian does not consume *M. oleifera* due to the misconception of increasing blood pressure by using the plant. In the current world with 6 billion population, drugs and foods are not fully accessible to all the people. To solve the problem, plant-based food and medication could be a way to ensure better health which can be achieved through proving those misconception wrong. For this, more and more research work have to be done in this particular field with clinical trials showing the therapeutic effects of different medicinal plant on human. For the plant *M. oleifera*, we are working on two clinical trial-based articles to analyze the data on the basis of its effectiveness on hypertension from which one article clinical trials data shows significant effect on lowering the blood pressure and other shows not any significant change in blood pressure. So, we can't declare or decide the efficacy of *M. oleifera* on the basis of clinical trials data of these two articles. More clinical trials-based research requires for the plant to be declare as the plant to reduce blood pressure and there are huge scope remains as the research for the plant start in recent years. But the plant-based medication was used from the ancient time when drug for the disease like hypertension doesn't even exist. To reduce the drug-based side effects and dependency on drugs plant-based medication or implantation of plant-based diet should be included into our lifestyle.

References:

Aju, B. Y., Rajalakshmi, R., & Mini, S. (2019). Protective role of *Moringa oleifera* leaf extract on cardiac antioxidant status and lipid peroxidation in streptozotocin induced diabetic rats. *Heliyon*, *5*(12), e02935. https://doi.org/10.1016/j.heliyon.2019.e02935

Al-Asmari, A. K., Albalawi, S. M., Athar, M. T., Khan, A. Q., Al-Shahrani, H., & Islam, M. (2015). *Moringa oleifera* as an anti-cancer agent against breast and colorectal cancer cell lines. *PLoS ONE*, *10*(8). https://doi.org/10.1371/journal.pone.0135814

Anwar, F., Latif, S., Ashraf, M., & Gilani, A. H. (2007). *Moringa oleifera*: A Food Plant with Multiple Medicinal Uses. *Phytother. Res*, *21*, 17–25. https://doi.org/10.1002/ptr

Anzano, A., Ammar, M., Papaianni, M., Grauso, L., Sabbah, M., Capparelli, R., & Lanzotti, V. (2021). *Moringa oleifera* lam.: A phytochemical and pharmacological overview. In *Horticulturae* (Vol. 7, Issue 10). MDPI. https://doi.org/10.3390/horticulturae7100409

Beevers, G., Lip, G. Y. H., & O'brien, E. (n.d.). *The pathophysiology of hypertension*. www.bmjbooks.com

Chan Sun, M., Ruhomally, Z. B., Boojhawon, R., & Neergheen-Bhujun, V. S. (2020). Consumption of *Moringa oleifera* Lam Leaves Lowers Postprandial Blood Pressure. *Journal of the American College of Nutrition*, *39*(1), 54–62. https://doi.org/10.1080/07315724.2019.1608602

Chen, L., Deng, H., Cui, H., Fang, J., Zuo, Z., Deng, J., Li, Y., Wang, X., & Zhao, L. (2018). Oncotarget 7204 www.impactjournals.com/oncotarget Inflammatory responses and inflammation-associated diseases in organs. In *Oncotarget* (Vol. 9, Issue 6). www.impactjournals.com/oncotarget/

Chowdhury, M. A. B., Islam, M., Rahman, J., Uddin, M. T., Haque, M. R., & Uddin, M. J. (2021). Changes in prevalence and risk factors of hypertension among adults in Bangladesh: An analysis of two waves of nationally representative surveys. *PLoS ONE*, *16*(12 December). https://doi.org/10.1371/journal.pone.0259507

Chowdhury, M. A. B., Uddin, M. J., Haque, M. R., & Ibrahimou, B. (2016). Hypertension among adults in Bangladesh: Evidence from a national cross-sectional survey. *BMC Cardiovascular Disorders*, *16*(1). https://doi.org/10.1186/s12872-016-0197-3

Chowdhury, M. Z. I., Rahman, M., Akter, T., Akhter, T., Ahmed, A., Shovon, M. A., Farhana, Z., Chowdhury, N., & Turin, T. C. (2020). Hypertension prevalence and its trend in Bangladesh: Evidence from a systematic review and meta-analysis. *Clinical Hypertension*, *26*(1). https://doi.org/10.1186/s40885-020-00143-1

