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Research Article

Development and Characterization of Solid Self Nanoemulsifying Drug Delivery System Containing Polyherbal Tablet to The Treatment of Diabetes Mellitus

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ABSTRACT

The liquid nanoemulsifying drug delivery systems, also known as SNEDDS, have shown remarkable results in regard to the enhancement of the oral bioavailability of medicines that are poorly soluble. "an isotropic and thermodynamically stable system comprising of drug, oils, surfactants, and co-surfactant or co-solvents," is the definition of a self-emulsifying drug delivery system, also known as a SEDDS. SEDDS are administered in the form of an oil-in-water mixture, and when they come into touch with the contents of the stomach, they produce an emulsion that is either coarse, micro-, or nano-sized, depending on the composition of the stomach and the formulation process. The key process that helps SEDDS increase the dissolving rate is the natural formation of an emulsion inside the gastrointestinal tract as a result of moderate agitation generated by stomach movement. This is the mechanism that promotes SEDDS. The decrease in the size of the droplets leads to an increase in the interfacial area, which in turn facilitates the absorption of the medicine when it is administered. As a consequence of this, SEDDS improves the solubility of hydrophobic medicines in settings that include water. It has been shown that the use of SEDDS causes improvements in drug solubility, permeability, and lymphatic uptake, all of which contribute to an increase in the absorption of medications.

Keywords: SNEDDS, Tablet, Diabetes, Polyherbal formulations, Oils, Co-solvent

Introduction:

Self-emulsifying drug delivery systems (SEDDS) are also known as self-emulsifying oil formulations. These formulations are mixtures of oils and surfactants, ideally isotropic, and sometimes contain co-solvants [1]. When introduced into aqueous phase agitation, these formulations emulsify spontaneously to produce fine oil in water emulsion. Oral bioavailability of poorly water-soluble medicines may be improved by the use of self-nanoemulsifying drug delivery systems (SNEDDS), mild self microemulsifying drug delivery systems (SMEDDS), and self-emulsifying drug delivery systems (SEDDS) [2]. A nano-emulsion that is made of a fine oil-in-water mixture is produced by a drug delivery system known as a SNEDDS when it is exposed to aqueous media, such as the fluids present in the gastrointestinal tract. This nano-emulsion is produced by using a combination of oils, surfactants, and co-surfactants. It is possible for this system to enhance the solubility and bioavailability of pharmaceuticals that are difficult to dissolve, which eventually leads to an improvement in the therapeutic efficacy of these treatments [3]. This system is thermodynamically stable and possesses all of these capabilities. An SA self-nano-emulsion, also known as an SA-SNE, is a possible drug delivery system that has been created with the intention of enhancing the solubility, absorption, and bioavailability of SA. In order to develop an SA-SNE, it is vital to choose the oils, surfactants, and co-surfactants that work together in the most effective manner. When it comes to achieving a self-nanoemulsifying formulation that is not only efficient but also stable, the selection of these components is of the highest significance [4]. The oils, surfactants, and co-surfactants that were selected for this examination were eventually selected on the basis of the information that was acquired from the research that was

conducted in the past]. In the case of SNEDDS, the selection of oils is of the highest significance since these oils are accountable for the stabilization of the emulsion and the definition of the many characteristics that it has. These oils were selected because it is well-established that they are potent emulsifiers that are able to generate oil-in-water (O/W) emulsions when they come into contact with an aqueous phase. The term "self-nano emulsifying drug delivery system" (SNEDDS) refers to isotropic combinations of oil, surfactant, co-surfactant, and drug that, when injected into aqueous phases with mild agitation, result in the formation of a thin oil-in-water nanoemulsion [5]. It is easy for SNEDDS to move throughout the gastrointestinal system, and the digestive motility of the stomach and the intestines provides the agitation that is required for self-emulsification to occur. The proposed study on "Formulation and Evaluation of SNEDDS Loaded with Polyherbal Formulation to Treat Diabetes" has a comprehensive scope that encompasses various aspects of research and application. The study aims to develop a self-nanoemulsifying drug delivery system (SNEDDS) that can effectively encapsulate a polyherbal formulation for the treatment of diabetes [6]. This entails formulating an optimized SNEDDS by selecting appropriate lipids, surfactants, and co-surfactants to ensure stability and efficiency. The study also focuses on enhancing the solubility and bioavailability of poorly water-soluble active compounds present in the polyherbal formulation, which can lead to improved therapeutic outcomes. Additionally, the physical and chemical stability of the SNEDDS formulation will be evaluated to determine its shelf life and long-term viability. In vitro studies will be conducted to assess parameters such as drug release, dissolution rate, and permeability, providing insights into the performance of the SNEDDS formulation. Furthermore, in vivo evaluations may be performed to investigate the pharmacokinetic and pharmacodynamic profiles of the formulation. The study also includes assessing the antidiabetic activity of the SNEDDS-loaded polyherbal formulation through the measurement of blood glucose levels, insulin sensitivity, and markers of diabetes control.

