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A REVIEW: POLY HERBAL FORMULATION FOR DIABETES

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ABSTRACT

Diabetes mellitus is a major global epidemic over the past few decades. The prevalence of diabetes has been increased worldwide and has reached alarming levels around the world, 463 million people have diabetes in the world and there are about 88 million people in the Southeast Asia region. Of this 88 million people, 77 million are from India. According to the IDF the prevalence of diabetes in the population is 8.9%. Although, synthetic oral hypoglycemic agents/insulin is the mainstream treatment of diabetes and effective in controlling hyperglycemia, they have prominent side effects and have failed to significantly alter the course of diabetic complications. This forms the main reason for an increasing number of people finding alternative therapies that may have less severe or almost no side effects. The present study was based on Polyherbal formulations and the products available in market for treatment of Diabetes.

Keywords: Diabetes mellitus, Poly herbal formulation, Marketed formulation, Ayurvedic

INTRODUCTION

Diabetes mellitus (DM) is one of the oldest diseases, having been referenced in Egyptian literature three thousand years ago. Around 1500 B.C., Indian physicians recognised the sweetness of diabetic patients' urine and named it "Madhumeha." [1]. As per WHO DM referred as diabetes, characterized by

hyperglycemia may be a chronic disease, which occurs when pancreas produces insufficient insulin or there's decreased insulin sensitivity in cells. By the year 2025,300 million people worldwide will be affected by most common disorder called diabetes. Diabetes affects 69 percent of

adults in underdeveloped countries and 20% of those in industrialized countries. With increased number of population, diabetes mellitus is emerging as a major health problem.

Types of DM Type -I or Insulin Dependent Diabetes Mellitus (IDDM)/ juvenile-onset diabetes is immune mediated characterized by beta cells destruction of pancreas by T-cell mediated immune attack and life span of pancreatic cell is decreased by one third along with keto acidosis in body tissues and fluid.

Type-II or Non-insulin Dependent Diabetes Mellitus (NIDDM)/ adult-on-set diabetes is due to lack of insulin secretion in response to blood glucose levels demonstrates NIDDM. Reduced insulin sensitivity is predominant abnormality, leading to hyperglycemia can be reversed by drugs improving insulin sensitivity or reducing glucose production by liver.

Gestational Diabetes Mellitus (GDM) In a non-diabetic pregnant woman, gestational diabetes develops nearly to the end of the 3rd trimester or beginning of 4th trimester. It is characterized by intolerance of carbohydrate due to body's inability to use insulin as a result of pregnancy induced hormonal changes. 4% of pregnancies are affected by

gestational diabetes, which further disappears after child birth [2].

TREATMENT

Insulin and oral hypoglycemic medications are two types of oral hypoglycemic medications. Insulin therapy should strive to imitate nature's achievement in minimising postprandial hyperglycemia and preventing hypoglycemia between meals. Insulin injections can be given intramuscularly or intravenously, and the site of administration is equally critical for improved and safe insulin action. Human insulin, cow insulin, and pork insulin are among the insulin formulations available. Insulin therapy is not without its drawbacks and side effects. When an incorrect dose of insulin is used and there is a mismatch between meals and insulin injection, the most serious side effects include weight gain and hypoglycemia. Weight gain is an unavoidable side effect of initiating insulin therapy for uncontrolled diabetes because of increasing truncal fat and muscle development. This is also attributable to lower glycosuria-related energy losses.

Oral hypoglycemic medicines include sulphonyl ureas like glibenclamide and glipizide, as well as biguanides like metformin and phenformin. Hypoglycemia is caused by sulfonylureas, which stimulate insulin release from pancreatic β -cells. They

bind to sulfonylurea (SUR) receptors on the plasma membrane of the β -cell, triggering the closure of ATP-sensitive potassium channels and depolarization of the cell. This opens voltage gated channels, allowing calcium ions to enter and produced insulin granules to be secreted. Sulfonylureas enhance insulin secretion from the pancreas and may also increase insulin levels by lowering hepatic clearance of the hormone in type 2 diabetes patients [3].

TRADITIONAL MEDICINES

TM is the world's oldest type of health care, and it's used to prevent and treat physical and mental disorders. Various societies have evolved beneficial healing strategies to tackle a variety of health- and life-threatening disorders throughout history. TM is also known as complementary and alternative medicine, as well as ethnic medicine, and it continues to play an important role in many nations today. The majority of the medicines used in TM are made from natural ingredients.

