

Review on Nellyathi kasayam in the management of Diabetes Mellitus (Neerizhivu)

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Abstract- Globally diabetes is one of the major health challenges disease. This disease directly impacts the socio-economical level in person and country. Diabetes Mellitus is caused by lack of insulin activity. In type 2 diabetes there is resistance to the action of relative insulin; it causes insulin deficiency. Ancient Siddha text Sarabentira Vaithiya Muraigal has mentioned that Neerizhivu and their management under the Neerizhivu Sigitchai. Neerizhivu can be correlated with the Diabetic mellitus. Nellyathi kasayam is mentioned for the treatment of Neerizhivu (diabetic). *Nellyathi kasayam* is a polyherbal formula which includes the following herbs such as *Phyllanthus emblica*, *Strychnos potatorum*, *Tereminalia bellirica*, *Cissampelos pareira*, *Cyperus rotundus*. The objective of this study (review) was to assess the efficacy and safety of Nellyathi kasayam management of diabetes. A review of research work had been done in web search (PubMed, Google Scholar, Medline and Science Direct) journals and herbs-related books. Each herb in the drug has anti-diabetic effect. Following are the common Mechanism of action when the herbs do the anti-diabetic pharmacological action such as reduced insulin resistance in tissues, stimulates insulin secretion, regenerated β -cells, hypoglycemic effect, inhibits intestinal absorption (inhibitory effects on α -glucosidase and α -amylase activities) and antioxidant action. For this pharmacological action, the most of the ingredients of this drug contain the bioactive constituents of polyphenols, flavonoids, alkaloids, terpenoids, saponins, glycosides, and tannins. Therapeutic activity of this drug had been alternate the pathological changes of the diabetes mellitus and improvement of illness. This study had been given scientific explanation for ancient drug of Nellyathi kasayam use of diabetic. It can be concluded that Nellyathi kasayam can be used as a Siddha drug in treatment of diabetes mellitus. Further scientific evidence based on clinical studies are recommended with appropriate study design, adequate sample size, and statistical evidence to prove its therapeutic action.

Index Terms- Diabetes Mellitus, *Phyllanthus emblica*, *Strychnos potatorum*, *Tereminalia bellirica*, *Cissampelos pareira*, *Cyperus rotundus*.

I. INTRODUCTION

Diabetes mellitus is one of the Non-Communicable Diseases. It is a major public health problem in the present era. In the world, day to day, the prevalence and incidence rate of diabetic mellitus⁽¹⁾. WHO reports show about 422 million people worldwide have diabetes, particularly in low- and middle-income

countries, population who will be in the age 45-64 year. The following reasons are mentioned by 'WHO' such as ageing population growth, unhealthy diets, obesity and sedentary lifestyles⁽²⁾.

Diabetes is a chronic metabolic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin and it produces. Insulin is a hormone that regulates blood sugar. Hyperglycaemia, or raised blood sugar, which in turn damages many of the body's systems, in particular the blood vessels and nerves. In the management of diabetes involves diet, physical activity, and oral medication, but may also require insulin^(2,3,4).

Siddha Medicine is one of the ancient (more than 10000 years ago) traditional Medicine⁽⁵⁾. This system plays a prominent role in traditional health care system in the Northern and Eastern parts of Sri Lanka, especially in Jaffna. In particular, Siddha medicine had been established by the relationship of South India⁽⁶⁾. Herbs are the main source of the Siddha medicines and also used inorganic substances and animal products⁽⁵⁾. Interest in traditional systems of medicine and, in particular, herbal medicines, has increased substantially in both developed and developing countries over the past two decades⁽⁷⁾. In general, herbal secondary metabolites exhibit a wide array of biological and pharmacological properties⁽⁸⁾. The people believe that the herbal remedies from natural origin are harmless and carry no risk. Eighty per cent (80%) of the people in this world depend on traditional medicine for their primary health care needs⁽⁹⁾.

Sarabentira Vaithiya Muraigal is one of the Indian ancient Siddha books which is an abstract of palm script; it is edited by Mr. Vasudevasasthiri and Dr. Venkatramaiyer, published by *Saraswathimahala* library in *Thanjavur*. This book has mentioned that *Neerizhivu* and its management under the *Neerizhivu Sigitchai*. *Neerizhivu* can be correlated with the Diabetic mellitus⁽¹⁰⁾. The disease *Neerizhivu* is called by different names in Siddha books such as *Neerilivu*, *Mathumeham*, *Salarogam*, *Mihuneer*, *Vehumooththiram*, *Inippuneer*, *Mehaneer*, *Theanneer*⁽¹¹⁾.

