

HYPOGLYCEMIC ACTIVITY OF NIDDWIN, A POLYHERBAL FORMULATION IN NORMAL RATS

T.SRUTHI^{1*}, D.SATYAVATI², RAJNEEKAR DASARI³, V.JYOTHI¹, P.ROSHAN ALI¹

¹Teegala Krishna Reddy College of Pharmacy, Medbowli, Meerpet, Saroornagar, Hyderabad, Andhra Pradesh, India -500097, ²Sree Dattha Institute of Pharmacy, Sheriguda, Ibrahimpatnam, Hyderabad, Andhra Pradesh, India, ³Mallareddy Institute of Pharmaceutical sciences, Dhulapally, Maisammaguda, Quthbullapur, Rangareddy Dist, Hyderabad, Andhra Pradesh, India. Email: thatipamulasruthi@gmail.com

Received: 20 October 2013, Revised and Accepted: 12 November 2013

ABSTRACT

Objective: The present study was focused to evaluate the hypoglycemic activity of NIDDWIN, a polyherbal formulation in normal rats.

Methods: Male Albino Wistar Rats (180-200gms) were divided into four groups of five animals each. Group-I was given aqueous suspension of 2% gum acacia, Group-II was given aqueous suspension of NIDDWIN 50mg/kg, Group-III was given aqueous suspension of NIDDWIN 100mg/kg, Group-IV was given aqueous suspension of Glibenclamide 10mg/kg were given orally for 10 days. The blood samples were collected before and after administration drugs at 0hrs, 2hrs, 4hrs, 6hrs, and 8hrs on 1st, 5th, and 10th days from retro-orbital sinus and serum was separated and estimated for glucose, cholesterol and triglycerides by using analytical method [1,2].

Results: NIDDWIN showed significant hypoglycemic activity at 4hrs on 1st, 5th, and 10th days was found to be effect in comparable with standard Glibenclamide 10mg/kg.

Conclusion: NIDDWIN a polyherbal formulation concluded that it possesses hypoglycemic activity in normal rats and should be evaluated for its antidiabetic activity

Keywords: NIDDWIN, Glibenclamide, Glucose Kit, Cholesterol kit, Triglyceride Kit, UV-Spectrophotometer.

INTRODUCTION

Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both [3, 4]. It is one of the refractory diseases identified by Indian council of medical research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a growing problem in the contemporary world [5]. Today India has become the diabetic capital of the world with over 20 million diabetic patients and this number is likely to increase to 57 million by 2025 [6]. This astronomical increase in the prevalence of diabetes has made diabetes a major public health challenge for India and is become important human ailment afflicting many from various walks of life in different countries and once again the whole world being looked upon ayurvedic the oldest healing system of medicine for the treatment of diabetes [3]. Although there are many synthetic medicines developed for patients, but it is the fact that it has never been reported that someone had recovered that totally from diabetes [7]. The modern oral hypoglycemic agents procedure undesirable side effects thus in the recent years considerable attention has been directed towards the antidiabetic potential of medicinal plants and their herbal formulation in the management of disease.

The concept of polyherbalism is peculiar to ayurveda although it is difficult to explain in term of modern parameters. It is evident that there are many herbal formulations of varying potency since these preparation act by different mechanism, it is theoretically possible that different combination of these extract will do better job in reducing blood glucose. In the traditional system of plant medicine it is usual to use plant formulation and combined extract of plant are used as a drug of choice rather than individual ones [8] to get the benefit of synergism and to find suitable antidiabetic and antioxidant combination therapy. Polyherbal formulation which appear to be most effective relatively nontoxic and have substantial documentation of efficacy.

NIDDWIN a polyherbal formulation which include 11 antidiabetic herbs and 1 mineral the 12 constituents of NIDDWIN were individually proved to be having antidiabetic activity but the combination of these 12 constituents called NIDDWIN for its antidiabetic activity was not yet reported in the market.