To improve therapeutic efficacy and reduce drug toxicity in TCM, proper processing and dose management are critical. Clinical investigations have yielded a significant amount of data, and TM has aided in the creation of contemporary medications in this way. TM has advantages over other kinds of

medicine in areas such as the discovery of lead compounds and drug candidates, the examination of drug-like action, and the exploration of physicochemical, biochemical, pharmacokinetic, and toxicological features because to its use of natural ingredients. If any kind of TM is successfully implemented, it may un-expectedly aid in the development of new pharmaceuticals, leading in numerous benefits, including large cost savings [4].

SINGLE HERBAL VERSUS POLYHERBAL FORMULATION

In Ayurveda, medication formulation is founded on two principles: single-drug usage and multiple-drug usage, the latter of which is known as PHF. Polypharmacy or polyherbalism is a fundamental traditional therapeutic herbal method that involves mixing many medicinal herbs to increase therapeutic effectiveness. The Ayurvedic literature "Sarangdhar Samhita," which was written hundreds of years ago in 1300 A. D., has stressed the concept of polyherbalism in this ancient therapeutic system. Plant formulations and mixed extracts of plants are preferred over separate ones in the ancient Indian medical system. Ayurvedic herbals are known to come in a variety of dose forms in which mostly all of them are PHF.

Even while the active phytochemical elements of certain plants have been identified, they are frequently present in trace amounts and are never enough to produce the desired therapeutic effects. For this reason, scientific researchers have showed that combining various plants of various strength can possibly give a bigger outcome than using the plant alone. Synergism is the term for the phenomena of favorable herb-herb interactions. Certain pharmacological activities of herbal active ingredients are only noticeable when potentiated by those of other plants, but not when administered alone. There are two processes through which synergism works, depending on the nature of the relationship (i.e., pharmacodynamics and pharmacokinetic).

Polyherbalism gives various benefits not present in single herbal formulations due to synergism. It is clear that a single multi-constituent formulation can achieve a superior therapeutic impact. To achieve desired pharmacological action, a lesser dose of the herbal preparation would be required, lowering the likelihood of harmful side effects. Furthermore, PHFs promote patient convenience by reducing the need to take more than one single herbal formulation at a time, which leads to enhanced compliance and therapeutic impact. When compared to

single herbal formulations, all of these advantages have resulted in the popularity of PHF on the market.

REASON OF USING POLY HERBAL FORMULATION

As previously said, PHF is just recently gaining popularity around the world, owing to the fact that it offers several benefits not found in allopathic medications. To begin with, PHFs are well-known for their excellent efficacy in a wide range of disorders. The therapeutic impact of herbal medicines is mediated by the presence of several phytoconstituents, as previously stated and the effects are further potentiated when compatible herbals are formulated together in PHFs. Many studies on PHF have been conducted to date in order to assess their effectiveness, and these studies have been published in international publications. Srivastava *et al.* (2012), for example, reported a variety of anti-diabetic PHFs in their investigation, including Dihar, Diabeta, Diasol, Dianex, DRF/AY/5001, Diashis, Diabrid, Diakyur, Diasulin, and others, all of which have been verified to have comparable effects to traditional allopathic treatments. According to a statistical study conducted in the United Kingdom, the main reason for the usage of medical herbalism is the treatment's effectiveness and beneficial effects [5].

MEDICINAL PLANT FOR DIABETES

Our Vedic literatures, such as the Charak Samhita, already mention the use of plants, herbs, and their derivatives to treat diabetes. More than 400 plants are incorporated in approximately 700 recipes which are wont to treat DM in almost two thirds of the planet population. A large number of in vivo studies

are conducted on animals to check the claimed activity have demonstrated the hypoglycemic property of the many plants, already reported in various literatures. Various medicinal plants have been reported for their anti diabetic actions are as follows [6].