Cuellar-Núñez, M. L., Gonzalez de Mejia, E., & Loarca-Piña, G. (2021). *Moringa oleifera* leaves alleviated inflammation through downregulation of IL-2, IL-6, and TNF-α in a colitis-associated colorectal cancer model. *Food Research International (Ottawa, Ont.)*, *144*, 110318. https://doi.org/10.1016/j.foodres.2021.110318

Díaz-Prieto, L. E., Gómez-Martínez, S., Vicente-Castro, I., Heredia, C., González-Romero, E. A., Martín-Ridaura, M. D. C., Ceinos, M., Picón, M. J., Marcos, A., & Nova, E. (2022). Effects of *Moringa oleifera* Lam. Supplementation on Inflammatory and Cardiometabolic Markers in Subjects with Prediabetes. *Nutrients*, *14*(9). https://doi.org/10.3390/nu14091937

Fang, J., Chang, T., Wang, G., & Loustalot, F. (2020). Association between cost-related medication nonadherence and hypertension management among US adults. *American Journal of Hypertension*, *33*(9), 879–886. https://doi.org/10.1093/ajh/hpaa072

Gayatri balasaheb, -pachorkar, & Gayatri Shashikant Mr-Lade Harish Ravsaheb -Sayali Jagdish Chothave, -Dhakane. (2023). *Moringa oleifera: A Review Article on its Nutritional Properties and Prospects in Nepal*. www.ijnrd.org

Hall, J. E. (2016). Response to Morris et al. In *Circulation* (Vol. 133, Issue 9, p. 893). Lippincott Williams and Wilkins. https://doi.org/10.1161/CIRCULATIONAHA.115.017923

Huang, Q., Liu, R., Liu, J., Huang, Q., Liu, S., & Jiang, Y. (2020). Integrated Network Pharmacology Analysis and Experimental Validation to Reveal the Mechanism of Anti-Insulin Resistance Effects of *Moringa oleifera* Seeds. *Drug Design, Development and Therapy*, *14*, 4069–4084. https://doi.org/10.2147/DDDT.S265198

Jafarain, A., Asghari, G., & Ghassami, E. (2014). Evaluation of cytotoxicity of *Moringa oleifera* Lam. callus and leaf extracts on Hela cells. *Advanced Biomedical Research*, *3*(1), 194. https://doi.org/10.4103/2277-9175.140668

Khan, M., Yu, B., Rasul, A., Al Shawi, A., Yi, F., Yang, H., & Ma, T. (2012). Jaceosidin Induces Apoptosis in U87 Glioblastoma Cells through G2/M Phase Arrest. *Evidence-Based Complementary and Alternative Medicine : ECAM*, *2012*, 703034. https://doi.org/10.1155/2012/703034

Kou, X., Li, B., Olayanju, J. B., Drake, J. M., & Chen, N. (2018). Nutraceutical or pharmacological potential of *Moringa oleifera* Lam. In *Nutrients* (Vol. 10, Issue 3). MDPI AG. https://doi.org/10.3390/nu10030343

Krawczyk, M., Burzynska-Pedziwiatr, I., Wozniak, L. A., & Bukowiecka-Matusiak, M. (2022). Evidence from a Systematic Review and Meta-Analysis Pointing to the Antidiabetic Effect of Polyphenol-Rich Plant Extracts from Gymnema montanum,

Momordica charantia and *Moringa oleifera*. In *Current Issues in Molecular Biology* (Vol. 44, Issue 2, pp. 699–717). MDPI. https://doi.org/10.3390/cimb44020049

Kumar Biswas, S., Chowdhury, A., Das, J., Roy, A., & Zahid Hosen, S. (2012). PHARMACOLOGICAL POTENTIALS OF *MORINGA OLEIFERA* LAM.: A REVIEW. *IJPSR*, *3*(2), 305–310. www.ijpsr.com

Leone, A., Spada, A., Battezzati, A., Schiraldi, A., Aristil, J., & Bertoli, S. (2015). Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of *Moringa oleifera* leaves: An overview. In *International Journal of Molecular Sciences* (Vol. 16, Issue 6, pp. 12791–12835). MDPI AG. https://doi.org/10.3390/ijms160612791

