Journal of Research in Biomedical Sciences (JRBMS)
A Peer reviewed Indexed International Journal (IF 0.92)
An Official Publication of BioSci Group of Research I ***An UGC Approved Journal***

REVIEW ARTICLE

Phytopharmacology and ethnomedical approach of Uloga chendooram, Siddha Herbo-mineral drug for the Management of Neerizhivu (Diabetes Mellitus) - A Review.

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ABSTRACT

Siddha system of medicine is a pioneer traditional medicine which is in practice since several centuries before. As per Siddha classical text, Agasthiyar vaidiya rathna churukanaadi diseases are classified into 4448 types, one among them is meganoi. Based on three humours vatha, pitha, kabha meganoi is classified into 20 types according to *Yugi Vaithiya Chinthaamani, Madhumegam (neerizhivu)* is one of the meganoi, which comes under *Pitha* type called *Thithippu Neer*. The causes, signs and symptoms of *Neerizhivu (madhumegam)* are associated with Diabetes Mellitus in modern system *Mathumegam* is a clinical condition characterized by increased frequency of micturition, urine with 'sweetness' ultimately worsens the seven body constituents, leads to avathaikal, which is the complications of long term poorly controlled hyperglycemia. In most developing countries diabetes mellitus is one of the major health problems. Being a lifestyle disorder its management is still a challenge for modern system of medicine. Increase in the number of diabetic patients, high cost for medical treatments, unsatisfactory treatment response are the major reasons for people to switch over to traditional medicinal systems. At current scenario, Siddha system among Indian systems of medicine is gaining more attention worldwide and it serves as a hope in controlling this dreadful disease and preventing its high risk complications. Siddha drugs include herbal, mineral and herbo-mineral drugs. Among which herbomineral medicines serve the purpose in the management of uncontrolled diabetes. This review article focuses on one such herbomineral Siddha formulation 'uloga chenduram' as mentioned in text Agasthiar attavanai vaagadam, specifically indicated for neerizhivu, hepatic disorders.

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KEYWORDS

Neerizhivu, diabetes mellitus, herbomineral drug, Siddha medicine.

Received: May 2020. Revised: Jun 2020. Accepted: Jun 2020

To Cite: R Gomathi et al, Phytopharmacology And Ethnomedical Approach Of Uloga Chenduram, Siddha Herbomineral Drug For The Management Of Neerizhivu (Diabetes Mellitus) – A Review, J Res Biomed Sci, 3(2), 2020, 52-61.

J Res Biomed Sci

INTRODUCTION

Siddha is a wide-ranging system that places equal emphasis on the body, mind and spirit to restore the innate harmony of the individual it develops methods and medication that strengthen the body, mind, soul. Siddha system has its own principles which are based on 96 thathuvaas, [1] [2] [3]. Siddha system helps to revitalize and rejuvenate the deranged organ. Siddha system is an exclusive system compared to other systems as it is both medically, socially, intellectually and spiritually enriched.

Diabetes is a comparable condition with 'Madhumegam' *or* Neerizhivu in Siddha literature,

As per Theraiyar, Madhumegam (Neerizhivu) is mentioned as

Neeriru vinai gunathai neeyaru virithu solvoom
Neerinai perukkalondru neerinai yarukka ondru
neerizhivudanae.....[4]

Hence Madhumegam (Neerizhivu) is one among the neerinai perukkal noi in our Siddha literature. Meganoi is classified into twenty types in which four comes under Vatham, six under Pitham and ten under Kabam. Madhumegam/Neerizhivu (Diabetes mellitus) comes under pitham. [5]

The Major cause of meganoikal is due to dearrangement in pitha humour, Sage Theraiyar says "*Pakar pitha vinthaiyalaathu megam vaarathu"* in Pini mutharkaaranam (6).

Initially in meganoikal, increased Pitha humour which enhances vaayu, which in turns affect iyam and vali. Three thodam affects the function of seven udal thathukkal, hence the nutrients supporting body life are released through urine, which affects Mukutram, five pranaathi vaayukal and seven udal thaathukkal [7].Agasthiyar said that excess food intake, irregular diet, stress, irregular sexual behaviour leads to Mathumegam. As per Yugi text Mathumegam exhibit the following symptoms like polyuria, nocturia, polydipsia, polyphagia, body pain, weight loss, tiredness, burning feet and genital pruritus [8].

