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REVIEW OF NISHA AMALAKI –AN AYURVEDIC FORMULATION OF TURMERIC AND INDIAN GOOSE BERRY IN DIABETES

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ABSTRACT

Introduction- *Nishamalaki* or *Nisha Amalaki* representing various combination formulations of Turmeric (*Nisha, Haridra, Curcuma longa L.)* and Indian gooseberry (*Amalaki, Emblica officinalis* Gaertn.) is recommended in Ayurvedic classics, proven efficacious and widely practiced in the management i.e. treatment of Diabetes along with management and prevention of complications of *Madhumeha* (Diabetes). **Aims and objectives-**Inspite of many pharmacological, clinical researches of *Nishamalaki* on Glucose metabolism and Glycemic control, their review is not available, hence present study was conducted. **Material and methods-** Evidence based online published researches of *Nishamalaki* on Glucose metabolism and Glycemic control and its efficacy in the management of complications of Diabetes from available databases and search engines were referred for review through. Summary of published researches was systematically arranged, analyzed and presented. **Observations and results-**Review of online Published original research studies reveals total were found to be 13 in number, comprising of 3 in vitro studies and animal experimental pharmacological researches each and 7 clinical researches. **Discussion and Conclusion-** *Nishamalaki* is group of various combination formulations of *Haridra* and *Amalaki.* It is effective in the clinical management of *Madhumeha, Prameha* and Diabetes. *Nishamalaki* possess antihyperglycemic, Antidiabetic, insulinomimetic, α-Amylase inhibitory and α-glucosidase inhibitory, antioxidant properties. It improves insulin sensitivity, increases glucose uptake by skeletal muscles and is beneficial in the management of *Madhumeha, Prameha* and Diabetes as well as prevention of its complications microvascular- like diabetic nephropathy, neuropathy, retinopathy, gastropathy and macrovascular like atherosclerosis. **Conclusion-** *Nishamalaki* is group of various combination formulations of *Haridra* and *Amalaki.* It is effective in the clinical management as well as prevention of complications of *Madhumeha, Prameha* and Diabetes.

KEYWORDS: Inspite of many pharmacological, clinical researches of *Nishamalaki.*

INTRODUCTION

Formulation "*Nishamalaki*" or "*Nisha Amalaki*" may be considered as a composition formulation or drug combination or mode of administration of drug or Fixed drug combination.[1]

Nishamalaki or *Nisha Amalaki* [(NA), various combination formulations of *Haridra* and *Amalaki*][2,3,4] is recommended in Ayurvedic classics, proven efficacious and widely practiced in the management (treatment, prevention of complications) of *Madhumeha* (Diabetes Mellitus).

AIMS AND OBJECTIVES

Inspite of many pharmacological, clinical researches of *Nishamalaki* on Glucose metabolism and Glycemic control, their review is not available, hence present study was conducted.

MATERIAL AND METHODS

Search method-Published researches on *Nishamalaki* in the management of Diabetes (Antihyperglycemic effect, Hypoglycemic effect, Antidiabetic effect, insulinomimetic effect and effect on glucose uptake, effect on glucose utilization, Glucose regulation, Diabetic complication (microvascular and macrovascular complications) i.e. prevention of Diabetic nephropathy, Diabetic neuropathy, Diabetic retinopathy, Cataract formation, antioxidant activity, Cardiomyopathy) were compiled from relevant published research papers in various databases of research journals and search engines like J gate, Springer, Elsevier, Pub med, Yahoo, Worldwidescience.org, NISCARE online periodicals, Biomed central, Biomed search, Google, Google India, Google scholar. Inclusion criteria- Articles either exclusively, predominantly on above mentioned pharmacological activities or from studies of other

research areas were included. Articles displayed in minimum first 2 pages of website of respective search engines (else till display of webpage page without relevant matter) were included. Exclusion criteria-Articles predominantly on literature review, Safety and toxicity study, other pharmacological studies (other than mentioned above) and principally Pharmaceutical, Analytical, pharmaceutico-analytical studies were excluded from the review. Researches which are mentioned as only title or only as an abstract, their details are included in review.

Repeated same research work in different publications was considered as one. Summary of published researches was systematically arranged, analyzed and presented.

