Optimising Medicinal Plants Values Grown in Nigeria for Prevention, Controlling and Treatment of Infectious Diseases, Determinant Factors of Infant Mortality Using Mathematical Modelling Protégé

Oludare Temitope. Osuntokun[1*] and Adeyemi O. Binuyo[2]

[1]*Department of Microbiology, Faculty of Science, Adekunle Ajasin University, Akungba Akoko, Ondo State, Nigeria.*
[2]*Department of Mathematical Sciences, Faculty of Natural Sciences, Ajayi Crowther University, Oyo, Oyo State, Nigeria.*

Authors' contributions

This work was carried out in collaboration between both authors. Author OTO designed the activity of medicinal plants on infectious diseases for prevention, controlling and treatment of infectious diseases among infant and author AOB designed the materials and methods using first-order non-linear ordinary differential equations and numerical simulations of mathematical modelling protégé. Both authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Infant mortality is a challenge for third-world countries like Nigeria where there is little next to non-availability of conventional drugs, and if available, it is costly and out of the reach of the common populace. It is a fact that medicinal plant is a gift from Mother Nature, but its uses and efficacy have been overlooked over the century because of the over super-imposed of conventional drugs but its medicinal plants efficacy is still intact. The objectives of this work are to optimise medicinal plants values being grown in Nigeria, West Africa, in the prevention, control and treatment of infectious diseases which is a determinant factors of infant mortality using mathematical model protégés. the research/review scientific point of view. The x-rays features of this paper is to

_____

Corresponding author: Email: osuntokun4m@gmail.com, osuntokun4m@yahoo.com;

formulate and analyse a mathematical model that extends and complements the ones in the literatures by incorporating medicinal plant class denoted by M(t). Mathematical models are widely used to examine, explain and predict the dynamics of infectious diseases transmission. Models have played important roles in developing public health strategies for control and prevention of infectious diseases. The mathematical model is a system of first-order non-linear ordinary differential equations which are partitioned into five different compartments. Two equilibria states exist, the disease-free equilibrium and endemic equilibrium which are locally asymptotically stable if the basic reproductive number is less than one and unstable if the basic reproductive number is greater than one. Numerical simulations were performed using hypothetical values for the parameters used in the model. The model shows that an increase in the medicinal plants grown or found in the country leads to low disease prevalence among the susceptible infant population considered in this work. Therefore, our medicinal plants become a very alternative for the prevention, control, and treatment of infectious diseases to reduce or prevent infant mortality among infants, especially in rural areas. Also, this will elevate the knowledge from African trado-medical practice and rejuvenate our ethno-botanical properties and characteristics for future uses.

Keywords: Mathematical modelling; basic reproductive number; numerical simulation; infectious diseases; infants; Nigeria.

1. INTRODUCTION

A medicinal plant is any plant which, in one or more of its organs, contains substances that can be used for therapeutic purposes or which are precursors for the synthesis of useful drugs. This description makes it possible to distinguish between medicinal plants whose therapeutic properties and constituents have been established scientifically, and plants that are regarded as medicinal but which have not yet been subjected to a thorough scientific study.

Medicinal plant has been used for ages in the treatment of various infectious diseases and it was not known where or when plants first began to be used, but the connection between plants and health has existed for thousands of years [1]. There is limited documentation of medicinal plants used in the treatment of infants mortality/diseases in Nigeria, but several ethno-botanical studies focusing on medicinal plants have been documented all over the world [2-5].

Medicinal plants possess various arrays of chemical substances that support certain physiological and biochemical activities in the human system/body, they are known as phytochemicals or secondary metabolite which is the active core physiological and therapeutic ingredient in all plants. These chemicals are non-nutritive substances used to prevent, control and treat various infectious diseases, as well as provide disease preventive properties [6,7]. Pharmacological activity of medicinal plants resides in their secondary metabolites, which are relatively smaller in quantity in contrast to the primary molecules such as carbohydrates, proteins, and lipids. These metabolites have a clue to manufacture new structural types of antimicrobial and antifungal chemicals/agents that are comparatively safe to humans being [8].

Secondary metabolites have different classes with greater antimicrobial properties; they are flavonoids (flavones, flavonols, flavanols, isoflavones, anthocyanidins), phenolic acids (hydroxybenzoic, hydroxycinnamic acids), stilbenes, lignans, quinones, tannins, coumarins (simple coumarins, furanocoumarins, pyrano coumarins), terpenoids (sesquiterpene lactones, diterpenes, triterpenes, polyterpenes), alkaloids, glycosides, saponins, lectins, steroids, and polypeptides [9].

Medicinal plants produce a boundless quantity of secondary metabolites that have great antimicrobial activity [6]. Medicinal plant-produced low molecular weight antibiotics are classified according to two types, namely [1] phytoanticipins, which are involved in microbial inhibitory actions, and [2] phytoalexins, which are generally anti-oxidative and synthesized de novo by plants in response to microbial infection [7]. These compounds have copious mechanisms that underlie antimicrobial activity, e.g., disturbing microbial membranes, weakening cellular metabolism, control biofilm formation, inhibiting bacterial capsule production, attenuating bacterial virulence by controlling quorum-sensing, and reducing microbial toxin production [10]. All this antimicrobial activity helps to reduce and prevent the scourge and menace of infectious diseases,

A World Health Organization (WHO) expert group defined Traditional Medicine as the sum total of all knowledge and practices, whether explicable or not, used in diagnosis, prevention and elimination of physical, mental, or social imbalance and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing. In view of the fact that infant mortality/diseases are widely observed in Nigeria due to the attitude of mothers, to some illness which are supposed to be treated, non-availability of health care practitioners and the cost of accessing orthodox mode of treatment. It is paramount to document some ethno-botanicals used in the treatment of infant mortality/diseases in Nigeria, West Africa. The following infant diseases were treated with medicinal plant, they are Blood Shortage (Anaemia), Infant Constipation, Infant Convulsion, Infant Cough, Infant Diarrhea, Infant Dysentery, Jaundice, Helminthic infestation, Malaria, Measles, Small Pox/Chicken Pox, Teething.

The medicinal plants used for this treatment include *Sorghum bicolor* shoots,*Mangifera indica* and *Theobroma cacao, Annanasc omosus,* sweet orange, *Allium cepa*, *Allium sativum, Zingiber officinale, Xylopia aethiopica, Alstonia boonei, Perquatina nigrescence,* Matured unripe pawpaw,*Azadira chtaindica, Morinda lucida, Momordica charantia, Rauwolfia vomitoria,* indigofera, *Cajanus cajan* and stem of sugar cane, just to mention a few. Emphasis on the use of medicinal plants has been placed on the treatment rather than prevention of infectious diseases.

