

#### REVIEW ARTICLE WORLD JOURNAL OF AYURVEDA SCIENCE

e-ISSN 2456-0227

### RASAYANA THERAPY IN DIABETIC NEUROPATHY

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Received on 06/05/2017

Accepted on 15/05/2017

Reviewed on 08/06/2017

Published on 20/07/2017

#### **ABSTRACT**

Neuropathy is the most common complication of Diabetes Mellitus. Main factors playing vital role in development of neuropathy are metabolic as well as vascular which causes degeneration of neurolema resulting in impaired nerve conduction. It is presented in the patients as Dysaesthesia / Parasthesia.

In Ayurveda Diabetes has been described as 'Madhumeha' which is a 'Vata' predominating disease causing derangement of body tissues. 'Vata' is vitiated either due to 'Dhatu Kshaya' (quantitative or qualitative loss of tissue factors) or vitiation of vata due to obstruction in microchannels responsible for nourishment and maintenance of tissue fators. As per description available in Ayurvedic literature derangement of body tissues starts much before appearance of characteristic clinical features of 'Madhumeh'. 'Pani Pad Tala Dah' (burning sensation in palms and soles) a symptom of afflicted nervine tissue is mentioned as purvaroopa (pre diabetic stage) i.e a stage wherein vitiated doshas have just started to effect tissue factors.

'Rasayana' is a unique to bring and to maintain the metabolic activities in equilibrium, bringing normalcy in body tissues thus improving resistance and immunity against diseases, prolonging the life, developing the positive health and improving the quality of life. 'Rasayana' act at the level of 'Dhatus' (body tissues), 'agni' (metabolic activities) and 'srotansi' (micro circulation).

A number of 'Rasayana' drugs are in use to combat diabetic neuropathy in Ayurveda such as shilajita, Guduchi etc .Various different researches have been reviewed in order to understand the importance of Rasayanas in general health and their uses and the active principles behind the drugs along with their mechanism of action in breaking the pathogenesis of Diabetes and its complications esp. Diabetic neuropathy. Many drugs have been found out having the quality of both the Rasayana and anti- Diabetic and also improving the status of its complications

Key words Rasayana Agni, Madhumeha

#### INTRODUCTION

Diabetes mellitus refers to a group of heterogeneous metabolic disorders that share the phenotype of hyperglycemia.<sup>1</sup>

The prevalence of diabetes is increasing dramatically in both developed and developing countries. The prevalence as estimated to be 2.8 % affecting 171 million people worldwide, in year 2000. With current trends, the prevalence worldwide is estimated to reach 4.4%, affecting 366 million people by the year 2030. Diabetes and its complications are the major causes of mortality, morbidity and decreased quality of life.<sup>2</sup>

Diabetic neuropathy is one of the common microvascular complication characterised by sensory abnormalities like paraesthesia, burning sensation, cutaneous hyperaesthesia and numbness and loss of tendon reflexes<sup>3</sup>

The prevalence of diabetic neuropathy is rising with the global burden of type 2 diabetes given that diabetics effect approximately 246 million people worldwide it is estimated that 20 to 30 affected million people are neuropathy. symptomatic diabetic Neuropathy is a leading and independent risk factor for mortality and morbidity.<sup>2</sup>

#### TYPES OF DIABETIC NEUROPATHY<sup>3</sup>

- Chronic distal symmetrical sensory
   motor poly neuropathy
- Autonomic neuropathy
- Focal/ asymmetrical neuropathies

#### PATHOGENESIS (SAMPRAPTI) OF DIABETIC NEUROPATHY

KAPHA PRADHAN NIDANA



DOSHA PRAKOPA

(KAPHA PRADHAN TRIDOSHA)