Material and Methods

The soxhlet extractor, manufactured by Perfit India Ltd., was used to extract the plant material. This was accomplished by using a vacuum rotary evaporator (Buchi R-114, Switzerland) to concentrate the extracts. When producing TLC plates, a CAMAG twin trough development chamber was used as the chamber of choice.

Preparation of SNEDDS (Self-Nanoemulsifying Drug Delivery Systems) tablets

The ratio of sesame oil: span 80:propylene glycol was made with comparison from 1:1:1 to 1:9:1. The determination of the percentage of each component is 1:1:1 (lower limit) until 1:9:1 (upper limit) with a total weight of SNEDDS was 5.0 grams. The formulation SNEDDS containing all herb extract 1.0 gram (1:1:1) with Curcuma longa, Tinospora cordifolia, Gymnema sylvestre. Weigh all ingredients, then vortexed for 1 minute, sonication for 15 minutes and incubation at a temperature of 45 °C [7].

Table 1: Various composition of SNEDDS containing (1:1:1) with *Curcuma longa, Tinospora cordifolia, Gymnema sylvestre*

F. Code	Proportion of sesame oil: span 80: propylene glycol (ratio)	Sesame oil	Span 80	Propylene glycol
PS1	01:01:01	1.67	1.67	1.67
PS2	01:02:01	1.25	2.5	1.25
PS3	01:03:01	1	3	1
PS4	01:04:01	0.83	3.33	0.83
PS5	01:05:01	0.71	3.57	0.71
PS6	01:06:01	0.62	3.75	0.62
PS7	01:07:01	0.56	3.89	0.56
PS8	01:08:01	0.5	4	0.5
PS9	01:09:01	0.25	4.5	0.25

Solidification of SNEDDS

Solidification of selected SNEDDS (PS9) was done by the solid carrier adsorption method. Briefly, 20 g of SNEDDS formulation was blended with 24 g of microcrystalline cellulose to obtain a wet mixture. Later, 6 g of Aerosil 200 was added to the wet mixture and mixed to obtain S-SNEDDS [8].

Tablet Preparation of SNEDDS

For the preparation of S-SNEDDS loaded tablets, listed ingredients were weighed accurately and sifted through sieve number 60. The ingredients were mixed until a uniform mixture was obtained and was again sieved. Lubricant and glidant were added, mixed and the mixture was directly compressed using a 8 station punching machine [9].

Table 2: Composition of solid formulation (SNEDDS tablets)

Ingredients	Category	PST7 Amount in (mg)	PST8 Amount in (mg)	PST9 Amount in (mg)
The powder contains 50 mg of the drug	Drug loaded solid self-nanoemulsifying drug delivery system	120	120	120
PVP K30	Binder	20	20	20
Sodium CMC	Disintegrant	40	40	40
Magnesium stearate	Lubricant	10	10	10
Talc	Glidant	10	10	10

Evaluation of Polyherbal tablet preparation

Appearance: The manufactured herbal tablets' appearance and colour were evaluated. In this study, colour, odour, and taste were noted.

Hardness

Five tablets were chosen at random from each batch to test the crushing strength using Monsanto's tablet hardness tester.

Angle of repose

The angle of repose was calculated using the fixed height method in order to forecast the flow characteristics of the physical mixtures in each formulation. A funnel with a 10mm inner diameter stem was suspended from the platform at a height of 2 cm. 10g of material were transferred gradually and contacted the steam in the funnel. A preliminary estimation of the radius of the powder cone was obtained by rough circling the base of the pile. The average radius and the following formula were used to get the angle of repose [10].

$\theta = \tan^{-1}(h/r)$

Where, θ = Angle of repose, h = Height of the pile, r = Average radius of the powder cone

Friability

25 randomly chosen tablets were weighed out, placed in an Electro lab friabilator, and rotated at 25 rpm for 4 minutes to assess the friability. The percentage of friability was

$\%F = (1-WI/WF) * 100$

Where, WI=Initial weight of the 25 tablets; WF=Final weight of 25 tablets

Weight Variation

In compliance with IP 2018, the weight fluctuation of 20 randomly selected pills was assessed.

Disintegration test

The determination of tablet disintegration time was conducted utilising the digital microprocessor-based disintegration test equipment, namely the basket rack assembly from Lab India. A single pill was placed into each tube and thereafter a disc was inserted. The assembly was placed in a 1000 mL beaker that was filled with water. The water volume was sufficient for the wires to intersect at their maximum point, which was positioned at least 25 mm below the water's surface. Similarly, at its minimum point, the wires were positioned at least 25 mm above the bottom of the beaker. The equipment was operated and maintained at a temperature of 37±2 ºC. The duration necessary for all pills to undergo disintegration and traverse a wire mesh was recorded [11].