Infant mortality is the unconditional death of little children from ages 1 to 5. Some school of thought describes infant mortality as the death of an infant before his or her first birthday. The infant mortality rate is the number of infant deaths for every 1,000 live births. In 2013, the leading causes of infant mortality include birth defects [11]. Other leading causes of infant mortality include birth asphyxia, pneumonia, congenital malformations, term birth complications such as abnormal presentation of the fetus umbilical cord prolapsed, or prolonged labor, [12] neonatal infection, diarrhea, malaria, measles and mal-nutrition [13].

One of the most common preventable causes of infant mortality is smoking during pregnancy [14]. Lack of prenatal care, alcohol consumption during pregnancy, and drug use also cause complications which may result in infant mortality [15]. Many environmental factors and seasonal variation may contribute to infant mortality, such as the mother's level of education, environmental conditions, political and medical infrastructure [15]. Improving sanitation, access to clean drinkingwater, immunization against infectious diseases and the use of medicinal plants.

However, there exists in the literature considerable report in recent times on research work on the use of medicinal plants and their constituents in disease prevention. Babies born in low to middle income countries in sub-Saharan Africa like Nigeria are at the highest risk of neonatal death. Bacterial infections of the bloodstream, lungs, and the brain's covering (Meningitis) may be responsible for 25% of neonatal deaths. Newborns can acquire infections during birth from bacteria that are present in their mother's reproductive tract. The mother may not be aware of the infection. These bacteria can move up the vaginal canal into the amniotic sac surrounding the baby [16].

Seven out of ten childhood deaths are due to infectious diseases: acute respiratory infection, diarrhea, measles and malaria. Acute respiratory infection such as pneumonia, bronchitis and bronchiolitis account for 30% of childhood deaths; 95% of pneumonia cases occur in the developing world. Diarrhea is the second-largest cause of childhood mortality in the world, while malaria causes 11% of childhood deaths. Measles is the fifth-largest cause of childhood mortality [17].

Infant mortality rate (IMR) is the number of deaths per 1,000 live births of children under one year of age. The rate for a given region is the number of children dying under one year of age, divided by the number of live births during the year, multiplied by 1,000 [18].

The x-rays features of this paper is to formulate and analyse a mathematical model that extends and complements the ones in the literatures by incorporating medicinal plant class denoted by M(t). Mathematical models are widely used to examine, explain and predict the dynamics of infectious disease transmission and models of specific diseases of global importance have played important role in developing public health strategies for control and prevention of infectious diseases.

2. MATERIALS AND METHODS

2.1 Mathematical Modelling Protégé

2.1.1 Formulation of the mathematical model

We formulate a non-linear deterministic model for the transmission dynamics of the infectious diseases among the infants. The model subdivides the infant population into five different compartments depending on the epidemiological status of the infants. The compartments are Susceptible class S, Exposed class E, Infected class I, Medicinal plant used class M and the Recovered class R.

To indicate this mathematically, we have the following systems of ordinary differential equations as:

$$S^{'}(t) = \Lambda + (1-P)A + \delta R(t) - \beta S(t)I(t) - (\mu + \eta)S(t); \tag{1}$$

$$E^{'}(t) = \beta S(t)I(t) + \eta S(t) - (\mu + \sigma)E(t); \tag{2}$$

$$I^{'}(t) = \sigma E(t) - (\mu + \tau)I(t); \tag{3}$$

$$M^{'}(t) = PA + \tau I(t) - (\mu + \omega)M(t); \tag{4}$$

$$R^{'}(t) = \omega M(t) - (\mu + \delta)R(t). \tag{5}$$

The following assumptions were considered to formulate the above mathematical model.

1. All susceptible infants can be exposed and infected through a direct contact with an infected infant in the community.
2. Infants are only born into the susceptible class.
3. Birth rate is not equal to the death rate.
4. Susceptible infants get infected with the infectious diseases at a rate proportional to the susceptible population.
5. All parameters used in the mathematical model are non-negative.
6. Some infectious diseases are re-infected in the community among the infants.

The Table 1 below shows the definitions and the hypothetical values of the parameters used in the formulation of the mathematical model.

Table 1. Parameter hypothetical values for the model

Parameters	Definition	Hypothetical values	Source
Λ	rate of newborn infants into the susceptible infant class	100	Estimated
P	fraction of infants who are given herbal medicine plants	0.305	Estimated
A	number of infants with infectious diseases	1500	Binuyo (2014)[19]
μ	mortality or death rate of the infants in the community	0.2	Assumed
δ	rate at which re-infection of the infectious diseases occur	0< δ < 1	Binuyo (2012)[20]
β	rate of transmission of the infectious diseases in the community	0.5	Assumed

Parameters	Definition	Hypothetical values	Source
η	rate at which the susceptible infants are exposed to infectious diseases	0.4	Assumed
σ	rate at which the exposed infants become infected with infectious diseases	0.1	Binuyo (2012)[20]
τ	rate at which infected infants are treated, controlled and prevented from infectious diseases	0.35	Binuyo (2014)[19]
ω	rate at which the efficacy of the herbs reduces leading to re-infection of the infectious diseases in the community.	0.0182	Assumed
S_0	initial value of susceptible infant class with time	1.6568	Estimated
E_0	initial value of exposed infant class with time	4.4367	Estimated
I_0	initial value of infected infant class with time	0.8066	Estimated
M_0	initial value of medicinal plant used infant class with time	5.8356	Estimated
R_0	initial value of recovered infant class with time	4.0856	Estimated

2.1.2 Equilibrium states of the mathematical model

The mathematical model (1) – (5) exhibits two states of equilibrium i.e. disease free equilibrium and the endemic equilibrium such that $\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dM}{dt} = \frac{dR}{dt} = 0$.

