FORMULATION AND PHARMACOLOGICAL EVALUATION OF POLYHERBAL FORMULATION FOR ANTIDIABETIC ACTIVITY BY USING STREPTOZOCIN INDUCED DIABETIC RATS

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ABSTRACT

Aim

The main aim of the study is to design, optimization and pharmacological evaluation of polyherbal formulation for antidiabetic activity by using STZ induced diabetes.

Methodology

Four polyherbal formulations (A, B, C and D) were prepared by mixing specific plant extracts at documented therapeutic levels to enhance antidiabetic efficacy and bioavailability. The sustained release polymer matrix tablets were prepared by dry granulation using polyethylene oxide, xanthan gum, HPMC, sodium alginate and Kollidone SR as matrix components. Evaluation of thickness, friability, weight fluctuation and homogeneity of content. Acute oral toxicity studies were conducted in compliance with OECD Guideline 423. Antidiabetic activity was evaluated in Streptozotocin (STZ) induced diabetic Wistar rats. Animals were divided into four groups standard, diabetic, formulation treated and normal. Blood glucose levels were determined before and after the treatment and the formulation with the best glucose lowering action was selected.

Result and Discussion

All the plant extracts and polyherbal formulations were found to be safe and did not produce any behavioral abnormalities or mortality at dose level up to 2000 mg/kg. Individual extracts significantly reduced blood glucose levels in streptozotocin induced diabetic rats. Sustained-release matrix tablets prepared with different polymers showed good physicochemical characteristics and controlled drug release profiles. The formulations FA1 and FD1 at the dose of 200 mg/kg showed significant antidiabetic activity among the evaluated formulations. FD1 achieved the maximum reduction in blood glucose levels which was comparable with the conventional drug. Statistical analysis showed that the improved polyherbal formulation was effective and produced highly significant changes ($p < 0.001$) as compared with diabetic control animals.

Conclusion

The study showed that the polyherbal sustained-release preparations were safe and effective and could significantly reduce blood glucose levels in streptozotocin-induced diabetic rats. The regular drug and the studied formulations were compared and FD1 showed the best antidiabetic effect among them. The improved matrix tablet exhibited excellent safety, controlled drug release and satisfactory physicochemical characteristics up to 2000 mg/kg. The results suggest that polyherbal sustained release formulation is a promising therapeutic approach for successful treatment of diabetes mellitus.

Keywords: Streptozotocin (STZ), OECD, Cinnamomum camphora, polyethylene oxide, xanthan gum, HPMC, sodium alginate and Kollidone SR.

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1. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia due to defects in insulin secretion, action, or both. It is one of the most common non-communicable

diseases in the world and a serious public health threat due to its increasing prevalence and associated problems.[1,2] Statistics on global health show that the number of people with diabetes continues to increase, particularly in developing countries. Long-term uncontrolled diabetes can significantly adversely affect quality of life and increase healthcare costs, including nephropathy, neuropathy, retinopathy, cardiovascular disorders, and impaired wound healing.[3,4]

Conventional antidiabetic drugs, such as insulin preparations, biguanides, thiazolidinediones and sulfonylureas, are commonly used in the treatment of diabetes.[5] But these treatments often have drawbacks like side effects, resistance to drugs, cost of treatment and poor compliance from patients. Hence, alternative therapy strategies that are efficient, safe, affordable and capable of providing long term glycemic control are gaining popularity.[6,7] Medicinal plants are used for centuries in traditional medical systems for the treatment of diabetes and other metabolic diseases. Phytoconstituents such as flavonoids, alkaloids, phenolics, tannins, terpenoids, and glycosides have exhibited remarkable antihyperglycemic, antioxidant, anti-inflammatory, and insulin sensitizing activities.[8,9] Polyherbal formulations are the use of several medicinal plants in a single dose form that have attracted a lot of interest because of the synergistic therapeutic effects, increased efficacy and decreased toxicity compared to single herb preparations. The synergy of several bioactive compounds might target multiple pathways involved in the pathophysiology of diabetes such as glucose metabolism, insulin secretion, insulin sensitivity, oxidative stress, and inflammatory responses.[10,11]

The development of sustained release drug delivery systems to maintain the plasma drug levels and improve the patient compliance is to enhance the therapeutic efficacy. Matrix tablets can be formulated for controlled release of the herbal ingredients over long periods of time by reducing the frequency of dose and increasing bioavailability with the right polymers. Polyherbal sustained release formulations are an attractive way for the treatment of diabetes mellitus.[12,13]

