Original Research Article

Mathematical Modelling (Seipr) and Epidemiological Applicability/Therapeutic and Pharmacological Efficacy of *Mangifera Indica* (Mi) *Linn.* Against Selected Recalcitrant Health Challenges in Third-World Countries.

Abstract:

Mango with the botanical name of Mangifera Indica (MI)*Linn. is* one of the traditionally used herb tree in the third world country used for different curative and prophylaxis measure for different health challenges. This article presents an updated information on its mathematical modeling using SEIPR theoretical/analytical methods and epidemiological applicability of therapeutic /pharmacological efficacy of *Mangifera indica* (MI) *linn.* against selected recalcitrant diseases in third-world countries**.** To introduce the mathematical model that connects all the necessary parameters and variables on the epidemiological applicability of therapeutic /pharmacological efficacy of the mango(*Mangifera Indica* (MI) *Linn)* leaf and stem bark to cure the ravaging health challenges . The basic reproductive number of the model was obtained. This parameter was obtained to show that, the use of the mango (*Mangifera Indica* (MI) *Linn)* leaf and stem bark can cure the he**alth challenges** mathematically such that, as the use of the mango leaf and stem bark increases, the rate of the ravaging health challenges among the populace reduces. It is a fact that the medicinal plant is a good source of medicine for developing countries especially in the third world like Africa and Asia, taking Nigeria as a case study. This write-up is premeditated from the fact that there should be a cure for recalcitrant ailments like high blood pressure, diabetes and etc. without the use of conventional medicine. We should be able to use the local herbs for the known health debacle without any side effects. As scientists, we decided to research various medicinal plants that can be used. During the process of search, mango leaf shines like a bright star and there is a need to make a thorough and further searchlight for the wonderful medicinal plant, because of its various therapeutic uses on ravaging **health challenges** in Nigeria and other third world countries.

Keyword; Pharmacologically, Therapeutic Efficacy, Mango (Mango (Mangifera Indica L.), Mathematical Modelling, Basic Reproductive Number.

Introduction

"Mangifera Indica (MI) *Linn.* has been an important herb in the traditional and indigenous medical systems for over 4000 years. *Mangifera Indica* (MI) *Linn.* belongs to the genus *Mangifera* which consists of about 30 species of tropical fruiting trees in the flowering plant family Anacardiaceae. According to various researcher, varied medicinal properties are attributed to different parts of the mango tree" [1]. One of the important chemical constituent isokated from the mango tree is Mangiferin.

"Various parts of the *Mangifera Indica* (MI) *Linn* plant are used as a dentifrice, antiseptic, astringent, diaphoretic, stomachic, vermifuge, tonic, laxative, and diuretic therapeutic activities. and to treat diarrhea, dysentery, anaemia, asthma, bronchitis, cough, hypertension, insomnia, rheumatism, toothache, leucorrhoea, hemorrhage and piles" [2]. "All *Mangifera Indica* (MI) *Linn* plant parts are used to treat abscesses, broken horn, rabid dog or jackal bite, tumor, snakebite, stings, datura poisoning, heat stroke, miscarriage, anthrax, blisters, wounds in the mouth, tympanitis, colic, diarrhea, glossitis, indigestion, bacillosis, bloody dysentery, liver disorders, excessive urination, tetanus, and asthma" [2].

Mangifera Indica (MI) *Linn* plant were domesticated separately in South and East Asia and other third world countries over centuries, resulting in two distinct genetic populations in modern mangoes – (1)the "Indian type" and (2) the "Southeast Asian type". Mangoes, but in a place like Nigeria , we have the Southeast Asian type. [3].