Following are the common challenges when the diabetic patients are facing their quality of life.

1. Diabetic patient can't control their blood sugar level.
2. Continuously treated with high dosage of Allopathic drugs therefore they suffer with a lot of side effects.

Therefore, safety and efficacy of Siddha drugs are needed for them. WHO reports say that the herbal medicines, therapeutic activity refers to the successful prevention, diagnosis and treatment of physical and mental illnesses; improvement of symptoms of illnesses; as well as beneficial alteration or

regulation of the physical and mental status of the body. However, scientific research is needed to provide additional evidence of its safety and efficacy⁽⁹⁾.

Nelliyathikasayam is mentioned for the treatment of *Neerizhivu* (diabetic). *Nelliyathikasayam* is a poly herbal formula which includes the following herbs such as *Phyllanthus emblica*, *Strychnos potatorum*, *Tereminaliabellirica*, *Cissampelos pareira*, and *Cyperus rotundus*. All these herbs are easily available. Any institution can simply producing these drugs and increase the patient benefit with less expensive. To the best of our knowledge, there are no previous studies done in this drug and relevant information's are also not available. In other way thus this review for evidence base study if this drug is found to be effective for- *Neerizhivu*. The objective of this study was to assess the efficacy and safety of *Nelliyathikasayam* management of diabetes. Therefore, this study review will be scientific evident base of its safety and efficacy. This study will provide suggestions to the based on the results obtained.

II. METHODOLOGY

A review of research work had been done in web search (Pub med Google Scholar, Medline and Science Direct) journals and herbs related books. Following key words had been used in this study anti-diabetic effect of *Phyllanthus emblica*, *Strychnos potatorum*, *Tereminaliabellirica*,

Cissampelospareira, *Cyperusrotundus*. A totally 50

scientific papers had been review for this study which were published from 2000 to 2019.

III. RESULT AND DISCUSSION

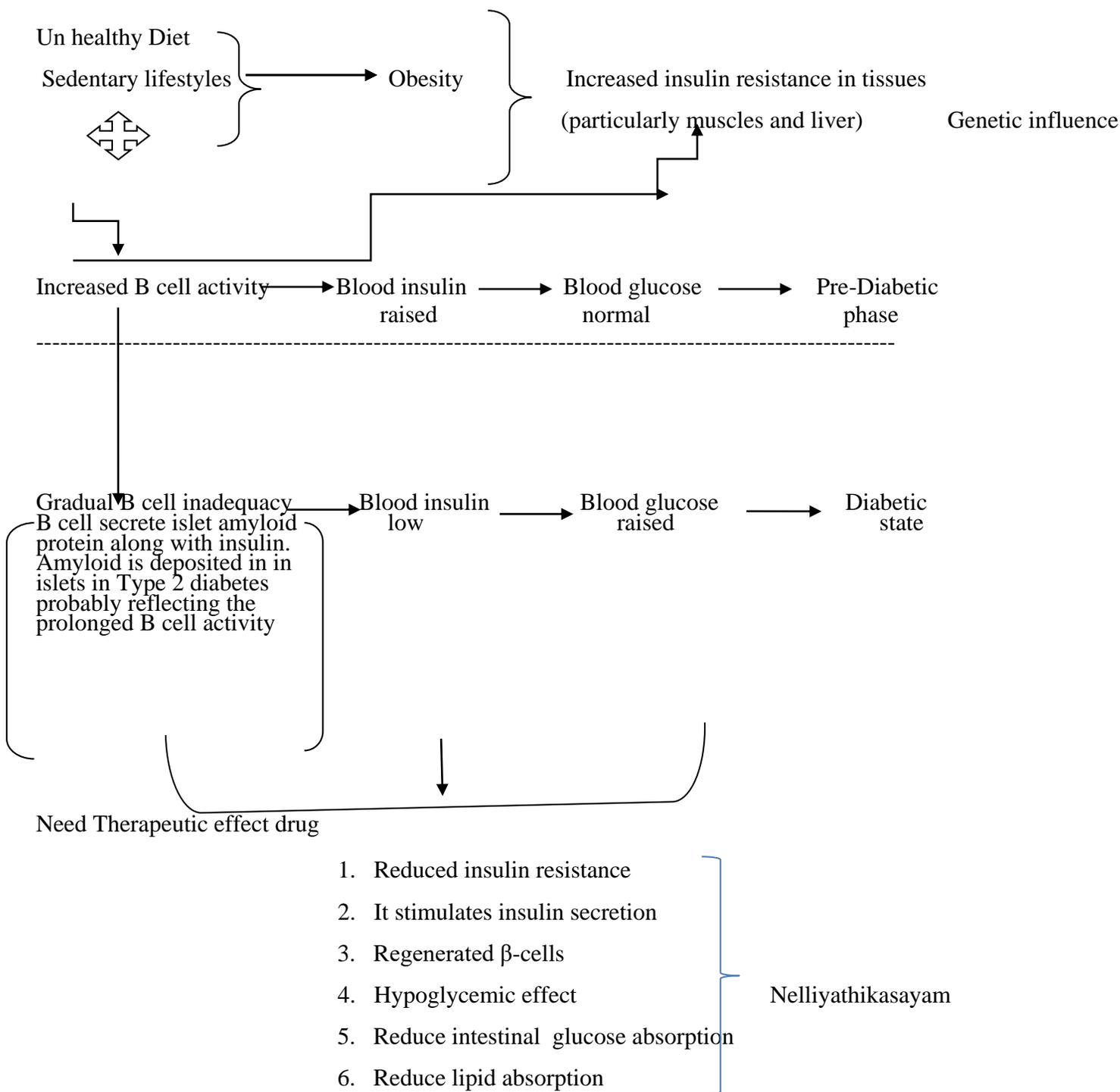
Majority of the articles were in review and animal studies. According this search all ingredients of *Nelliyathikasayam* herbs (*Phyllanthus emblica*, *Strychnos potatorum*, *Tereminalia bellirica*, *Cissampelos pareira*, and *Cyperus rotundus*) have anti-diabetic effect. These herbal secondary metabolites exhibit the anti-diabetic effect in through various multiple mechanisms of action. As show in the table (2.2) describe in the herbs detail, description, phytochemicals, and mechanism of action which ingredients of *Nelliyathi kasayam*.