RESULTS AND DISCUSION

Review reveals that total Published original researches were found to be 15 in number, comprising of 5 animal experimental pharmacological researches (3 antidiabetic (including research on antioxidant effect, prevention of Dibaetic complications like nephropathy, cataract formation and neuropathy), 2 antihyperglycemic), 3 in-vitro studies (2 Alpha Amylase inhibitory and one Alpha glucosidase inhibitory study) and 7 clinical researches (6 in diabetic patients and one in healthy volunteers for evaluation of drug-drug interaction)(Table 1).

Table-1.

Type of Research	In vitro	In Vivo(Animal)		Clinical		Total
		Anti-hyperglycemic	Anti-diabetic	Diabetic	Healthy volunteers	
Published researches	3 (2 α Amylase and 1 α glucosidase inhibitory study)	2	3	6	1 (Drug Drug Interaction)	15

Summary of Published research works
Experimental studies-08
In-vitro study
α-amylase inhibitory and α-glucosidase inhibitory effect

Screening of *Nishamalaki Churna* (fine powder of *Curcuma longa* and *Emblica officinalis* 1:1) by α-amylase inhibition by starch iodine method and dinitrosalicylic acid method (DNSA) showed potent α-amylase inhibition IC_{50} 89.44 µg/mL by starch iodine method and IC_{50}100.0 µg/mL by DNS method.[5]

Sadiya Anjum *et al*, "Preliminary studies on the inhibitory effect of '*Nishamalaki Rasayana*' on pancreatic alpha-amylase and intestinal alpha-glucosidase", conference paper, "International Symposium on Phytochemistry (ISP-2015)", At Kerala Academy of Sciences, Thiruvananthapuram, Kerala, India April 2015. Details are not available online.

***In-Vivo* studies**
Animal studies
Antihyperglycemic

The *Nishamalaki Churna* (fine powder of *Curcuma longa* and *Emblica officinalis* 1:1) significantly reduced ($p< 0.05 – 0.01$) hyperglycemia at the dose levels of 90 and 180 mg/kg, compared with glucose treated group (group-2). The glucose control group showed significant ($p< 0.01$) increase in glucose levels after 30 min of glucose administration in all the animals when compared with normal group animals. The hypoglycemic effect of *Nishamalaki Churna* comparably equivalent to the standard metformin.[6]

Antihyperglycemic study of *Nisha Amalaki yoga* [ASBNAC, prepared with 16 times levigation (*Bhavana*) of mixture of fine powder of turmeric and *Emblica officinalis* (1:1) with fruit pulp juice of later in half the quantity of mixture for each levigation] at 2 dose levels (43.29 and 260mg/kg) and Standard control (SC) Glibenclamide (0.065 mg/kg) in Swiss albino mice, per orally showed that, ASBNAC at both the dose level showed comparative reversal of BSL at all test intervals after 30 minutes, whereas Glucose control group had shown statistically significant hyperglycemia. *Nisha Amalaki yoga* exhibited dose related antihyperglycemic effect at 43.29 and 260mg/kg, orally corresponding to 0.33gms and 2gms single human dose.[7]

Antidiabetic
Effect on Hyperglycemia

Nisha Amalaki (Mixture of Powder of *Haridra* and *Amalaki* in equal proportion), in animal dose of 0.9 g/kg wt of rats, showed significant lowering of plasma glucose and glycated hemoglobin in diabetic rats ($p<0.001$ when compare with Diabetic Control) as that of Glyburide (36 mg/kg) and Troglitazone(4 mg/kg).[8,9]

Nisha Amalaki was prepared from powder of *Curcuma longa* Linn. And fresh juice of *Emblica officinalis* Gaertn. According to Ayurvedic literature and administered with honey. *Nisha Amalaki* treatment (0.9 gm/kg) achieved significant ($p<0.01$) lowering of blood glucose in diabetic rats comparable to that of the Pioglitazone treated group. Pharmaceutical details of drug are lacking.[10]

Prevention of diabetic complications

Nisha Amalaki was prepared by *Bhavana* with *Amalaki Swarasa* (0.9 gm/kg). *Nisha Amalaki* showed protective effect on diabetic nephropathy & also delayed the progression of cataract in rats. Administration of *Nisha*

Amalaki was observed to be more effective in prophylactic groups.[11]