Table 1: List of Herbs used in treatment of Diabetes

Scientific Name	Family	Local Name	Mode of Use
<i>Coccinia grandis</i>	Cucurbitaceae	Ivy Gourd	Leaf juice given twice or thrice a day
<i>Annona squamosa</i>	Annonaceae	Seetaphal	Young leaves taken early in the morning
<i>Gymnema sylvestre</i>	Asclepiadaceae	Gurmar	Leaf juice is taken early in the morning in empty stomach
<i>Eugenia jambolana</i>	Myrtaceae	Jamun	Seed Powder is taken
<i>Terminalia bellirica</i>	Combretaceae	Bahera	Dried fruit is taken
<i>Aloe barbadensis</i>	Asphodelaceae	Aloe vera	At 200 mg/kg, aloe vera gel has significant anti-diabetic activity.
<i>Marrubium vulgare L</i>	Lamiaceae	White horehound	Aqueous extract at 200 and 300 mg/kg/ twice daily for two weeks

MECHANISM OF ACTION OF HERBAL ANTI DIABETICS

The antidiabetic activity of herbs depends upon sort of mechanisms.

The mechanism of action of herbal antidiabetic might be grouped as-

- Stimulation of Adrenomimeticism, pancreatic beta cell potassium channel blocking, cAMP (2nd messenger)
- Renal glucose reabsorption is inhibited
- Insulin secretion from beta cells of islets or/and inhibition of insulin degradative processes is stimulated
- Insulin resistance reduction

- Necessary elements like calcium, zinc, magnesium, manganese and copper for the beta-cells are provided
- Regenerating and/or repairing of pancreatic beta cells
- Increasing the dimensions and number of cells within the islets of Langerhans
- Stimulation of insulin secretion
- Stimulation of glycogenesis and hepatic glycolysis
- It has a protective effect against the destruction of beta cells.
- Digestion improves as blood sugar and urea levels drop.

- Prevention in pathological conversion of starch to glucose
- Inhibition of the β -galactocidase and α -glucocidase

