FORMULATION AND EVALUATION OF SYNERGISTIC ANTIDIABETIC ACTIVITY OF *WITHANIA COAGULANS DUNAL* AND *HIBISCUS ROSA SINESIS.*

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Abstract:
Hyperglycaemia is characterized by elevated blood glucose levels, stands as the most prevalent metabolic endocrine disorder. It is the chronic condition, caused due to the improper insulin production in body or due to insulin resistance, high blood glucose level and low blood glucose level leads to diabetic condition. The aim of the present research study was to formulate and evaluate poly herbal anti -diabetic tablet for medicinal purpose. The polyherbal tablets of *Withania coagulans dunal* and *Hibiscus rosa-sinensis* were prepared as side effects free, safer, cheaper and much effective medicine Granules prepared by wet granulation method, were performed preformulation studies based on the preformulation studies powder flow properties are good and Weight variation of F3 and F7was ±1.99 and ± 2.13 respectively, Hardness of F3 and F7 was 4.1± 0.01 kg/cm^2 and 4.2± 0.03 kg/cm^2 respectively, Friability of F3 and F7 are 0.73 ± 0.01% and 0.69 ± 0.01% respectively. Thickness of F3 and F7 was measured as 4.6± 0.02 mm and 4.4± 0.02 mm respectively, Disintegration time of both F3 and F7 are 15min15 sec good. The formulated tablets were subjected to in vitro release study and from which the formulation F7 was selected as optimized formulation which shows 91.68% drug release for *Withania coagulans dunal* and 81.88% drug release for *Hibiscus rosa-sinensis.*

Keyword: Withania coagulans Dunal, Hibiscus rosa-sinensis, Antidiabetic action, polyherbal tablet, Wet granulation method.

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INTRODUCTION:

Introduction of Diabetes Mellitus:

Diabetes mellitus is a persistent condition affecting the metabolism of carbohydrates, fats, and proteins. A defective or deficient insulin secretary response, which translates into impaired carbohydrates (glucose) use, is a characteristic feature of diabetes mellitus, is the resulting hyperglycaemia. [1]

The main types of Diabetes Mellitus are Insulin Dependent Diabetes Mellitus (Type1 IDDM) is also called autoimmune diabetes and previously known as juvenile-onset or ketosis prone diabetes. Non-Insulin Dependent Diabetes Mellitus (Type2 NIDDM) is also known as adult-onset diabetes. [2] The underlying insulin resistance sets the stage for the progressive defect in insulin secretion. [3] Diabetes Mellitus in that glucose intolerance occurring for the first time or diagnosed during pregnancy is referred to as gestational diabetes mellitus (GDM).[4] Other Specific Type (Monogenic Types) are most common form of monogenic types of diabetes is developed with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1a. They also referred to as genetic defects of beta cells.[5] Causes of Diabetes Mellitus [6] are aging, obesity, insufficient energy consumption, alcohol drinking, smoking etc. Symptoms of diabetes [7] are increase thrust, frequently urination, extreme hunger**,** weight loss, fatigue, polyuria, polydipsia, glycosuria etc.

The widespread utilization of polyherbal formulations across the globe can be attributed to their significant medicinal and therapeutic benefits. It has also known as polyherbal therapy or herb-herb combination.[8] Every medical system endeavor to bring healing and wellness to those who are unwell. In India, contemporary medicine coexists harmoniously with traditional healing practices, offering patients diverse medical options. In India, two coexisting medical systems, modern and traditional, run in parallel, offering diverse healthcare approaches to the population. Traditional treatments include herbal medicines, dietary interventions, and massage.[9] Combining drugs in treatments frequently yields a more promising and effective outcome compared to using a single drug. The synergy of multiple herbs in a polyherbal approach offers superior diabetes management with fewer side effects compared to using single herbs in most traditional systems.[10]

MATERIAL AND METHODS:

1. Drug profile:

1.1 *Withania coagulans dunal.*

Fig- 1: *Withania coagulans* fruits.

Botanical name- *Withania coagulans dunal*
Common name -Paneer phool, Paneer dodi, Vegetable rennet etc.
Family – Solanaceae.
Plant part used – Fruits.
Appearance – Yellow to brown.

1.2 *Hibiscus rosa sinesis*

Fig- 2: *Hibiscus rosa sinesis* flower.

Botanical name – *Hibiscus rosa sinesis.*
Common name – China rose, Gudhal etc.
Family – Malvaceae.
Plant part used – Flowers.