Prevention of Diabetic Neuropathy

Streptozotocin induced Diabetic rats were treated with *Nishamalaki* at lower and high dose, Glibenclamide, Pioglitazone and Epalrestat. Animals received drug treatment for next 12 weeks. Monitoring of Blood Sugar Level (BSL) was done every 15 days. Walking function test was performed to assess motor function. Dose-dependent improvement was observed in thermal hyperalgesia (Eddy's hot plate and tail immersion test) & cold allodynia in NA groups. Activity of NA was more than Glibenclamide, Epalrestat and Pioglitazone in high dose and comparable in low dose. *Nishamalaki* improved lipid profile. The diameter of nerve fibres in cross-section was markedly reduced suggesting the shrinkage of nerve fibres and marked axon atrophy and myelin vacuolization was evident in the cross-sectional view of the sciatic nerve in diabetic control group. Normal arrangement of fibres and density of myelinated fibres was well maintained in NA group. Few areas of partial loss of fibres were evident in Glibenclamide and Epalrestat treated groups. Apart from controlling hyperglycaemia, *Nishamalaki* effectively prevented the development of diabetic neuropathy (sensory and motor component).

Antihyperlidemic effect

Streptozotocin induced Diabetic Rats were fed with High Fat High Fructose diet were treated with *Nishamalaki* at lower and high dose, Glibenclamide, Pioglitazone and Epalrestat. Animals received drug treatment for next 12 weeks. Monitoring of Blood Sugar Level (BSL) was done every 15 days and lipid profile at the end. Serum cholesterol levels in diabetic control group shows significant increase ($p< 0.001$) than normal control. NA in 0.9gm/kg dose showed significant decrease ($p< 0.01$) in cholesterol levels. Glibenclamide and Pilglitazone showed less effect then NA ($p< 0.05$). In case of Serum triglycerides, similar pattern was observed in diabetic control group. There was significant reduction in the levels with both the doses of NA ($p<0.001$). *Nishamalaki* reduced lipid profile comparatively.[12]

Antioxidant property

Nisha Amalaki (Mixture of Powder of *Haridra* and *Amalaki* in equal proportion), in animal dose of 0.9 g/kg wt of rats, in antidiabetic study lowered Erythrocyte membrane lipid peroxidation to a comparable extent by the three drugs ($p<0.001$ as that of Diabetic control(DC)). *Nishamalaki* treated rats showed greater improvement in erythrocyte reduced glutathione (GSH) level and glutathione peroxidase (GSH-Px) activity (both $p<0.001$ as that of Diabetic Control) than Gliburide treated rats ($p>0.05$ vs DC for GSH and $p<0.05$ vs DC for GSH-Px) and this was comparable to the results of Troglitazone treated rats. Erythrocyte superoxide dismutase (SOD) activity was restored to a similar extent by the three drugs ($p<0.01$ vs DC).[13]

Sciatic nerve antioxidant effect

Levels of Malondialdehyde (MDA) were increased significantly ($p<0.001$) in diabetic control group compared to control, indicative of oxidative stress. Decrease in the levels of MDA was seen with high dose of *Nishamalaki* (NA). There was increase in levels SOD ($p<0.001$) and catalase ($p<0.001$) in NA group.[14]

Clinical studies-7

In Diabetic patients

Study-1- 14 diabetic patients were administered with *Amalaki Rasayana* (levigated powder of *Emblica officinalis* fruit pulp with of fresh juice of fruit pulp, 21 times) 8 Gm. per day and *Haridra* 16 Gm. per in four divided doses for 60 days. GTT and Serum Cholesterol tests were repeated at an interval of each 15 days.

Fasting blood sugar statistically significantly reduced on 45 days ($P <0.05$) and 60 days ($P <0.01$). Similarly 1st hr. blood sugar level was found statistically significantly reduced after 45 days ($P <.0.01$). The drug also showed significant reduction at 60^{th} day of treatment ($P < 0.01$). Similarly 2^{nd} hr. blood sugar level was significantly reduced on 30^{th} day ($P <0.01$) and on 60^{th} day ($P <0.05$) of treatment. The reduction in blood sugar level at 1^{st}, 2^{nd} and 2.5^{th} hr during GTT was 56.86 mg, 55.29mg and 58.16mg respectively. The drug showed symptomatic effect on symptoms of *Medodusti*. Initially 5 symptoms of *Kleda Dushti* were present out of these drug showed marked effect on *Mukha Shosha*, *Avilamutrata*, *Pipasa* and *Daha*.[15]