Solving equations (6) – (10) below,

$$\Lambda + (1-P)A + \delta R(t) - \beta S(t)I(t) - (\mu + \eta)S(t) = 0; \tag{6}$$

$$\beta S(t)I(t) + \eta S(t) - (\mu + \sigma)E(t) = 0; \tag{7}$$

$$\sigma E(t) - (\mu + \tau)I(t) = 0; \tag{8}$$

$$PA + \tau I(t) - (\mu + \omega)M(t) = 0; \tag{9}$$

$$\omega M(t) - (\mu + \delta)R(t) = 0. \tag{10}$$

We obtain the following results;

(i) Disease free equilibrium (DFE) i.e. in the absence of any infection (I = 0), then the disease free equilibrium points are:

$$(S^*, E^*, I^*, M^*, R^*) = (\frac{\Lambda + (1-P)A}{\mu + \eta}, 0, 0, 0, 0) \tag{11}$$

(ii) The Endemic Equilibrium State (EE) i.e. in the presence of the infection (I ≠ 0), we obtain;

$$S^* = \frac{(\mu + \sigma)(\mu + \tau)I^*}{\sigma(\beta I^* + \eta)}, E^* = \frac{(\mu + \tau)I^*}{\sigma}, M^* = \frac{PA + \tau I^*}{(\mu + \omega)}, R^* = \frac{\omega(PA + \tau I^*)}{(\mu + \delta)(\mu + \omega)} \tag{12}$$

For I^* is the positive root of the quadratic equation $AI^{*2} + BI^* + C = 0$ where

$$A = \beta \omega \tau (\mu + \delta)(\mu + \omega)(\mu + \sigma)(\mu + \tau) - \beta \sigma \delta \omega \tau \sigma \omega \tau \tag{13}$$

$$B = \omega\tau(\mu+\delta)(\mu+\omega)(\mu+\eta)(\mu+\sigma)(\mu+\tau) - PA\tau\omega\delta\omega\sigma\beta - \sigma\tau\omega\delta\omega\tau\eta - (\Lambda+A-PA)(\mu+\delta)(\mu+\omega)\omega\tau\sigma\beta \quad (14)$$

$$C = \eta\omega\tau\sigma(\mu+\delta)(\mu+\omega)(\Lambda+A-PA) + PA\sigma\tau\omega\eta\delta\omega \quad (15)$$

With these values for S*, E*, I*, M* and R*, the positivity and uniqueness of the endemic equilibrium are guaranteed if and only if $R_0 > 1$ where R_0 is the basic reproductive (21) number given in the form;

$$R_0 = \frac{\sigma\beta}{(\mu+\sigma)(\mu+\tau)} \quad (16)$$

In the endemic disease state, the number of infected infants is strictly positive and constant. So, if some of the solutions of the system of equation I (t) approach as time goes to infinity, the number of infective will remain strictly positive for a long time and approximately equal to me (t). Thus, the disease remains in the population and becomes endemic except adequate measures are done to control or prevent the rapid spread of the disease among the infant population. Therefore, in the event of an epidemic, the theoretical determination of condition that can make R_0 less than unity is of great public health interest such that the disease can be greatly reduced or eventually eradicated among the infant population [22].

2.1.3 Numerical simulations of the model

Numerical simulations were carried out to graphically explain the long term effects of preventing, controlling and treating on the infectious diseases determinant factor among the infants using the medicinal plants grown in Nigeria. In order to support the analytical results, graphical representations showing the time graphs of different state variables are provided.
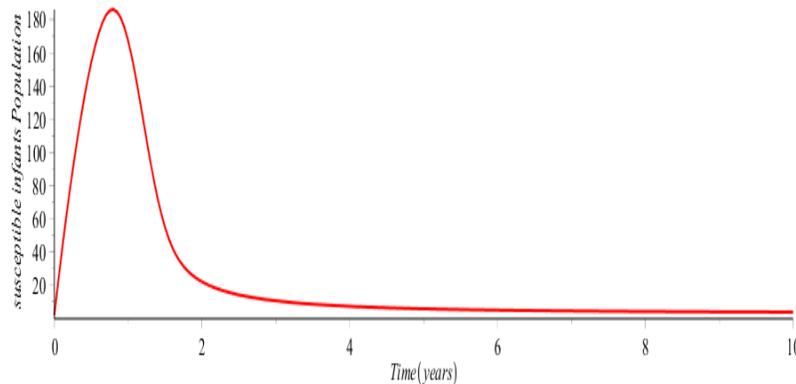

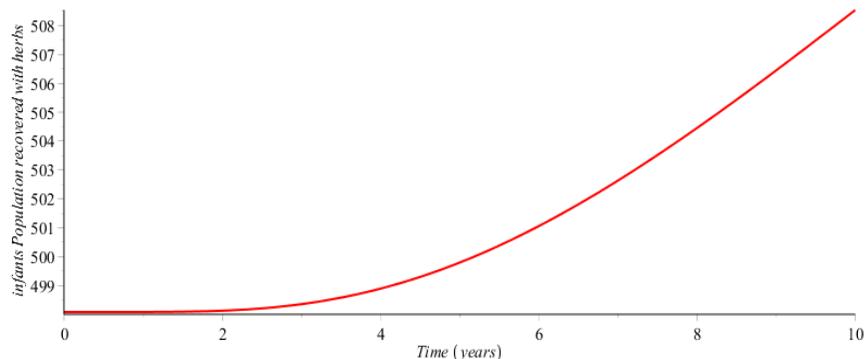**Fig. 1. Simulation of susceptible infant's population**

Fig. 2. Simulation of Recovered Infants Population from infectious diseases using medicinal plants (Herbs)
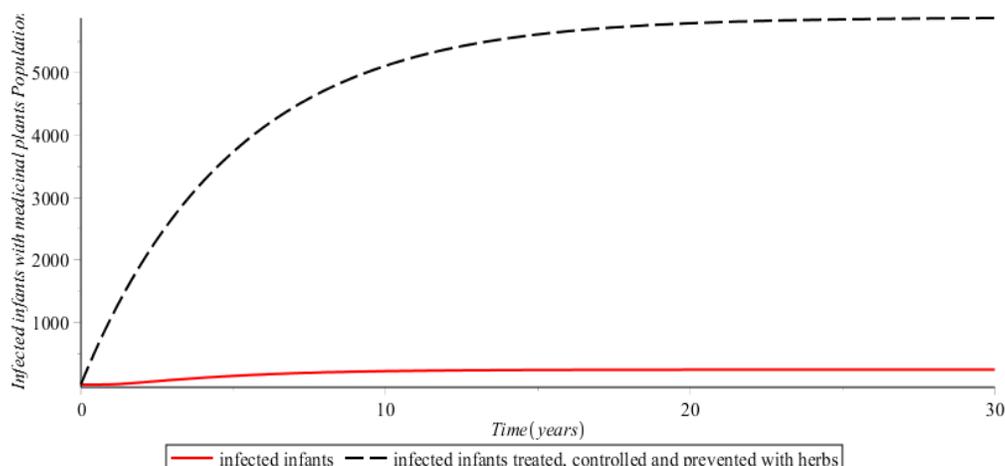
Fig. 3. Simulation of infected infants treated, controlled and prevented with medicinal plants

3. RESULTS

Numerical simulations were carried out to graphically illustrate the long term effect of controlling the dynamics of infectious diseases determinant factor using the medicinal plants (herbs) among the infant mortality. In order to support the analytical results, graphical representations showing the time graphs of different state variables are provided.