2. METHODOLOGY

2.1 Formulation of Poly herbal (PHB) Matrix tablet

Maltodextrin, Xanthan gum, hydroxypropyl methyl cellulose (HPMC K100 LV and HPMC K4M), polyherbal (PHB), dicalcium phosphate anhydrous and other excipients were weighed accurately as per the formulation design. All the materials except magnesium stearate were passed through a #20 mesh sieve and mixed well in a box blender for 10 minutes. The mixture was passed through the same mesh as before to ensure homogeneity. Lubricated blend was produced by adding previously sifted magnesium stearate through a #40 mesh sieve and stirring for two minutes. The lubricated mixture was compressed into slugs by using 16 mm flat punches on a 20-station rotary tablet compression machine at a speed of 20-25 rpm and hardness of 70-80 N. The prepared slugs were ground in a multimill with 8 mm screen and 1.5 mm screen at modest speed using knife forward operation. The resulting granules were screened through a #20 mesh sieve to get uniform particle size. The sized granules were lubricated for two additional minutes with magnesium stearate (#40 mesh) in a box blender. The final blend was compressed into sustained-release matrix tablets on a 20-station rotary tablet compression machine using 8.0 mm biconvex punches (B tooling). Tablets were compressed at machine speed 20-25 rpm and hardness 50-70 N. The fabricated tablets were evaluated for various physicochemical parameters and in-vitro drug release characteristics.

Sr. No.	**Ingredients**	**B. No. S01/09**	**B. No. S02/09**	**B. No. S03/09**	**B. No. S04/09**	**B. No. S05/09**	**B. No. S06/09**	**B. No. S07/10**	**B. No. S08/10**	**B. No. S09/10**	**B. No. S10/10**
mg/tab											
1	Poly Herbal (PHB)	30	30	30	30	30	30	30	30	30	30
2	Dicalcium phosphate, anhydrous	79.9	51.5	60	55	49	50	50	48	50	50
3	Maltodextrin	15	72.5	57	57	57	57	57	57	57	57
4	Hydroxypropyl methyl cellulose	34	44	44	44	50	44	44	46	44	44

	(HPMC K100 LV)										
5	Hydroxypropylmethylcellulose (HPMC K 4 M)	5	10	10	15	15	15	15	15	44	44
6	Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Lubrication											
7	Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
	Average wt. (mg)	200	200	200	200	200	200	200	200	200	200

Table 1. Composition of formulation

Table 2 Composition of Poly Herbal (PHB) SR tablets 30 mg with polyethylene oxide (PEO) as release rate controlling polymer B. Size: Each batch of 100 tablets

Sr. No.	**Ingredients**	**B. No. HX01/09**	**B. No. HX02/09**	**B. No. HX03/09**	**B. No. HX04/09**
mg/tablet					
1	Poly Herbal (PHB)	30	30	30	30
2	Dicalcium phosphate, anhydrous	58	76	86	101
3	Maltodextrin	50	50	50	50
4	Magnesium stearate	2.0	2.0	2.0	2.0
Lubrication					
5	Xanthan gum	58	40	30	15
6	Magnesium stearate	2.0	2.0	2.0	2.0
	Average weight	200 mg	200 mg	200 mg	200 mg

Table 3 Composition of formulation

2.2 Evaluation of Matrix Tablet

2.2.1 Thickness

The thickness of the polyherbal sustained release matrix tablets were determined by using Vernier calliper. From each batch of formulation, ten tablets were selected randomly and the thickness of each tablet was determined individually. Measurements were taken in millimetres (mm) and mean thickness and standard deviation calculated. The test was conducted to ensure the uniformity of the tablets, and the consistency of the compression process.

2.2.2 Friability

Friability of the polyherbal sustained release matrix tablets was evaluated by Roche friabilator. Ten pre-weighed tablets of each formulation batch were taken in friabilator and rotated 100 times at the speed of 25 rpm. At the end of the test the tablets were removed, cleaned and re-weighed. The percentage friability was calculated as the difference between the initial and final weight of the tablets.

Friability turned into calculated the usage of following components.

Percentage friability = (Initial weight – Final weight) × a hundred / Initial weight

2.2.3 Uniformity of Weight

The weight uniformity of the polyherbal sustained release matrix tablets was determined by randomly selecting 20 tablets from each batch of formulation and weighing them individually. The mean weight of the tablets was determined and the weight of each tablet was compared with the mean weight. It was considered that the formulation met the pharmacopeial specifications if the weight of the tablets did not differ from the average weight by more than the permissible percentage limit. The test was conducted to determine the uniformity of distribution of the ingredients of the formulation and the consistency of the tablet weight.