These symptoms can be correlated with Non-Insulin Dependent Diabetes Mellitus (NIDDM) in modern medicine. Diabetes mellitus (DM) is a major public health problem worldwide. Current global estimates indicate that this condition affects 415 million people and is set to escalate to 642 million by the year 2040 [9].

This prevalence is expected to rise to 366 million people by the year 2030.Several epidemiological and clinical studies indicate a direct relationship between hyperglycemia and neuropathy, retinopathy, atherosclerosis and coronary artery disease (10).

In diabetes chronic hyperglycemia in synergy with the other metabolic aberrations can cause damage to various vital organs by stems, leading to the development of disabling and life-threatening health complications, most prominent of which are microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications leading to increased risk of cardiovascular diseases [11].

Several categories of drugs that have been currently used for the treatment of diabetes which can acts by multiple different mechanisms, such as stimulation of the release of insulin (e.g., sulfonylureas), reduction of hepatic glucose output and enhancement of the peripheral uptake of glucose (e.g. biguanidines) [12,13]

This has led to an increase in the demand of natural products with antihyperglycemic activity having lesser side effect. In madhumegam, seven udal thaathukkal get affected. In order to strengthen the seven udal thaathukkal several mineral formulations are used, one such Siddha herbomineral formulation is uloga chenduram (internal medicine) [14]

INGREDIENTS OF ULOGA CHENDURAM

Purified uloga manduram (ferrouso ferric oxide) -336gm

Naaval pattaichaaru (stem bark juice of Syzygium cumini) -672 ml

Kaiyaanchaaru (juice of Eclipta prostrata) - 672 ml

Tripala decotion -672 ml

METHOD OF PURIFICATION: [15]

Mandooram was placed in the ural pounded and then it is placed in a pan, added 4 parts of tamarind leaves and 8 parts of water, boiled for 1 saamam (3hrs). Then the leaves and powder was washed and dried, and then winnowed from which the leaves are separated. After that mandooram was powdered in a kalvam and put it in a pan with 4 parts of cow's urine, boiled until it dries then washed with water.

METHOD OF PREPARATION:

At first instance the purified ulogamandooram was well soaked in both naaval pattaichaaru, kaiyaan chaaru and then dried well. Now it was ground well with tripala decotion and made in to small round cakes (villai) and subjected to pudam (7 times).

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Allowed to cool itself then chenduram was collected.

STUDY DRUG REVIEW:

MANDOORAM: [16]

Scientific name :Ferroso ferric oxide

English name :Iron rust impure of iron

Synonyms :loga mandooram, kittam, sittam, aya-kittam

Organoleptic characters: [16]

Taste : Bitter, Astringent, sour

Quality : Heat

Division : Pungent

Action : Tonic, Hepatotonic

Character: [16]

Chittamonraar sobai kilaiveeka mathisuram

Thuttavida paakam suvaasamaiyam kettakodum

Paandiirupal neeraamai paazhum piramiyamun

Thaandividum mandurath thaathu

SCIENTIFIC REVIEW:

HEPATOPROTECTIVE EFFECT:

Sapkal et.al studied the hepatoprotective activity of mandur bhasma (Mb) in paracetamol induced hepatotoxicity in rats, results says that the effectiveness of Mb as better hepatoprotective was also supported by the results of histopathological studies. These studies revealed that paracetamol caused 80% to 85% necrosis of liver and treatment with Mb could reduce it to 5% to 10%. This shows that Mb was most effective in protecting the liver from paracetamol induced hepatotoxicity. [18]

KARISALAI: [17]

Botonical Name : Eclipta prostrata

English Name : Eclipta

Family : Asteraceae

Synonyms : Karisalai, Bringarajam, Kaiyanthakarai

Part Used : Whole plant

Organoleptic characters: [17]

Taste : Bitter

Quality : Heat

Division : Pungent

Action : Cholagouge, Tonic, Alterative, Emetic, Purgative, Hepatotonic, Deobstruent

Character: [17]

Kuralkammal kaamalai kuttamodu sobai

Paandu pannoo ozhiya niratsonne

Meiyaanth thakaraiyotha meelinnu natpullathuk

Kaiyaanth thakaraiyoththa kaal – (Siddha materiamedica p.no:230)

CHEMICAL CONSTITUENTS:

Studies yield presence of tannins, terpenoids, wedelolactone and demethylwedelolactone, pholabatannins, resins, lipids and fats, steroids, tannins, terpenoids, reducing sugars, phenols, carbohydrates, anthraquinone, catchol, sterols, and flavonoids, Study of leaf extracts yield major constituents of 2-Tridecanone (CAS) (4.51%), n-(methoxy phenyl methylene) carbamic acid ethyl ester (1.65%), and 9,12,15-Octadecatrienoic acid, methyl ester, (Z,Z,Z) (13.68%).Phytochemical screening of leaves yielded alkaloids, glycosides, flavonoids, saponins, steroids, and carbohydrates.

SCIENTIFIC REVIEW:

Anticonvulsant activity, analgesic, neurological, antioxidant and cytotoxic activities, antioxidant activity, hepatoprotective activity, α-Amylase and α-Glucosidase Inhibitory Activities [19, 20, 21].

HEPATOPROTECTIVE EFFECT:

Naveen et al. (2012) evaluated for its hepatoprotective effect in cadmium chloride- induced (3mg/kg, i.v) hepatotoxicity in albino rats, the Liv-52,2ml/kg/p.o used as a standard drug. Rats treated with CdCl2 showed a significant hepatic damage as observed from elevated serum level of hepato specific enzymes SGOT, SGPT and Total bilirubin as well as severe alteration in different liver parameters. Treatment with the aqueous extract of Wedelia chinensis leaves caused significant protection against cadmium chloride-induced hepatotoxicity by decreasing the serum enzyme levels and bilirubin in a dose responsive manner. In histopathology, the cadmium chloride-induced histological changes were reduced by extract treatment in a dose dependent manner.

HYPOGLYCEMIC EFFECT:

Nguyen Phuong Thaoet.al studied the α-Amylase and α-Glucosidase Inhibitory Activities. In their study new cyclohexyl ethanoid derivative was isolated from the leaves of Wedelia chinensis (Osbeck.) Merr. Structures of the compounds were conducted via interpretation of their spectroscopic data (1D and 2D NMR, IR, and MS), and the absolute configurations of compound was determined by the modified Mosher's

method. MeOH extract of W. chinensis and the compounds isolated from this extract inhibit α-amylase and α-glucosidase inhibitory activities. Furthermore, compound showed the strongest effect with IC50 values of 112.8±15.1 g/mL (against α amylase) and 785.9±12.7 g/mL (against α-glucosidase). [22] W. Chinensis reveals antioxidant, anti-inflammatory, analgesic, sedative, antistress, antiulcerogenic, anticancer, and antifungal, anticonvulsant, hepatoprotective and steroid suppressing activities [23, 24, 25].

NAVAL PATTAI: [17]

Botonical Name :Eugenia Jambolana

English Name :Jambul

Family :Myrtaceae

Synonyms : Navval, Sambu, Surabipathirai, Sathavam, Sambal

Part Used : Whole parts

Organoleptic characters: [17]

Taste : Astringent

Quality : Coolant

Division : Pungent

Action : Astringent, Tonic, Diuretic, Stomachic

Character: [17]

Aasiyanooi kaasam asirkkaranju vaasavinai

Kesamuru paala kiraganoi pesariya

Maaviyanga laanjanamiv vanpiniyae laamegum

Naavalaru pattaiyathanaal – (Siddhamateria medica p.no: 571)

CHEMICAL CONSTITUENTS:

The stem bark includes friedelin, kaempferol, ellagic acid, gallotannin, betulinic acid, β-sitosterol, eugenin (Singh & Kaur, 2016; Baslingappa Shrikant et al, 2012). [26]

Eugenia-triterpenoid-B, Ellagic acid, Pentacyclic triterpenoid- Betulinic acid, Pentacyclic triterpenoid - Friedelin, Resin-Myricetine, Phytosterol-B, Sitosterol-Myricyl alcohol [27].

Stem bark of Syzygium cumini includes betulinic acid, ß-sitosterol, friedeanol, epi-friedeanol and eugenin. It also contains ß-sitosterol-D-glucoside, Kamepferol-3-0-glucoside, quercetin, myricetin, astragalin, and gallic acid (Sengupta and Das, 1965; Bhargava et al., 1974). [28].