Fig. 1 is the diagram showing the dynamics of the susceptible infant population. The susceptible population increases initially as the newborns are introduced into the community and later decreases as time increases. This decrease was possibly because of the high rate of introduction of the medicinal plants in order to control, prevent and treat the infected infants among the susceptible population of the infants.

Fig. 2 shows the graph of the infant population that are recovered from the infectious diseases determinant factor using the medicinal plants. It is observed that as the rate of infectious diseases determinant factor increases, the infant population of the recovered infants shows some rapid increase due to the treatment of the infants with the medicinal plants among the infected infants.

Fig. 3 shows the graph of the combination of the infected infants and the infants treated prevented and controlled with the medicinal plants. Observe that, as the population of the infected infants

increases, the population of the infants that are using medicinal plants are increasing with time.

Tables 2 & 3 show the various medicinal plants that are used to prevent, control and treat infectious diseases determinant factor among the infant which can reduce the infant mortality. The medicinal plants were *Sorghum bicolor* shoots, *Mangifera indica* and *Theobroma cacao, Annanas comosus,* sweet orange, *Allium cepa, Allium sativum, Zingiber officinale, Xylopia aethiopica, Alstonia boonei, Perquatina nigrescence,* Matured unripe pawpaw, *Azadira chtaindica, Morinda lucida, Momordica charantia, Rauwolfia vomitoria,* indigofera, *Cajanu scajan.*

4. DISCUSSION

The objective of this work is to optimise medicinal plants value being grown in Nigeria, West Africa, in the prevention, control and treatment of Infectious diseases which is a determinant factor of infant mortality using different mathematical model protégé as the research/review scientific point of view. The x-rays features of this paper is to formulate and analyse a mathematical model that extends and complements the ones in the literatures by incorporating medicinal plant class denoted by M(t). Mathematical models are widely used to examine, explain and predict the dynamics of infectious disease transmission and models of specific diseases of global importance have played important role in developing public health strategies for control and prevention of infectious diseases.

Table 2. Selected profile of plants used in the control & prevention of infant mortality/diseases

S/N	Botanical names	Family	Common name	Local names	Plant parts used	Medicinal uses
1.	*Sorghum bicolor*	Poaceae	Guinea corn	Oka baba (Y)	Shoots, Leaves	Blood tonic, malaria, fever
2.	*Mangifera indica*	Anacardiaceae	Mango tree	Mangoro (Y)	Leaves, Barks	Malaria, fever, Anaemia
3.	*Theobroma cacao*	Sterculiaceae	Cocoa	Koko (Y)	Leaves, Barks	Blood tonic, tooth ache
4.	*Annanas comosus,*	Bromeliaceae	Pineapple	OpeOyinbo (Y)	Fruits	Malaria, Dysentery
5.	*Xylopia aethiopica*	Annonaceae	Ethiopian pepper	Eeru (Y)	Fruits	Cough, convulsion, stomach ache
6.	*Allium sativum & Allium cepa*	Liliaceae	Garlic	AlubosaAyuu (Y)	Bulbs	Convulsion
7.	*Zingiber officinale*	Zingiberaceae	Ginger	Atale (Y)	Rhizomes	Fever, malaria, digestive disorder, liver disease, typhoid.
8.	*Alstonia boonei*	Apocynaceae	Stool wood	Ahun (Y)	Leaves, Barks	Fever, Convulsion, Diarrhoea
9.	*, Perquatina nigrescence*	Periplocaceae	African parquatina	Ogbo (Y)	Leaves	Anti-anaemic, dysentery, stomach disorber, skin disease
10.	*Azadira chtaindica*	Meliaceae	Neem tree	Dongoyaro (H) Igikasia (Y)	Leaves, Stem	Dysentery, Fever
11.	*Morinda lucida*	Rubiaceae	Brime stone tree	Oruwo (Y)	Leaves	Jaundice, fever, malaria
12.	*Momordica charantia*	Cucurbitaceae	African cucumber	Ejinrin were (Y)	Leaves	Convulsion, Disorder, measles, chicken pox
13.	*Rauwolfia Vomitoria*(Benth.) Swizzlestick	Apocynaceae	Serpent wood	Asofeyeje (Y)	Leaves	Nervous disorder, jaundice, scabies, diarrhoea
14.	*Theobroma cacao*	Sterculiaceae	Cocoa	Koko (Y)	Leaves, Barks	Blood tonic, tooth ache
15.	*Vernonia Amygdalina*	Asteraceae	Bitter leaf	Ewuro (Y)	Leaves, Stem	Stomach disorder, dysentery, skin infection,

S/N	Botanical names	Family	Common name	Local names	Plant parts used	Medicinal uses
	Schreb.					malaria
16.	*Aframomum melegueta* (Sonn.) K. Schum	Zingeberaceae	Alligator pepper	Ataare (Y)	Fruits	Small Pox, Chicken Pox, Cough
17.	*Cajanusc ajan*(L.) Millsp.	Mimosaceae	Pigeon Pea	Otili (Y)	Leaves, Seeds	Small pox, Measles
18.	*Carica papaya L.*	Caricaceae	Pawpaw	Ibepe (Y)	Leaves	Malaria, Jaundice, Convulsion
19.	*Cymbopogon citrata*(DC.) Strapt.	Poaceae	Lemon grass	Kookooba (Y)	Leaves	Malaria, Cough
20.	*Garcinia kola* Heckel	Gutiferae	Bitter Kola	Orogbo (Y)	Nuts	Cough, Catarrh, Jaundice

Source; Fatoba et al,. 2018 [23]

