

RUMI HERBALS - DIARUN PLUS

Diarun Plus, is a polyherbal formulation developed by Rumi Herbals R&D Centre after extensive research on traditional medical literature and is manufactured by Rumi Herbals Private Limited, Chennai. Diarun Plus contains chosen herbal ingredients of therapeutic value for Diabetes Mellitus such as *Salacia reticulate*, *Curcuma longa*, *Mimordica charantia*, *Gymnema sylvestre*, *Trigonella foenum gracum*, *Embllica officinalis* and *syzygium cumini*. The product is in the market since 2005, that has benefited thousands of diabetic patients.

Extensive pre clinical and clinical studies have been carried out on this formulation and are presented in the following sections for better appreciation.

1. Safety studies on Diarun Plus: The herbal formulation diarun plus was tested in animal models according to OECD guidelines (Senthil vel *et al* 2007).

Acute toxicity study:

- Acute toxicity studies did not reveal any abnormal behavioural or toxic effect even in a dose of 2000mg/kg body weight.
- Histo-pathological studies of the organs (Liver, kidney, heart, cerebrum, cerebellum, lungs, spleen, testis and ovary) of diarun plus treated animals did not reveal any changes and the herbal formulation were found to be safe in the dose tested.

Sub-acute Toxicology:

- Due to its safety in acute studies it was further subjected for sub acute toxicity studies for 28 days in animals as per OECD guidelines
- Since the clinical dose of the formulation has been prescribed up to 6g/day, the doses 2.7g/kg, 5.4g/kg, 10.8g/kg/body weight were chosen for this study.
- There was a gradual increase in body weight of diarun plus treated animals similar to the control group of animals. The water and food intake and behaviour were unaltered.
- The haematological, biochemical and histopathological studies (Liver, kidney, heart, cerebrum, cerebellum, lungs, spleen, testis and ovary) were normal when comparable to that of control group.
- Hence the No Observed Adverse Effect Level (NOAEL) of the test drug was estimated to be 10g/kg.b.w. Hence the above studies conclusively proved the safety of Diarun plus in the experimental animals.

2. Tests for contamination:

- A major concern for the use of herbal preparations is contamination with heavy metals, pesticides and microbes.
- Diarun Plus has been subjected to intense scrutiny and found to be free from above contaminants.
- This observation further strengthens the recommendation for regular use in humans.

3. Investigations on mechanism of action (in-vitro studies):

- ✓ Apart from the deficiency and resistance to insulin action several other mechanisms like free radical damage of beta-cells of islet of Langerhans have been proposed for the development of diabetes mellitus.
- ✓ Another new approach in the treatment of diabetes mellitus targets the enzyme alpha glucosidase. This enzyme decreases the availability of glucose for absorption from the intestine.
- ✓ The above possibilities have been investigated for the formulation diarun plus as well as for the individual herbs present in the formulation.

3a. Alpha glucosidase inhibition:

- A potent inhibition of alpha glucosidase activity was evident for diarun plus and its constituents in the in-vitro assays. This observation indicates that alpha glucosidase inhibition may be one of the important mode of action of diarun plus

3b. Free radical scavenging/Antioxidant effect: Several parameters that reveal the antioxidant efficacy of a compound have been studied with diarun plus. Even in a very low concentration (15 microgram/ml), diarun plus markedly inhibited nitric oxide free radical generation to about 91% and DPPH free radical to about 86%. In higher concentrations diarun plus was able to inhibit lipid peroxidation by 80%. Further, the total antioxidant activity of diarun plus was nearly 30% to that of vitamin-E and 20% to that of vitamin C

S.NO	Antioxidant activity	Concentration	% of Free radical inhibition
1	Lipid Peroxidation	600µg/ml	80
2	Nitric oxide scavenging	15µg/ml	91
3	DPPH	15µg/ml	86
4	Total antioxidant capacity	30% to that of vitamin-E	
5	Total antioxidant capacity	20% to that of vitamin C	

The protection of beta cells of islets Langerhans against free radical damage by diarun plus may help in restoration of insulin secreting capacity of beta cells.

4a. Effect of diarun plus on experimental animals: Non diabetic animals: Diarun plus administration had the ability to restore normal euglycemic status in situations of extreme variation in blood sugar level.