The stem bark of S-Cumini includes betulinic acid, ß-sitosterol, friedeanol, epi-friedeanol and eugenin. It also contains ß-sitosterol-D-glucoside, Kamepferol-3-0- glucoside, quercetin, myricetin, astragalin, and gallic acid [29, 30, 31]

SCIENTIFIC REVIEW:

ANTI-INFLAMMATORY EFFECT:

Pandey et al studied the methanolic extract of s. cumini bark and reported to showed anti-inflammatory activity against histamine, serotonin and prostaglandin [32, 33]

ANTIDIABETIC EFFECT:

Tripathi et.al, studied antidiabetic activity of bark extract of Syzygium cumini (L.) on streptozotocin (STZ)-induced diabetic Wistar albino rats. They stated that 30 minutes prior administration of Syzygium cumini (L.) extracts before oral glucose loading significantly decreased ($p<0.001$) the rise in postprandial blood glucose levels in treated rats as compared to control rats however the result was less significant than glibenclamide. Every day, Continuous oral treatment of STZ-induced diabetic with various Syzygium cumini (L.) extract for 3 weeks lead to significant reductions in fasting blood glucose levels as compared to diabetic controls

CARDIO-PROTECTIVE EFFECT:

Madhulika Pradhan et.al studied the hydro-alcoholic extract of Syzgium cumini was evaluated for its antihypertensive, and vasorelaxant effect. Polyethylene catheters were inserted into the inferior vena cava and lower abdominal aorta in the anaesthetized rats for dosing and measuring blood pressure. The extract at the doses of 0.5; 1; 5; 10; 20 and 30 mg/kg, i.v. was able to induce hypotension (due to reduction in endothelium mediated peripheral resistance) and bradycardia [33].

ANTIHYPERLIPIDEMIC EFFECT:

Ravi et.al, [34] studied the Antihyperlipidemic effect of Eugenia jambolana seed kernel on streptozotocin-induced diabetes in rats, the efficacy was compared with standard hypoglycemic drug, glibenclamide. The effect of oral administration of ethanolic extract of EJs-kernel (100 mg/kg body weight) was examined on the levels of cholesterol, phospholipids, triglycerides and free fatty acids in the plasma, liver and kidney tissues of STZ (55 mg/kg body weight)-induced diabetic rats. The plasma lipoproteins and tissues fatty acid composition were also monitored. STZ-induced diabetic rats, showed significant increase in the levels of cholesterol, phospholipids, triglycerides and free fatty acids which were considerably restored to near normal in EJs-kernel

or glibenclamide treatment. It may be concluded that, EJs-kernel possesses hypolipidemic effect, which may be due to the presence of flavonoids, saponins, glycosides and triterpenoids in the extract. The hypolipidemic effect mediated by EJs-kernel may also be anticipated to have biological significance and provide a scientific rationale for the use of EJs-kernel as an anti-diabetic plant.

KADUKKAI [17]

Botonical Name	:	Terminalia Chebula
English Name	:	Chebulic Myrobalan
Family	:	Combritaceae
Synonyms	:	Amirtham, Arithaki, Jeevanthi, Haimavathy, Vanathurkki
Part Used	:	Tender fruit,Fruit

Organoleptic characters: [17]

Taste	:	Astringent, Sweet, Pungent, Bitter, Sour
Quality	:	Heat
Division	:	Sweet
Action	:	Astringent, Tonic,

Character: [17]

Thaadai thazhuththakki thaalu kurivida

Peedai silipathamum pethividam aadai aadaiettaath

Thoolamidi punvaatha sonikaa maalaiiran

Taalamidi poom varikaayaal – (Siddha material medica p.no:207)

Chemical constituents:

Terflavin A, Terchebin, Chebulaginic acid, Neo-chebulic acid, Gallic acid, Casuarinin, Chebulanin, Corilagin, Methyl(S)-flavogallonate, Methyl neochebulagate, Eugenol, Ascorbic acid, Triethyl chebulate, Tannic acid, phloroglucinol pyragallol, Terpenoids and Triterpene Saponins, Arjungenin, Arjunolic acid, Arjunic acid, Terminolic acid, Chebuloside II, β-caryophyllene, β-Sitosterol, Daucosterol, Behenic acid, Stearic acid, Palmitic acid, Oleic acid, Arachidic acid, Linoleic acid, Cyclododecane, 9-Octadecene, Hexadecane, Cylohexane, Tritetracontane, Phthalic acid, Linoleic acid ethyl ester, Heptafluorobutyric acid.