Diabetes Mellitus is caused by lack of insulin activity. Commonly this is the result of diminished production of insulin. In type 2 diabetes there is resistance to the action of insulin i.e there is a relative insulin deficiency. Following are the main results when the lack of insulin such as Inability to control carbohydrate metabolism, increased fat catabolism, and increased catabolism of amino acids prevents proper protein synthesis⁽¹²⁾. As show in diagram (2.1) accommodates aetiology and pathology of the diabetes mellitus were correlate the pharmacological action of drugs. The treatment is in contrast to nature and temperament of the disease. Therefore the elimination of the root cause is the main treatment regime.

The table (2.2) describe in the herbs which ingredients of Nelliyathi kasayam

Botanical name	<i>Phyllanthus emblica</i>	<i>Strychnos potatorum</i>	<i>Tereminalia bellirica</i>	<i>Cissampelos pareira</i>	<i>Cyperus rotundus</i>
Family	Euphorbiaceae	Loganiaceae	Combretaceae	Menispermaceae	Cyperaceae.
Name Tamil:- English:- Sinhala:-	Nelli Emblic myrobalan tree Ambulla	Tetta Cleaning nut tree Ingini	Tanri Bellericmyrobalan Bulu	Ponmusueddi, Velvet-leaf Diyanmitta	Koori Coco-grass Muisthka(17)
Description	Tree(about 10m in high) spreading branches leaves single alternative very numerous ⁽¹⁷⁾	A small moderate sized tree with a blackish grey corky barks Leaves simple opposite 7.5-12.5 cm long Seeds:- black 1-2 cm diameter, circular bluntly ⁽¹⁸⁾	A large deciduous tree with straight buttressed trunk. long Leaves simple alternate without stipules placed at the ends of branches' 10-20 cm long Fruit ; - brownish-yellow tomentum stone large woody with a large seed cavity ⁽¹⁷⁾	perennial climber leaves simple alternative, ovate-orbicular Flowers small unisexual Rootstock woody, perennial ⁽¹⁹⁾	Perennial weed with slender, scaly creeping rhizomes, The tubers are externally blackish in colour and reddish white inside, The stems grow to about 25 cm tall and the leaves are linear, dark green ⁽²⁰⁾ .
Distribution	India, malay China, Ceylon(very common)	Ceylon (North,central, province), India, Myanmar;	Ceylon (kurunegala, Gal-oya). India, Barma, Malaya	Tropical and subtropical India, Ceylon, Singapore, Philippine	tropical, subtropical and temperate regions In Asia Ceylon(very common)
part used	Fruit	seeds	Fruit	Leaves	Rhizome
phytochemicals	Carbohydrates, Vitamin C, amino acids, minerals. polyphenol (Ellagic acid)flavonoids,HydrolysableTannins, Alkaloids(Phyllanthine, Phyllembein, Phyllantidine) ^(13,14)	Alkaloids(diaboline), flavonoids, glycosides, lignins, phenols, saponin, sterols triterpenes, mannogalactans and tannins	polyphenolic (gallic acid, ellagic acid, and chebulagic acid) triterpinoids (arjungenin, bellericagenin and belleric acid)	phenols, tannins, flavonoids, alkaloids, terpenoids, sterols, and reducing sugars. Potassium, calcium, and iron	flavonoids, tannins, glycosides, furochromones, monoterpenes, sesquiterpenes, sitosterol, alkaloids saponins, terpenoids, essential oils, starch, carbohydrates, protein, separated amino acids
Mechanism of action	inhibitory effects against both alpha-glucosidase and alpha-amylase activities ⁽¹⁵⁾ inhibitory action of lipase ⁽¹⁶⁾ antioxidant activity	Secretion of insulin by inhibiting the opening of the K ⁺ ATP sensitive channel ⁽³²⁾	Reduced insulin resistance, Antioxidant action, regeneration of β -cells, ^(22,23)	It stimulates insulin secretion from the remnants of β -cells or from regenerated β -cells ⁽²⁶⁾	inhibitory effects against both alpha-glucosidase and alpha-amylase activities antioxidant activity ⁽³¹⁾