2.2.4 Uniformity of Content

For content homogeneity of polyherbal sustained release matrix tablets, one tablet was placed in 100 mL volumetric flask containing 50 mL phosphate buffer (pH 7.4). The mixture was sonicated for 15 min for complete extraction of active ingredients and then cooled and diluted to volume with the same buffer. Filtration of the resultant solution and dilution of an exactly determined aliquot of the filtrate with phosphate buffer (pH 7.4) gave the final test solution. The absorbance was measured at 274 nm by using a UV-visible spectrophotometer.

2.3 Acute oral toxicity Studies of extracts

The acute oral toxicity of the polyherbal formulation was determined by fixed dose method in adult female albino rats as per OECD Guideline 423. Wistar albino rats of both intercourse weighing among one hundred–one hundred fifty gm of both sexes have been received from primary animal residence Department of Pharmacy, Oriental University, Indore (M.P.). The animals were dosed after overnight starvation. The test formulation was administered orally at the dose of 2000 mg/kg body weight, suspended in 0.5% w/v sodium carboxymethyl cellulose (CMC). Animals were continuously observed for changes in behaviour, neurologic function, and autonomic function during the first 3 hours after injection. The next three hours saw further observations at 30-minute intervals. Then, a 14-day observation period was performed to determine signs of toxicity or death up to 24 hours later. All observations were recorded according to Irwin's parameters of observation.

2.3.1 Induction of diabetes mellitus

Experimental diabetes mellitus (DM) was induced in Wistar albino rats by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 60 mg/kg body weight. Freshly prepared streptozotocin was given in 0.1 M citrate buffer (pH 4.5) after an overnight fast. Blood glucose levels were determined by glucose oxidase method using an Accu-Chek glucometer before and 72 hours after STZ injection. Blood samples were collected from the tail veins of the animals. Diabetic rats were selected for further study by selecting animals with fasting blood glucose levels >250 mg/dL. Diabetic animals were further used for the evaluation of antidiabetic activity of the prepared polyherbal formulations.

2.3.2 Treatment Groups

1. Group I (NC): Normal Control
2. Group II (DC): Diabetic Control
3. Group III (AS-ETOH): Diabetic rats orally dealt with suspension of ethanolic extract of dried leaves of *Alstonia scholaris* suspended in zero.5 % w/v sodium CMC.
4. Group IV (CA-ETOH): Diabetic rats orally dealt with suspension of ethanolic extract of dried leaves of *Centella asiatica* suspended in 0.5 % w/v sodium CMC.
5. Group V (CT-ETOH): Diabetic rats orally handled with suspension of ethanolic extract of dried leaves of *Cinnamomum camphora* suspended in zero.5 % w/v sodium CMC.
6. Group VI: Diabetic rats orally treated with Glipizide suspended.

2.3.3 Treatment Groups: polyherbal formulations:

After 72 hr. Of STZ injection animal with BGL ≥ 250 mg/dl had been divided into specific corporations (with 5 animals each) for anti-diabetic have a look at of Formulations.

1. **Group I (NC)**
2. **Group II (DC)**
3. **Group III (PC)**
4. **Group IV (FA1)**
5. **Group V (FA2)**
6. **Group VI (FB1)**
7. **Group VII (FB2)**
8. **Group VIII (FC1)**
9. **Group IX (FC2)**
10. **Group X (FD1)**
11. **Group XI (FD2)**

2.4 Biochemical examinations in diabetic rats

For dimension of blood glucose stage, blood become drawn from the tail vein and the glucose level changed into envisioned by using glucose oxidase approach by means of the use of Accu-Chek Glucometer.

3. RESULT AND DISCUSSION

3.1 Acute toxicity studies

S. No.	Treatment	Acute Oral Toxicity
1	*Alstonia scholaris* Ethanol Extract	Safe
2	*Centella asiatica* Ethanol Extract	Safe
3	*Cinnamomum camphora* Ethanol Extract	Safe

Table 4. Acute toxicity studies of ethanolic extracts of leaves of *Alstonia scholaris, Centella asiatica*, and *Cinnamomum camphora*

3.2 Effect of different plant leaves extracts on blood glucose level

The effect of ethanolic extracts of leaves of *Alstonia scholaris, Centella, asiatica and Cinnamomum camphora* has been proven as anti-diabetic. All the leaves extract of 4 different plants has showed decrease in blood glucose level 74.17, 79.60, 86.30 and 82.0 mg/dl significantly lower than as 386.5 compared to diabetic control group. The Positive control group treated with standard drug Glipizide showing blood glucose level 71.83 mg/dl.