Table 3. Enumeration of the Medicinal plants recipes for the treatment of various infant diseases

s/n	Disease condition	Recipes	Modes of Administration and Dosage
1)	Blood Shortage (Anemia)	*Sorghum bicolor* shoots, barks of *Mangifera indica* and *Theobroma cacao* are boiled together for 30 minutes with 2 liters of water, two tins of milk and 4 cubes of sugar are added to the herbal preparation	5 ml of the decoction taken orally thrice daily
2)	Infant Constipation	The juice of *Annanas comosus* and sweet orange are extracted for drinking.	The Juice is taken orally; 0-12 months old taken 5 ml thrice daily; 1-5years old taken 5 ml five times daily.
3)	Infant Convulsion	*Allium cepa*, *Allium sativum* and *Zingiber officinale* are ground together. The ground material is mixed with palm oil.	The mixture is applied topically all over the body of the baby and should be allowed to enter the eyes. About 21/2 ml is given orally to the affected child
4)	Infant Cough	The fruits of *Xylopia aethiopica* are added to fried oil. The fruits are then separated after 8 minutes and sugar is then added to the extract.	It is taken Orally by licking.
5)	Infant Diarrhoea	The leaves of *Alstonia boonei* is squeezed to obtain the juice.	The Juice is Orally by using 5 ml of the juice thrice daily
6)	Dysentery	Leaves of *Perquatina nigrescence* are squeezed. The juice extracted is mixed with a pint of salt.	5 ml of the juice taken orally every three hours
7)	Jaundice	Matured unripe pawpaw is cut into pieces and soaked in fermented maize water (Omiidun) for three days.	2.5ml taken orally five times daily
8)	Helminthic infestation	The leaves of *Azadira chtaindica* is squeezed with water. Lime and garlic are added to the infusion.	10 ml of the infusion taken orally twice daily
9)	Malaria	Extract of the leaves of *Morinda lucida* is squeezed out using water	5 ml taken orally thrice daily
10)	Measles	The leaves of *Momordica charantia* is boiled in water	The decocted material is used to bathe every day and night until the measles cure.
11)	Small Pox/Chicken Pox	The leaves of *Rauwolfia vomitoria,* indigofera and *Cajanus cajan* are boiled in water for 45minutes.	It is taken orally, 15 ml four times daily; the decoction is also used for bathing
12)	Teething	The juice is extracted from the stem of sugar cane	Taken orally (5 ml) every three hours.

Source; Fatoba et al,. 2018 [23]

Prevention and chronic disease management are proactive approaches to health care that stresses prevention at different points along the health care continuum. Health promotion and disease prevention strategies focus on keeping people well and preventing diseases from occurring. These strategies are referred to as primary prevention activities. Prevention is categorized into three levels.

Primary Prevention, which seeks to reduce the number of new cases of a disorder or illness. At this level of prevention we have: the health promotion/education, and specific protective measures (such as immunization). Secondary Prevention, which seeks to lower the rate of established cases of a disorder or illness in the population (prevalence). This level essentially involves measures that ensure early diagnosis (such as screening) and prompt management. Tertiary Prevention, which seeks to decrease the amount of disability associated with an existing disorder. This level involves the Disability limitation and Rehabilitation.

Disease prevention should focus on strategies that reduce the risk of disease, identify risk factors, or detect disease in its early, most treatable stages. Examples of disease prevention activities include well-baby visits, immunizations, calcium and Vitamin D supplements to reduce the risk of osteoporosis, blood pressure and cholesterol assessments during annual health exams, and screening for illnesses such as breast, cervical, colorectal and prostate cancer [24,25,26].

Prevention and treatment of infant mortality is one of the basic issues in the review, medicinal plants are the magical bullet to prevent and treat basic causes of infant mortality. Medicinal plant can be classified into, primary and secondary prevention strategy which is under the scope of this review work. This is the reason; mechanism of action of this plant must be dealt with, to illustrate the action of medicinal plants on recalcitrant infectious diseases. Some of the mechanisms are as follows, Inhibition of Biofilm Formation, Inhibition of Cell Wall Construction, Inhibition of Prokaryotic DNA Replication and Inhibition of Energy Production. Mechanism of action otherwise known as the modus operandi of medicinal plants against infectious diseases should be discussed in the context of this review. If the medicinal plants not reactive against the medicinal plants, then the issue at hand will be in jeopardy. There is need to discuss that activity of

it modus operandi against infectious diseases. However, medicinal plant activity are Promote Cell Wall Disruption and Lysis, Phenolic compounds are a family of aromatic rings consisting of a hydroxyl functional group (-OH) which is alleged to absolute toxicity to microorganisms, although increased reactions of hydroxylation result in microbial cell lysis [27]. Example are Quercetin, Rutin, Naringenin, sophoraflavanone, Tiliroside, 2, 4, 6-trihydroxy-30-methyl chalcone, etc

Inhibition of Biofilm Formation is one of the key features of bacteria developing biofilms are generally 100–1000 times more resistant to antimicrobial drugs while related to their usual plank tonic forms [28]. Interestingly, numerous researchers have described how flavonoids cause the aggregation of multicellular composites of bacteria and inhibit bacterial growth after aggregation, which indicates that flavonoids are potent antibiofilm compounds. The bioactive flavonoids such as galangin [29]: isovitexin [30], EGCG and 3-O-octanoyl-epicatechin [31], as well as 5, 7, and 40-trihydroxyflavanol [32]. Induce pseudo multicellular aggregation of *S. aurous* and *S. mutans* [33].

Inhibition of Cell Wall Construction is another way to eradicated bacteria in infectious diseases. Bacterial cell wall is accountable for osmoregulation, respiration, the transport mechanism, and biosynthesis of lipids. For the execution of these functions, membrane integrity is very important, and its disruption can directly or indirectly cause metabolic dysfunction eventually leads to bacterial death. Catechins [34]. Attract lipid bilayers of the membrane which involves the following mechanisms [35]. Catechins form hydrogen bonds, which attract polar head groups of lipids at the membrane edge. Epicatechin [36] and epigallocatechin gallate [37]. Alter phospholipids, which can alter structural changes in the cell membrane [38].

Inhibition of Prokaryotic DNA Replication is another major tool to prevent infectious diseases. Alkaloids are nitrogenous compounds characterized by their alkaline nature, which aids the inhibition of cell respiration, intercalates with DNA, and inhibits various enzymes involved in replication, transcription, and translation [39]. Plant-based bioactive compounds such as quercetin [40], nobiletin [41], myricetin [42], tangeritin [43] genistein [44], apigenin [45], chrysin [46], kaempferol [47], and 3, 6, 7, 30, 40-

pentahydroxyflavone [48] have been recognized as noteworthy DNA gyrase inhibitors, which are essential for DNA replication in prokaryotes including *V. harveyi, B. subtilis, M. smegmatis, M. tuberculosis,* and *E. coli* [49].