In vitro Dissolution test

The investigation was conducted with a basket type tablet dissolving test device manufactured by Lab India. A dissolving media with a volume of 900 mL was prepared by adding 0.1 M hydrochloric acid to the apparatus vessel. The medium was then heated to a temperature of 37±1ºC and stirred at a speed of 50 rpm for duration of 2 hours. Samples of 10 mL were extracted from a region located at the midpoint between the surface of the dissolving medium and the top of the revolving blade at specified time intervals. Subsequently, an equivalent volume of new dissolution medium, maintained at the same temperature, was introduced to the system. The samples were subjected to analysis by using a UV-visible spectrophotometer (Shimadzu UV-1700) to measure the absorbance at a wavelength of 365 nm. The calculation of the cumulative percentage of drug release was performed using an equation derived from a standard curve [12].

Evaluation of Antidiabetic activity

The polyherbal formulation which was safe were assessed in normal, glucose loaded hyperglycemic and alloxan-induced diabetic rats. In all studies, the animals were fasted overnight for 12 hrs with free access to water throughout the duration of the experiment.

Oral Glucose Tolerance Test

Experimental Design

Overnight fasted rats were separated into different groups. Animals of all groups were administered with glucose (2g/kg b.w.) orally. Animals in group normal were given normal saline (0.9% w/v NaCl). Positive control group was received standard drug glibenclamide 5mg /kg b.w., Group 3 to 9 were treated orally with Polyherbal formulation 100 mg/kg b.w., all animals were monitored daily for their health status and signs of any detectable abnormalities.

Table 3: various animal group for in-vivo study

Group no.	Investigated material	Content / Dose
Group 1	Normal Control	Received normal saline (0.9% NaCl)
Group 2	Positive Control	Treated with Glibenclamide5mg/kg b.w
Group 5	PST7	Polyherbal tablet containing 1:7:1 sesame oil: span 80: propylene glycol
Group 4	PST8	Polyherbal tablet containing 1:8:1 sesame oil: span 80: propylene glycol
Group 3	PST9	Polyherbal tablet containing 1:9:1 sesame oil: span 80: propylene glycol

Blood sample collection and analysis: Blood samples were collected by tail pricking method of each animal just after oral glucose administration at 0, 30, 60,120 and 180 min for the estimation of glucose by accu-chek glucometer [13].

Antidiabetic activity of polyherbal formulation

Experimental Design

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of freshly prepared alloxan (150 mg/kg b.w.) in 0.1 M citrate buffer-pH 4.5. After 72 hrs ALLOXAN-induced fasted rats having blood glucose levels greater than 250 mg/dl were considered as diabetic and were used for further study. The animals had free access to 5% glucose solution overnight to overcome the drug induced hypoglycemia. Six rats were separated into various groups for the current investigation. The basal blood glucose levels of each animal were recorded, and then six animals were divided to serve as a typical control. The remaining animals each received a single intra-peritoneal injection of Alloxan monohydrate in water for injection at a dose of 150 mg/kg. Blood glucose levels were calculated after four days of Alloxan administration, and animals with readings between 280 mg/dl and 380 mg/dl were selected and divided into groups. The control group in Group 1 is untreated saline water; the diabetic group in Group 2 is given Alloxan 150 mg/kg; the diabetic group in Group 3 is given glibenclamide 10 mg/kg; and the diabetic groups in Groups 4 through 6 are given Polyhebal formulation PST7, PST8 and PST9. Statistical Analysis Data were assessed by comparing outcomes for various treatment groups with figures for individual controls. Analysis of variance (one-way ANOVA) was utilized in the most recent piece of software to look at significant variations in values. The information is displayed as X (Mean) SEM, with n=6 for all the gathered results. The experimental animals were divided into different groups of 6 rats in each group to determine the antidiabetic activity of polyherbal formulation. The actions of the polyherbal formulation were compared with that of the standard oral hypoglycemic agent, glibenclamide [14].

Table 4: various animal group for in-vivo antidiabetic study

Group no.	Investigated material	Content / Dose
Group 1	Normal Control	Normal saline (0.9% NaCl)
Group 2	Diabetic Control	ALLOXAN 60mg/kg + normal saline (0.9% NaCl)
Group 3	Positive Control	Diabetic rats treated with glibenclamide5 mg/kg b.w
Group 4	PST9	Polyherbal tablet containing 1:9:1 sesame oil: span 80: propylene glycol
Group 5	PST8	Polyherbal tablet containing 1:9:1 sesame oil: span 80: propylene glycol
Group 6	PST7	Polyherbal tablet containing 1:9:1 sesame oil: span 80: propylene glycol

Effect of polyherbal formulation on the body weight

All animals ingested normal amounts of food and water during the study period; hence the body weights of all the rats were taken before and during the experimental protocol.