Groups → / Parameters ↓	**Normal Control (NC)**	**Diabetic Control (DC)**	***Alstonia scholaris* Ethanol Extract (AS-ET**	***Centella asiatica* Ethanol Extract (CA-ET**	***Cinnamomum camphora* Ethanol Extract (CCAM-ETOH)**	**Positive Control Glipizide (PC)**

			OH)	OH)		
Blood Glucose (mg/dl) On 11th day	74.53 ± 1.956	386.5± 7.140 ***	74.17± 1.978 ***	79.60± 2.717 ***	86.30 ± 3.870 ***	71.83± 0.758 ***

Table 5. Effect of different plant leaves extracts on blood glucose level

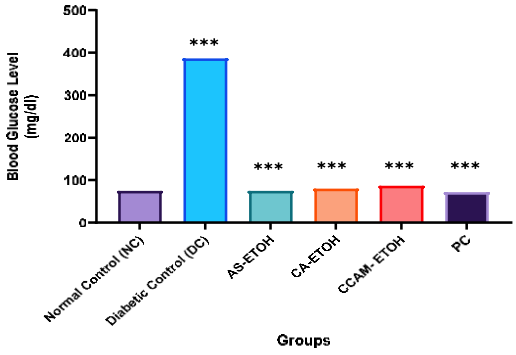

Figure 1. Blood Glucose level of plant leaves extracts

3.3 Evaluation of physiochemical properties of Polyherbal SR Matrix tablets

Granule parameters	B. No. P01/09	B. No P02/09	B. No P03/09	B. No P04/09	B. No P05/09	B. No P06/09	B. No P07/09	B. No. P08/09	B. No. P09/09
Loss on drying (%) NMT3 %	1.5	1.48	1.52	1.5	1.62	1.5	1.5	1.5	1.48
Tapped Density	0.714	0.824	0.784	0.716	0.822	0.789	0.717	0.828	0.787
Bulk Density	0.6	0.7	0.6	0.6	0.7	0.6	0.6	0.7	0.6
	66	21	95	68	29	91	60	25	94
Compressibility index	6.72	12.5	11.35	6.78	12.4	11.42	6.92	12.2	11.25
Hausner's Ratio	1.071	1.14	1.12	1.078	1.16	1.13	1.074	1.13	1.15
Finished product parameters									
Hardness (N)	65	70	73	65	65	80	76	65	70
Thickness ± 0.3 mm	3.2	3.1	3.2	3.1	3.0	3.4	3.1	3.2	31
Average wt. (mg) ± 3%	203	204	201	198	200	201	205	203	204
Friability	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Table 6. Granule and finished product evaluation of formulations with PEO

Granule parameters				
Parameters	**B. No. HX01/09**	**B. No. HX02/09**	**B. No. HX03/09**	**B. No. HX04/09**
Loss on drying (%)NMT3%	1.5	1.48	1.52	1.5
Tapped Density	0.678	0.624	0.784	0.716
Bulk Density	0.612	0.627	0.695	0.666
Compressibility index	9.72	9.5	8.35	9.78
Hausner's Ratio	1.15	1.17	1.14	1.072
Finished product parameters				
Hardness (N)	68	75	73	65
Thickness ± 0.3 mm	3.3	3.1	3.2	3.4
Average wt. (mg) ± 3%	203	205	207	195
Friability	Nil	Nil	Nil	Nil

Table 7.Granules and finished product evaluation of the formulations with Xanthan gum as polymer

Granule parameters	B. No. P01/09	B. No P02/09	B. No P03/09	B. No P04/09	B. No P05/09	B. No P06/09	B. No P07/09	B. No P08/09	B. No. P09/09
Loss on drying (%)NMT3%	1.5	1.48	1.52	1.5	1.65	1.5	1.5	1.5	1.48
Tapped Density	0.724	0.8334	0.785	0.7226	0.8227	0.781	0.7118	0.8233	0.788
Bulk Density	0.666	0.721	0.6955	0.6668	0.729	0.6911	0.6660	0.7225	0.6944
Compressibility index	6.72	12.5	11.35	6.78	12.4	11.42	6.92	12.2	11.25
Hausner'ls Ratio	1.071	1.14	1.12	1.078	1.16	1.13	1.074	1.13	1.15
Finished product parameters									
Hardness (N)	65	70	74	65	65	82	76	67	71
Thickness ± 0.3 mm	3.2	3.1	3.2	3.1	3.0	3.4	3.1	3.2	31
Average wt. (mg) ± 3%	203	204	201	198	200	201	205	203	204
Friability	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil	Nil

Table 8. Granule and tablet parameters of Polyherbal matrix tablets with HPMC as polymer

3.4 Dissolution profile of polyherbal sustained release matrix tablet formulations with different polymers

PEO WSR Coagulant was used as a release retarding polymer in the formulation of polyherbal sustained release matrix tablets. The first batch with 47.5 % polymer had acceptable physical properties releasing about 75 % of the medication in ten hours. To optimize the dissolving profile, subsequent formulations were prepared with different polymer concentrations. The optimized batches were evaluated by comparing their dissolution behavior with that of Diamicron 30 mg SR tablets. The f_2 similarity factor was used to evaluate the similarity of dissolution profiles; values greater than 50 indicated similar release characteristics and satisfactory formulation optimization.