Hypoglycemic polyherbal formulations:

Some of the polyherbal formulations which are in the market are: Diabet, Dianex, DRF/AY/5001, Diabrid, Diakur, Diasulin, Diabecure, EFPTT/09, 5EPHF, Karmin plus, Okudiabet,

Formulation of NIDDWIN

Tinospora cordifolia – 50mg, *Gymnema sylvestre* – 50mg, *Terminalia tomentosa* – 50mg, *Asphaltum* – 50mg, *Tribulus terrestris* – 50mg, *Emblica officinalis* – 58mg, *Mucuna pruriens* – 50mg, *Sida cordifolia* – 50mg, *Withania somnifera* – 25mg, *Terminalia bellerica* – 8mg, *Terminalia chebula* – 8mg, *Momordica charantia* – 10mg.

Therefore, the present study was focused to evaluate the hypoglycemic activity in normal rats of the polyherbal formulation NIDDWIN.

MATERIALS AND METHODS

Plant Material

NIDDWIN a polyherbal formulation containing 11 antidiabetic herbs and 1 mineral was manufactured by IMIS pharmaceuticals Pvt ltd., Vijayawada is evaluated for hypoglycemic activity.

Animals

Male albino wistar rats weighing 180-200gms were obtained from authorized animal house (Albino research center, Hyderabad). Animals were housed at room temperature 25°C with a 12hrs light and 12hrs dark cycle. The animals had free access to standard rat pellet diet and tap water. After one week of acclimatization, the animals were considered for suitable study and the experiments were conducted according to CPCSEA guidelines.

Acute toxicity study

The animals were divided into four groups each containing 5 animals NIDDWIN a polyherbal formulation was given orally in increasing dose 30, 100, 300 and 1000mg/kg. The rats were observed continuously for 2hrs for behavioural, neurological and autonomic profiles and after 24 hours and 72 hours for any lethality [9, 10].

STUDY DESIGN

Experimental study was done in the department of pharmacology in Teegala Krishna Reddy College of Pharmacy, Hyderabad.

The animals were randomly divided into four groups with 5rats in each group and all the drugs were given orally for 10days as follows [11, 12, 13, and 14].

Group – I: This group was given aqueous suspension of 2% gum acacia as control

Group –II: This group was given aqueous suspension of NIDDWIN 50mg/kg

Group – III: This group was given aqueous suspension of NIDDWIN 100mg/kg

Group – IV: This group was given Glibenclamide 10mg/kg

The blood samples were collected before and after administration of drugs at 2, 4, 6 and 8hrson 1st, 5th and 10th days[15] of from retro orbital sinus puncture. The serum was separated from the blood samples by centrifugation and was analysed for glucose, cholesterol and triglycerides by analytical method [1, 2]. The concentration of glucose, cholesterol, and triglycerides [16] in the blood at each time interval was calculated and expressed as mg/dL. Percentage

reduction of glucose, cholesterol, and triglycerides in blood from each group at different time intervals was calculated and given in tables 1 – 3.

Statistical Analysis

Results were analyzed using one way ANOVA using InStat3 software, followed by Dunnet's test. The percentage reduction values were expressed in Mean±SEM.

RESULTS

Acute toxicity studies

Acute toxicity studies revealed the toxicity with 1000mg/kg after 24hrs of treatment.

Percentage reduction of glucose, cholesterol and triglycerides levels in blood with 2% gum acacia control in normal rats.

The percentage reduction of glucose, cholesterol and triglycerides in blood with 2% gum acacia control group was found to be (Day-1) 11.81, 8.336 and 6.39 (Day-5) 11.58, 9.992 and 7.656 (Day-10) 13.128, 11.692 and 10.73 after 4hrs of administration.

Table 1: Consolidated table showing Mean ±SEM values of percentage reduction of blood glucose, cholesterol and triglycerides levels with 2% gum acacia of normal rats after continuously for 10 days treatment.