- Lowering activities of Cortisol
- Alpha-amylase inhibition

POLYHERBAL FORMULATIONS FOR DIABETES

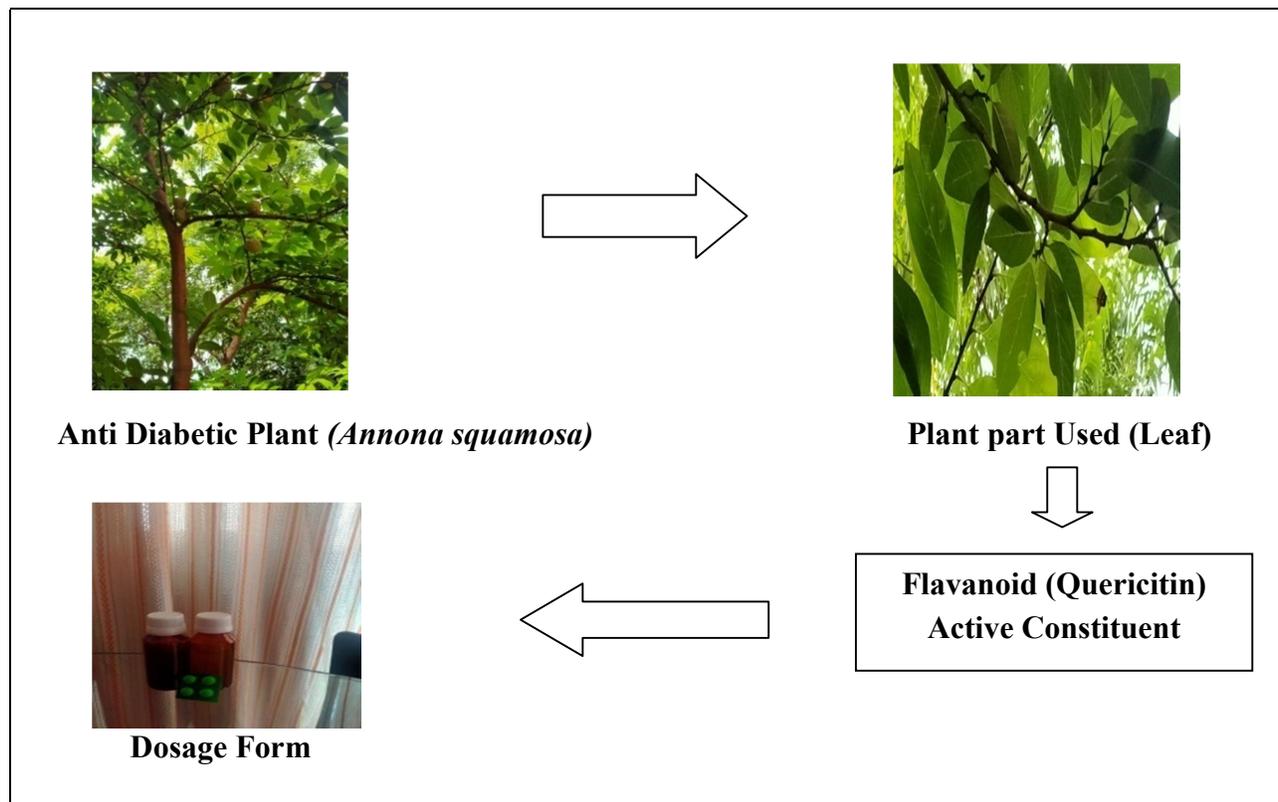


Figure 1: Graphical Representation of Poly herbal formulation

POLY HERBAL MARKETED FORMULATION

Epinsulin- Epicatechin, a benzopyran, is the active component of Epinsulin, which is marketed by Swastik formulations. Epicatechin enhances the islet's cAMP concentration, which is linked to enhanced insulin release. It plays a crucial role within the conversion of proinsulin to insulin by increasing cathepsin activity. It also has an insulin-like impact on human erythrocyte

osmotic fragility and inhibits Na/K ATPase activity in the patient's erythrocytes. It corrects the neuropathy, retinopathy and disturbed metabolism of glucose and lipids. It is reported to be a curative for diabetes, Non Insulin Dependent Diabetes Mellitus (NIDDM) and a good treatment for people with insulin-dependent diabetes mellitus (IDDM) to help them need less insulin.

Bitter gourd powder marketed by Garry & Sons lowers blood & urine sugar levels. It

strengthens the body's immune system and purifies the blood. Bitter Gourd has excellent medicinal virtues. It has antidote, antipyretic, palatable, stomachic, antibilious, and laxative properties. It contains bitter glycosides, saponins, alkaloids, reducing sugars, phenolics, oils, free acids, polypeptides, sterols, 17-amino acids including methionine, and a crystalline product called p-insulin, which is used as a traditional remedy for diabetes. In addition to being antihaemorrhoidal, astringent, stomachic, emmenagogue, hepatic stimulant, anthelmintic, and blood purifier, it has been found to have hypoglycemic activity [7].

Dihar is a polyherbal formulation containing eight different herbs *Syzygium cumini*, *Momordica charantia*, *Emblica officinalis*, *Gymnema sylvestre*, *Enicostemma*, *Azadirachta indica*, *Tinospora cordifolia* and *Curcuma longa*. In Strptozotocin (STZ, 45 mg/kg IV single dose) caused type 1 diabetic rats, a combination of these eight herbs showed effective anti-hyperglycemic activity, according to the literature. When compared to control, treatment with Dihar (100 mg/kg) for 6 weeks resulted in lower STZ-induced serum glucose and lipid levels and higher insulin levels.

Diabeta is an Ayurvedic Herbal Health Products which is a poly herbal formulation

containing *Curcuma longa*, *Coscinium fenestratum*, *Strychnos potatorum*, *Phyllanthus reticulatus*. *Tamarindus indica*, *Tribulus terrestris* was investigated for its glucose tolerance and antidiabetic activity in alloxan induced diabetic rats. At a dose of 500mg/kg, normal rats were used in the glucose tolerance test and hypoglycemic experiments. At a dose of 500 mg/kg, the substance was effective, although it had no hypoglycemic impact.

Diasol *Eugenia jambolana*, *Foenum graceum*, *Terminalia chebula*, *Quercus infectoria*, *Cuminum cyminum*, *Taraxacum officinale*, *Emblica officinalis*, *Gymnema sylvestre*, *Phyllanthus nerui*, and *Enicostemma littorale* plant extracts make up Diasol, a polyherbal antidiabetic medication. Previous investigation showed Diasol reduces 63.4 % of blood glucose level in a dose of 125 and 250 mg/kg and proved to be effective antidiabetic polyherbal formulation.