Appearance – Red.
The fresh flowers of *Hibiscus rosa sinesis* were collected from local area of Pandharpur.While the fruits of *Withania coagulans dunal* were purchased from local market of Pandharpur.Both the drugs were authenticated at Department of Botany, Karmaveer Bhaurao Patil Mahavidyalaya, Pandharpur, Punyashlok Ahilyadevi Holkar Solapur University, Solapur, India.

2.Methods:

2.1 Preformulation study:

2.1.1 Morphology: It encompasses the assessment of a drug based on its color, smell, size, shape, taste, and unique attributes, such as touch and texture.

2.1.2 Solubility: Amount of a substance that dissolve in a unit volume of a liquid substance to form a saturated solution under specified conditions of temperature and pressure is called the solubility of the solute. For the quantitative or crude solubility, a known amount of drug (1 mg) was suspended in a series of different solvents at room temperature in tightly closed test tubes and shaken on the shaker for 2 hours. The crude solubility was perceptible solely through visual observation.

2.2 Methodology For extraction of Withanolide from *Withania coagulans dunal*:

Withania coagulans dunal fruit are collected from market. They are manually sorted. The fruits of Withania coagulans were coarsely powdered. And extracted with methanol using Soxhlet. To the extract water was added (1: 1) and fractionated using chloroform (2: 1) in a separating funnel. Both the fractions chloroform and hydroalcoholic were concentrated. Dried in a Rota evaporator initially and then in vacuum desiccator

2.3 Methodology For extraction of Anthocyanin from *Hibiscus rosa sinesis*:

The flowers dried under shade. Powdered and passed through 40 mesh sieve. Extracted with ethanol at 60°C- 80°C for 48 hours. Dried in a Rota evaporator initially and then in vacuum desiccator.

2.4 Preparation of polyherbal tablets of *Withania coagulans dunal* and *Hibiscus rosa sinesis*:

The wet granulation method was utilized to prepare all the formulations. The *Withania coagulans dunal* and

Hibiscus rosa sinesis and all other ingredients were individually passed through sieve ≠ 60. All the ingredients were mixed thoroughly by triturating for up to 15 minutes, ensuring complete mixing. After combining the binder solution with the powder mixture, an adhesive mass is produced, which can then be granulated. The quantity of binding agent and fluid needed to create a damp mass is crucial for the process. The wet massed powder blend is screened using 18 to 20 mesh screens to prepare wet granules. The screened moist granules are dried in a hot air oven at a controlled temperature not exceeding 50 0C.The dried granules was lubricated with talc. The single punch tablet machine (CADMACH) was used for the compression of the floating tablets. Use of ingredients in the formulation: Carbopol was used as rheology modifiers. Microcrystalline cellulose (MCC) was used as the diluent. Ethyl cellulose and PEG 4000 was used as binder and dibasic calcium phosphate act as filler. The direct compression method was employed to prepare the tablets.

Table - 1: Formulation of polyherbal tablets of *Withania coagulans dunal* and *Hibiscus rosa sinesis*:

Sr. No.	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)
1	Withania coagulans dunal	170	180	190	130	120	110	200	160
2	Hibiscus rosa sinesis.	130	120	110	170	180	190	100	140
3	Carbopol	20	30	40	-	-	-	-	-
4	Ethyl cellulose	-	-	-	20	30	40	40	30
5	Microcrystalline cellulose	40	40	40	40	40	40	40	40
6	Dibasic calcium phosphate	30	20	10	30	20	10	10	20
7	PEG 4000	10	10	10	10	10	10	10	10
8	Methyl paraben	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
9	Weight per Tablet	400	400	400	400	400	400	400	400

3.Evaluation for tablet:

3.1 Pre-compression study:

3.1.1 Bulk density and Tapped density: [11]

Both loose bulk density and tapped density were determined. Each formulation's powder, having been gently shaken to disperse any clumps, was then carefully poured into a 10 ml measuring cylinder. Following the initial volume observation, the cylinder was repeatedly dropped from a height of 2.5 cm onto a hard surface at 2-second intervals.