SCIENTIFIC REVIEW:

ANTI HYPERGLYCEMIC EFFECT:

Murali et.al studied the Antihyperglycemic effect of water extract of dry fruits of Terminalia chebula in experimental diabetes mellitus, Water extract of dry fruits of Terminalia chebula at a dose of 200 mg/kg body weight improved the glucose tolerance as indicated by 44% of reduction in the peak blood glucose at 2(nd) hour in glucose tolerance test in diabetic (streptozotocin induced) rats [35, 36].

ANTI-OXIDANT EFFECT:

Bajpai et al. [37] investigated the high phenolic content and anti-oxidant activity of leaves, fruits and bark of T.chebula. The TPC of fruits, leaves and bark of T. chebula were 144.7, 162.1 and 150.7 mg/g GAE, respectively. Kim et al. [38] showed the free radical scavenging activity in methanol aqueous extract of T.Chebula

HEPATO PROTECTIVE EFFECT:

Tasduq SS reported that Ethanol extract of T. chebula was found to be a good hepatoprotestive thus it prevents the hepatotoxiocity caused by the administration of rifampicin, isoniazid and pyrazinamide (combination) in sub-chronic model (12 weeks). Lee HS et al. in their study, a mixture of chebulic acid (CA) and its minor isomer, neochebulic acid with a ratio of 2:1 isolated from ethanolic extract of T. chebula fruits showed strong hepatoprotective activity [39]

NEPHROPROTECTIVE EFFECT:

Nalamolu Koteswara Rao et al. [40] evaluated the chloroform extract of T. Chebula exhibited significant renoprotective activity and also more effectively inhibited the incidence of diabetic nephropathy.

ANTI-DIABETIC EFFECT:

Kannan VR et al. showed that T. chebula fruit and seeds exhibit antihyperglycemic property, it provides dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in short term and long term study. Sabu M.C et al. [41] and Senthilkumar GP et al [42] reported that Tripala extract has reduced the blood sugar level in normal and alloxan (120mg/kg) induced diabetic rats significantly.

NELLIKAI [17]

Botonical Name	:	Embilica officinalis
English Name	:	Indian Goseberry
Family	:	Euphorbiaceae
Synonym	:	Amalakam, Ambal, Miruthubala, Thathiri
Part Used	:	Leaf, Fruit, Root,Seed,Bark

Organoleptic characters: [17]

Taste	:	Astringent,Sweet,Sour
Quality	:	Coolant
Division	:	Sweet

Action :Astringent, Tonic, Refrigerant, Laxative, Diuretic

Character: [17]

Pithmana laiyam peenisam vaaineer vaanthi
Maththamala kaadum mayakkamumil othavuru
Villikka yammarungaa mennatkaa lanthernthae
Nellikaai marunthu nee – (Siddha materiamedica p.no:621)

CHEMICAL CONSTITUENTS:

These fruits are reputed to contain high amounts of ascorbic acid (vitamin C) [43]and have bitter taste that may derive from a high density of ellagitannins, such as emblicanin A (37%), emblicanin B (33%), punigluconin (12%), and pedunculagin (14%) [44] Amla also contains punicafolin and phyllanemblinin A, phyllanemblin other polyphenols, such as flavonoids, kaempferol, ellagic acid, and gallic acid [45, 46]

SCIENTIFIC REVIEW:

ANTIDIABETIC EFFECT:

The hypoglycemic and antioxidant activity of methanolic extracts of the leaves of Terminalia arjuna, T. bellerica, T. chebula (tripala) Were estimated for total phenolic, flavonoid, and tannin content, and in vitro antioxidant potential with DPPH, ORAC, and FRAP assays. The extracts hypoglycemic activities were evaluated by hypoglycemic screening and an oral glucose tolerance test (OGTT) in normal rats. Results states that the T. chebula extract had a better hypoglycemic effect in normal and glucose induced hyperglycemic rats ($p < 0.001$) than that of T. bellerica and T.arjuna, respectively [47]. Latha P.C.R et al.,(2010) investigated that Hexane, Ethylacetate and Methanolic extracts of TB fruit at the doses of 200, 300 and 400 mg/kg, p.o for 60 days to Streptozotocin induced diabetic rats significantly ($p < 0.05$) increased the plasma insulin, , c- peptide, glucose tolerance levels, body weight body weight, serum total protein. The effect was more pronounced in methanol extract treated rats. In addition the plant extracts significantly decreased the serum levels of total cholesterol, triglycerides, low density lipoprotein cholesterol, urea, uric acid and creatinine in diabetic rats. [48].