Plate 1. Mango tree(Mango (Mangifera indica L.)(4)

The chemical constituent of *Mangifera Indica* (MI) *Linn* leaf, stem, and bark is another important subject of discussion and the therapeutic importance of mango leaf and stem bark .Mangiferin, being a polyphenolic has antioxidant and glucosyl xanthone properties, it has a strong anti-oxidant, anti-lipid peroxidation, immunomodulation, cardiotonic, hypotensive, wound healing, anti-degenerative, and anti-diabetic therapeutic activities. Pharmacologically active hydroxylated xanthone(C-glycoside) is extracted from *Mangifera Indica* (MI) *Linn* plant at low/high concentrations from the stem, bark, and leaves [5]. Example of such substance is Allergenic urushiols i,e phenolic substances are present in the fruit peel which can trigger contact dermatitis in sensitized individuals.

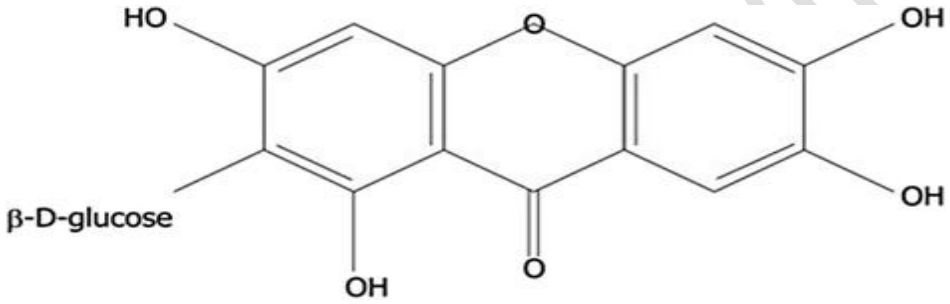

Fig 1a: Chemical structure of mangiferin[6].

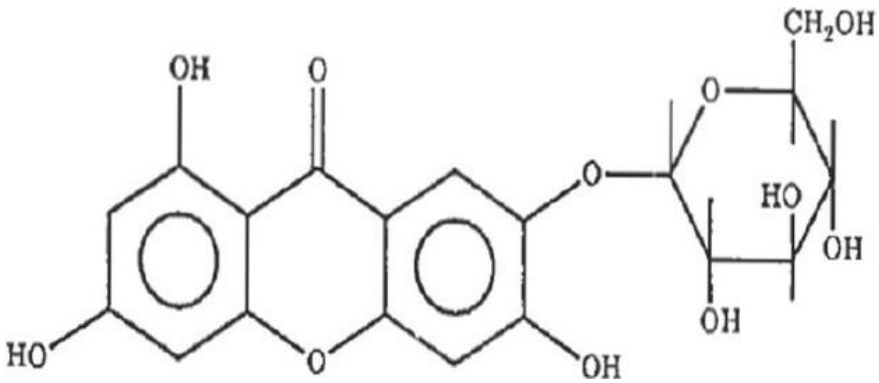

Fig 1b: Chemical structure of mangiferin[6].

"The leaf and flower of *Mangifera Indica* (MI) *Linn* plant possesses an essential oil containing humulene, ocimene, linalool, nerol, and many others. This essential oil has various pharmacological and therapeutic antecedents with various pharmaceutical index of relcacitract infections. The fruit pulp contains vitamins A and C, β-carotene,xanthophylls and unusual fatty acid, cis-9, cis-15-octadecadienoic acid" [5][6],

The extensive survey of literature revealed that **mangiferin from** *Mangifera Indica* (MI) *Linn.* has mangiferonic acid [Figure 2], hydroxymangiferin, polyphenols, and carotenes. Many different pharmacological activities, like antioxidant, radioprotective, immunomodulatory, anti-allergic, anti-inflammatory, antitumor, antidiabetic, lipolytic, anti bone resorption, monoamine oxidase-inhibiting, antimicrobial and antiparasitic, have been reported by some selected researcher.