Inhibition of Energy Production should be discussed to prevent and treat infectious diseases. Energy production or ATP synthesis is the supreme vital requirement for the existence and development of bacteria as these chemicals are the main source of living systems. The treatments of flavonoids such as isobavachalcone [50] and 6 prenylapigenin [51] with S. aureus cause membrane depolarization, resulting in bacterial cell wall lysis [52]. Similarly, licochalcones inhibited oxygen consumption in M. luteus, interrupting the electron transport system eventually killing the bacteria [53]. It has been described that flavonoids such as baicalein [54], morin [55], silibinin [56], quercetin [57], isoquercetin [58], quercitrin [59], and silymarin [60] can constrain the F1FO Apace system of E. coli and result in the obstruction of ATP synthesis [61].

Inhibition of Bacterial Toxins, It is noteworthy that catechins and other flavonoids can cause bacterial cell wall destruction, resulting in an inability to discharge toxins [62]. Catechins [63], pinocembrin, kaempferol, EGCG [64], gallocatechingallate [65], kaempferol-3-O-rutinoside [66], genistein [67], quercetin glycoside [68], and andproanthocyanidins [69] are suggested to neutralize bacterial toxic factors initiating from *V. cholerae, E. coli, S. aureus, V. vulnificus, B. anthracis, N. gonorrhoeae, and C. botulinum* [70].

Bacterial hyaluronidases are enzymes formed by both Gram-positive and Gram-negative bacteria and directly interact with host tissues, causing the permeability of connective tissues and reducing the viscosity of body fluids due to hyaluronidase-mediated degradation [71]. Flavonoids such as myricetin [72] and quercetin [73] have been identified as hyaluronic acid lyase inhibitors in Streptococcus equisimilis and Streptococcus agalactiae [74,75].

5. CONCLUSION

We conclude that effective control, prevention and treatment of infectious diseases determinant factor among infants by medicinal plants have greater benefits and reduce the rapid progression of infection in the community. It was observed that the mathematical model produced an asymptotically stable population such that the infectious diseases determinant factor among the infants die out from the infant population as time increases when adequate measures (medicinal herbs in large quantity) are encouraged, administered and used for the infants in appropriate quantity.

ORCID

Osuntokun Oludare temitope-
https://orcid.org/0000-0002-3954-6778.

Osuntokun Oludare temitope- Web of Science Researcher ID;L-4314-2016

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Faleyimu OI, Oluwalana SA. Medicinal value of forest plant seeds in Ogun State, Nigeria. World Journal of Biological Research. 2008;1(2):1-6.
2. Cox PA. The seven pillars of ethnomedical wisdom. Ethnobotany. 2005;17:24-34.
3. Kumar A, Tewari DD, Sharma R, Pandey VO. Practices of folk phytoveterinery in Devipatan division, Uttar Pradesh. India Journal Natcon. 2005;17(1):153-161.
4. Singh NK, Singh DP. Ethnobotanical survey of Balrampur. Flora- fauna. 2001; 7(2):59-66.
5. Wang, Yu-hua, Pei, SJ, Xu JC. Sustainable management of medicinal plant resources in China: Literature review and implications. Resources Science. 2005;24(4):81-88.
6. Belman S. Onion and garlic oils inhibit tumor promotion. Carcinogenesis. 1983; 4(8):1063–1065.
7. Botterweck AAM, Verhagen H, Goldbohm RA, Kleinjans J, Van den Brandt PA. Intake of butylated hydroxyanisole and

butylated hydroxytoluene and stomach cancer risk: Results from analyses in the Netherlands cohort study. Food Chem Toxicol. 2000;38:599–605.

8. Ngono Ngane A, Biyiti L, Bouchet P, Nkengfack A, Amvam Zollo PH. Antifungal activities of *Piper guineense* of Cameroun. Fitoter. 2003;4(5):464–468.

9. Antony ML, Singh SV. Molecular mechanisms and targets of cancer chemoprevention by garlic-derived bioactive compound diallyltrisulfide. Indian J Exp Biol. 2011;49(11):805–816.

10. Alam A, Khan N, Sharma S, Saleem M, Sultana S. Chemopreventive effect of Vitisvinifera extract on 12-O-tetradecanoyl-13-phorbol acetate-induced cutaneous oxidative stress and tumor promotion in murine skin. Pharmacological Research. 2002;46(6):557–564.

11. Mathews TJ, MacDorman MF, Menacker F. Infant mortality statistics from the 1999 period linked birth/infant death data set"(PDF). National Vital Statistics Reports. 2002;50(4):1–28.
DOI: 10.1037/e 558952006-001.

12. Complications -- the Basics. WebMD. Retrieved 2017-03-16. Basic Labor and Delivery; 2017.

13. Infant Mortality, Newborn Health. Women and Children First; 2017. Retrieved 2017-04-25

14. Hall ES, Venkatesh M, Greenberg JM. A population study of first and subsequent pregnancy smoking behaviors in Ohio. Journal of Perinatology. 2016;36(11): 94895 3.
DOI:10.1038/jp.2016.119

15. Genowska A, Jamiołkowski J, Szafraniec K, Stepaniak U, Szpak A, Pająk A. Environmental and socio-economic determinants of infant mortality in Poland: an ecological study. Environmental Health. 2015;14:61.
DOI:10.1186/s12940-015 0048-1.

16. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE. Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis.PLOSMedicine.2013;10(8):e1001 502.
DOI:10.1371/journal.pme.1001502. PMC 3 747 995

17. Nussbaum M. Creating capabilities. The Belknap Press of Harvard University Press; 2011.
ISBN 978-0-674-05054-9

18. Andrews KM, Brouillette DB, Brouillette RT. Mortality, Infant. Encyclopedia of Infant and Early Childhood Development. Elsevier. 2008;343–359.
DOI:10.1016/B978-012370877-9.00084-0. ISBN 9780123708779.

19. Binuyo, Adeyemi O. A deterministic model for the transmission dynamics of infectious diseases among infants. Elixir Appl. Math. 2014;78 (2015):29761-29764.

20. Binuyo AO, Komolafe O. Stability Analysis of an SEIRC epidemic model for an infectious disease. Elixir Appl. Math. 2012;42:6062–6064.

21. Diekmann O and Heesterbeek JAP. Mathematical Epidemiology of infectious diseases: model building, analysis and interpretation. Chichester: Wiley; 2000.