The tapping persisted until no additional alteration in volume was observed. Bulk density is calculated by using a formula:

$$Bulk\ density = \frac{Weight\ of\ sample\ in\ gm}{Volume\ occupied\ by\ sample\ in\ ml}$$

The final volume was recorded and the tap density was calculated by the following equation:

$$Tapped\ density = \frac{Weight\ of\ sample\ ingm}{Volume\ occupied\ by\ sample\ in\ ml}$$

3.1.2 Carr's index: [12]

A straightforward assessment method has been devised to measure the friability of a powder, involving the assessment of its poured (fluff)

density, tapped density, and the packing rate. A useful empirical guide is given by Carr's index.

$$Compressibility\ index = \frac{Bulk\ density - Tapped\ density}{Tapped\ density}$$

Hausner discovered that the correlation between tapped density and bulk density was indicative of interparticle friction and could be employed as a predictive measure for powder flow characteristics.

$$Hausner's\ ratio = \frac{Bulk\ density}{Tapped\ density}$$

3.1.3 Hausner's Ratio: [13]

Table2: Relationship between % compressibility and flowability

%Compressibility	Flowability	Hasuner's ratio
5-15	Excellent	1.00-1.11
12-16	Good	1.12-1.18
18-21	Fair to passable	1.19-1.25
23-25	Poor	1.26-1.34
33-38	Very poor	1.35-1.45
>40	Very very poor	1.46-1.59

3.1.4 Angle of repose: [14]

The angle of repose is used to measure the flow characteristics. Improper flow of powder is due to frictional forces are qualified by angle of repose. Angle of repose is defined as the maximum angle between the surface of a pile of the powder and the horizontal plane. Angle of repose for blend for each formulation was determined by fixed funnel method. The funnel is secured with its tip with height h (2 cm), above a plane of paper kept on a flat horizontal surface The powders were meticulously poured through the funnel, ensuring that the conical pile formed reached the tip of the funnel's apex with precision. Angle of repose was determined by substituting the values of the base radius 'r' and height of the pile ' h ' in the given equation given below,

Tan θ = h/r

Where,

θ = Angle of repose,

h = Height of pile, r = Radius of base.

Table 3: Relationship between Angle of repose and flow property

Sr. No.	Angle of repose	Flow property
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	>40	Very poor

3.2Post-compression study: [15]

The complete set of matrix tablets that were evaluated for both official and unofficial parameters.

3.2.1 Appearance:

The tablets were identified by checking the difference in colour.

3.2.2 Thickness:

The uniformity of tablet size depended on the tablet thickness. Thickness was measured by using screw gauze on 3 randomly selected samples.

3.2.3 Hardness:

Hardness of the all tablet formulations were determined by Monsanto hardness tester. For each formulation the hardness of 5 tablets was determined, the average was calculated and presented with standard deviation is expressed in kg/cm.

3.2.4 Friability:

The friability testing procedure was conducted using the Roche friabilator. Twenty tablets were precisely measured and then placed inside the plastic chamber, which was set to rotate at 25rpm for 4 minutes, causing the tablets to descend six inches with each revolution. After accurately weighing twenty tablets, they were carefully placed inside the plastic chamber, which rotated at 25rpm for 4 minutes, causing the tablets to drop six inches with each revolution. Following 100 revolutions, the tablets underwent reweighing, allowing for the calculation of the percentage decrease in tablet weight

3.2.5 Weight Variation:

To assess weight variation, a total of twenty tablets were randomly chosen from each formulation and weighed individually. The permissible weight variation, as per USP guidelines, encompassed the subsequent percentage deviate.

Table 4: Weight variation tolerance for uncoated tablets:

Sr. No.	Average mass	Percentage deviation
1	130 or less	±10
2	More than 130 mg and less	±7.5
3	324 mg or more	±5

In all formulations, the tablet weight was 120 mg, hence a maximum deviation of ± 10% from the average tablet weight was allowed.

3.2.6 Drug content: [16]

For determination of drug content at least five tablets from each formulation were weighed individually, crushed and diluted to 100 ml with sufficient amount of phosphate buffer of pH 6.8 (USP 2000). Then aliquot of the filtrate was diluted suitably and analysed spectrophotometrically at 205 nm against blank. Drug content was calculated using standard curve. All parameters of post compressional studies of the prepared matrix tablet.