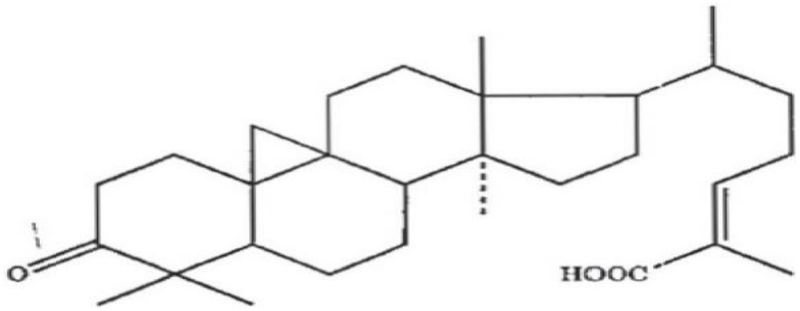

Fig 2: Structure of Mangiferonic acid(7)

Mangiferin is a (xanthone glycoside) major active constituent, derivatives of isomangiferin, tannins & gallic acid. Stem bark of *Mangifera Indica* (MI) contains protocatechic acid, Catechin, Epicatechin, Epigalocatetin, Mangiferin, Alanine, Glycine, γ-aminobutyric acid, kinic acid, shikimic acid, and the tetracyclic triterpenoids cycloart-24-en-3β,26diol, 3-ketodammar-24 (*E*)-en-20S,26-diol, C-24 epimers of cycloart-25 en 3β,24,27-triol and cycloartan-3β,24,27-triol.[1]. "It also contains Indicoside A and B, manghopanal, mangoleanone, friedelin, cycloartan-3β-30-diol and its derivatives, mangsterol, manglupenone, mangocoumarin, n-tetacosane, n-heneicosane, n-triacontane and mangiferolic acid and methyl ester, this validates it medicinal efficacy on the recalcitrant infection" (26).

1. Mathematical Formulation

The SEIPR mathematical model is partitioned into compartments of Susceptible population class (S), the Exposed population class (E), the Infected population class (I), the class of population who believes in the Therapeutic and Pharmacological Efficacy of mango leaf (P) and the temporary Recovered population class after being cured by the mango leaf (R). The proportion of Λare the incoming population into the susceptible class [8, 27,28,29]. This compartment reduces due to the expiration of the duration of pharmacological efficacy of the mango leaf and stem bark at the rate ω and also by a natural death at the rate of μ. The susceptible population

increases at the rate of δ due to the coming in of the people from the temporary recovered class as a result of the expiration of the duration of pharmacological efficacy of the mango leaf and stem bark at the rate ω. The susceptible population is also reduced due to the natural death rate μ and infection with a contact rate of infection β. The population dynamics of the exposed population class at the latent period grow with the incidence rate of βSI. This class reduces by the natural death rate μ and the occasional breakdown of the exposed people at the latent period into the infected class at the rate of σ. The class of people with the therapeutic and pharmacological efficacy of mango leaf, stem, and stem bark is denoted by P, but, because the efficacy of the mango leaf and stem bark is not one hundred percent such that it can wane at the rate of ω, the recovery class increases with temporary immunity at the rate of δ which are transferred back to the susceptible class and decreases by natural death rate μ.

The model equation is given in the form systems of ordinary differential equation as follows:

$$\frac{dS}{dt} = \Lambda + (1-m)A + \delta R(t) - \beta S(t)I(t) - (\mu+\eta)S(t), \qquad S(0) = S_0 \qquad (1)$$

$$\frac{dE}{dt} = \beta S(t)I(t) + \eta S(t) - (\mu+\sigma)E(t), \qquad E(0) = E_0 \qquad (2)$$

$$\frac{dI}{dt} = \sigma E(t) + cP(t) - (\mu+\tau)I(t), \qquad I(0) = I_0 \qquad (3)$$

$$\frac{dP}{dt} = mA + \tau I(t) - (\mu+\omega+c)P(t), \qquad P(0) = P_0 \qquad (4)$$