Time in Hrs	% dissolution										
	Diamicron SR tablets	B. N. H01/09	B. N. H02/09	B. N. H03/09	B. N. H04/09	B. N. H05/09	B. N. H06/09	B. N. H07/09	B. N. H08/09	B. N. H09/09	B. N. H10/09
1	7	5.2	4.6	14.4	14.3	7.5	9.3	11.6	11.9	13.3	12.4
2	15.8	10.3	8.6	18.8	21.7	18.3	21.3	16.0	16.7	28.8	25.7
4	36.6	28.1	19.8	36.7	39.2	44.5	50.2	35.4	32.3	44.3	41.2
6	54.2	44.7	45.8	55.4	56.5	65.7	74.0	55.1	50.8	62.9	56.6
8	80.9	64.7	62.1	70.7	67.1	72.	86.4	70.2	67.2	84.7	81.3
10	93.3	75.8	70.4	74.1	75.2	78.4	94.0	90.1	81.4	97.2	92.4

Table 9. Comparative % dissolution profile of polyherbal SR tablets containing PEO WSR coagulant as polymer with Diamicron SR tablets

3.5 Polyherbal sustained release matrix tablet with Xanthan as polymer

Time in Hrs Time in Hrs	% dissolution				
	Diamicron SR tablets	B. N. HX01/09	B. N. HX02/09	B. N. HX03/09	B. N. HX04/09
1	6.8	1.8	1.4	2.1	4.2
2	16.7	3.4	3.8	4.0	6.8

4	38.8	7.1	7.9	8.1	10.5
6	57.4	15.4	16.8	13.1	14.9
8	78.3	20.7	24.8	18.3	21.7
10	89.6	24.6	27.9	23.9	34.6

Table 10. Comparative % dissolution profile of polyherbal SR tablets containing Xanthan gum as polymer with Diamicron SR tablets

3.6 Polyherbal sustained release matrix tablet with Hydroxypropyl methyl cellulose (HPMC) as polymer

Time in Hrs	% dissolution											
	Diamicron SR tablets	B. No. H01/09	B. No. H02/09	B. No. H03/09	B. No. H04/09	B. No. H05/09	B. No. H06/09	B. No. H07/09	B. No. H08/09	B. No. H09/09	B. No. H10/09
1	7	9.45	16.4	10.4	9.9	12.6	12.7	11.1	3.2	4.8	10.5
2	15.8	17.9	21.4	17.5	10.2	14.7	15.9	16.8	12.8	14.9	15.9
4	36.6	31.4	45.1	36.4	23.4	3.7	39.8	37.2	25.8	28.8	39.6
6	54.2	61.7	60.4	56.6	34.4	44.5	58.2	54.1	44.9	48.9	56.6
8	80.9	75.4	66.7	74.3	52.7	49.7	31.6	79.4	58.7	62.3	81.7
10	93.3	92.5	86.5	78.1	70.1	64.2	78.9	94.6	63.5	91.5	92.8

Table 11. Comparative dissolution profile of Polyherbal SR tablets with HPMC as polymer with Diamicron SR tablets

Pilot scale trials were conducted to see the scale out of improved polyherbal sustained release formulation developed in the laboratory. The aim was to develop a reliable, reproducible and low-cost manufacturing process that can be scaled up for mass production. During the scale-up critical process parameters were identified and monitored to ensure constant product quality. The study demonstrated successful technology transfer of the optimized formulation from laboratory scale development to pilot scale manufacture with maintenance of the intended release profile and physicochemical properties.

S. No.	Ingredients	Mg/tablet, B. No. FL/10	Qty. in g. / 1000 tablets
1	Polyherbal Extract Mix	200	200
2	Microcrystalline cellulose	160	160
3	Maltodextrin	60	60
4	Hydroxypropyl cellulose	40	40
5	Purified water	q.s	q.s
		500	500

Table 12. Composition of Polyherbal Sustained release tablets scale up batch – 1000 tablets

Time in hrs.	B. No. T1	B. No. T2			B. No. T3		B. No. T4	
	(% drug released)	RSD (%)	(% drug release)	RSD (%)	(% drug released)	RSD (%)	(% drug released)	RSD (%)
1	5.6-7.2	17.68	4.5–11.8	63.34	6.9–9.4	21.69	5.4-11.2	50.12
4	32.5-33.8	2.77	28.97–38.95	20.78	38.5–40.4	3.41	34.5-42.5	25.1
6	69.8-71.3	1.5	66.9–79.5	12.17	70.4–74.3	3.81	68.2-78.3	12.75
10	89.5-91.6	1.64	79.5-89.6	8.45	89.6-92.5	2.25	82.98-96.45	10.62