In animals which are rendered hyperglycaemic by exogenous dextrose administration or made hypo glycaemic by swim stress, drastic variation in blood glucose level was not observed when pretreated with diarun plus

This observation suggests that sudden fall in blood glucose (Hypoglycemia) may not be a consequence of diarun plus administration.

4b. Effect of diarun plus on diabetic animals: Streptozotocin (STZ) induced diabetic animals: The elevated hyperglycemic status in streptozotocin animals was attenuated to 28% in animals which received diarun plus alone.

However when diarun plus was co administered with half the maintenance dose of insulin (1 IU/wk), near euglycemic status (comparable with insulin, 2 IU/wk received groups) was achieved.

S.NO	Group	Treatment Regimen	Initial B.S level mg %	Final B.S level mg %
1	A	Control	130	131
2	B	STZ+DP	160	132
3	C	STZ+ 2 U of Insulin	240	128
4	D	STZ+1 U I + DP	230	125

Diarun plus therapy in combination with insulin significantly attenuated the STZ induced hyper glycaemia. It is suggesting that, Diarun plus administration possibly might reduce the daily insulin requirements and can avoid the development of insulin resistance.

5a. Clinical studies on diarun plus: The efficacy and tolerability of diarun plus in 54 type-2 diabetes mellitus patients was reported by Senthilvel et al (2004).

In newly diagnosed type-2 diabetic patient's diarun plus alone could effectively bring down the blood sugar level. Three months treatment with diarrun plus did not reveal any serious adverse effects in these patients. For the sake of safety liver function and kidney function tests were done and found to be normal.

5b. Add on therapy: Diarun plus was introduced as an add on therapy (Two, 500mg capsule per day) and near normal blood sugar levels (RBS 135mg/dl, HbA1C reduced from 10.5 to 6.5%) were achieved in 4 months. No side effect was observed in the patient who had been

followed up for nearly 8 years. This study further strengthens the efficacy and safety of diarun plus in diabetic patients.

5c. Diarun plus in the treatment of newly diagnosed type-2 diabetes mellitus patients: In a well designed clinical trial (Amarnath et al,2015) the clinical efficacy of diarun plus was investigated in 16 newly diagnosed type-2 diabetes mellitus patients as well as in patients who did not respond adequately to oral hypoglycemic agents alone and were unwilling over to or take additional insulin therapy. The protocol was approved by the Institutional Ethical Committee number IEC/C-P/41/2014 dated 27.03.2014.

S.No	Drug dose	Duration	Before treatment		After treatment	
			FBS	PPBS	FBS	PPBS
1	Cap. DP 500mg 1-1-1	15 days	170	236	130	180

*The above mentioned is mean values

This observation is in consonance with the earlier report Senthilvel et al (2004) that in newly diagnosed type-2 diabetes mellitus patients mono therapy with diarun plus alone may effectively regulate blood sugar level.

5e. Effect of diarun plus in refractory diabetes patients:

In some type-2 diabetes mellitus patients even after employing more than one oral hypoglycemic agent hyperglycemia persists and these patients are advised to receive insulin injection. However, some of them are aversive to insulin injection and insist on oral medication only. Eighteen such patients volunteered to take diarun plus in addition to their routine medication. These patients were on one or more of the following oral hypoglycemic drugs. Metformin, glybenclamide, glimipride and pioglitazone. Diarunplus(Three,500mg capsule per day dose) was included as an add on therapy without any interference to their oral hypoglycemic drug regimen. Fasting and post prandial blood glucose levels were monitored at the time of inclusion in the study and at the end of 15 days the mean fasting and post prandial blood sugar levels are mentioned below.

S.No	Drug dose	Duration	Before treatment		After treatment	
			FBS	PPBS	FBS	PPBS
1	Cap. DP 500mg 1-1-1	15 days	190	295	130	208

Based on the observations it was concluded that diarun plus may be a useful antidiabetic agent suitable for patients who are inadequately controlled with routine oral hypoglycemic drugs. It may be recommended as an add on therapy to modern medicine in type-2 diabetes mellitus patients (Amarnath,2015)

The observations on other two refractory patients is worth mentioning. These two patients had fasting blood sugar 310 and 402 mg/dl and post prandial blood sugar 480 and

509 mg/dl respectively. Unwilling to receive insulin injection, they sought the advice of Ayurvedic Physician and were prescribed diarun plus(3,500mg capsule per day) along with their routine oral hypoglycemic drugs. Two weeks later their fasting blood sugar were 217 and 216 mg/dl and post prandial blood sugar levels were 333 and 317 mg/dl respectively.