Biochemical Analysis

Collection of Blood and Separation of Plasma Serum

At the end of the experimental period i.e., after 28 days, rats were sacrificed by cervical dislocation under mild anesthesia. Blood samples were collected through arterial Jugular with EDTA. Plasma and serum were separated by centrifugation at 3000 rpm for 10 min and the supernatant was transferred into labeled sample bottles. Were analyzed for various biochemical parameters associated with diabetes.

Estimation of lipid profile
All the estimations were done by commercially available diagnostic kit using Chemistry Analyzer (BS-120), Mindray Medical India Pvt. Ltd. The assessment of serum lipid profile included were total cholesterol, triglycerides, HDL, LDL and VLDL cholesterol [114].

Estimation of total cholesterol
Total cholesterol in the serum was estimated by the enzymatic method. Test sample was added with 1.0 ml of cholesterol oxidase enzyme reagent and mixed well and incubated at 47° for 5 minutes. Cholesterol standard were also processed similarly. The absorbance was measured at 505 nm using spectrophotometer (UV-1800, Shimadzu).

Estimation of triglyceride
Triglycerides in the serum were estimated using the diagnostic kit based on the enzymatic method described by**.** Test sample was added with 1.0 ml of enzyme reagent, mixed well and incubated at 37° for 10 minutes. Triglyceride standard were also processed similarly. The absorbance was measured at 546 nm using a spectrophotometer.

Estimation of HDL Cholesterol
HDL-cholesterol was estimated using the diagnostic kit based on the enzymatic method described by (Friedewald *et al*., 1972).Test sample was mixed with 0.1 ml of precipitating reagent and allowed to stand at room temperature for 5 minutes and centrifuged at 2000-3000 rpm, for 10 minutes. The clear supernatant was used for the estimation of HDL cholesterol as described earlier [15].

Estimation of VLDL and LDL cholesterol
These were calculated using the formula
VLDL cholesterol = TG/5
LDL cholesterol = TC- (HDL cholesterol + VLDL Cholesterol)

Estimation of glycosylated hemoglobin
At the end of the experimental period, the animals were sacrificed and blood samples were collected into heparinized tubes by cardiac puncture. Plasma 0.5ml was separated and cells were washed twice (0.154 M saline) and stored at −20°C. Oxalic acid (1 ml, 0.3 M) wasadded to an aliquot (2 ml) of adjusted hemolysate, mixed, and placed immediately in aboiling water bath at 100°C for exactly 60 min. Evaporation was minimized by placing glass marbles on each test tube. After incubation samples were cooled in cold water for 2min and deproteinization carried out by the addition of1 ml of 40%w/v TCA (Trichloroacetic acid). The tubes were vortexed (30 sec) and then centrifuged (1500 g x 15 min). Thiobarbituric acid (0.5ml, 0.05 M) was added to the clear supernatant (2 ml), mixed, and incubated at 40°C for60 min. The color developed was noted at 443 nm. Incubated in each assay were a blank using distilled water instead of hemolysate, aqueous standards of 5-HMF (0.01 mM/L - 0.05 mM/L), aqueous standards of fructose (1mM/L - 4 mM/L) [16].

Results and Discussion

Procurement and Authentication of Plant material
A systematic approach is necessary in pharmacognostic study, which helps in confirmation and determination of identity, purity and quality of a crude drug. The plant specimen was authenticated,

Evaluation of Physical Properties of SNEDDS
A polyherbal tablet containing ethanolic leaf extract of *Curcuma longa* (rhizome), *Tinospora cordifolia* (leaves), *Gymnema sylvestre* (leaves) was evaluated for appearance, hardness, friability, weight variation, and disintegration speed.

Table 5: Physical evaluation of solid formulation

Formulation Code	Weight variations (%)	Hardness (kg/cm²)	Friability (%)	Disintegration time (min)
PST7	7.01±0.11	3.18±0.21	0.74±0.12	7.01±0.12
PST8	7.21±0.05	3.29±0.29	0.32±0.52	5.22±0.11
PST9	6.21±0.31	3.84±0.12	0.27±0.24	4.66±0.01

The results show that polyherbal tablets are perfect. The result demonstrates that the data for each formulation code for which it was acquired are under the IP limit.
Animal models produced by alloxan were used to examine the anti-diabetic effects of PST9, PST8 and PST7, and the results revealed that PST9outperformed conventional medicine.