Table 13. Dissolution profile of Polyherbal Sustained release tablets in pH 6.8 Phosphate buffer with RSD

Time in	Formulation T1	Formulation T2	Formulation T3	Formulation T4	Diamicron MR

Hrs					
0	0	0	0	0	0
1	11.1	7	10.3	10.3	7
2	16.8	15.6	17.2	17.2	15.8
4	37.02	40.3	35.6	35.6	36.6
6	54.12	58.5	57.8	57.8	54.2
8	79.4	76.8	81.3	81.3	80.9
10	90.1	89.7	92.4	92.4	93.3

Table 14. Comparative dissolution profile of Polyherbal SR Matrix tablet formulations with Diamicron SR tablet

3.7 Acute toxicity study of polyherbal formulation

STZ-induced diabetic rats treated with all six formulations did not show any discernible change in behaviour up to the dose level of 2000 mg/kg body weight. No sign of mortality was observed during the observation of 14 days.

Group	**No of rats**	**Wt. of rats (gm)**	**Dose of Formulation**	**No. of dead animals**
I	3	150	250 mg/kg b.wt	Nil
		148		
		150		
II	3	151	500mg/kg b.wt	Nil
		145		
		156		
III	3	150	1000 mg/kg b.wt	Nil
		150		
		152		
IV	3	155	2000 mg/kg b.wt	Nil
		142		
		145		

Table 15. Results of Toxicity study of Formulation A

Group	**No of rats**	**Wt. of rats (gm)**	**Dose of Formulation**	**No. of dead animals**
I	3	160	250 mg/kg b.wt	Nil
		145		
		155		
II	3	150	500mg/kg b.wt	Nil
		140		
		155		
III	3	150	1000 mg/kg b.wt	Nil
		150		
		155		
IV	3	155	2000 mg/kg b.wt	Nil
		140		
		145		

Table 16. Results of Toxicity study of Formulation B

Group	**No of rats**	**Wt. of rats (gm)**	**Dose of Formulation**	**No. of dead animals**
I	3	150	250 mg/kg b.wt	Nil
		150		
		152		
II	3	151	500mg/kg b.wt	Nil
		145		
		156		
III	3	150	1000 mg/kg b.wt	Nil
		148		
		150		
IV	3	155	2000 mg/kg b.wt	Nil
		142		
		145		

Table 17. Results of Toxicity study of Formulation C

Group	**No of rats**	**Wt. of rats (gm)**	**Dose of Formulation**	**No. of dead animals**
I	3	150	250 mg/kg b.wt	Nil
		140		
		155		
II	3	155	500mg/kg b.wt	Nil
		140		
		145		
III	3	160	1000 mg/kg b.wt	Nil
		145		
		155		
IV	3	155	2000 mg/kg b.wt	Nil
		150		
		150		

Table 18. Results of Toxicity study of Formulation D

3.8 Antidiabetic activity of polyherbal formulations

Under blood glucose level examination from induction of diabetes to final day treatment of polyherbal tablet formulation. All formulation gives their beneficial antidiabetic activity. Amongs all formulation with two different dose regimen (200 & 400 mg/kg), the dose 200 mg/kg of Formulation FA1 and FD1 showed more beneficial blood glucose lowering effect as compared to diabetic control nontreated animals. While the formulation FD1 showed most potent antidiabetic activity in form of blood glucose lowering effects was observed similar to positive control animals and significantly different from Normal and diabetic control animals.

Groups → / Parameters ↓	**Dose**	**Zero Day (Fasting Blood Gluco**	**3rd Day (After STZ induction of Dia**	**5th Day (After induction of diabetes with Trea**	**10th Day (After induction of diabetes with Trea**	**15th Day (After induction of diabetes with Trea**