$$\frac{dR}{dt} = \omega P(t) - (\mu+\delta)R(t), \qquad R(0) = R_0 \qquad (5)$$

in which S(t), E(t), I(t), P(t) and R(t) represent the population of susceptible class, exposed class but not yet infected, the infected class, the therapeutic and pharmacological efficacy class and the temporary recovered class respectively. The parameters in the mathematical model are positive and the Tables 1 and 2 provide the definitions for the model parameters. The model assumes a varying population of N(t) so that N(t)= S(t)+E(t)+I(t)+P(t)+R(t) and it is given in the form; $N(t) = D + Ce^{-\mu t}$ for D = $\frac{\Lambda+A}{\mu}$. From the above system of equations (1) to (5), we use the following conceptthat: $\frac{dS}{dt} = 0$, $\frac{dE}{dt} = 0$, $\frac{dI}{dt} = 0$, $\frac{dP}{dt} = 0$ and $\frac{dR}{dt} = 0$. Also, let $\frac{S(t)}{N} = s(t)$, $\frac{E(t)}{N} = e(t)$, $\frac{I(t)}{N} = i(t)$, $\frac{P(t)}{N} = p(t)$ and $\frac{R(t)}{N} = r(t)$ to get the following re-scaled system of equations as:

$$\frac{ds}{dt} = \Lambda + (1-m)A + \delta r(t) - \beta s(t)i(t) - (\mu + \eta)s(t), \qquad s(0) = s_0 \qquad (6)$$

$$\frac{de}{dt} = \beta s(t)i(t) + \eta s(t) - (\mu + \sigma)e(t), \qquad e(0) = e_0 \qquad (7)$$

$$\frac{di}{dt} = \sigma e(t) + cp(t) - (\mu + \tau)i(t), \qquad i(0) = i_0 \qquad (8)$$

$$\frac{dp}{dt} = mA + \tau i(t) - (c + \mu + \omega)p(t), \qquad p(0) = p_0 \qquad (9)$$

$$\frac{dr}{dt} = \omega p(t) - (\mu + \delta)r(t), \qquad r(0) = r_0 \qquad (10)$$

Table 1: The interpretation of the parameters in the equations

Parameters	Definitions
Λ	recruitment rate of people into the susceptible class
A.	number of people with **r**ecalcitran**t Health Challenges**
m.	fraction of people who are using mango leaf, and stem bark cure the recalcitrant **Health Challenges**
(1 – m)	fraction of people who are not using mango leaf and stem bark to cure the recalcitrant **Health Challenges**
μ.	The mortality or death rate of the people
τ.	rate at which the infected are being cured with mango leaf and stem bark
β.	Transmission coefficient
ω.	rate at which the re – infection occurs
σ.	rate at which the exposed becomes infected with the recalcitrant i **Health Challenges.**
c.	rate at which the therapeutic and pharmacological efficacy of the mango leaf and stem bark occurs
δ.	rate at which re-infection of the **Health Challenges** occurs

η.	rate at which the susceptible infants are exposed to the diseases

Table 2: Variables and definition of sub-population used as variables

Variables	Definition
N_0	Initial value of the total population at time t
S_0	Initial value of the susceptible at time t
E_0	Initial value of the exposed at time t
I_0	Initial value of the infected at time t
P_0	Initial value of the therapeutic and pharmacological efficacy of mango leaf and stem bark at time t
R_0	Initial value of the temporary recovered at time t

In the next section, the basic reproductive number of the mathematical model shall be obtained using the next generation matrix [9].

2. BASIC REPRODUCTIVE NUMBER OF THE MODEL

It is easy to see that the region {(S,E,I,P,R):S> 0, E ≥ 0, I ≥ 0, P ≥ 0, R ≥ 0} is positively invariant for the model. Summing up the five equations in the model, we have,

$$\frac{d(S+E+I+P+R)}{dt} = \mu[\frac{A+A}{\mu} - (S+E+I+P+R)] \quad (11)$$

The basic reproductive number, R_0, is defined as the expected number of secondary cases produced by a single infection in a completely susceptible population. R_0 is a dimensionless number and not a rate which would have units of per time [27,28]. [10]Hefferman *et al* (2005) provided "a nice readable introduction for calculating R_0 in structured population models" [11, 12]. Using the next generation matrix method, the basic reproductive number is defined as the spectral radius of the next generation matrix of the form $\rho(FV^{-1})$, where F is a nonnegative