22. Hethcote HW. The mathematics of infectious disease. SIAM Review. 2000; 42(4):599-653.

23. Fatoba POSB. Adeyemi AA. Adewole, Fatoba MT. Medicinal plants used in the treatment of infant diseases in South Western Nigeria, Nigerian Journal of Basic and Applied Science. 2018;26(1):14-22.
DOI:http://dx.doi.org/10.4314/njbas.v26i1.2

24. Family Health Teams, author. Guide to Health Promotion and Disease Prevention. Ontario: Canada; 2006.

25. Di Pierro F, Rapacioli G, Ferrara T, Togni S. Use of a standardized extract from Echinacea angustifolia (Polinaceae) for the prevention of respiratory tract infections'. Altern Med Rev. 2012;17(1).

26. Ramakrishna Y, Goda H, Baliga MS. Munsh AK. Decreasing cariogenic bacteria with a natural alternative prevention therapy using phytochemistry (plant extracts). J Clin Paediatr Dent. 2011; 36(1):55–63.

27. Ganesan K, Xu B. A critical review on phytochemical profile and health promoting e_ects of mung bean (*Vigna radiata*). Food Sci. Hum. Wellness. 2018; 7:11–33.

28. Kahaliw W, Ase_a A, Abebe M, Teferi M, Engidawork E. Evaluation of the antimycobacterial activity of crude extracts and solvent fractions of selected Ethiopian medicinal plants. BMC Complement. Altern. Med. 2017;17.

29. Dewapriya P, Khalil ZG, Prasad P, Salim AA, Cruz-Morales P, Marcellin E, Capon RJ, Talaropeptides A-D. Structure and biosynthesis of extensively n-methylated linear peptides from an Australian Marine

tunicate-derived *Talaromyces* sp. Front. Chem. 2018;6.

30. Nath D, Banerjee P, Shaw M, Mukhopadhyay MK. Bottle Gourd (*Lagenaria Siceraria*). In Fruit and Vegetable Phytochemicals: Chemistry and Human Health, 2nd ed.; John Wiley& Sons, Ltd: Hoboken, NJ, USA. 2018;II: 909–920.

31. Mabona U, Viljoen A, Shikanga E, Marston A, Van Vuuren S. Antimicrobial activity of southern African medicinal plants with dermatological relevance: From an ethno-pharmacological screening approach, to combination studies and the isolation of a bioactive compound. J. Ethnopharmacol. 2013;148:45–55.

32. Prasannabalaji N, Muralitharan G, Sivanandan RN, Kumaran S, Pugazhvendan SR. Antibacterial activities of some Indian traditional plant extracts. Asian Pac. J. Trop. Dis. 2012;2,S291–S295.

33. El-Adawi H. Inhibitory effect of grape seed extract (GSE) on cariogenic bacteria. J. Med. Plants Res. 2012;6.

34. Kariu T, Nakao R, Ikeda T, Nakashima K, Potempa J, Imamura T. Inhibition of gingipains and Porphyromonas gingivalis growth and biofilm formation by prenyl flavonoids. J. Periodontal Res. 2016; 52:89–96.

35. Reygaert WC. The antimicrobial possibilities of green tea. Front. Microbiol. 2014;5.

36. Spathodeacampanulata Beauv. In Springer Reference; Springer: Berlin, Germany; 2016.

37. Muhaisen HMH, Ab–Mous MM, Ddeeb FA, Rtemi AA, Taba OM, Parveen M. Antimicrobial agents from selected medicinal plants in Libya. Chin. J. Integr. Med. 2015;22:177–184.

38. Oludare temitope Osuntokun AO, Oluduro TO Idowu, Omotuyi AO. Assessment of Nephrotoxicity, Anti-inflammatory and Antioxidant properties of Epigallocatechin, Epicatechin and Stigmasterol phytosterol (synergy) Derived from ethyl acetate stem bark extract of Spondiasmombin on Wister Rats Using Molecular method of analysis, Journal of Molecular Microbiology. 2017;1(1):103:1-11.

39. Zielin´ ska S, Wójciak-Kosior M, Dzia¸gwa-Becker M, Glen´ sk M, Sowa I, Fijałkowski K, Rura´ nska-Smutnicka D, Matkowski A, Junka A. The activity of isoquinoline

alkaloids and extracts from chelidonium majus against pathogenic bacteria and *Candida* sp. Toxins. 2019;11:406.

40. Mozirandi W, Tagwireyi D, Mukan ganyama S. Evaluation of antimicrobial activity of chondrillasterol isolated from *Vernonia adoensis* (Asteraceae). BMC Complement. Altern. Med. 2019;19.

41. Zhou J-X, Braun M, Wetterauer P, Wetterauer B, Wink M. Antioxidant, cytotoxic, and antimicrobial activities of *Glycyrrhiza glabra* L., Paeonialactiflora Pall., and *Eriobotrya japonica* (Thunb.) Lindl. Extracts. Medicines. 2019;6:43.

42. Mickymaray S, Al Aboody MS. *In Vitro* antioxidant and bactericidal E_cacy of 15 common spices: Novel Therapeutics for Urinary Tract Infections? Medicina. 2019; 55:289.

43. Arefin MK, Rahman MM, Uddin MZ, Hassan MA. Angiosperm flora of Satchari National Park, Habiganj, Bangladesh. Bangladesh J. Plant. Taxon. 1970;18:117–140.

44. Vinodhini R, Moorthy K, Suresh M. Incidence and virulence traits of Candida dubliniensis isolated from clinically suspected patients. Asian J. Pharm. Clin. Res. 2016;9:77.

45. Houlihan AJ, Conlin P, Chee-Sanford JC. Water-soluble exudates from seeds of Kochia scoparia exhibit antifungal activity against *Colletotrichum graminicola*. PLoS ONE. 2019;14:e0218104.

46. Lim SS, Selvaraj A, Ng ZY, Palanisamy M, Mickmaray S, Cheong PCH, Lim RLH. Isolation of actinomycetes with antibacterial activity against multi-drug resistant bacteria. Malays. J. Microbiol; 2018.

47. Akhalwaya S, van Vuuren S, Patel M. An in vitro investigation of indigenous South African medicinal plants used to treat oral infections. J. Ethnopharmacol. 2018; 210:359–371.

48. Rawat S, Jugran AK, Bahukhandi A, Bahuguna A, Bhatt ID, Rawal RS, Dhar U. Anti-oxidant and anti-microbial properties of some ethno-therapeutically important medicinal plants of Indian Himalayan Region. 3 Biotech. 2016;6:154.