Table 6: Effect of polyherbal formulation on oral glucose tolerance test in normal rats

Treatment	Blood glucose level (mg/dL)				
	0 min	30 min	60 min	90 min	120 min
Normal Control	79.30± 0.21	148.23± 0.98	154.23± 0.67	148.21± 0.99	104.17± 0.55
Positive Control	80.27±0.68	141.93± 0.82	138.14± 0.73	110.20± 0.84	89.98± 0.86**
PST7	81.53± 1.15	144.53± 1.46	140± 1.53	115± 1.73	94± 1.42**
PST8	80.23± 1.05	148.63± 1.16	144.26± 1.49	121.31± 1.76	96.41± 1.25*
PST9	81.23± 0.94	142.53± 1.37	139± 1.64	112± 0.89	91.42 ± 1.71**

n=6 rats) ± SD, Values are statistically significant at *p<0.05, more significant at **p<0.01

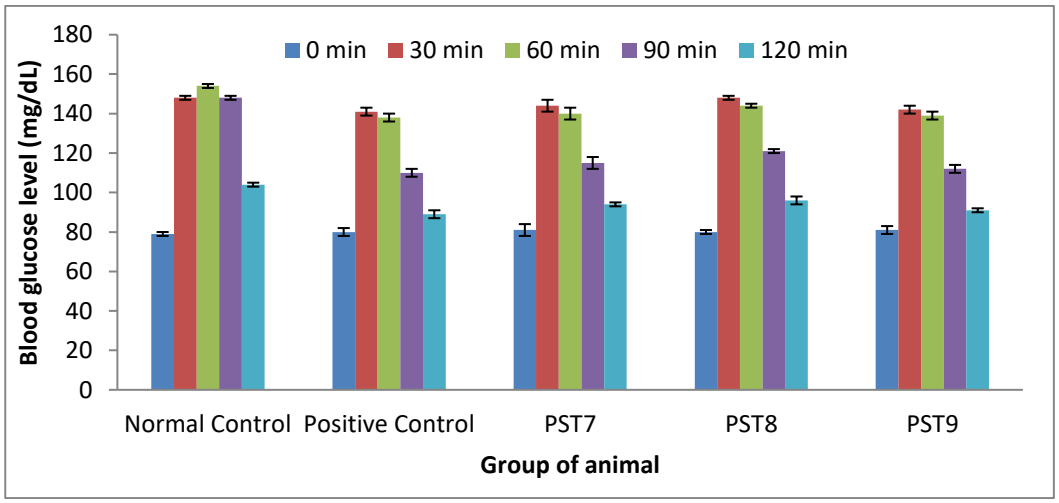

Figure 1: Effect of polyherbal formulationon oral glucose tolerance test in normal rats

Oral glucose tolerance is determined to check whether the drug substance has effect on elevated blood glucose levels after carbohydrate challenge. It measures the body's ability to use glucose which is the body's main source of energy. This test can be used to diagnose pre-diabetes and diabetes.

The formulation PH1 when administered 60 min before glucose challenge was found to have significant blood glucose lowering effect at 30th min post glucose challenge The OGTT was performed on normal glycemic rats. After glucose administration the blood glucose levels increased in the first 30 mins in all four groups. It gradually started decreasing after 120 min and got normalized in 180 min. The OGTT study it was also revealed that, oral administration of PST9 significantly ($p<0.01$) reduced the blood glucose concentrations by 80.53 % to the normal as positive control (80 %).

The oral glucose tolerance test (OGTT) widely used to evaluate apparent insulin release and insulin resistance in various clinical setting. In oral glucose tolerance test after administration of different test extracts and standard drug, 2 g/kg b.w., glucose was given orally and blood glucose level was estimated at different time intervals. The result it was revealed that drug significantly improved the OGTT in rats and exhibited potent antidiabetic activity, which could be either due to the result of the accumulation of their common active constituents or synergic action of different compounds present. This improvement in glucose tolerance would be beneficial even in prediabetes and diabetes condition to control the blood glucose levels.

Antidiabetic activity of polyherbal formulation

The experimental animals were divided into different groups of 6 rats in each group to determine the antidiabetic activity of polyherbal formulation. The actions of the extracts were compared with that of the standard oral hypoglycemic agent, glibenclamide.

Table 7: Effect of polyherbal formulation on the blood glucose levels in diabetic rats

Animal Groups	Fasting blood glucose levels(mg/dl)			
	0 Day	7 Day	14 Day	28 Day
Normal Control	80.34±3.37	81.66±3.25	83.16±3.48	84.17±2.19
Diabetic Control	256.17±4.70	250.53±5.81	254.20±4.80	255.16±3.66
Positive control	254.10±3.06	208.84±3.99	160.42±3.92	90.5±2.43**
PST7	254.43±3.32	222.31±3.41	172.23±3.67	102.21±2.76**
PST8	256.43±2.36	218.31±4.45	166.23±2.68	95.21±3.59**
PST9	258.46±2.72	217.32±3.28	159.44±3.56	94.2±3.52**

