

Review Article

Pharmacotherapy of Herbal Medicines to prevent Diabetes and Diabetic Retinopathy.

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ABSTRACT:

Diabetic retinopathy is an eye disease caused by prolonged uncontrolled blood sugar levels. Consistently high blood sugar damages the retinal blood vessels which results in blood leakage inside the retina. There occurs leakage of the blood inside the retina. This increased fluid and swelling of the retina cause complications in the eye's functioning and results in progressive vision loss. A diabetic person with high cholesterol, high blood pressure, tobacco and alcohol is more prone to develop the symptoms of diabetic retinopathy.

The prevalence of retinopathy is strongly linked to the duration of diabetes. Changes in the retina are observed by 10 years of Diabetes history or even earlier due to modified lifestyle in present era.^[3] Even with the better understanding of its pathogenesis, satisfactory treatment is yet to be established. Ayurveda is well recognized for its role in preventing the disease, so *Ayurvedic* treatment purely lies on the basis to pacify the pathological changes which occurs in eye as a result of diabetes according to modern parameters. This review gives understanding of the Pathophysiology of diabetic retinopathy with a view to understand therapeutic target and discusses the possible role of Ayurveda in its management.

KEY WORDS: Ayurveda, Diabetes, Retinopathy

INTRODUCTION:

Diabetes mellitus (DM) is a metabolic, disorder characterized primarily by hyperglycemia and glycosuria. It occurs in one of two forms: Type1 or Insulin Dependent Diabetes Mellitus (IDDM) and Type2 or Non-Insulin Dependent Diabetes Mellitus (NIDDM).^[1] The prevalence of diabetes mellitus is increasing globally with a rise from about 30 million cases in 1985 to 177 million cases in 2000 and worldwide estimates project that more than 360 million individuals will have diabetes by the year 2030.^[2] Diabetic retinopathy, one of the common complications of diabetes, is a major cause of blindness in developed as well as developing countries. This disease results in generalized macro and micro vascular complications linked to glycaemic control and resulting in poor vision or even blindness. The prevalence of retinopathy is strongly linked to the duration of diabetes. Changes in the retina are observed by 10 years of Diabetes history or even earlier due to modified lifestyle in present era.^[3] Even with the better understanding of its pathogenesis, satisfactory treatment is yet to be established. Ayurveda is well recognized for its role in preventing

the disease, so *Ayurvedic* treatment purely lies on the basis to pacify the pathological changes which occurs in eye as a result of diabetes according to modern parameters. This review gives understanding of the Pathophysiology of diabetic retinopathy with a view to understand therapeutic target and discusses the possible role of Ayurveda in its management.

AIMS & OBJECTIVES:

- Conceptual study of pharmacotherapy of diabetic retinopathy with comprehensive integration of principles of treatment of Madhumeha, Rasayana and Dristigataroga
- Integration of recent herbal research on management of Diabetes mellitus and consequent retinopathy with Ayurvedic principles
- To understand the Pathophysiology of diabetic retinopathy with a view to understand therapeutic target and discusses the possible role of Ayurveda in its management.

STUDY DESIGN:

Electronic literature search of MEDLINE, PUBMED, Available clinical studies published in the English language that used human participants and examined glycaemic control were included.

Screening of these dravyas with reference to their action on Tridoshas, Netrahitkara and Madhumeha.

Pathology of Diabetic Retinopathy:^[3]

Diabetic retinopathy includes micro aneurysm formation and intra retinal hemorrhage micro vascular damage leads to abnormalities and intra retinal micro vascular abnormalities (IRMA). During this stage increased vasopermeability can result in retinal thickening (edema) and or exudates that may lead to a loss in central visual acuity. The proliferative stage results from closure of arterioles and venules with secondary proliferation of new vessels on the disc, retina, iris, and in the filtration angle. These new vessels then lead to traction retinal detachments and neovascular glaucoma, respectively. Vision can be lost in this stage as a result of capillary nonperfusion or edema in the macula vitreous hemorrhage and distortion or traction retinal detachment.^[3]

Ayurveda Pathology

There is a common etiological factor for *Timira* and *Prameha*. *Nidana Sevana* like *amla rasa, sukta-aranala, maasha, vegadharana, swapnaviparyaya* are *achakshushya* factors in *Prameha* which leads to *Timira samprapti*.