Diakyur is apolyherbal formulation (composed of *Cassia javanica*, *Cassia auriculata*, *Salacia reticulate*, *Gymnema sylvestre*, *Mucuna pruriens*, *Syzygium jambolaum*, *Terminalia arjuna*), scientifically proved to be a potential antidiabetic formulation in previous studies. Diakyur has been demonstrated to have strong

hypoglycemic and antilipid peroxidative activity, indicating that it can be utilized as an adjuvant to allopathic therapy of diabetes as well as to prevent the late consequences of diabetes. So, concluded that Diakyur at a dose of 1600 mg/kg p.o is safe for long term treatment in diabetic condition.

Diasulin is a polyherbal formulation containing *Cassia auriculata*, *Coccinia indica*, *Curcuma longa*, *Emblica officinalis*, *Gymnema sylvestre*, *Momordica charantia*, *Scoparia dulcis*, *Syzygium cumini*, *Tinospora cordifolia*, *Trigonella foenum graecum*. Previous research suggests that increases glycolysis and decreases gluconeogenesis, resulting in a decreased requirement for pancreatic insulin in treated rats than in untreated rats. Because it modulates the activity of hepatic glucose metabolic enzymes, this is possible. It also resulted in significant decrease in tissue lipids and lipid peroxide formation.

Diabecon a polyherbal formulation containing *Gymnema sylvestre*, *Pterocarpus marsupium*, *Glycyrrhiza glabra*, *Casearia esculenta*, *Syzygium cumini*, *Asparagus racemosus*, *Boerhavia diffusa*, *Sphaeranthus indicus*, *Tinospora cordifolia*, *Swertia chirata*, *Tribulus terrestris*, *Phyllanthus amarus*, *Gmelina arborea*, *Gossypium herbaceum*, *Berberis aristata*, *Aloe vera*,

Triphala, *Commiphora wightii*, *shilajeet*, *Momordica charantia*, *Piper nigrum*, *Ocimum sanctum*, *Abutilon indicum*, *Curcuma longa*, *Rumex maritimus* has been shown to improve peripheral utilisation, elevate glucagon levels in the liver and muscles, promote B cell repair and regeneration, and enhance c peptide levels. It protects B cells from oxidative stress and possesses antioxidant effects. It reduces glycated haemoglobin levels, normalises microalbuminuria, and modulates the lipid profile, acting similarly to insulin. It minimizes long term diabetic complications. Diabecon has also been shown in previous studies to be a safe treatment for diabetic people who want to avoid issues like retinopathy. Antiinflammatory qualities improved the absorption of hard and soft exudates and resolved retinal and vitreal haemorrhages and their subsequent prevention. Studies concluded that Diabecon can be used as in patients with NIDDM and IDDM as a supplement to standard treatment. **Glyoherb** is a polyherbal preparation that was tested against normal and streptozotocin-induced diabetic rats for its antihyperglycemic, antihyperlipidemic, and antioxidant properties. In STZ-induced type 1 diabetic mice, Glyoherb sugar control granules lower serum glucose levels and

improve glucose tolerance, suggesting that they may have anti-diabetic properties. In addition to lowering serum cholesterol and triglyceride levels, this polyherbal mixture has antihyperlipidemic efficacy. In STZ-induced impaired kidney and liver functioning, glyoherb had no harmful effects. It was discovered that it improved kidney and liver functions. Furthermore, Glyoherb has antioxidant potential, since it reduces lipid peroxidation and improves antioxidant status in diabetic rats. Glyoherb's anti-diabetic benefits could potentially be linked to its antioxidant qualities. Thus previous research concluded that it may be regarded as a promising natural and safe remedy for the prevention or delay of diabetic complications.

Karmin Plus is an indigenous polyherbal formulation containing *Momordica charantia*, *Azadirachta indica*, *Picrorrhiza kurroa*, *Ocimum sanctum* and *Zinziber officinale* was evaluated for antidiabetic activity and it was found that product showed effectiveness at two dose levels at 200 mg/kg and 400 mg/kg b.w for antidiabetic activity [8].