Group	Control 2% gum acacia (Day – 1)				Control 2% gum acacia (Day – 5)				Control 2% gum acacia (Day – 10)			
	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs
% Reduction of Glucose	6.138	11.81	13.55	6.17	6.162	11.58	10.08	7.54	6.74	13.1	11.95	7.386
	±	±	±	2	±	±	±	4	4	28	±	±
	0.471	0.497	0.564	±	0.0611	0.878	2.194	±	±	±	1.387	0.786
	7	0	6	0.45				1.36	0.1	0.99		4
				5				7	6	4		
% Reduction of Cholesterol	6.32	8.336	6.626	5.91	5.926	9.922	8.062	7.06	6.03	11.692	9.73	7.772
	±	±	±	2	±	±	±	6	2	±	±	±
	0.272	0.506	0.23	±	0.129	0.601	1.411	±	±	0.71	1.188	1.191
		3	0	0.38	8			0.99	0.3	19		
				8				81	3			
%Reduction of Triglycerides	4.082	6.39	5.87	4.43	4.878	7.656	6.774	4.87	5.38	10.7	8.69	5.04
	±	±	±	±	±	±	±	8	2	3	±	±
	0.534	0.959	1.057	0.33	0.1412	0.6006	1.074	±	±	±	1.318	0.2835
		0	0					0.14	0.26	0.76		
								12	6	99		

Percentage reduction of glucose, cholesterol and triglycerides levels in blood with NIDDWIN 50mg/kg in normal rats.

The percentage reduction of glucose, cholesterol and triglycerides levels in blood with NIDDWIN 50mg/kg was found to be (Day – 1) 22.93, 14.824 and 10.88 (Day – 5) 27.296, 20.98 and 15.544 (Day – 10) 32.38, 24.24 and 17.19 after 4hrs of administration.

Table 2: Consolidated table showing Mean ±SEM values of percentage reduction of blood glucose, cholesterol and triglycerides levels with NIDDWIN 50mg/kg of normal rats after continuously for 10 days treatment.

Group	NIDDWIN 50mg/kg (Day – 1)				NIDDWIN 50mg/kg (Day – 5)				NIDDWIN 50mg/kg (Day – 10)			
	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs
% Reduction of Glucose	9.05	22.93	15.73	5.74	12.22	27.29	15.51	7.93	17.1	32.3	18.93	8.49
	±	±	±	±	±	±	±	2	4	8	±	±
	1.326	1.514	0.997	0.87	1.207	1.788	3.170	±	±	±	1.66	1.59
		*	**	9***		*	***	0.32	0.88	1.42	0***	1**
								8**	1**	2***		
% Reduction of Cholesterol	7.74	14.82	7.44	6.22	12.03	20.98	14.41	7.40	13.3	24.2	16.55	9.6
	±	4	±	±	±	±	±	±	3	4	±	±
	0.51	±	0.46	0.87	1.44	0.87	0.82	0.59	±	±	0.79	1.02
	8*	0.91	0*	5*	7*	0**	4*	3*	0.90	1.45	**	1*

		9*				5*				9**			
%Reduction of Triglycerides	of	5.68	10.88	6.72	4.12	9.03	15.54	9.03	6.97	8.66	17.1	10.89	8.43
		±	±	±	±	±	±	±	±	±	±	±	±
		0.22	0.56	0.94	0.42	1.00	1.35	1.00	0.84	0.85	±	0.55	0.87
		6*	4*	4*	8*	6*	8*	6*	4*	8*	7*	7*	7**

Each value is SEM of 5animals:***P<0.0001, **P<0.001, *P<0.01. Comparison made between normal control rats and NIDDWIN 50mg/kg treated group rats

Percentage reduction of glucose, cholesterol and triglycerides levels in blood with NIDDWIN 50mg/kg in normal rats

The percentage reduction of glucose, cholesterol and triglycerides in blood with NIDDWIN

100mg/kg was found to be (Day - 1) 25.644, 16.944 and 16.00 (Day - 5) 32.074, 24.17 and 20.796 (Day - 10) 36.74, 26.14 and 23.556 after 4hrs of administration.

Table 3: Consolidated table showing Mean ±SEM values of percentage reduction of blood glucose, cholesterol and triglycerides levels with NIDDWIN 100mg/kg of normal rats after continuously for 10 days treatment.