Ma, J., & Chen, X. (2022). Advances in pathogenesis and treatment of essential hypertension. In *Frontiers in Cardiovascular Medicine* (Vol. 9). Frontiers Media S.A. https://doi.org/10.3389/fcvm.2022.1003852

Mbikay, M. (2012). Therapeutic potential of *Moringa oleifera* leaves in chronic hyperglycemia and dyslipidemia: A review. *Frontiers in Pharmacology*, *3 MAR*. https://doi.org/10.3389/fphar.2012.00024

Mills, K. T., Bundy, J. D., Kelly, T. N., Reed, J. E., Kearney, P. M., Reynolds, K., Chen, J., & He, J. (2016). Global disparities of hypertension prevalence and control. *Circulation*, *134*(6), 441–450. https://doi.org/10.1161/CIRCULATIONAHA.115.018912

Moura, M. C., Napoleão, T. H., Coriolano, M. C., Paiva, P. M. G., Figueiredo, R. C. B. Q., & Coelho, L. C. B. B. (2015). Water-soluble *Moringa oleifera* lectin interferes with growth, survival and cell permeability of corrosive and pathogenic bacteria. *Journal*

of Applied Microbiology, *119*(3), 666–676. https://doi.org/10.1111/jam.12882

Neergheen-Bhujun, V. S., Ruhomally, Z. B., Dunneram, Y., Boojhawon, R., & Chan Sun, M. (2020). Consumption patterns, determinants and barriers of the underutilised *Moringa oleifera* Lam in Mauritius. *South African Journal of Botany*, *129*, 91–99. https://doi.org/10.1016/j.sajb.2019.01.027

Olsen, M. H., Angell, S. Y., Asma, S., Boutouyrie, P., Burger, D., Chirinos, J. A., Damasceno, A., Delles, C., Gimenez-Roqueplo, A. P., Hering, D., López-Jaramillo, P., Martinez, F., Perkovic, V., Rietzschel, E. R., Schillaci, G., Schutte, A. E., Scuteri, A., Sharman, J. E., Wachtell, K., & Wang, J. G. (2016). A call to action and a lifecourse strategy to address the global burden of raised blood pressure on current and future generations: the Lancet Commission on hypertension. In *The Lancet* (Vol. 388, Issue 10060, pp. 2665–2712). Lancet Publishing Group. https://doi.org/10.1016/S0140-6736(16)31134-5

Paikra, B. K., Dhongade, H. K. J., & Gidwani, B. (2017). Phytochemistry and pharmacology of *Moringa oleifera* Lam. In *Journal of Pharmacopuncture* (Vol. 20, Issue 3, pp. 194–200). Korean Pharmacopuncture Institute. https://doi.org/10.3831/kpi.2017.20.022

Parvin, S., Abu Shuaib Rafshanjani, M., Abdul Kader, M., Afia Akhtar, M., Sharmin, T., & Parvin Assistant Professor, S. (2014). Phytochemical screening and studies of analgesic potential of *Moringa oleifera* Lam. stem bark extract on experimental animal model. *Shumaia Parvin et Al*, *4*(5), 128. https://doi.org/10.7439/ijpp

Randriamboavonjy, J. I., Loirand, G., Vaillant, N., Lauzier, B., Derbré, S., Michalet, S., Pacaud, P., & Tesse, A. (2016). Cardiac Protective Effects of *Moringa oleifera* Seeds

in Spontaneous Hypertensive Rats. *American Journal of Hypertension*, *29*(7), 873–881. https://doi.org/10.1093/ajh/hpw001

Razis, A. F. A., Ibrahim, M. D., & Kntayya, S. B. (2014). Health benefits of *Moringa oleifera*. In *Asian Pacific Journal of Cancer Prevention* (Vol. 15, Issue 20, pp. 8571–8576). Asian Pacific Organization for Cancer Prevention. https://doi.org/10.7314/APJCP.2014.15.20.8571