ANTIOXIDANT EFFECT:

XiaoliLiu et.al studied the phenolic contents of methanolic extracts of emblica (*Phyllanthus emblica* L.) e of the commercial compounds (quercetin and BHA). It might be considered as a potential plant source of antioxidants. [49].

HEPATOPROTECTIVE EFFECT:

fruit from six regions in China were measured in this work, Methanolic extracts of emblica fruit from some selected regions exhibited stronger antioxidant activities compared to those of the commercial compounds (quercetin and BHA). It might be considered as a potential plant source of antioxidants. [49].

HEPATOPROTECTIVE EFFECT:

The methanol extracts of P. polyphyllus, P. emblica and P. indofischeri showed high levels of hepatoprotective activity with EC50 values of 12, 19 and 28 µg/mL and IC50 of 3.77, 3.38 and 5.8 µg/mL for DPPH scavenging activity respectively against an IC50 of 3.69 µg/mL for ascorbic acid. [50]

THANDRIKAI [17]

Botonical Name : *Terminalia bellerica*
English Name : Bellaric Myrobalan
Family : combretaceae
Synonyms : Akkantham, Kanthakatpalam, Thanikkai, Amutham, Boothavasakam, Erikatpalam
Part Used : Leaf, Fruit, Seed,

Organoleptic characters [17]

Taste : Astringent
Character : Heat
Division : Sweet
Action : Astringent, Tonic, Expectorant, Laxative

Character: [17]

Sillanthividam kaamiyapun seelaana megam
Kalanthuvarum vaathapitha kaaloo – ularnthu udalil
Oondrikkaai veppa muthirapiththa ungarakakkunth
Thaandrikai kaiyileduth thaal – (Siddha materiamedica p.no:513)

CHEMICAL CONSTITUENTS:

Fruits contain hexahydroxydiphenic acid, methyl ester, β-sitosterol, gallic acid, ellagic acid, ethyl gallate, galloyl glucose, chebulagic acid, mannitol, glucose, galactose, and rhamnose [51] Two new lignans named termilignan and thannilignan, Flavonoids, sterols and tannins, antraquinone glycoside, saponins, polysaccharides, Steroid, Tannin, Arjungenin, belleric acid, bellericoside, rhamnopyranoside, sitosterol, chebulagic acid, galloyl glucose, mannitol, fructose, Gallo-tannic acid and glycoside bellericanin, phenol, tannins and Glycosides, flavonoids, tannins, phenols, saponin, carbohydrates and proteins.[52]

SCIENTIFIC REVIEW:

ANTIHYPERTENSIVE EFFECT:

Terminalia belerica was screened for the antihypertensive effect by Arif Ullah Khan et al., 2008. After administration of Terminalia belerica, they observed that fall in the arterial BP of rats under anaesthesia. In isolated guinea-pig atria, inhibition of force and rate of atrial contractions noted. In rabbit thoracic aorta, relaxation was observed after the induction of contractions which was induced by phenylephrine. [53]

ANTIOXIDANT EFFECT:

Arya A et.al, studied the hypoglycemic, antioxidant activity, it shows Continuous administration of dried 75% methanolic extract of fruits of Terminalia belerica (Combretaceae) suspended in water was studied in antioxidant defense mechanism in rats. Alloxan induced oxidative stress was found to be significantly lowered by the administration of T. belerica extract. This was evident from a significant decrease in thiobarbituric acid reactive substances, conjugated dienes and hydroperoxides in blood and liver respectively. [47]

HEPATOPROTECTIVE EFFECT:

Hazra et. al studied the ameliorating effect of 70% methanol extract of Terminalia bellarica (TBME) on iron overload induced liver injury, along with its in vitro iron chelating and DNA protection studies. Treating with different doses (50, 100 and 200 kg body weight) of TBME showed dose dependent reduction in liver iron, lipid peroxidation, protein oxidation, liver fibrosis, serum enzymes and ferritin. The antioxidant enzymes levels were enriched and the reductive release of ferritin iron increased significantly with gradually increasing concentrations of TBME. [54]