matrix that consists of the rate of new infections and matrix V consists of the rate of recovery, deaths and other transitions from one compartment to another given in the form $F = \frac{\partial F_i(x_0)}{\partial x_j}$ and $V = \frac{\partial V_i(x_0)}{\partial x_j}$where x_0 is the disease free equilibrium state and R_0 is the dominant eigenvalue of the matrix (FV^{-1}) [9]. Consider the system of equations (6) to (10). Let the vector disease states be represented by $X_i = (s, e, i, p, r)^T$, (i = 1,2,3,4,5) such that at the disease free equilibrium point $x_0 = (1,0,0,0, 0)$. Hence, the Jacobian matrix for equations (7) to (9) is given as

$$J = \begin{pmatrix} -(\mu+\sigma) & \beta & 0 \\ \sigma & -(\mu+\tau) & c \\ 0 & \tau & -(c+\mu+\omega) \end{pmatrix}, \quad (12)$$

with

$$F = \begin{pmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad (13)$$

and

$$V = \begin{pmatrix} \mu+\sigma & 0 & 0 \\ -\sigma & \mu+\tau & -c \\ 0 & -\tau & (c+\mu+\omega) \end{pmatrix}. \quad (14)$$

Therefore, the basic reproductive number of the mathematical model (6) to (10), denoted by R_0 is given in the form,

$$R_0 = \rho(FV^{-1}) = \frac{\sigma\beta(c+\mu+\omega)}{\mu^3+\mu^2(c+\omega+\sigma+\tau)+\mu(c\sigma+\omega\sigma+\omega\tau+\sigma\tau)+\omega\sigma\tau}. \quad (15)$$

In the context of epidemiology modelling, it is generally known that, if $R_0 < 1$, the disease-free equilibrium is locally asymptotically stable and the disease will be eradicated from the community with time among the populace using the curable measures like mango leaf.Thus, the basic reproductive number R_0 is a threshold quantity that determines when an infection invades a population or does not [13, 14, 15].

3. Results and Discussion

From the mathematical expressions obtained above, we can now discuss some infections that the mango leaf, stem and stem bark can be cured in third-world countries. The recalcitrant health challenges include diabetes, blood pressure, weight gain, etc. Mango (*Mangifera Indica* (MI) *Linn* leaf, stem fruit, contains pre-biotic dietary fiber, vitamins, minerals, and *poly-phenolic flavonoid* compounds. Mango is a very good source of Vitamin-A and *beta-carotene*, *alpha-carotene*, and *beta-cryptoxanthin*. Together; these compounds are known to have antioxidant properties and are essential for vision. Maintaining healthy mucus membranes and skin vitamin A is required. Consumption of natural fruits rich in carotenes is known to protect body from lung and oral cavity cancers.

Diabetes is one of the most common killer diseases in Nigeria and other third-world countries. We need to follow the school of thought that foreign medicine should not be used to control health challenges, we should be able to use our God's given medicinal plants for the control of diabetes [16,17]. The mango leaf and stem bark contain tannins and anthocyanidins which has pharmacological and therapeutic index in the treatment of diabetes mellitus. In powdered dry mango leaf, has pharmacological and therapeutic index in the treatment of angiopathy, retinopathy diabetes and hyperglycemia in the human brain. The pharmaceutical functional ingredient in the mango(*Mangifera Indica* (MI)*Linn*)leaf and stem bark should be mention for scholastic purposes. It contains 3 beta taraxerol which along with ethyl acetate. 3 beta taraxerol helps proper brain function during cerebral activity.