Group	NIDDWIN 100mg/kg (Day - 1)				NIDDWIN 100mg/kg (Day - 5)				NIDDWIN 100mg/kg (Day - 10)			
	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs
% Reduction of Glucose	12.79	25.644	13.40	9.68	14.80	32.07	17.6	9.46	17.3	36.7	20.99	10.12
	±	±	±	±	±	4	3	±	0	4	±	±
	1.845	2.40	1.11	1.13	3.74	±	±	0.54	±	±	1.07	0.71
		1**	7***	1**	3	4.000	1.34	6**	2.88	2.12	4**	7**
						***	****		2**	2***	**	
% Reduction of Cholesterol	9.93	16.94	11.30	10.9	12.22	24.17	17.38	11.4	16.8	26.1	18.75	12.51
	±	4	±	5	±	±	±	1	7	4	±	±
	0.77	±	0.65	±	0.87	1.39	1.36	±	±	±	0.55	1.41
	6*	1.36	4**	0.44	3**	8***	8***	0.96	1.28	1.51	7***	2**
		4***		0**				7**	1**	0***		
%Reduction of Triglycerides	10.55	16.00	10.69	9.36	14.46	20.79	15.64	11.0	15.5	23.5	18.03	11.20
	±	±	±	±	±	±	±	1	5	56	±	±
	0.346*	0.81	0.77	0.31	1.35	0.44	0.88	±	±	±	0.95	0.44
		7**	3*	7*	0**	6***	2**	0.62	1.54	0.71	5**	1*
								3**	0**	9***		

Each value is SEM of 5animals: *P<0.05, **P<0.1, ***P<0.01, ****P<0.001. Comparison made between normal control rats and NIDDWIN 100mg/kg treated group rats.

Percentage reduction of glucose, cholesterol and triglycerides levels in blood with Glibenclamide 10mg/kg in normal rats

The percentage reduction of glucose, cholesterol and triglycerides in the blood with Glibenclamide 10m/kg was found to be (Day - 1) 27.292, 14.57 and 12.164 (Day - 5) 36.644, 17.36 and 14.07 (Day - 10) 38.922, 21.908 and 17.19 after 4hrs of administration.

Table 4: Consolidated table showing Mean ±SEM values of percentage reduction of blood glucose, cholesterol and triglycerides levels with Glibenclamide 10mg/kg of normal rats after continuously for 10 days treatment.

Group	Glibenclamide 10mg/kg (Day - 1)				Glibenclamide 10mg/kg (Day - 5)				Glibenclamide 10mg/kg (Day - 10)			
	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs	2hrs	4hrs	6hrs	8hrs
% Reduction of Glucose	13.06	27.29	15.40	10.3	18.30	36.644	23.15	14.4	20.7	38.9	23.59	13.38
	±	2	±	6	±	±	±	8	2	22	±	±
	1.847	±	1.41	±	2.441	2.59	2.10	±	±	±	1.67	1.65
		2.618	9**	0.42		0***	9***	1.56	2.51	2.51	7***	2**
		***		5**				7**	0**	0***		
% Reduction of Cholesterol	7.46	14.57	7.12	4.66	9.55	17.36	10.17	6.70	13.3	21.9	16.55	9.6
	±	±	±	±	±	±	±	±	3	08	±	±
	0.40	0.92	1.31	0.56	0.46	1.15	1.83	0.57	±	±	0.79	1.02
	4*	4**	8*	3*	7*	9***	0**	7*	0.90	1.51	0**	1*
									5**	9***		
%Reduction of Triglycerides	4.86	12.16	7.28	4.73	6.29	14.07	9.69	6.29	17.1	17.1	10.89	8.43
	±	4	±	±	±	±	±	±	9	9	±	±
	0.28	±	1.20	0.33	0.36	1.01	0.795	0.36	±	±	0.55	0.87
	3*	1.20	1*	2*	4*	5**	*	4*	0.44	0.44	7*	7*
		9*							7**	7**		

Each value is SEM of 5animals:***P<0.0001, **P<0.001, *P<0.01. Comparison made between normal control rats and Glibenclamide 10mg/kg treated group rats.

DISCUSSION

The blood glucose level in the body is maintained mainly by insulin and glucagon secreted from beta cells of islets of langerhans of pancreas. Insulin reduces blood glucose while glucagon raises it. Insulin plays a crucial role in lowering blood glucose levels by

inhibiting glycogenolysis and gluconeogenesis while stimulating glycogen synthesis and stimulates uptake of glucose, amino acids. It is known to increase fatty acids and triglycerides synthesis [17]. As NIDDWIN also showed reduced in the glucose levels at 4hours same as Glibenclamide. It indicates that may be NIDDWIN also as same mechanism of action as Glibenclamide.