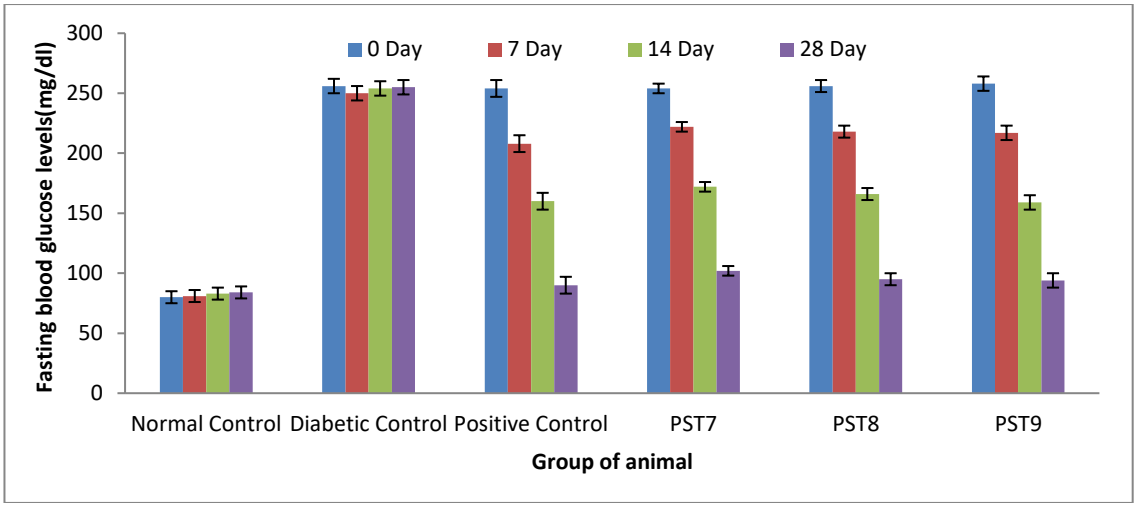

Figure 2: Effect of polyherbal formulation on the blood glucose levels in Diabetic Rats

Alloxan induces diabetes similar to type II diabetes mellitus. In study, it was found that fasting blood glucose level, which significantly elevated in alloxan–induced diabetic rats by 205.72%, as compared to the normal control, got reduced on administration of PST7, PST8, PST9for 28 days. polyherbal formulation significantly $p<0.05$ reduced the blood glucose level by 56 % and 53 % toward normal as compared to diabetic control group, whereas positive control group showed 49 % reduction.

Effect of polyherbal formulation on the body weight

Body weight assessment

All animals ingested normal amounts of food and water during the study period; hence the body weights of all the rats were taken before and during the experimental protocol. Slightly reduced body weight due to alloxan induced diabetes, significantly reverted to normal in all animals except diabetic control group, Whereas, in diabetic control group body weight reduced during 28thdays' diabetes study, this was not observed with various formulations.

Table 8: Effect of polyherbal formulation on body weight of animals

Groups	Before induction	After induction	After treatment
Normal Control	191.7±1.21	192.9±2.12	194.12±1.98
Diabetic control	190.16±2.08	161.73±2.12	145.15±1.13
Positive control	187.23±1.21	162.35±1.98	183.45±2.19
PST7	188.16 ±5.21	160.17±3.23	174.87±3.31
PST8	190.16±2.91	162.73±5.62	184.21±3.97
PST9	189.69±4.09	175.56±3.71	191.96±4.29

n=6 rats) ± SD, Values are statistically significant at *p<0.05, more significant at **p<0.01

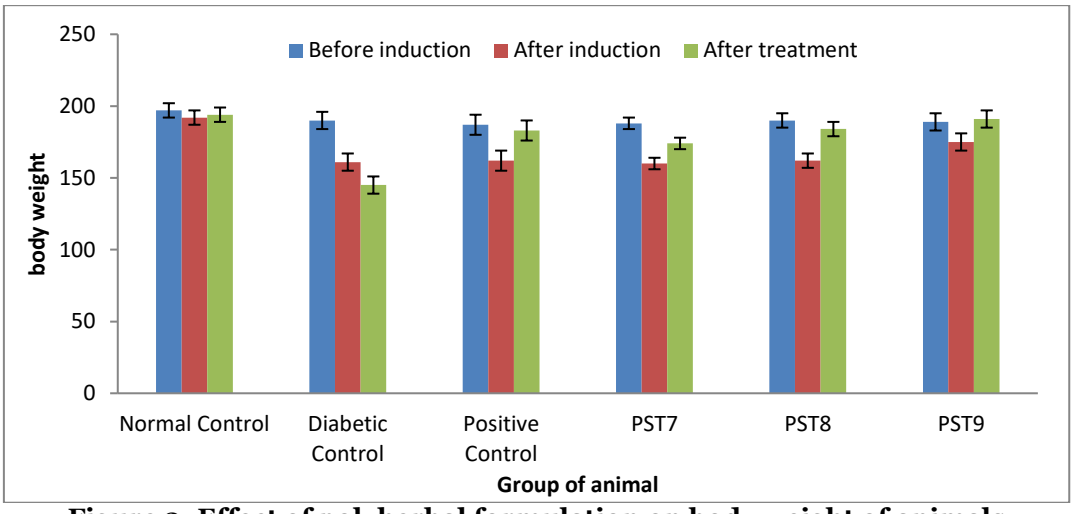

Figure 3: Effect of polyherbal formulation on body weight of animals

Body weights of all the diabetic rats were found to be statistically less (p<0.001) as compared to normal rats. All animals ingested normal amounts of food and water during the study period. Significantly reduced body