3.2.7 In vitro Release Studies:[17]

Based on the particle size and *in vitro* buoyancy studies, all the formulations were subjected to *in vitro* release studies. The studies were carried out by paddle method (USP apparatus II) at 50 rpm using 900 ml of simulated gastric fluid (pH 1.2) maintained at 37±0.5 ◦C. The samples were evaluated spectrophotometrically at 260 nm (λmax). The experiments were conducted three times to ensure reproducibility and consistency in the results. The samples were collected at specified intervals from the dissolution media, and fresh dissolution media with corresponding pH levels were replenished in their place. The samples were analysed by UV-Visible Spectrophotometer (Lab India 3000+). The quantification of drug concentrations in the samples was achieved using calibration curves derived from reference standards. The plotted graph illustrates the percentage of drug released over designed time intervals.

RESULT AND DISCUSSION:

1.Preformulation studies of herbal drugs:

The pure drug *Withania coagulant dunal* used in the study was obtained from local market. The drug was identified by light absorption in the range of 227 nm according to Indian pharmacopeia. The absorbance of drug solution was 0.485 at λ max 227 nm, which obeys Indian pharmacopeia. The result is given in Table No. 5.

The pure drug *Hibiscus rosa sinesis* used in the study was obtained from local market. The drug was identified by light absorption in the range of 520 nm according to Indian pharmacopeia. The absorbance of drug solution was 0.309 at λ max 520 nm, which obeys Indian pharmacopeia. The result is given in Table No. 5.

Table 5: Preformulation studies of *Withania coagulans dunal* and *Hibiscus Rosa Sinesis.*

Sr. No.	Drugs	Identification parameter reported
1.	*Withania coagulans dunal*	λ max at 227 nm
2.	*Hibiscus rosa sinesis*	λ max at 520 nm

2 Solubility study of *Withania coagulans dunal* and *Hibiscus Rosa Sinesis*:

Withania coagulans dunal solubility checked in water, ethyl acetate, n-hexane, ethanol, acetone. The *Withania coagulans dunal* soluble in methanol, ethanol, chloroform. The result is given in Table No. 6

Table 6: Solubility tests of *Withania coagulans dunal* in various solvents

Sr.No.	Solvents	Solubility behaviour
1	Ethyl acetate	Freely soluble
2	Methanol	soluble
3	Water	Insoluble
4	Acetone	Partially soluble
5	Ethanol	soluble
6	chloroform	Soluble
7	Benzene	Partially Soluble

Hibiscus rosa sinesis solubility checked in Water, methanol, n-hexane, ethanol, acetone. The Hibiscus rosa sinesis soluble in ethanol, methanol, benzene. The result is given in Table No. 7

Table 7: Solubility tests of *Hibiscus Rosa Sinesis* in various solvents

Sr.No.	Solvents	Solubility behaviour
1	Ethyl acetate	Freely soluble
2	n-Hexane	Freely soluble
3	Water	soluble
4	Acetone	Partially soluble
5	Ethanol	soluble
6	Methanol	Soluble
7	Benzene	Soluble

3. Evaluation for tablets:

3.1 Pre-compression study:

3.1.1 Angle of Repose:

The angle of repose (θ) serves as a distinctive indicator of the internal friction or cohesion of particles; hence, cohesive powders will exhibit a higher value, while non-cohesive powders will demonstrate a lower angle of repose. The angle of repose of all formulations was found to be good in the range of 23.60±0.58 to 33.30±0.22 there was no much difference in flow property. Formulation F1, F2, F3, F4, F6, F7 showed angle of repose as 29.1±0.23, 32.0±0.12, 23.60±0.42, 30.96±0.34, 26.5±0.12. Formulations F2, F6, F8 showed a higher angle of repose. The lower angle of repose 23.60±0.42 was shown by formulation F3.

3.1.2 Bulk density and Tapped density:

The ratio of mass of the powder to the volume required to occupy that respective mass is represented as bulk density. A product with increased bulk density is always desired so as to reduce the volume that can be occupied. All formulations showed bulk density in the range of 0.440±0.004 to 0.510±0.003. All formulations showed tapped density in the range of 0.500±0.004 to 0.560±0.005.

3.1.3Carr's Index:

Carr's index up to 21 is considerable of acceptable flow properties. Bulk density and tapped density are simple tests that have been developed to evaluate the flowability of powder. There are important properties to calculate % compressibility of the powder. All formulations possess acceptable flow properties. Formulations F1, F2 showed carr's index 12.50±1.01, 15.56±0.74 respectively. Formulations F3, F4 showed Carr's as 10.87±0.73, 13.64±0.96 respectively, While F5, F6 showed Carr's index as 11.76±1.28, 27.91±0.76 respectively. Formulations F7, F8 showed Carr's as 14.38±0.73, 21.70±1.70 respectively.