CONCLUSION

The present study suggested that the polyherbal formulation NIDDWIN possess a potent hypoglycemic activity as it significantly reduced blood glucose levels. In addition it also shown to reduce cholesterol, triglycerides levels in normal rats.

As NIDDWIN is shown to have potent hypoglycemic activity. Therefore further studies are planned to conduct antidiabetic activity and antihyperlipidemic activity.

REFERENCES

1. Trinder, P., Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. *Ann. Clin. Biochem.* 1969; 6:24-27
2. Gochman N, Ryan WT, Sterling RE, and Widdowson GM, Interlaboratory Comparison of enzymatic methods for serum glucose determination. *Clin. Chem.* 1975; 21:359
3. Joseph B, Jini D. An insight in hypoglycemic effect of traditional Indian herbs used in the treatment of diabetes, *Research Journal of Medicinal plant.* 2011; 5:352-376.
4. Mutalik S, Sulochana B, Chetana M, Udupa N, Uma Devi UP. Preliminary studies on acute and sub acute toxicity of an antidiabetic herbal preparation, Dianex. *Indian Journal of Experimental Biology.* 2003; 4:316- 320.
5. Piyush MP, Natvarlal MP, Ramesh KG. Holistic classification of herbal antidiabetics: A review. *Pharma Times*, 2006; 38: 19-25.
6. Cooke DW and Plotnick L. Type I diabetes mellitus in pediatrics. *Pediatrics review*, 2008; 29:374-385.
7. Li WL, Zheng H.C, Bukuru J. Natural medicines used in traditional Chinese medical system for therapy of diabetes mellitus. *Journal of Ethno pharmacology.* 2004; 92(1): 1-21.
8. Kumar Jaya. Herbal medicine for Type 2 diabetes. *International Journal of Diabetes Developing Countries*, 2010; 30: 111-112.
9. M.A Turner, *Screening Methods in Pharmacology*, Academic Press, New York, NY, USA 1965.
10. Lithfeild JT, Wilcoxon F. A simplified method of evaluating dose effect experiments. *J Pharmacol Exp Ther* 1949; 96:99-133.
11. Augusti KT. Studies on the effects of a hypoglycemic principal from *Allium Cepa* Linn. *Indian Journal of Medicinal Research.* 1973; 61:1066-1071.
12. Gupta RK, Kesari AN, Murthy PS, Chandra R, Tandon V., Watal G. Hypoglycemic and hypoglycemic effect of ethanolic extract of leaves of *Annona squamosa* L. in experimental animals. *Journal of Ethnopharmacology.* 2005; 99: 75-81.
13. Khan, BA, Abraham, A, Leelamma, S. Hypoglycemic action of *Murraya koeingii* (curry leaf) and *Brassica juncea* (mustard): mechanism of action. *Indian Journal of Biochemistry and Biophysics.* 1995; 32:106-108.
14. Pari, L., and Venkateswaran, S. Hypoglycaemic activity of *Scoparia dulcis* L. in Alloxan induced hyperglycaemic rats. *Phytotherapy Research.* 2002; 16:662-664.
15. NW Abueze patrick okechukwu. Hypoglycemic and free radical scavenging activity of partially purified fraction E from DCM stem extract of *Cosinium fenestratum*. *Asian journal of pharmaceutical and clinical research.* 2012; 5: 30 - 36.
16. Soumya P. Rout, Durga M.Kar, Santhosh B. Mohapatra, Sharada P. Swain. Anti - hyperglycemic effect *Annona reticulata* L. leaves on experimental diabetic rat model. *Asian journal of pharmaceutical and clinical research.* 2013;6: 56-60.
17. Rang HP, Dale MM, Ritter JM. The Endocrine pancreas and the control of blood glucose. In: Barbara simmons, *Pharmacology*, 3rd edition, U.K, Longman Group Ltd, 1991, 403 - 410.