weight of alloxan induced diabetic rats as compared to normal control rats, significantly restored to normal in all animals except diabetic control group, Whereas, in diabetic control group body weight reduced during 28th days' diabetes study. The body weight of the diabetic rats treated various formulations were found to significantly improved. The percent decrease in diabetic control and increase treated groups in body weight on 28th day was indicating that the formulation was more effective in controlling blood glucose levels and weight.

Induction of diabetes by alloxan leads to loss of body weight due to the increased muscle wasting and loss of tissue proteins. The failure of diabetic animals to significantly gain weight during the course of time is due to continuous excretion of glucose because of the defect in peripheral uptake and impairment of liver's capacity to synthesize glycogen.

Biochemical Analysis

Estimation of lipid profile

In alloxan induced diabetic rats, there was a significant increase of triglycerides (TG), total cholesterol (TC), low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol and significant decrease in high density lipoprotein (HDL) cholesterol in serum compared with normal control was observed. Thus, the formulation PH1 used in the study significantly reverted *lipid profile* as compared to diabetic control the disturbed lipid profile parameters.

Alloxan induced diabetic rats were observed with increased serum lipids, which are responsible for several cardiovascular disorders. The higher levels of serum lipids such as cholesterol triacylglycerol and LDL-cholesterol of diabetic rats are due to increase in mobilization of free fatty acids from peripheral depots and also due to the lipolysis caused by hormones.

Table 9: Effect of polyherbal formulation on lipid profiles

Groups	Serum lipid level on 28th Day				
	Triglyceride (mg/dl)	Total Cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Normal Control	94.23±1.37	80.16±2.93	49.01±0.92	45.03±0.91	15.76±0.94
Diabetic Control	169.04±4.28	135.32±1.42	27.95±1.26	103.16±1.93	37.08±0.76
Positive Control	96.15±0.67**	81.04±1.45**	45.89±0.92**	49.08±1.67**	17.86±0.87**
PST7	101.93±1.64*	85.97±1.42**	43.38±1.28**	57.03±1.45**	20.24±1.27*
PST8	101.2±2.48**	84.6±0.69**	42.5±1.51**	52.23±1.58**	18.96±0.85**
PST9	96.57±1.49**	81.97±1.34**	45.58±1.37**	52.33±1.58**	17.06±0.35**

(n=6 rats) ± SD, Values are statistically significant at *p<0.05, more significant at **p<0.01