Study-2- Short term Hypoglycemic effect of drug was studied on 10 healthy volunteers. Before and after GTT was done. Three doses of *Amalaka Rasayana* (levigated powder of *Emblica officinalis* fruit pulp with of fresh juice of fruit pulp, 21 times) 2 gms and *Haridra* 4 gms were given 12 hrs, 5 hrs, and 2 hrs before GTT for only two days without any dietary restrictions. These effects of the drug were statistically insignificant (P 0.05).[16]

Study 3- *Nisha Amalaki* was given 1gm, 2 times/day with water for 6 weeks in 100 patients of *Madhumeha* (diabetic patients) in an open labeled clinical trial which showed moderate hypoglycemic effect. There was reduction in fasting blood sugar level and symptoms of *Madhumeha*.[17]

Study 4-*Nisha Amalaki* was given 1gm 2 times/d for 6 weeks in 25 patients of *Madhumeha* with different *prakriti* in one group and placebo "barley" in another group. Statistically less significant results ($P<0.1$) were observed in fasting and post prandial blood sugar levels in *Nishamlaki* treated group along with reduction signs and symptoms of the disease (*Prabhut Mutrata*, *Avila mutrata*, *Kshudha* and *Trusha*). *Kaphaja Prakriti* patients showed better response to *Nishamalaki*. Pharmaceutical details of drug failed to procure.[18]

Study 5- Tablets *Nisha Amalaki* (reference sushrut Samhita) were administered in the dose of 1gm 2 times/dy for 2 months in 10 patients of *Prameha.* They showed8.6 and 15.7% reduction in FBS and 9.8 and 13.4% reduction in PPBS after 1 and 2 months respectively. Pharmaceutical details of drug used for study are not published.[19]

Study 6-Gopakumar K; Bharathi K, "Clinical study in "*Nisha Amalaki Churna*" In *Ikshumeha* (Diabetes Mellitus", The antiseptic, 2005,Volume 102,Issue 5,Page 270-272.

Details are not available online.

Study in healthy volunteers
Drug-drug interaction
Study 7-Healthy volunteers were studied in two groups (6/group). Volunteers were randomized to oral metformin (500 mg single dose) alone or with concurrent DMFN01 (10 g) (*Mamejawa Ghana vati*), or DMFN02 (750 mg) *Nishamalaki churna*. Plasma metformin concentrations were measured within 0 to 24 h interval after administration.750mg single dose of *Nisha Amalaki churna* with metformin reduced 51% absorption of later when compared with metfomrin alone suggesting need to explore drug- drug interaction with metformin.[20]

Nishamalaki refers to group of various combination formulations of *Haridra* and *Amalaki*. It is effective in the clinical management of *Madhumeha, Prameha* and Diabetes. As per literature both the drugs are mentioned to have many benefits in healthy and diseased state and are mentioned to possess rejuvenating property (*Rasayana)*. *Nisha* and *Amalaki* are considered as drug of choice in the management of *Prameha* (Diabetes). *Amalaki* is recommended as dietary intervention for treatment of *Prameha.* Both Many research works had been carried out on *Nisha* (Curcuma longa), *Amalaki* (*Emblica officinalis* Gaertn), their extracts and chemical ingredients in these two drugs for their effects on *Prameha, Madhumeha,* Diabetes Mellitus, complications of Diabetes, Antihyperglycemic effects and effects on Blood glucose regulation. the drugs *Nisa (Nisha-Curcuma longa*) and *Amalaki* (*Emblica officinalis* Gaertn.) are abundantly cultivated in our country, hence affordable, congenial and can drastically reduce the cost of treatment of the disease, making it accessible to poor people. Hence combination *Nishamalaki* best suits for Diabetes management, which affects multisystem, multifunction and multiple organs.

Nishamalaki possess antihyperglycemic, Antidiabetic, insulinomimetic, α-Amylase inhibitory and α-glucosidase inhibitory, antioxidant properties. It improves insulin sensitivity, increases glucose uptake by skeletal muscles and is beneficial in the management of *Madhumeha, Prameha* and Diabetes as well as prevention of its complications microvascular- like diabetic nephropathy, neuropathy, retinopathy, gastropathy and macrovascular like atherosclerosis.

CONCLUSION

Nishamalaki refers to group of various combination formulations of *Haridra* and *Amalaki.* It is found effective in the clinical management as well as prevention of complications of *Madhumeha, Prameha* and Diabetes through in vitro, in vivo (animal and clinical) studies.

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