KLEDAKA KAPHA PRAKOPA



**AAM** 



**JATHARAGNIMANDHYA** 



**DHATWAGNIMANDHYA** 



HAMPERED DHATU POSHAN KARMA



MALA FORMATION OF DHATUS



BHAHU DRAVA SHLESHMA

## BAHU ABADHA MEDA **ABHISHYANDA SROTORODHA** AVRAN OF VATA VATA PRAKOPA **AVARANA** DHATU KSHAYA AYURVEDA MODERN AYURVEDA **MODERN** VATA PRAKOPA STHANA SANSHRAYA **HYPERGLYCEMIA** HYPERGLYCEMIA IN DHATUS & DUE TO DHATU-**UPDHATUS** KSHAYA PRODUCTION OF END GLYCATION **PRODUCTS** LONG STANDING **ACTIVATION OF** LOCAL DHATUS + FREE RADICALS ALDOSE REDUCTASE AAMAVASTHA + VATA PRAKOPA (POLYOL PATHWAY) **EMACIATION OF OXIDATIVE STRESS SOTHA** GLUCOSE SORBITOL LOCAL DHATUS (NAADIS) ACCUMULATION OF SORBITOL INJURY TO **APOPTOSIS** IN NERVE TISSUES + DEPLETION NAADI VASONEURON OF NEURONS **KSHAYA** OF MYO-INOSITOL MICROANGIOPATHY **INFLAMMATION** OF VASA NERVORUM OSMOTIC SWELLING ISCHEMIA & HYPOXIA DEGENERATION OF MYELINATED Na<sup>+</sup> K<sup>+</sup> ATPase ACTIVITY & NON MYELINATED NERVE FIBRES **DECREASE**



SOTHA

PERIPHERAL NEUROPATHY

VATA – SPARSH VAIGUNYA PITTA – HASTA-PADA DAHA KAPHA – HASTA-PADA SUPTATA

ABNORMAL PROPRIOCEPTION
VIBRATION & TOUCH SENSATION,
BURNING PAIN, ABNORMAL HEAT
SENSATION, ABNORMAL COLD & PRESSURE
SENSATION DEEP & LANCATING PAIN
BOWEL, BLADDER & SEXUAL DYSFUCTION

**Rasayana**, is a sanskrit word, with the literal meaning: Path (āyana) of essence (rasa).<sup>4</sup>

Medicines which invigorate a healthy persons and alleviate the diseases are *Rasayanas* (rejuvenators).<sup>5</sup>

## Types of Rasayana

- *Pranakamya* Promoter of vitality and longevity
- *Medhakamya* Promoter of intelligence.
- *Srikamya* Promoter of complexion.
- Naimittika Rasayanas help to fight a specific disease.

#### **METHODOLOGY**

- (I) Critical study of Ayurvedic literature with aim to understand diabetic neuropathy in Ayurveda.
- (II) Internet search on Google, Wikipedia, DOAJ, PUBMED ETC with keywords *prameha*, *madhumeha*, *rasayana*, Diabetes, Diabetic neuropathy.

#### TABLE NO. 1 OBSERVATION

S.NO	NO. OF ARTICLES	NO.	OF	ARTICLES
		FOUN	D SUIT	ABLE
MADHUMEHA	5	4		
PRAMEHA	10	8		
DIABETES	20	15		

DIABETIC	10	8
NEUROPATHY		
RASAYAN	8	3
TOTAL	53	38

TABLE No.2 RASAYANA USEFUL IN DIABETES AND DIABETIC NEUROPATHY

S No.	Name Of the Research Paper	Properties
1. GUDUCHI	Anti-Diabetic claims of	(i)Anti-hyperglycemic
Tinospora	Tinospora cordifolia. Critical	(ii)Adaptogenic
cordifolia	Appraisal and role in therapy.	(iii)Hepeto-pancreato
	Rohit sharma, Hetal	protective.
	Amin, Galib, Pradeep kumar prajapati.	(iv)Hormones regulator.
	Asian Pacific Journal of Tropical	
	biomedicine.2015;5(1):68-78.	
2. GOKSHUR	α-Glucosidase and Aldose reductase	$\alpha$ -Glucosidase and Aldose
Tribulus	inhibiting activity in vitro and Anti-	reductase inhibitor
terrestris	diabetic activity in vivo of tribulus	
	terrestris.	
	HARMIDER SINGH LAMBA,	
	CHANDER SHEKHAR	
	BHARGAVA, MAYAK THAKUR,	
	SHILPI BHARGAVA.	
	International journal of pharmacy and	
	pharmaceutical sciences. Vol 3, Issue	
	3, 2011.	
3. SHILAJEET	Evaluation of effects of Shilajatu on	(i)Ojovardhak
Asphalthum	Madhumeh.	(ii)Pramehagna
punjabinum		(iii)Agnideepak
	World Journal of Pharmacy and	(iv)Sroto shodhak
	Pharmaceutical Sciences Vol 4, issue	
	07 2015	
4. PUNARNAVA	Hypoglycemic effects of Traditional	↑ Hexokinase activity
Boerhavia	Herbs used in the treatment of	↑ Plasma insulin
Diffusa	Diabetes.	↓ Glucose-6- phosphatase
	Baby Joseph and D.Jini	
	Research Journal of Medicinal	
5 VIII VIII D	plants.5(4) 352-376,2011.	
5. VIJAYSAR	Hypoglycemic effects of Traditional	(i)Pterostilbene rejuvenate
Pterocarpus	Herbs used in the treatment of	β cells in pancreas.
marsupium	Diabetes.	(ii)Reduces inflammation
	Research journal medicinal plant	and insulin resistances
C CHIA DAIA	5(4) 352-376,2011	(:\ A 1 1
6. SWARNA	Madhumeh with current evidence and	(i)Agnideepak
MAKSHIK	intervention with Ayurvedic	(ii)Vrshya
	rasaushadhi. Das, Banani, Mitra,	(iii)Rakthposhak