For pharmacological and therapeutic uses of mango (*Mangifera Indica* (MI)*Linn*)leaf against diabetes, it is advisable for diabetics patient to drink mango leaf tea 2 times a day. To demonstrate the pharmaceutical /efficacious index of mango(*Mangifera Indica* (MI) *Linn*)leaf, boil around 10 to 15 leaf of the mango tree, Leave the water overnight to pre-cool, and drink early in the morning [18]. Mango(*Mangifera Indica* (MI) *Linn*)leaf stimulates β-cells,to release insulin, this is proposed to be the mechanism of action of Mango(*Mangifera Indica* (MI) *Linn*)leaf, thereby stimulating different pharmaceutical/chemical constituent of mango(*Mangifera Indica* (MI) *Linn*)leaf like polyphenolics, flavonoids triterpenoids, and mangiferin [8].

Blood pressure is another health debacle in third-world countries like Nigeria. The use of conventional medicine like Visoprim(5mg), Nefediprine (5mg, and Amlodipine(5/10mg), may

not be the answer to the control of high blood pressure. It was observed that there is a hidden side effect generated by these conventional tablets as time goes on. i.e later in life, mango(*Mangifera Indica* (MI)*Linn.*) leaf and stem bark maybe the answer to this health challenges.

"Mango(*Mangifera Indica* (MI) *Linn*)leaf contains numerous nutrients which helps in reducing blood pressure levels. It is very effective in making the blood vessels strong which is essential in the treatment of varicose veins" [19].To demonstrate the pharmaceutical /efficacious index of Mango(*Mangifera Indica* (MI) *Linn*)leaf against blood pressure. Tea from Mango leaf should be taken two times a day. Boiled mango leaves. Drink either a warm /cold state early in the morning. To reduce the scourge of High blood pressure. It should be noted that patients with low blood pressure should take caution in the use of mango leaves to control low blood pressure; this may be a major health hazard. [20]. Fresh mango is a very rich source of potassium. Potassium is a very important component of cells and body fluids that helps control heart rate and blood pressure [21].

Weight gain and loss is one of the major challenges in both developing and developed countries in the world. Populate in the third-world countries may not be affected by these health challenges because of inadequate of fatty and pretentious foods, more carbohydrate food, this is not the same with the developed countries, with more fatty and proteinous food (Sandwiches and etc). Therapeutic use of mango leaf should be encouraged for the populate in developed countries. Mango (*Mangifera Indica* (MI) *Linn*) leaf and stem bark contains several categories of essential nutrient which may be helpful in weight reduction. Eg, Enzyme Papain. Papain boosts digestion, increases and eliminates the production of leptin hormone, to regulates the accumulation of fats in the body[20]. To demonstrate the pharmacological and therapeutic uses of mango leaves against weight loss, add mango leaves to your diet for around a month. Drink mango leaf tea early in the morning [21].

Dysentery/ Bleeding dysentery may be caused by different factors, it may be as a result of microbial ingestion, this includes *Staphylococcus aureus*, *Vibro cholera*, *Shigella bacteria or Entamoeba histolytica* and etc, this may be difficult to handle unless the use of various antibiotics. If there are no antibiotics, we can results in the use of natural medicinal plants like Mango leaf, stem and bark. The mango leaf contains many phytochemicals that are active against the different degrees of microorganisms. These phytochemicals are easily metabolized in the

human system. This natural arrays of chemical plays a major role in the physical well-being of the human system example of these arrays of natural chemical (phytochemicals) are tannins, Saponin, alkaloids, and flavonoids. To demonstrate the pharmaceutical /efficacious index of Mango(*Mangifera Indica* (MI) *Linn*)leaf and stem against Dysentery, the patient should take dry Powder mango leaf twice times in a day. if bleeding is observed along with Dysentery, take dry Powder mango leaves twice times in a day[22].

"A cough, also known as pertussis, is a voluntary or involuntary act that clears the throat and breathing passage of foreign particles, microbes, irritants, fluids, and mucus; it is a rapid expulsion of air from the lungs. Coughing can be done deliberately or as part of a reflex.Cough is an upper respiratory tract infection. In the conventional method of treatment of cough via Codeine, dextromethorphan, and other cough suppressants. Mango leaf and stem presents another alternative remedy in the treatment of cough. Boil two ot three leaves and small cut from the stem branch , pre-cool the extract and drink three times daily" [22]. The mechanisms of action of mango leave and stem were made possible because of the present of flavonoids.