Roush, G. C., & Sica, D. A. (2016). Diuretics for hypertension: A review and update. In *American Journal of Hypertension* (Vol. 29, Issue 10, pp. 1130–1137). Oxford University Press. https://doi.org/10.1093/ajh/hpw030

Segers, P., Rietzschel, E. R., & Chirinos, J. A. (2020). How to Measure Arterial Stiffness in Humans. In *Arteriosclerosis, Thrombosis, and Vascular Biology* (Vol. 40, Issue 5, pp. 1034–1043). Lippincott Williams and Wilkins. https://doi.org/10.1161/ATVBAHA.119.313132

Siahaan, S. C. P. T., Santoso, B., & Widjiati. (2022). Effectiveness of *Moringa oleifera* Leaves on TNF-α Expression, Insulin Levels, Glucose Levels and Follicle Count in Rattus norvegicus PCOS Model. *Diabetes, Metabolic Syndrome and Obesity : Targets and Therapy*, *15*, 3255–3270. https://doi.org/10.2147/DMSO.S385492

Sreelatha, S., Jeyachitra, A., & Padma, P. R. (2011). Antiproliferation and induction of apoptosis by *Moringa oleifera* leaf extract on human cancer cells. *Food and Chemical Toxicology : An International Journal Published for the British Industrial Biological Research Association*, *49*(6), 1270–1275. https://doi.org/10.1016/j.fct.2011.03.006

Taher, M. A., Nyeem, M. A. Bin, Ahammed, M. M., Hossain, M. M., & Islam, M. N. (2017). *Moringa oleifera* (Shajna): the wonderful indigenous medicinal plant. *Asian*

Journal of Medical and Biological Research, *3*(1), 20–30. https://doi.org/10.3329/ajmbr.v3i1.32032

Thapa, K., Poudel, M., & Adhikari, P. (2019). *Moringa oleifera*: A Review Article on Nutritional Properties and its Prospect in the Context of Nepal. *Acta Scientific Agriculture*, *3*(11), 47–54. https://doi.org/10.31080/asag.2019.03.0683

Unger, T., Borghi, C., Charchar, F., Khan, N. A., Poulter, N. R., Prabhakaran, D., Ramirez, A., Schlaich, M., Stergiou, G. S., Tomaszewski, M., Wainford, R. D., Williams, B., & Schutte, A. E. (2020). 2020 International Society of Hypertension Global Hypertension Practice Guidelines. *Hypertension*, *75*(6), 1334–1357. https://doi.org/10.1161/HYPERTENSIONAHA.120.15026

Vergara-Jimenez, M., Almatrafi, M. M., & Fernandez, M. L. (2017). Bioactive components in *Moringa oleifera* leaves protect against chronic disease. In *Antioxidants* (Vol. 6, Issue 4). MDPI. https://doi.org/10.3390/antiox6040091

Xie, J., Qian, Y.-Y., Yang, Y., Peng, L.-J., Mao, J.-Y., Yang, M.-R., Tian, Y., & Sheng, J. (2021). Isothiocyanate From *Moringa oleifera* Seeds Inhibits the Growth and Migration of Renal Cancer Cells by Regulating the PTP1B-dependent Src/Ras/Raf/ERK Signaling Pathway. *Frontiers in Cell and Developmental Biology*, *9*, 790618. https://doi.org/10.3389/fcell.2021.790618

Zhou, B., Carrillo-Larco, R. M., Danaei, G., Riley, L. M., Paciorek, C. J., Stevens, G. A., Gregg, E. W., Bennett, J. E., Solomon, B., Singleton, R. K., Sophiea, M. K., Iurilli, M. L. C., Lhoste, V. P. F., Cowan, M. J., Savin, S., Woodward, M., Balanova, Y., Cifkova, R., Damasceno, A., … Zuñiga Cisneros, J. (2021). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a

pooled analysis of 1201 population-representative studies with 104 million participants. *The Lancet, 398*(10304), 957–980. https://doi.org/10.1016/S0140-6736(21)01330-1

Zhou, B., Perel, P., Mensah, G. A., & Ezzati, M. (2021). Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. In *Nature Reviews Cardiology* (Vol. 18, Issue 11, pp. 785–802). Nature Research. https://doi.org/10.1038/s41569-021-00559-8