		se Level)	**betes Blood Glucose Level)**	**tment Blood Glucose Level)**	**tment Blood Glucose Level)**	**tment Blood Glucose Level)**
Group-I Normal Control (NC)	Vehicle 2 ml/kg	75.83± 1.956	76.21± 0.598	75.26± 0.297	77.52± 0.264	75.22± 0.176
Group-II Diabetic Control (DC)	STZ (60 mg/kg)	76.5± 0.140***	386.5± 0.241***	408.2± 0.549***	410.2± 0.524***	412.2± 0.521***
Group-III Positive Control Glipizide (PC)	5 mg/kg	72.67± 0.978***	385.5± 0.751***	210.6± 0.185***	168.4± 0.364***	70.05± 0228***
Group-IV Formulation (FA1)	200 mg/kg	73.50± 0.717***	341.4± 0.632***	268.9± 0.110***	187.1± 0.368***	85.62± 0.875***
Group-V Formulation (FA2)	400 mg/kg	76.30± 0.870***	378.7± 0.421***	245.5± 0.548***	210.6± 0.332***	140.6± 0.115***
Group-VI Formulation (FB1)	200 mg/kg	75.00± 0.840***	366.1± 0.205***	288.9± 0.124***	207.1± 0.361***	95.12± 0.412***
Group-VII Formulation (FB2)	400 mg/kg	78.83± 0.758***	356.4± 0.212***	295.5± 0.548***	224.6± 0.332***	152.7± 0.126***
Group-VIII Formulation (FC1)	200 mg/kg	72.00± 0.840***	382.5± 0.141***	272.9± 0.105***	210.1± 0.355***	105.18± 0.121***
Group-IX Formulation (FC2)	400 mg/kg	73.83± 0.758***	387.3± 0.541***	262.5± 0.148***	221.2± 0.216***	145.7± 0.264***
Group-X Formulation (FD1)	200 mg/kg	76.00± 0.840***	396.5± 0.211***	265.8± 0.153***	182.8± 0.421***	75.66± 0.587***
Group-XI Formulation (FD2)	400 mg/kg	78.83± 0.758***	388.2± 0.268***	240.5± 0.561***	170.5± 0.246***	110.2± 0.652***

Table 19. Effect of Polyherbal SR Matrix Tablet Formulations (A,B,C & D) on blood glucose level

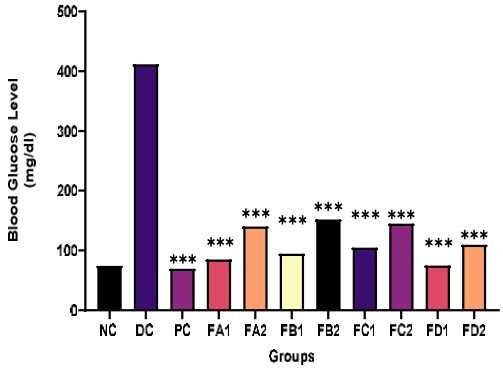

Figure 2. Blood Glucose level of Polyherbal SR Formulations

4. SUMMARY & CONCLUSION

The main objective of the present study was to prepare, optimize and evaluate polyherbal sustained release (SR) matrix tablets for management of diabetes. The present study investigated different matrix forming polymers such as Polyethylene oxide (PEO), Xanthan gum and Hydroxypropyl methylcellulose (HPMC) to obtain regulated and sustained drug release profile comparable to marketed Diamicron® SR tablet. Early formulations with higher doses of PEO had slower drug release but acceptable physical properties. The release

properties were acceptable with 22.5% PEO and the dissolution profile was improved by the optimization of the polymer concentration. Xanthan gum-based formulations showed good tablet properties. This approach was abandoned because the desired release profile could not be achieved even with a reduced concentration of the polymer. The polymer with the closest dissolution profile to the reference formulation was the HPMC at 44% concentration.

All the prepared formulations met the pharmacopeial standards for tablet quality parameters like weight fluctuation, assay, content consistency and limitation of impurities. The optimized formulation was scaled up 15 folds without any compromise in the quality of the final product. The effective optimization of critical process parameters such as blending time, compression speed, tablet hardness, milling settings and granulation factors showed the stability and repeatability of the manufacturing process . The slugging technique helped to reduce larger batch production and scale up.

Hydrophilic polymers were used to improve the controlled release behavior; polyethylene glycol 8000 and HPMC were mixed with hydrophobic excipients like hydrogenated castor oil and stearic acid. The improved formulation showed good stability and predictable release profile during the scale-up testing.

The antidiabetic activity of the new polyherbal sustained-release tablets was confirmed in vivo in streptozotocin-induced diabetic rats. The combination was therapeutically effective over the long term and lowered blood glucose levels. The study revealed that the optimized polyherbal sustained-release matrix tablet was a safe, repeatable and efficient dosage form which can produce potent anti diabetic action and controlled drug release. These findings support its potential for large scale production and future clinical use in treating diabetes mellitus.