However, Mangiferin is one of the important phytochemicals present in the leaves of a mango leaf. It shows a promising activity against, *Bacillus pumilus, B. cereus, Staphylococcus aureus, S. citreus, Escherichia coli, Salmonella agona, Klebsiella pneumoniae,* and *Saccharomyces cerevisiae*. The basic reason it has activity against cough and cold (23). To demonstrate the pharmaceutical /efficacious index of mango(*Mangifera Indica* (MI) *Linn*)leaf and stem against Cough and Cold, Add a little honey to the water containing three leaves, boil and drink. The mechanisms of action of mango(*Mangifera Indica* (MI) *Linn*)leaf and stem against Cough and Cold is bactericide/ bacteriostatic i.e totally inhibits and destroy all form of microbial habitat colonizing the throat area.[23].

Mango(*Mangifera Indica* (MI)*Linn*.leaf and stem bark contains various degree of vitamin for different physiological activity in the human system. They are present in appreciable amount. They include vitamin B_6 (pyridoxine), vitamin C, and vitamin E. Consumption of fruits rich in vitamin C like Mango(*Mangifera Indica* (MI) helps the body to develop resistance against infectious agents and scavenge harmful oxygen-free radicals(ROS). Vitamin B_6 is required for GABA hormone production in the brain i.e mental alertness and proper functioning of the cerebral cortex.there is abundant supply of Vitanin B6 *in Mangifera Indica* (MI). Vitanin B_6 also controls homocysteine levels in the blood, which may otherwise be harmful to blood vessels

resulting in CAD and stroke [23].this the basic reason *Mangifera Indica* (MI) rich Vitamin B_6 is used in traditional medication to reduce the scourge of high/ low blood pressure in the third world countries where little or less availability of conventional he medicine. Most of time people may not be able to assess free medical healthcare, *Mangifera Indica* (MI) may be the viral solution

Furthermore, *Mangifera Indica* (MI) contain some trace element like copper, manganese and zinc, this is another subject of discussion for the pharmacological and therapeutic properties of *Mangifera Indica* (MI) leaf and stem bark. "Copper is a co-factor for many vital enzymes, including cytochrome c-oxidase and superoxide dismutase Copper is also required for the production of health red blood cells. Mango peels are also rich in phytonutrients, such as the pigment antioxidants like carotenoids and polyphenols" [24].

"Mangiferin, an important chemical constituent of mango (*Mangifera Indica* (MI) leaf and stem bark mediates the down-regulation of NF-*x*B, suppresses NF-*x*B activation induced by inflammatory agents, including tumor nuclear factor (TNF), increases the intracellular glutathione (GSH) levels and potentiates chemotherapeutic agent-mediated cell death; this suggests a possible role in combination therapy for cancer".[24] "It is likely that these effects are mediated through mangiferin ROS quenching and GSH rising; increased intracellular (GSH) levels are indeed known to inhibit the TNF-induced activation of NF-*κ*B".[24,25,26].

Conclusion

Mangifera indica (MI) leaf and stem bark, has been an important herbal medicine potentials, useful to indigenous medical systems .Varied medicinal properties are attributed to different parts of mango leaves such as anti-diabetic, anti-oxidant, and anti-viral and etc. The mathematical concept in the work especially the calculation of the basic reproductive number of the mathematical model has helped us to understand the concept of the epidemiological applicability of therapeutic /pharmacological efficacy of *mangifera indica* (MI)*linn.* against selected recalcitrant health challenges in third-world countries. Pharmacologically and medicinally important chemicals such as mangiferin, polyphenolic and a glucosyl xanthone, have antioxidants, immune modulation, hypotensive, hypetensive and other activities. This paper encourages third-world countries to use *mangifera indica* (MI)*linn.*

NOTE:

The study highlights the efficacy of "Ayurved" which is an ancient tradition, used in some parts of Nigeria India, and Pakistan. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

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