3.1.4 Hausner's ratio:

The ratio of tapped density to bulk density is used to determine Hausner's ratio. It was related to the inter particle friction. All formulations showed acceptable flow property as it showed Hausner's ratio in the range of 1.11±0.028 to 1.28±0.025.

Table No.8: Pre-compression study

Batch	Angle of repose (◦)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	29.1	0.48	0.54	12.50	1.13
F2	32.0	0.45	0.52	15.56	1.16
F3	23.6	0.46	0.51	10.87	1.11
F4	31.2	0.44	0.5	13.64	1.14
F5	27.47	0.51	0.57	11.76	1.12
F6	30.96	0.43	0.55	27.91	1.28
F7	26.5	0.47	0.53	14.38	1.15
F8	33.3	0.49	0.56	21.70	1.17

3.2 Standardization of formulated tablets:

3.2.1Thickness:

Thickness of tablets ranged from 4.4±0.02mm to 4.7±0.02mm the thickness of the tablet is depend upon the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material as well as the force applied during compression.

3.2.2 Friability:

All the matrix system had acceptable friability as none of the tested formulae had percentage loss in tablets weight exceed 1 % is an indication of good

mechanical resistance of the tablets. Friability of formulations ranges from 0.69 to 0.87. Formulations F1, F2 showed friability 0.69, 0.79 respectively. Formulations F3, F4 showed friability 0.73, 0.79 respectively. Formulations F5, showed friability 0.76. All formulations showed % friability less than 1% this ensures that tablets could withstand to the pressure, shocks during handling transportation and shifting processes.

3.2.3 Hardness:

The formulation should aim to achieve ideal tablet hardness while avoiding the use of excessive force. Hardness of all formulations was found to be in the range of 4.2±0.02kg/cm2 for F1 to 4.0±0.02kg/cm2 for F2. Formulations F3, F7 showed hardness 4.1±0.01kg/cm2, 4.2±0.03 respectively. Formulations F4, F5 4.1±0.03, 4.0±0.03 respectively. Formulations F6, F8 showed hardness 4.0±0.9 kg/cm2, 4.1±0.02kg/cm2 respectively.

3.2.4 Weight variation test:

Weight variation test revealed that the tablets of all formulations were within the range of pharmacopeial specifications, all the formulations passes weight variation test.

Table No. 9: Standardization of formulated tablets.

Batch	%Weight variation (±5%)	Hardness (Kg/cm2)	Thickness (mm)	%Friability (NMT 1%)	Disintegration time
F1	± 2.51	4.2 ± 0.02	4.5 ± 0.02	0.69 ± 0.01	19 min 50 sec
F2	± 2.48	4.0 ± 0.02	4.6 ± 0.02	0.79 ± 0.01	18 min 15 sec
F3	± 1.99	4.1 ± 0.01	4.6 ± 0.02	0.73 ± 0.01	15 min 15 sec
F4	± 2.60	4.1 ± 0.03	4.7 ± 0.02	0.79 ± 0.01	20 min 25 sec
F5	± 2.21	4.0 ± 0.03	4.6 ± 0.02	0.76 ± 0.02	17 min 30 sec
F6	± 2.71	4.0 ± 0.9	4.5 ± 0.02	0.87±0.02	17 min 30 sec
F7	± 2.13	4.2 ± 0.03	4.4 ± 0.02	0.69 ± 0.01	15 min 15 sec
F8	±2.34	4.1 ± 0.02	4.7±0.02	0.73 ± 0.01	14 min 15 sec

3.3 Drug content:

Percentage drug content of Withania coagulant dunal is estimated in two determinations. Percentage drug content of Withania coagulant dunal were determined by HPLC method and were found to be in the range of 83.60±1.56 to 92.30±3.49 the drug content of all batches was found to be within the limits.

Percentage drug content of Hibiscus rosa sinesis is estimated in two determinations. Percentage drug content of Hibiscus rosa sinesis were determined by HPLC method and were found to be in the range of 83.90±1.56 to 89.30±3.39 the drug content of all batches was found to be within the limits.

Table No.10 Drug content of *Withania coagulans dunal* and *Hibiscus Rosa Sinesis*.