	Achintya Hazra, Jayram.	(iv)Yogvahi
	Indian Journal of traditional knowledge 10(4): 624-628, Nov 2011.Pub-NISCAIIR-CSIR.	
7. <i>ATIBALA</i> Abutilon	Anti-diabetic activities of Abutilon indicum are mediated by enhancement	(i)Improves insulin sensitivity
indicum	of adipocyte differentiation. Chut wade	(ii)Glucose transport-1
	krisanapun, Seong-holee, Penchom	promoter activity
	Peungvicha, Rungravi temsirirkkul,	(iii)Analgesic
	Seung joon back.	
	Evidence based complementary and	
	alternative medicine. Vol 2011 article 1	
	D 167684.	

## Review of Rasayana and their effects on Diabetes and its complications.

#### *GUDUCHI*

- 1. Tinospora cordifolia (Guduchi) is found to be effective in hyperalgesia in experimental Diabetic neuropathy in streptozotocin induced diabetic rats. Aldose reductase inhibitory activity of Guduchi has also been found in-vitro.<sup>6</sup>
- 2.The different alkaloids like Magnoflorine, Palmetine, Jatrorrhizine, <sup>7</sup> tannins, cardiac glycosides, flavonoids, saponins, etc. <sup>8</sup> present in *Guduchi* (Tinospora cordifolia) have anti-diabetic activity.
- 3. Arial part of Tinospora Cordifolia may contain phytoconstituents like alkaloids, glycosides, flavonoids, steroids terpenoids. The analgesic activity of Guduchi (Tinospora Cordifolia) is due to the various flavonoid present in it which inhibits the production of prostaglandins,<sup>9</sup> hence reduces the inflammation. Also its stem contains methanol which decreases the activity of SOD, GPx in alloxan induced diabetic rats. 10,11 Leafs extract of Guduchi (Tinospora Cordifolia ) contains saponarin (an alpha-glucosidase inhibitor) which has a significant role as an antioxidant and hydroxyl radical activity. 12 scavenging All these

constituents helps in reversing the pathogenesis of the Diabetic Neuropathy.

4. The plant *Guduchi* (Tinospora cordifolia) has also been shown neuroprotective action by initiate the antioxidant system in rat hippocampal slices subjected to oxygen glucose deprivation. <sup>13</sup>

#### **GOKSHURA**

- 1.It has been found that when streptozocin induced diabetic rats were treated with T. alatus extract and T.terestris extract the atrophied and degenerated beta cells of pancreas were normalized when monitored histopathologically. But t. alatus showed its mechanism more than T. terestris. <sup>14</sup>
- 2.Phytochemical analysis of *Gokshura* (Tribulus Terestris) shows that it contain many major constituents like flavonoids, steroidal saponins, alkaloids, lignanamides which are found useful in the treatment of diabetes mellitus.<sup>15</sup>

#### *PUNARNAVA*

1.The extract of leaves of *Punarnava*(Boerhaavia diffusa) causes reduction in blood glucose as it rejuvenate beta cells of pancreas which has been shown in experiments on streptozotocin-induced NIDDM rats.<sup>16</sup>

- 2. *Punarnava* (Boerhavia diffusa) contain alkaloid punarnavaine, punarnavoside which increases the hexokinase activity, decreases glucose 6 phosphatase and fructose bi- phosphatase activity in glucose metabolism. Also it increases plasma insulin levels.<sup>17</sup>
- 3. The roots of *Boerhavia diffusa* L. possess diuretic action, anti-inflammatory. Its leaf extract has hypoglycemic effects. the effects of *B. diffusa* leaf extract on antioxidant in liver and kidney of alloxan diabetic rats are reported. <sup>18</sup>