By Astanga Sangraha and Charakacharya in *Pramehasamprapti* and *Prameha purvaroop* respectively, which clearly indicates involvement of vital organs like *Netra*. Diabetic Retinopathy is silent disorder as the patient will not realize the condition until he experiences blurred vision. *Timira* is important disease one among the *drishtigata rogas*, which means darkness / increased dampness (*kleda*) in the eye.

Prameha is a *kapha* dominant disease and the major *sampraptighataka* is *kleda* which contributes to *upadrava rogas*. *Timira* explained based on different *dosha* predominance can be compared to DR and can be termed as *Madhumehajanya Timira*.

Tejo *guna* dominated by *Pitta dosha* in *netra* will always have fear from *kapha dosha*. The combination of *kleda* and *kapha* in *Prameha*, through *pratilomagati* of *vyana vayu* and *rasavahinis* reaches *netra* and stimulate the process of *srotorodha* in *sukshma raktavahi srotases* which can be correlated to microvascular occlusion due to loss of pericytes and thickening of basement membrane causes occlusion (Capillaropathy).

Deformation of erythrocytes and rouleaux formation, increased platelets stickiness and aggregation of platelets (Hematological changes) causes endothelial cell damage.

Subsequently due to *srotorodha* their causes *atipravritti* of *utkleshitadoshas* which can be neovascularisations caused by vasoformative substances (growth factors) elaborated by hypoxic retinal tissue in an attempt to revascularise hypoxic retina.

- Further causing *siragranthi* can be justified to formation of aneurysms where there will be localised saccular outpouchings due to physical weakening of the retinal vessels.
- The *utkleshana* of *doshas* in *srotas* due to *srotorodha* deranges the vasculature and permeability of retinal vessels causing *srotoabhisyanda* and giving rise to hard exudates.
- Due to increased *kapha* and *kleda* in *Prameha* it increases *sara guna* and *drava guna* of *pitta* and *rakta* in *srotas* and also the *abhisyandi srotas* causes leakage of the blood vessels causing dot and blot haemorrhages, which simulates *raktapitta samprapti*.
- The *srotorodha* in *siras* resulting in *agnimandya* at the level of *dhatwagni* and *bhutagni* causes lack of circulation of *pitta* and *rakta* in those areas where there will be best *shanika pandu lakshana* which represents as cotton wool spots of the ischemic area of the retinal nerve fiber layer.^[4]

Treatment

Treatment of diabetes-related complications should be a part of routine care among all diabetic patients. Intensive treatment designed to keep glucose levels close to normal has been shown to reduce the risk of developing retinopathy. The natural history and screening recommendations for diabetic retinopathy must be understood, since even advanced disease can be asymptomatic. Till date, no effective medical management has been developed and available treatment is confined to photocoagulation and vitreous surgery. Apart from the effective management of DM, drugs like aldose reductase inhibitors, antiplatelet agents, interferon, vasodilators and growth hormone inhibitors are in use with variable result. There is Need to find a drug that can be effective in the management of diabetic retinopathy.^[7]

OBSERVATIONS & RESULTS:

To summarize the latest review on the molecular mechanisms of diabetic vascular complications, and evaluates the level of scientific evidence for common herbal medicines and their bioactive photochemical. Overall, herbal medicines exhibit anti-inflammatory and anti-oxidative properties provide a promising approach for the prevention and treatment of diabetic retinopathy.

Table No. 1: Some single herbs drugs used in Diabetes mellitus^[2]

Amalaki (<i>Emblica officinalis</i> Gaertn.)	Shilajit (<i>Black bitumen</i>)
Meshasringi (<i>Gymnema sylvestre</i> Retz.)	Vijaysar (<i>Pterocarpus marsupium</i>)
Karavellaka (<i>Momordica charantia</i> Linn.)	Jambu (<i>Syzygium cumini</i> Linn.)
Methika (<i>Trigonella foenum-graecum</i> Linn.)	Tvak (<i>Cinnamomum zeylanicum</i> Blume)
Tejpatta (<i>Cinnamomum tamala</i> Nees & Eberm)	Guduci (<i>Tinospora cordifolia</i> Willd.)
Bimbi (<i>Coccinia indica</i>)	Khadirasara (<i>Acacia catechu</i> Wild.)
Kakamaci (<i>Solanum nigrum</i> Linn.)	Devadaru (<i>Cedrus deodara</i> Roxb.)
Devadaru (<i>Cedrus deodara</i> Roxb.)	Daruharidra (<i>Berberis aristata</i> DC.)
Palash (<i>Butea monosperma</i> Lam.)	Shimshapa (<i>Dalbergia sisso</i> Roxb.)