49. Vijayakumar R, Aboody M, AlFonaisan M, Turaiki W, Mickymaray S, Mariappan P, Alsagaby S, Sandle T. Determination of Minimum inhibitory concentrations of Common Biocides to Multidrug-Resistant

Gram-negative bacteria. Appl. Med. Res. 2016;2:56.

50. Durairaj B, Dorai A. Antiplatelet activity of white and pink Nelumbonucifera Gaertn flowers. Braz. J. Pharm. Sci. 2010;46:579–583.

51. Bhattacharjee I, Chatterjee SK, Chandra G. Isolation and identification of antibacterial components in seed extracts of *Argemone mexicana* L. (Papaverace ae). Asian Pac. J. Trop. Med. 2010;3:547–551.

52. Yasukawa K, Demitrijevic SM, Evans FJ, Kawabata S, Takido M. Inhibitory effect of Prunus Cortex extract and its component, octacosylferulate, on tumor promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin. Phytotherapy Research. 1998;12(4):261–265.

53. Antony ML, Singh SV. Molecular mechanisms and targets of cancer chemoprevention by garlic-derived bioactive compound diallyltrisulfide. Indian J Exp Biol. 2011;49(11):805–816.

54. Banothu V, Neelagiri C, Adepally U, Lingam J, Bommareddy K. Phytochemical screening and evaluation of in vitro antioxidant and antimicrobial activities of the indigenous medicinal plant *Albiziaodor atissima*. Pharm. Biol. 2017;55:1155–1161.

55. Mickymaray S, Al Aboody MS, Rath PK, Annamalai P, Nooruddin T. Screening and antibacterial effcacy of selected Indian medicinal plants. Asian Pac. J. Trop. Biomed. 2016;6:185–191.

56. Chatterjee SK, Bhattacharjee I, Chandra GIsolation and identification of bioactive antibacterial components in leaf extracts of *Vangueria spinosa* (Rubiaceae). Asian Pac. J. Trop. Med. 2011;4:35–40.

57. Mozirandi W, Tagwireyi D, Mukan ganyama S. Evaluation of anti microbial activity of chondrilla sterol isolated from *Vernonia adoensis* (Asteraceae). BMC Complement. Altern. Med. 2019;19.

58. Gaziano R, Campione E, Iacovelli F, Marino D, Pica F, Di Francesco P, Aquaro S, Menichini F, Falconi M, Bianchi L. Antifungal activity of *Cardiospermum halicacabum* L. (Sapindaceae) against *Trichophyton rubrum* occurs through molecular interaction with fungal Hsp90. Drug Des. Dev. 2018;12:2185–2193.

59. Nefzi A, Ben Abdallah RA. Antifungal activity of aqueous and organic extracts from With aniasomnifera L. against *Fusarium oxysporum* f. sp. *Radicisly copersici*. J. Microb. Biochem. Technol. 2016;8.

60. Chahal SS, Matthews HR, Bradbury EM. Acetylation of histone H4 and its role in chromatin structure and function. Nature. 1980;287:76–79.

61. Walker EH, Pacold ME, Perisic O, Stephens L, Hawkins PT, Wymann MP, Williams RL. Structure determinants of phosphoinositide 3-kinase inhibition by wortmannin, LY294002, quercetin, myricetin and staurosporine. Mol. Cell. 2000;6:909–919.

62. Shah S, Stapleton PD, Taylor PW. The polyphenol (□)-epicatechingallate disrupts the secretion of virulence-related proteins by *Staphylococcus aureus*. Lett. Appl. Microbiol. 2007;46:181–185.

63. Kariu T, Nakao R, Ikeda T, Nakashima K, Potempa J, Imamura T. Inhibition of gingipains and Porphyromonas gingivalis growth and biofilm formation by prenyl flavonoids. J. Periodontal Res. 2016; 52:89–96.

64. Prasannabalaji N, Muralitharan G, Sivanandan RN, Kumaran S, Pugazhvendan SR. Antibacterial activities of some Indian traditional plant extracts. Asian Pac. J. Trop. Dis. 2012;2:S291–S295.

65. Muhaisen HMH, Ab–Mous MM, Ddeeb FA, Rtemi AA, Taba OM, Parveen M. Antimicrobial agents from selected medicinal plants in Libya. Chin. J. Integr. Med. 2015;22:177–184.

66. Pandian MR, Banu GS, Kumar GA. Study of the antimicrobial activity of *Alangium salviifolium*. Indian J. Pharm. 2006;38:203.

67. Vinodhini R, Moorthy K, Suresh M. Incidence and virulence traits of Candida dubliniensis isolated from clinically suspected patients. Asian J. Pharm. Clin. Res. 2016;9:77.

68. Arulmozhi P, Vijayakumar S, Kumar T. Phytochemical analysis and antimicrobial activity of some medicinal plants against selected pathogenic microorganisms. Microb. Pathog. 2018;123:219–226.

69. Mubarack H, Doss A, Vijayasanthi M, Venkataswamy R. Antimicrobial drug susceptibility of *Staphylococcus aureus* from subclinical bovine mastitis in

Coimbatore, Tamilnadu, South India. Vet. World. 2012;5:352.

70. Choi O, Yahiro K, Morinaga N, Miyazaki M, Noda M. Inhibitory e_ects of various plant poly phenols on the toxicity of Staphylococcal _-toxin. Microb. Pathog. 2007;42:215–224.

71. Ahmed SI, Hayat MQ, Tahir M, Mansoor Q, Ismail M, Keck K, Bates RB. Pharmacologically active flavonoids from the anticancer, antioxidant and antimicrobial extracts of Cassia angusti folia Vahl. Bmc Complement. Altern. Med. 2016;16.

72. Mickymaray S, Al Aboody MS. In vitro antioxidant and bactericidal E_cacy of 15 Common Spices: Novel Therapeutics for Urinary Tract Infections? Medicina. 2019;55:289.

73. Abe H. Catalase. In method of enzymatic analysis. New York: Academic Press. 1974:673–684.

74. Hertel W, Peschel G, Ozegowski J-H, Müller P-J. Inhibitory effects of triterpenes and flavonoids on the enzymatic activity of hyaluronic acid-splitting enzymes. Arch. Pharm. 2006;339:313–318.

75. Benevides Bahiense J, Marques FM, Figueira MM, Vargas TS, Kondratyuk TP, Endringer DC, Scherer R, Fronza M. Potential anti-inflammatory, antioxidant and antimicrobial activities of *Sambucus australis*. Pharm. Biol. 2017; 55:991–997.