Batch	%Drug content of *Withania coagulans dunal*	%Drug content of *Hibiscus rosa sinesis*
F1	83.6	87.6
F2	84.9	86.9
F3	92.3	89.3
F4	83.9	83.9
F5	85.4	85.4
F6	86.9	86.9
F7	91.3	88.7
F8	87.3	89.3

3.4 In vitro drug release studies:

3.4.1 In vitro drug release studies of *Withania coagulans dunal*:

The polyherbal tablets of *Withania coagulans dunal* prepared by using Wet granulation method. All the formulations F1, F2 showed % DR 88.23 ±1.12, 76.12± 0.13. F3, F4 showed 93.23 ±0.18, 86.69 ±26.15 and the formulations F5, F6 showed 75.62 ±1.56, 87.23 ±1.12 and formulations F7, F8 showed 91.68 ±1.45, 84.23±21.12 and formulations The more appreciating drug release was observed with the formulations F3, F7.

Table No.11: *In vitro* Drug dissolution (cumulative drug release) Profile of *Withania coagulans dunal* (Batch F1 toF8)

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
2	12.12	8.68	8.68	8.12	8	8.26	11.25	10.17
4	26.56	24.67	12.12	18.56	15.23	15.56	28.75	17.56
6	32.1	29.13	26.67	27.1	24	24.1	35.56	24.38
8	41.23	32.57	36.23	36.88	36.1	37.23	41.23	37.23
10	49.21	40.46	47.32	49.21	46.21	49.21	53.21	49.21
12	57.13	48.36	55.27	55.13	52.13	58.46	57.13	57.13
14	64.11	54.47	64.39	69.18	57.13	62.84	64.11	66.21
16	72.24	59.46	72.24	77.24	61.24	69.75	72.24	72.24
18	81.88	67.45	81.88	81.88	69.23	81.88	85.69	81.62
20	88.23	76.12	93.23	86.69	75.62	87.23	91.68	84.23

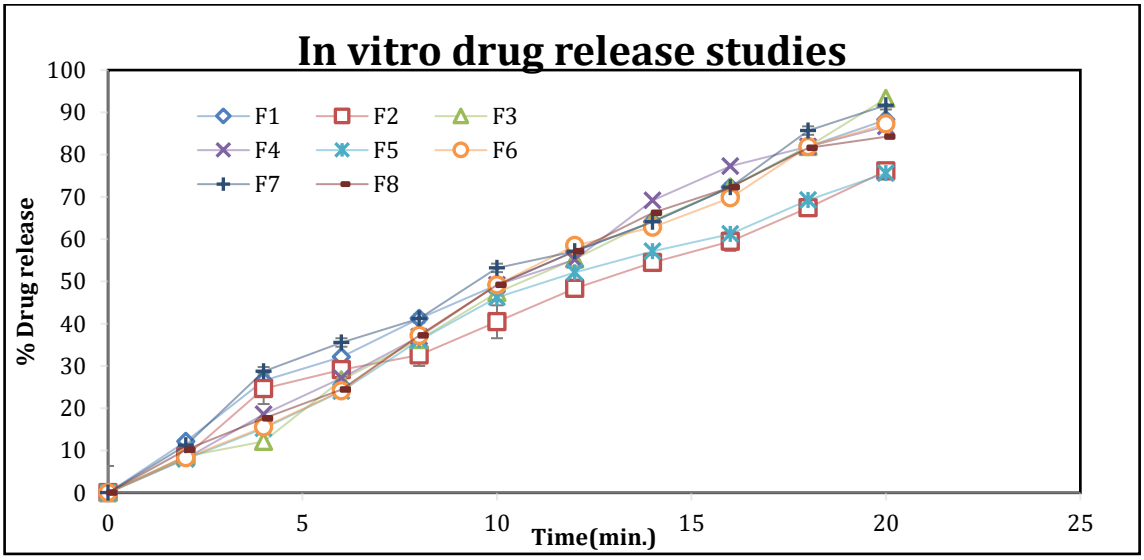

Fig 3: *In vitro* Drug dissolution (cumulative drug release) Profile of *Withania coagulans* dunal (Batches F1to F8)

3.4.2 In vitro drug release studies of *Hibiscus rosa sinesis*:

The polyherbal tablets of *Hibiscus rosa sinesis* prepared by using Wet granulation method. All the formulations F1, F2 showed % DR 76.12± 0.13, 70.23 ±2.12. F3, F4 showed 88.23 ±1.12, 75.62 ±1.56 and the formulations F5, F6 showed 69.23 ±1.12, 78.68 ±2.46 and formulations F7, F8 showed 86.69±26.15, 79.23±1.12 and formulations The more appreciating drug release was observed with the formulations F3, F7.