Table No. 2: Some single herbs used in Diabetes Retinopathy^[2]

Haridra (<i>Curcuma longa</i> Linn.)	Karvellaka (<i>Momordica charanti</i> Linn.)
Garlic (<i>Allium sativu</i>)	Jambu (<i>Eugenia jambolana</i> Lam.)
Methica (<i>Trigonella foenum graecu</i> Linn.)	Aloe (<i>Aloe vera</i>)
Draksha (<i>Vitis vinifera</i> Linn.)	Green tea (<i>Camellia sinensis</i>)

Table No. 3: Some single herbs for chakshuya acc. to Bhavprakash^[5]

Haritaki (<i>Terminaliya chebula</i> Retz.)	Lavanga(<i>Syzygium aromaticum</i> Linn.)
Bibhitaki (<i>Terminaliya bellerika</i> Roxb.)	Raktachandana (<i>Pterocarpus santalinus</i> Linn.f.)
Amalaki (<i>Emblica officinalis</i> Gaertn.)	Jeevanti(<i>Leptadenia reticulate</i> Retz.)
Jeeraka (<i>Cumium cymium</i> Linn.)	Mudgaparni (<i>Phaseolus trilobus</i> Ait.)
Yastimadhu (<i>Glycyrrhiza glabra</i> Linn.)	Nimbapatra (<i>Azadiracta indica</i> A. Juss)
Katakaphala (<i>Strychnos potatorum</i> Linn.f.)	Nirgundi (<i>Vitex negundo</i> Linn.)
Lodhra (<i>Symplocos racemosa</i> Roxb.)	Shatavari (<i>Asparagus racemosus</i> Willd.)
Lashuna (<i>Allium sativu</i>)	Kumari (<i>Aloe vera</i>)
Palandu (<i>Allium cepa</i> Linn.)	Kakamachi (<i>Solanum nigrum</i> Linn.)
Karpura(<i>Cinnamomum Camphora</i> Nees & Eberm.)	Draksha (<i>Vitis vinifera</i> Linn.)

Table No. 4: Herbs for Dristigataroga ^[6]

Haritaki (<i>Terminaliya chebula</i> Retz.)	Shunti (<i>Zingiber officinale</i>)
Vibhitaki (<i>Terminaliya bellerika</i> Roxb.)	Shigru (<i>Moringa pterygosperma</i> Gaertn.)
Amalki (<i>Emblica officinalis</i> Gaertn.)	Shatavari (<i>Asparagus racemosus</i> Willd.)
Yastimadhu (<i>Glycyrrhiza glabra</i> Linn.)	Ashwagandha (<i>Withania somnifera</i> Dunal.)
Haridra (<i>Curcuma longa</i> Linn.)	Bala (<i>Sida codifolia</i>)
Daruharidra (<i>Berberis aristata</i> DC.)	Sariva (<i>Hemidismus indicus</i>)
Pippali (<i>Piper longum</i> Linn.)	Manjistha (<i>Rubia cordifoliya</i> Linn.)
Maricha (<i>Piper nigrum</i> Linn.)	Nimba (<i>Azidarekta indica</i> A.Juss)
Vidanga (<i>Embelia ribes</i> Burm.f.)	Guduchi (<i>Tinospora cordifolia</i> Willd.)
Jeevanti(<i>Leptadenia reticulate</i> Retz.)	Bhumyamlaki(<i>phyllanthus niruri</i> Sensu Hook.f.)
Kataka Beej(<i>Strychnos potatorum</i> Linn.f.)	Chandana(<i>Santalum album</i> Linn.)
Karpura(<i>Cinnamomum camphora</i> Nees&Eberm)	Lavanga(<i>Syzygium aromaticum</i> Linn.)
Devdaru (<i>Momordica charantia</i> Linn.)	Punarnava (<i>Boerhavia diffusa</i> Linn.)
Nirgundi(<i>Vitex negundo</i> Linn.)	Bhrungraj(<i>Eclipta alba</i> L.)
Sarshapa(<i>Brassica campestris</i> Linn.)	Kumari (<i>Aloe vera</i>)
Patol(<i>Tricosanthes dioica</i> Roxb.)	Draksha(<i>Vitis vinifera</i> Linn.)