IMMUNOMODULATORY EFFECT:

The effects of Terminalia bellerica methanolic extract (0.1, 1, 10, 100 and 500 µg/ml) on the mouse immune system was investigated in vitro. Phagocytic activity and lymphocyte proliferation were assayed. The results indicated the effect of the extract (500 µg/ml) on the stimulation of macrophage phagocytosis, through the production of superoxide anions and acid phosphatase, with a phagocytic index (PI) value of approximately 1.5 and 1.3, respectively. In lymphocyte proliferation assay, the extract (500 µg/ml) with phytohemagglutinin exhibited maximal activation, with a stimulation index (SI) value of approximately 5.8. With concanavalin A, lipopolysaccharide, and pokeweed mitogen, similar activation (SI 4.5) of lymphocyte proliferation was observed. However, at low concentrations (0.1 µg/ml), T. bellerica extract with concanavalin A and pokeweed mitogen caused suppressant activity (SI 0.7). [55]

DISCUSSION

Uloga chenduram consists of uloga manduram (ferrousoferric oxide), juice of naval pattai (syzygium cumini) and juice of karisalai (eclipta prostata), The above ingredients are well known for their antihyperglycemic property [56,57] and hepatoprotective activity.

Manduram– astringent (veppa veeriyam) [16]

Naaval pattai– astringent (Thatpa veeriyam) [17]

Karisaalai– bitter, spicy (veppa veeriyam) [17]

Hence Naaval pattai reduces pitha, Manduram and karisalai balance kabam, vaatham. Hence Uloga chenduram balance the Mukutram and also strengthen the seven udal thaathukkal. Uloga chenduram was given in a tripala decoction (kadukai, nellikai, thaandrikai.)

Kadukkai (Terminalia Chebula) - Astringent, Sweet, Pungent, Bitter, Sour (veppa veeriyam)[17]

Nellikai (Embilica officinalis) - Astringent,Sweet,Sour (thatpa veeriyam) [17]

Thandrikai (*Terminalia bellerica*)- Astringent (veppa veeriyam) [17]

Kadukkai and Nellikai are karpa medicine, balances mukkutram. Thandrikai balance kaba, vatha humour. Hence as a whole uloga chenduram with tripala decotion helps to balance three humours. According to Siddha science, chronic uncontrolled disease comes under kabam (which has the quality of nilaithu nitral) [7], this drug uloga chenduram is used to control uncontrolled diabetes mellitus.

In view of the above mentioned pharmacological activities, ingredients of *uloga chenduram* are found to possess antidiabetic activity along with antioxidant, antihyperlipidemic, hepatoprotective, cardioprotective, antihypertensive, nephroprotective activities. Hence this drug acts in liver and maintain blood sugar level, indirectly it reduce the complication of diabetes mellitus by possessing nephroprotective, cardioprotective, antihypertensive activites. Thus the potency and efficiency of a drug is further enhanced. With this proven efficacy, easily available drugs to prepare, cost efficacy and safer treatment *uloga chenduram* serves as a promising anti diabetic drug for future research in the treatment of uncontrolled Diabetes mellitus which acts upon glucose metabolism thereby aiding in controlling blood sugar levels and by preventing its long term complications.

CONCLUSION

From this review it is proved that the ingredients have potent anti-diabetic and anti-hyperglycaemic activity. And it is certain that siddha system of medicine beside with its traditional life style and food habits can challenge to prevent and treat Diabetes on this scientific & modern world. Further clinical studies and statistical data analysis help in exploring this herbomineral siddha formulation.

ACKNOWLEDGEMENT

The author thanks Late.Dr.K.Natarajan sir and his wife Late.Mrs.N.Rathinammal, Vaithiyarathnam Dr.K.Natarajan Siddha Vaithiyasalai, Arumbakkam, Chennai, Dr.A.Mamallan, Assistant medical officer, Mallaankinar phc, Arupukottai, Dr S.Thamodaran Assistant medical officer, Saalavaakam phc, Chenkalpattu. for their teaching, valuable support, encouragement.

SOURCE OF FUNDING

The author received no financial support for the research and publication of this article.

CONFLICT OF INTEREST

The author declared no potential conflicts of interest with respect to the research and publication of this article.

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