The diagram (2.1) accommodates the aetiology, and pathology of the diabetes mellitus were correlate the pharmacological action of drugs.



Phyllanthus emblica

Anti-diabetic effect is in the *Phyllanthus emblica*. Sultana.et.al (2014) confirmed that the ethanolic extracts of fruit of *Phyllanthus emblica* has significant anti-diabetic effect. It is endowed with reduction of sucrose absorption and partly related to inhibition of disaccharides activity in the gut

(21).Krishnaveni.et.al also reported ethanolic extracts of fruit of *Phyllanthus emblica* has anti-diabetic action⁽¹³⁾. Bashir.et.al(2018) evaluated the Antioxidant and Antidiabetic activity of ethanolic extract of dry fruits of *Phyllanthus emblica* and the result indicated the presence of carbohydrates, tannins, phenols, alkaloids, flavonoids, saponins, glycosides, amino acids and proteins.

phenolic and flavonoid contents observed that *Phyllanthus emblica* is a potent antioxidant and antidiabetic agent⁽³⁶⁾. Srinivasan.et.al (2018) was reported the methanolic extracts of *Phyllanthus emblica* has major constituent Antidiabetic properties of quercetin. quercetin is a potential drug with anti-diabetic and anti hyperglycemic action mediated by changes in the levels of glucose, cholesterol, and triglycerides as indicated by in silico and in vivo studies⁽³⁷⁾. Fatima.et.al (2017) reported the *Phyllanthus emblica* can act as potent Anti-diabetic agent as it has active constituent, ellagic acid. Ellagic acid in *Phyllanthus emblica* exerts anti-diabetic activity through the action on β -cells of pancreas that stimulates insulin secretion and decreases glucose intolerance⁽³⁸⁾.

Terminalia bellerica

Ellagic and gallic acid are major ingredients of *Terminalia bellerica*. It has antioxidant activity it may be possible that these extracts may reduce the effect of inflammatory cytokine release during diabetes which may be one of the causative agents for the tissue destruction and insulin resistance⁽²²⁾. The hot water extract of *Terminalia bellerica* fruit active ingredients has gallic acid. It is the responsible for the inhibition of pancreatic lipase activity and suppression of the absorption of meal⁽²³⁾.

Latha et.al was carried out the animal and laboratory study. The compound was identified as gallic acid. Gallic acid was administered to streptozotocin (STZ)-induced diabetic male wistar rats at different doses for 28 days. Plasma glucose level was significantly ($p < 0.05$) reduced in a dose-dependent manner. Histopathological examination of the pancreatic sections showed regeneration of β -cells in addition, significantly decreased serum total cholesterol, triglyceride, LDL-cholesterol, urea, uric acid, and creatinine at the same time markedly increased plasma insulin of diabetic rats.⁽²⁴⁾

Another study with alloxan – induced rats given ethanolic extract of *Terminalia bellerica* suspended in water has shown significant decrease of the blood glucose (from 6th day of administration), as well as Oxidative stress produced by alloxan⁽²⁵⁾.