Table No. 5: Rasayana Herbs for Diabetis^[2]

Amalaki (<i>Emblica officinalis</i> Gaertn.)	Haritaki (<i>Terminaliya chebula</i> Retz.)
Haridra (<i>Curcuma longa</i> Linn.)	Shilajit (<i>Black bitumen</i>)
Guduci (<i>Tinospora cordifolia</i> Willd.)	Kumari (<i>Aloe vera</i>)
Khadira (<i>Acacia catechu</i> Wild.)	Jtamansi (<i>Nardostachys jatamansi</i> Dc.)
Daruharidra (<i>Berberis aristata</i> DC.)	Karvellak (<i>Momordica charantia</i> Linn.)
Patol(<i>Tricosanthes dioica</i> Roxb.)	Bilva (<i>Aegel marmelos</i> Linn.)

Table No. 6: Rasayana Herbs for Diabetic Retinopathy^[2]

Haridra (<i>Curcuma longa</i> Linn.)	Garlic (<i>Allium sativu</i>)
Jambu (<i>Eugenia jambolana</i> Lam.)	Draksha (<i>Vitis vinifera</i> Linn.)
Methica (<i>Trigonella foenum graecu</i> Linn.)	Karvellaka (<i>Momordica charanti</i> Linn.)

Table No. 7: Herbs for Atherosclerosis does action lekhan^[7]

Madanaphala (<i>Randia dumetorum</i> Lam.)	Udumbar (<i>Ficus racemosa</i> Linn)
Karpura (<i>Cinnamomum camphora</i> Nees & Eberm)	Plaksh (<i>Ficus lacer</i> Buch Ham)
Purana guggulu (old <i>Commiphora mukul</i> Engl.)	Parish (<i>Thespesia populnea</i> Linn.)
Vata (<i>Ficus bengalensis</i> Linn.)	Kapitha (<i>Myrica nagi</i> Thumb)
Ashwatha (<i>Ficus religiosa</i> Linn)	Ksudra Dhanya (Inferior grains)
Pinyaak (powder of seasmum)	Tila tail (Seasum oil)

Table No. 8: Herbs for hypertension^[8]

Ashwagandha (<i>Withania somnifera</i> Dunal.)	(<i>Cinnamomum zeylanicum</i> Breyn.)
Neem (<i>Azadiracta indica</i> A. Juss.)	Mandukparni (<i>Centella asiatica</i>)
Garlic (<i>Allium sativum</i> Linn.)	Shankhapushpi (<i>Convolvulus pluricaulis</i>)
Guduchi (<i>Tinospora cordifolia</i> Willd.)	Ashoka (<i>Saraka ashoka</i>)
Ajvayan (<i>Carom caticum</i>)	Rudraksha (<i>Guazuma ulmifolia</i>)
Olive tree (<i>Oleo europaea</i>)	Badar (<i>Gmelina Asiatica</i> Linn.)
Amsul (<i>Garcina indica</i> Choisy)	Amlavettas (<i>Garcina pedunculata</i> Roxb.)

DISCUSSION:

Pharmacotherapy of Diabetic Retinopathy should be based on its multifactorial etiopathogenesis. Hence management has to include multiple drugs with pharmacological activities which help to break the samprapti. Rasayana, Lekhana, Dhavagni Deepana, Medohara, Chakshushya activities along with Madhumehahara and Dristigatarogahara activity are to be administered. Survey of Ayurvedic literature for drugs with these activities and recent researches on herbal drugs on Diabetic Retinopathy and associated or predisposing conditions enables to understand its pharmacotherapy.

Above observations are providing a baseline for developing a better therapeutic planning for Diabetic Retinopathy integrating Ayurveda and modern herbal research. Further studies with proper planning would help the traditional practitioners in treating patients suffering from this disorder.

CONCLUSION:

Ayurveda portray distinct concepts and principles of management of diabetes and their complications, so efforts are being made to generate evidence on extent of use and efficacy of its approaches.

With these herb we have to break the samprapti. Rasayana, Lekhana, Dhavagni Deepana, Medohara, Chakshushya activities along with Madhumehahara and Dristigatarogahara activity are to be administered.

The Molecular Signaling Pathways and Mechanisms Implicated in the Development of Diabetic Vascular Inflammation and Some Suggestions on the Potential

Therapeutic Strategies in the Ayurvedic herbs on different path way we can be prevent the Diabetic Retinopathy.

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