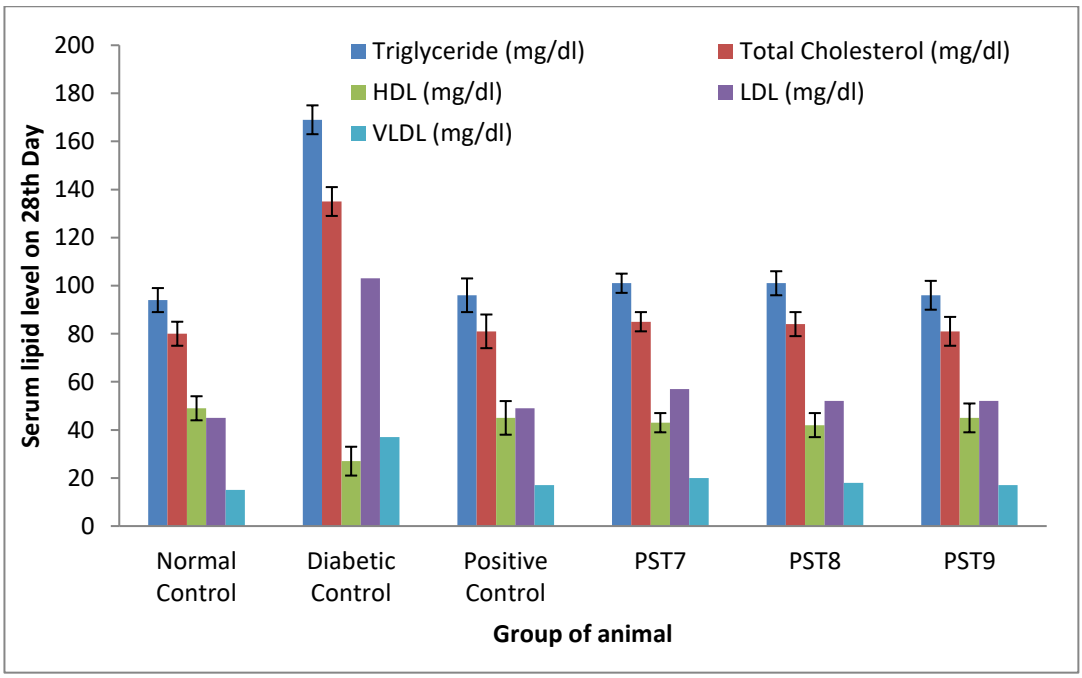

Figure 4: Effect of various polyherbal formulations on lipid profiles

The ability of extracts to reduce serum total lipids by normalization of lipogenesis could be due to presence of phytoconstituents which are responsible for increasing insulin releasing capacity of pancreatic beta cells or it could be due to achievement of normoglycemia where there was no further degradation of already accumulated lipid for otherwise glucose starved cells. The formulation PST9 are rich in, total phenolics and flavonoids content which responsible for antioxidant activity. The ability of beta sitosterols to reduce plasma cholesterol and triglycerides could be explained by the insulin releasing capacity of β-sitosterols. Also the ability of scavenging free radicals and antioxidant properties of the both the extracts may also participate in the hypolipidemic activity by inactivating hepatic HMG-CoA reductase, a key enzyme, in cholesterol synthesis. It is reported that flavonoids decrease liver HMG-CoA reductase activity in type II diabetic rat.

Estimation of glycosylated hemoglobin

In alloxan induced diabetic rats, there was a significant increase of Glycosylated hemoglobin compared with normal control. Whereas, polyherbal formulation PST9restored the elevated HbA1c profile compared to diabetic control, which was as significant as positive control (standard treated).

Table 10: **Effect of polyherbal formulation on glycosylated hemoglobin levels in animals**

Groups	Glycosylated hemoglobin (HbA1c %)
Normal Control	5.72±0.21
Diabetic Control	11.86±0.23
Positive Control	5.69±0.16**
PST7	6.89±0.21*
PST8	6.21±0.32**
PST9	5.88±0.18**

(n=6 rats) ± SD, Values are statistically significant at *p<0.05, more significant at **p<0.01

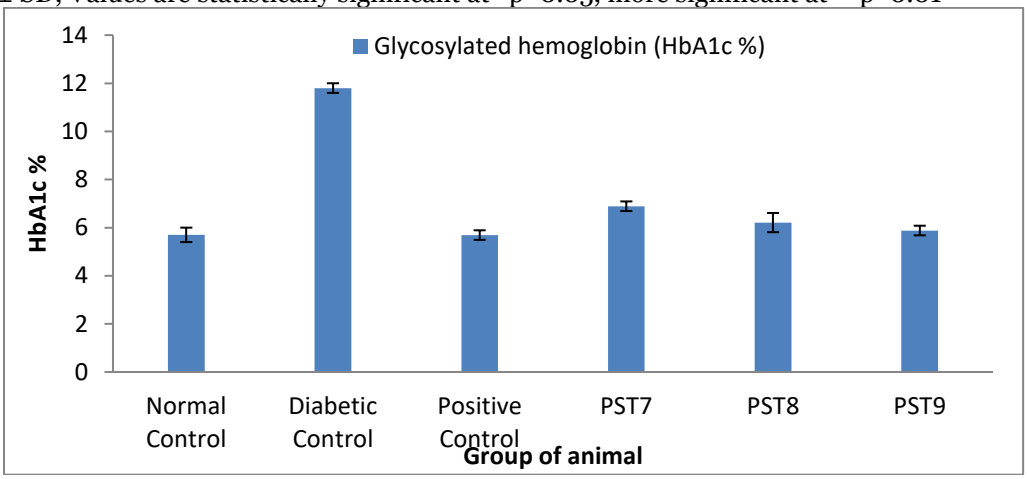

Figure 5: **Effect of polyherbal formulation on glycosylated hemoglobin levels in animals**

Summary and Conclusion

The overall results of this study indicated that an improved formulation of Curcuma longa, Tinospora cordifolia, Gymnema sylvestre SNEDDS tablets was successfully developed using the extrusion-spheronization technique. The resulting SE tablets exhibit uniform size and spherical shape and suitable hardness. It is possible to make the oral delivery of hydrophobic drugs possible by using SNEDDS, which have been demonstrated to significantly improve oral bioavailability. With the continued development of this technology, SNEDDS continue to enable novel applications in drug delivery. Through the use of surfactant- and co-surfactant-stabilized oil nanodroplets, SNEDDS is able to improve the efficacy of medications that are not very water-soluble. In the context of medication delivery, SNEDDS functions as a suitable carrier.

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