Cissampelos pareira

Basumata.et.al (2012) conducted an animal study to evaluate the anti-diabetic potential of *Cissampelos pareira* leaf extract. Fructose-alloxan-induced diabetic rats have shown the anti-diabetic effect. It stimulates insulin secretion from the remnants of β -cells or from regenerated β -cells. Light microscopic studies using Aldehyde-fuchsin staining technique showed significant higher islet volume and β -cells granulation scores in the *Cissampelospareira* treated diabetic rats compared to diabetic control rats⁽²⁶⁾.

Shanker.et .al(2013) was carry out animal study to the assessment of anti-diabetic effect of *Cissampelospareira* leaf extract and results support the medicinal uses of *Cissampelospareira* leaf in the treatment of diabetic⁽²⁷⁾. Other in vivo studies done by Piero.et.al (2015).The result show that the hypoglycemic activities and safety of *Cissampeols pareira*⁽²⁸⁾

Cyperusrotundus

Another study with streptozotocin-induced mice given, ethanolic extract of *Cyperusrotundus* rhizomes has shown significant anti-diabetic activity, improvement in body weight,

and reduction in elevated biochemical parameters such as SGPT, SGOT, cholesterol, and triglyceride levels⁽²⁹⁾.

Raut.et.al evaluate the Anti-diabetic activity of hydro-ethanolic extract of rhizomes of *Cyperusrotundus* and the result conform the Anti-diabetic activity of *Cyperusrotundus*. This anti-hyperglycemic activity can be attributed to its antioxidant activity as it showed the strong 11-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging action⁽³⁰⁾.

Tran.et.al was conducted a laboratory study to Identification of Phytochemical from methanol extract compounds of *Cyperus. rotundus* rhizomes responsible for the inhibition of Alpha-glucosidase and alpha-amylase. A new (2RS,3SR)-3,40,5,6,7,8-hexahydroxyflavane, together with three known stilbene dimers, cassigarol E, scirpusin A and B were isolated. Compound cassigarol E inhibited both Alpha -glucosidase and Alpha -amylase activities while the flavane 1 only showed effect on alpha-amylase, and compounds scirpusin A and scirpusinB were active on alpha-glucosidase. All four compounds showed significant 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity⁽³¹⁾.

Cyperus. rotundus has 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging Antioxidant action. *Cyperusrotundus* to suppress age formation and protein oxidation in a model of fructose-mediated protein glycoxidation. Scientists concluded that, since non-enzymatic glycation has been shown to correlate with severity of diabetes and its complications.⁽³²⁾

Strychnos potatorum

Strychnos potatorum has anti-diabetic action. It causes an enhanced secretion of insulin on the pancreatic Beta-cells in as much as they block the ATP sensitive K⁺ channel which initiates the membrane depolarization process. This leads to the activation of the voltage operated calcium channels. The latter event elevates the free intracellular Ca⁺⁺ concentrations which function as a coupling signal for the exocytosis of insulin that resides in the beta cells of pancreas. Potential to control post prandial hyperglycemia. Blood glucose lowering effect and significant increase in serum AST and ALT of ethanol extract of *Strychnos potatorum* was observed in alloxan diabetic rats as well as in fasted normal rats, this effect could, possibly be due to increased peripheral glucose utilization. Inhibition of the proximal tubular reabsorption mechanism for glucose in the kidney⁽³²⁾.

Biswas.et.al was carry out the animal study to evaluate the antidiabetic effect of *Strychnos potatorum* on streptozotocin induced male diabetic rats.in this study result conformed the *strychnos potatorum* has anti-diabetic action as it significantly reduce the blood sugar level⁽³³⁾. Biswas.et.al was carry out the another animal study to compared with glipizide and conformed the *Strychnos potatorum* has effective hypoglycemic compound. Mishra.et.al (2013) reported that the ethanolic extract of *Strychnospotatorum* showed significant anti-diabetic action and antioxidant.

IV. CONCLUSION

This study had been given scientific explanation for ancient drug of Nelliyaathi kasayam use of diabetic. That the Nelliyaathi kasayam can be used as a siddha drug in treatment of diabetes mellitus. Further scientific evidence base on clinical studies are

recommended with appropriate study design, adequate sample size, and statistical evidence to prove its therapeutic action.

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