S.NO	Patient	Before treatment		Drug dose with duration	After treatment	
		FBS	PPBS		FBS	PPBS
1	Patient I	310	480	DP 3500mg/day- 15 days	217	333
2	Patient II	402	509		216	317

5f.Renal function parameters: Blood urea and serum creatinine levels were determined in patients who received diarun plus (3,500mg capsule per day) alone for 15 days and also in patients who received oral hypoglycemic drugs (metformin/glybenclamide/pioglitazone) and diarun plus (3,500 mg capsule pre day) for 15 days. There were no significant changes in blood urea or creatinine level compared to pre treatment values in the above treatment groups.

Group	Blood Urea (mg)		Serum creatinine (mg)	
	Before	After	Before	After
DP alone	30.37	29.5	0.96	0.95
DP+ Modern Medicine	29.77	29.2	1.01	0.98

It is suggesting that long term use of Diarun plus will be worthwhile for the diabetic human community

SUMMARY OF SCIENTIFIC FINDINGS:

1. Diarun Plus formulation is based on Indian Traditional Systems of Medicine (ITSM) Knowledge “Food is medicine and medicine is food”
2. The poly herbal formulation is developed in Rumi Herbals R&D Centre approved by Tamil Nadu State Drug Licence issuing Authority, Government of Tamil Nadu; Manufactured by Rumi herbals Private limited a GMP Factory in Chennai.
3. Diarun Plus has been scientifically validated for its consistent quality, safety and efficacy.
4. Chemical and Microbiological studies proved the formulation to be free from heavy metals, pesticides and microbial contamination.
5. Biological screening in-vitro and in-vivo models established its safety on continued usage (Acute and Sub acute toxicity studies) and its therapeutic efficacy in diabetic animal models.

6. In-vitro studies on the individual ingredients and formulations established its benefit in regulating blood sugar and also its mechanism of action.
7. Clinical trial on human volunteers showed significant improvement of Type-2 diabetes.
8. Diarun plus also has a beneficial effect on Drug resistant Diabetes.
9. Diarun Plus, a Poly herbal formulation developed from the knowledge of Indian traditional systems of medicine with scientific validation and can be tried as a DIETARY SUPPLEMENT along with Modern Medicine as this product is currently used by more than 5000 patients since 2005.

Research Publications:

1. G.Senthilvel, M.Jegadeesan, Anoop Austin, P.Thirugnanasambantham, M.Balasubramanian and E.Mayisvren. **Evaluation of efficiency and tolerability of a herbal formulation in the management of type 2 diabetes mellitus in Indian patients**, Amla Research Bulletin, 24: 57-62 (2004)
2. G.Senthilvel, M.Jegadeesan, Anoop Austin, P.Thirugnanasambantham, M.Balasubramanian and E.Mayisvren, N.Narayanan and S.Viswanathan. **Effect of polyherbal formulation (Diarun plus) on streptozotocin induced experimental diabetes**, International Journal of Tropical Medicine 1(2): 88-92 (2006).
3. Winford Rollands.,Senthilvel. G.,AnoopAustin, Thirugnanasambantham.P., Mayisvren.E.,**Clinical report on Diarun Plus in controlling elevated blood sugar level**, The Antiseptic,103(6),348-349,(2006)
4. G.Senthilvel, M.Jegadeesan, Anoop Austin, P.Thirugnanasambantham, M.Balasubramanian and E.Mayisvren, N.Narayanan and S.Viswanathan. **Effect of a ployherbal formulation (Diarun plus) on glycemic status modified by physiological means in non-diabetic mice and rats**, International Journal of Pharmacology, 3 (2): 175-178 (2007).
5. S.Amarnath. Influence of certain Indian system of medicines on the Pharmacotherapy of Diabetes mellitus Patients in Puducherry-M.D.,Dissertaion submitted to Bharath University,Chennai(2015).