HypoNIDD marketed from Charak Pharma composed of Yashad Bhasma (*Zinc Calx*), Shilajit (*Purified Asphaltum*), Karela (*Momordica charantia*, bitter gourd), Haridra

(*Curcuma longa*, turmeric), Tarwar (*Cassia auriculata*, Avarakkai, Indian broad-beans), Amalaki (Amla, Indian Gooseberry, *Embllica officinalis*), Raja Jambu (*Eugenia jambolana*), Mamejavo (*Enicostemma littorale*), Meshashringi (*Gymnema sylvestre*), Vijaysaar (*Pterocarpus marsupium*), Guduchi (*Tinospora cordifolia*), Neem (*Melia azadirachta*), Kirat Tikta (*Swertia chirata*) [8]. HypoNIDD has been studied in diabetic rats for its potential antihyperglycemic and antioxidant effects. Streptozotocin (STZ) (45 mg kg⁻¹ body weight) was used to make rats diabetic. Hyponidd (100 mg kg⁻¹ and 200 mg kg⁻¹) was given orally for 45 days, resulting in considerable reductions in blood glucose and large increases in hepatic glycogen and total haemoglobin. An oral glucose tolerance test was also done in experimental diabetic rats, and the rats treated with hyponidd showed a considerable improvement in blood glucose tolerance. In diabetic rats, hyponidd treatment reduced glycosylated haemoglobin, plasma thiobarbituric acid reactive compounds, hydroperoxides, ceruloplasmin, and -tocopherol. Oral dosing of hyponidd dramatically increased plasma reduced glutathione and vitamin C levels. Hyponidd (200 mg kg⁻¹) was shown to be more effective than glibenclamide (600 mg kg⁻¹) in

returning values to near-normal levels. In STZ-induced diabetic rats, hyponidd was found to have antihyperglycaemic and antioxidant activities [9].

Dabur Madhu Rakshak marketed from Dabur Amla is a polyherbal formulation (*Phyllanthus emblica*), Tejpatra (*Cinnamomum tamala*), Vijaysar (*Pterocarpus marsupium*), Gurmar (*Gymnema sylvestre*), Jamun seed (*Eugenia jambolana*), Kali marich (*Piper nigrum*), Neem leaves (*Azadiracheta indica*), Methi (*Trigonella foenum-graecum*), Bahera (*Terminaliabelerica*), Bhavana Dravyas, Shudh Shilajit, karela fruit (*Momordica charantia*), Hareetaki (*Terminalia chebula*).

Madhumehari Granules marketed from Baidyanath contains gudmar (*Gymnema sylvestre*), Jamun guthali (*Syzygium cumini*), Gulvel (*Tinospora cordifolia*), Kkarela Beej (*Momordica charantia*), Khadir Chuma (*Acacla Catechu*), Haldi (*Curcuma Longa*), Amla (*Embllica-officinalis*), vijay-sar Kutki (*Picrorhiza kurroa*), (*Pterocarpus Marsupium*), Tejpatra (*Cinnamomum-Tamala*), Shilajit (*Asphaltum*), Gularphal Chuma (*Ficus Glomerata*), Kutki (*Picrorhiza kurroa*), Chitrak (*Plumbago Zeylanica*), Methi (*Trigonella-foenum graecum*), Bhavna

of Neem Patti (*Azadirachta - Indica*), Bilwa Patra (*Aegle Marmelos*) [10].

CONCLUSION

Diabetes is a developing problem in India, with an estimated 8.7% diabetic population between the ages of 20 and 70. Rapid urbanisation, sedentary lifestyles, bad diets, cigarette use, and increased life expectancy are all contributing to the rising prevalence of diabetes and other non communicable diseases. There has been increasing interest in the plant remedied in recent years. Herbal drugs are preferable to allopathic pharmaceuticals because of their safety, low cost, and complete accessibility, as well as their increased tolerance. More preclinical research is needed to investigate the antidiabetic potential of new plants/herbs that have not previously been explored, as well as the clinical establishment of antidiabetic plants that have already shown promise in preclinical testing. When compared to polyherbal formulations including a ratio of several plants, the pharmacological activity of a single plant is regarded to be weaker. The polyherbal mixture produces a more effective synergistic impact while simultaneously lowering the amounts of single herbs, decreasing side effects. Scientific validation of several Indian plant species has proved the ability of botanicals to

lower blood sugar levels could be considered medicinal in nature. Many different plants have been used to treat diabetes, either individually or as formulations.

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