The B. diffusa leaves are rich in alkaloids including sterols ursolic hypoxanthine-9-L-arabinofuranoside, punarnavine 1 and 2, myricyl alcohol, myristic acid and quinolizidine alkaloids<sup>33</sup>. These compounds may be responsible for the antioxidant and antidiabetic activity of B. diffusa leaves, which may attributed to its protective action on lipid peroxidation and to the enhancing effect cellular antioxidant defense on contributing to the protection against oxidative alloxanized damage diabetes.18

#### VI.JA YSAR

1. Vijaysar (pterocarpus marsupium) shows inhibition of ALR (aldose reductase) the alcoholic extract of P. marsupium prevents the accumulation of intracellular sorbitol. Which in turn reduces the injury to the nerve cells and prevent diabetic neuropathy.

Alcoholic extract showed remarkable antioxidant activity and/or free radical scavenging activity, antiglycation, property. 19

#### SWARNA MAKSHIKA

1. Age-Related macular degeneration Study-based micronutrients inhibit the development of diabetic retinopathy in rodents by inhibiting oxidative and nitrative stress. The use of minerals like vanadium, chromium, magnesium, zinc, selenium, copper and vitamins or cofactors

(tocopherol [vitamin E], ascorbic acid [vitamin C], ubidecarenone [ubiquinone; coenzyme Q], nicotinamide, riboflavin, thioctic acid [lipoic acid], flavonoids) are advised in diabetes, with a particular focus on the prevention of diabetic complications.<sup>20</sup>

2. Swarna makshika is found to be effective in lowering blood sugar levels<sup>21</sup>.

#### ATIBALA

1. Atibalamula shows highly significant reduction in the symptoms of Diabetic neuropathy including numbness, tingling, burning sensation and pain in lower limbs in the patients of Diabetic neuropathy.<sup>22</sup>

Out of all the *Rasayanas* found effective in Diabetes and Diabetic neuropathy most of the *Rasayanas* work on hyperglycemic condition and lowers the blood sugar levels which in turn prevent the complications of diabetes but *Shilajatu* which is mentioned as a *naimittik* rasayana shows direct effect on breaking the pathogenesis of neuropathy through various pathways.

#### **Detail description of** *SHILAJATU*

Shilajatu as per the word meaning is conqueror of mountains and destroyer of weakness.

## Vernacular name<sup>23</sup>

English- Black Bitumen, mineral pitch. Latin- Asphaltum punjabinum or Bitumen judiek.

Sanskrit- *Shilajatu*. Hindi- *shilajit*.

# Pharmcological and Therapeutical Properties of $Shilajatu^{:24,25}$

- Rasa- Tikta, Lavana, Kashya, Katu.
- Guna- Guru, Snigdha, Mrudu, Sheeta.
- Veerya- sheeta.

- Vipaka- Katu.
- Karma- Rasayana, Yogvahi, Sarvaroghara.
- Doshprabhava- kaphahara, Tridoshaghna.
- Vyadhiprabhava- kaphja roga, Kshaya, Prameha, Pleeha, Gulma, Unmada.

## Chemical composition<sup>26</sup>

Shilajatu is a humic substance produced by interaction of plants, algae, mosses, microorganisms and also the phytochemistry of vegetation around shilajatu bearing rocks constituted an important part. It contains Fulvic acids and Humic acids, phenolic acids, glucose, arabinose, rhamnose and xylose.

#### Bioactivity of Shilajatu

- 1. Fulvic acid is a strongest chelating agent act as a free radical scavengers. It converts harmful heavy metals into aluminium silicate which is safe for the body. It reduces the risks of degenerative disorders. <sup>27</sup>
- 2. *Shilajatu* may be associated with correction of blood glucose level and lipid regulation in circulation. Experimental studies reveal that may be associated with phenomenon of reducing direct sugar and lipid from gut, thereby affecting the overall metabolic syndrome.<sup>28</sup>
- 3. The anti-stress activity of these compounds was suggested by their augmentation of murine swimming endurance exercises. The results obtained till now are sufficiently impressive to warrant expectation that the *Ayurvedic Rasayana*, *Shilajit*, as more effective than several currently available clinically efficacious immunomodulators.<sup>29</sup>
- 4. Shilajatu is a rasayan dravya. It has very important role in mootravaha strotas. Shilajatu acts as diuretics and antioxidant. New research shows shilajatu contain 85 minerals in ionic form and it contains uvic acid, humic