5. REFERENCES

1. Hou, Y., Xuelin, C., Dong, L., Wanga, L., Chenga, B., Shia, Q., Luo, X., Bai, G., (2012). Bioactivity-based liquid chromatography-coupled electro spray ionization tandem ion trap/time of flight mass spectrometry for β2AR agonist identification in alkaloidal extract of *Alstonia scholaris. Journal of Chromatography A*, 1227, (2), 203– 209.
2. Arulmozhi, S., Mazumdar, P.M., Sathiyanarayanan, L., Thakurdesai, P.A., (2012). Analgesic, anti-inflammatory and antiulcerogenic activities of fractions of *Alstonia scholaris*. *Pharmacologia,* (3) 132–137.
3. Antony, M., Menon, D.B., James, J., Dev, L.M.S., Thankamani, V., (2011). Phytochemical analysis and antioxidant activity of *Alstonia scholaris. Pharmacognosy Journal*, (26), 13-18.
4. Yun-Li Zhao, Zi-Feng Yang, Bai-Fen Wu, Jian-Hua Shang, Ya-Ping Liu, Xin-Hua Wang, Xiao-Dong Luo, Indole alkaloids from leaves of Alstonia scholaris (L.) R. Br. protect against emphysema in mice, J Ethnopharmacol, 2020 Sep 15;259:112949.
5. Arulmozhi, S., Mazumder, P. M., Lohidasan, S., Thakurdesai, P. (2010). Antidiabetic and antihyperlipidemic activity of leaves of *Alstonia scholaris* Linn. R. Br. *Eur. J. Integr. Med.* 2, 23-32.
6. Jong-Anurakkun, N., Bhandari, M. R., Kawabata, J. (2007). α-Glucosidase inhibitors from Devil tree (*Alstonia scholaris*). *Food Chem.* 103, 1319-1323.
7. Pawan Kumar Verma a,* , Sheen Tukra a , Bhawani Singh a , Priyanka Sharma a , Gholamreza Abdi b,* , Zuhaib F. Bhat c, Unveiling the ethnomedicinal potential of Alstonia scholaris (L.) R. Br.: A comprehensive review on phytochemistry, pharmacology and its applications, Food Chemistry Advances, 6(2025), 100866, 1-12.
8. Shrestha De, Rajat Das, Mrittyunjoy Adhikari, Pallab Ghosh, Jyochhana Priya Mohanty and Chandrika Sharma, An updated review on Alstonia scholaris: A delightful therapeutic plant, Journal of Medicinal Plants Studies 2024; 12(2): 43-51.
9. Ahmad Nasir Labaran, Zakariyya Uba Zango, Giriraj Tailor, Ahmed Alsadig, Fahad Usman, Muhammad Tukur Mukhtar, Alhassan Muhammad Garba, Raed Alhathlool, Khalid Hassan Ibnaouf, Osamah A. Aldaghri, Biosynthesis of copper nanoparticles using Alstonia scholaris leaves and its antimicrobial studies, Scientific Reports, 14 (2024), 1-4.
10. Longmann O. (2005), Indian Medicinal Plants, International Book Distributors Book Sellers & Publisher India,1, 52.
11. Kumar VK, Gupta YK. (2002) Effect of different extracts of *Centella asiatica* on cognition and markers of oxidative stress in rats. J Ethanopharmacol; 79: 253-260.
12. Maquart FX, Bellon G, Gillery P, Wegrowski Y, Borel JP. Stimulation of collagen synthesis in fibroblast cultures by a triterpene extracted from *Centella asiatica. Connect Tissue Res.* 1990; 24(2): 107-20.
13. Montecchio GP, Samaden A, Carbone S, Vigotti M, Siragusa S, Piovella F. *Centella asiatica* Triterpenic Fraction (CATTF)

reduces the number of circulating endothelial cells in subjects with post phlebitic with post phlebitic syndrome. *Haematologica.* 1991 May- Jun.; 76(3):256-9.

Sr. No.	**Ingredients**	**Spec.**	**B. N. H01/09**	**B. N. H02/09**	**B. N. H03/09**	**B. N. H04/09**	**B. N. H05/09**	**B. N. H06/09**	**B. N. H07/09**	**B. N. H08/09**	**B. N. H09/09**
	mg/tablet										
1	Poly Herbal (PHB)	Ph. Eur.	30	30	30	30	30	30	30	30	30
2	Lactose monohydrate	Ph. Eur.	47.5	67.6	-	-	-	-	-	-	-
3	Dicalcium phosphate, Anhydrous	Ph. Eur.	-	-	77.6	82.6	87.6	97.6	87.6	77.6	72.6
4	Maltodextrin	Ph. Eur.	18	20	20	20	20	20	30	40	45
	Lubrication										
5	Polyethylene oxide (PEO)	In. Spec.	95	80	70	65	60	50	50	50	50
6	BHT (sifted through # 100 mesh sieve)	Ph. Eur.	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
7	Magnesium Stearate	Ph. Eur.	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0