- acid, hippuric acid, and benzopyrones. The active principle in *shilajatu* as uvic acid regenerates & prolongs the degeneration of essential nutrients in the cells. Fulvic acid restores electrical balance to damage cells, neutralizes toxins & eliminates food poisoning in a short duration. *Shilajatu* provides iron to the body that are necessary for making the red blood cells (RBC's). It also acts as a stimulant for immune system. It is a strong kidney tonic. <sup>30</sup>
- 5. The effect of *Shilajita*, as reported in the *Ayurvedic* literature, seems to suggest its influence on endocrine, autonomic, and brain functional changes. The discovery that these changes can be mediated by cytokines, released by activated immune cells, has opened up possibilities for similar mechanism of action of *Shilajita*.<sup>31</sup>
- 6. Certain combinations of the phenolic and triterpenoid constituents and the fulvic acids of *Shilajita* produced significant effects against restraint stress-induced ulcers. Similar anti-inflammatory, analgesic, anti-diabetic, immunomodulatory, anti-anxiety proper-ties of *Shilajita* have been seen.<sup>3</sup>
- 7. According to classical texts *Shilajita* is supposed to be the exudates from the top of the mountains, but after chemical analysis it is found to be a plant fossil mostly generated by Euphorbea royalena and Trifolium repens and many more bryophtes. It is a mineral enriched adaptogen. It has nearly 85 ionic minerals and mainly contains fulvic acid and humic acid. <sup>33</sup>

**Dose**<sup>34</sup>- For *vyadhi nashana*- Upto 1*tula* (100 *pala*) sevena. *Rogi* becomes *madhumeh mukta*.

#### **DISCUSSION**

Rasayana (rejuvenation therepy) is a therapeutic modality to achieve rasa

(primordial tissue factor) and other *dhatus* par excellence. Rasayanas are the drugs to maintain *swasthya*<sup>35</sup>(*healthy state*) and are uriaa (vigour) .Swastha (health) itself is defined as the state of samdosha<sup>36</sup> (equillibrium of body humours), sam agni (equilibrium of metabolic factors), sam dhatu (equilibrium of tissue factors) and sam mala kriya (adequate balance of excretory factors). It may be achieved only if Rasayan dravya act at the level of dhatu (body tissue), agni (metabo lic activities), srotasa (microcirculation). Rasayana helps in the formation of pure rasa through proper digestion of ahara taken at jathragni, bhutagni and dhatwagni level. The qualitative excellence achieved at rasa (primordial tissue) in turn improves the quality of subsequent dhatu.

Also the *sam agni* ensures *mala pachana* at *dhatu* level which in turn ensures the patency of srotas (*micro channels*) and henceforth improves nutritional supply to the various *dhatus*. All these together maintain a homeostasis in the body and reduces the risk of disease inside the body.

Diabetic neuropathy is believed to occur due to Avrana janya vata prakopa. Vitiated vata damages nervous tissues by local inflammatory process (shoth) simultaneously Avrana causes sroto avrodh(obstruction in microchannels) which lead to malformation of preceding Dhatu( progressive nutrition of tissues) leads to further *Dhatu kshya*( emaciation at tissue level as well as at microlevels).

Shilajatu (Asphalthum punjabianum) is anamla panchrasa, katu vipaka, sheeta virya and laghu. It causes agni deepan due to its laghu guna and sheeta virya. It is a srotosodhak(cleaning the microchannels) due to its katu vipaka and ojovardhak(innate immunity) due to its prabhava. With these qualities shilajatu helps in pachana of doshas(toxic metabolites) – removes avrana- sroto shodhana- pacifies vata- reduces nerve tissue degeneration. Ojovardhana property of shilajatu ensures

dhatu poshan (at cellular level and ultimately causes nerve cell regeneration. Therefore shilajatu a rasayana may be used as an ideal therapeutic agent to manage Diabetic neuropathy.

#### **CONCLUSION**

Rasayan therapy helps to attain optimal physical strength, quality of dhatus, longevity, immunity or bala and mental competence. Shilajatu, as reported in ayurvedic literatue, seem to suggest its influence on endocrine autonomic, and functional changes hence Shilajatu as a rasayana helps in combating both Diabetes mellitus and Diabetic Neuopathy.

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Source of support: Nil

Conflict of interest: None Declared