Table No. 12: *In vitro* Drug dissolution (cumulative drug release) Profile of *Hibiscus rosa sinesis* (Batch F1 toF8)

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
2	8.68	9.17	12.12	8	12.12	8.12	8.12	9.24
4	24.67	26.56	26.56	15.23	26.56	16.25	18.56	16.56
6	29.13	29.1	32.1	24	32.13	26.56	27.1	25.1
8	32.57	47.23	41.23	36.1	36.53	39.62	36.88	36.75
10	40.46	52.21	49.21	46.21	41.23	41.23	49.21	41.53
12	48.36	63.13	57.13	52.13	49.21	51.49	55.13	48.23
14	54.47	68.11	64.11	57.13	54.11	57.13	69.18	57.13
16	59.46	72.24	72.24	61.24	57.13	64.11	77.24	64.11
18	67.45	76.88	81.88	69.23	63.25	72.24	81.88	72.24
20	76.12	70.23	88.23	75.62	69.23	78.68	86.69	79.23

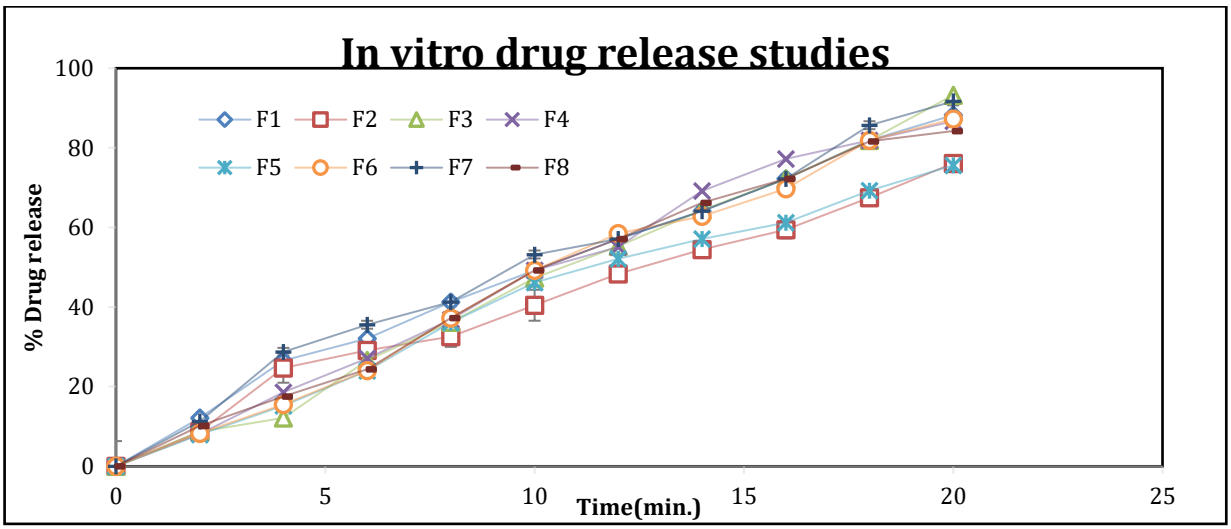

Fig 4: *In vitro* Drug dissolution (cumulative drug release) Profile of *Hibiscus rosa sinesis* (Batches F1to F8):

3.5 Kinetics treatment of Dissolution profiles:

3.5.1 Kinetics treatment of Dissolution profiles of formulations F1-F8 of *Withania coagulans dunal*:

To describe the kinetics of drug release of WCD from antidiabetic tablets, release data was analyzed according to different kinetic equations. The data were analyzed by the method of regression coefficient and regression coefficient values (r2) of all batches were shown in Table 11. After examining the regression coefficient values of all batches, it became evident that Batch F1, 2, 3, 4, 6, 7, and 8 tablets displayed nearly zero-order kinetics. Batch F-5 tablets followed Higuichi model. Results are shown in Table 11.

Table No.13: Kinetics treatment of Dissolution profiles of formulations F1-F8.

Batch	Zero order	First order	Higuchi	Korsemeyer Peppas	Best fitted
F1	0.99	0.93	0.97	0.92	Zero order
F2	0.99	0.94	0.93	0.86	Zero order
F3	0.99	0.88	0.99	0.97	Zero order
F4	0.98	0.97	0.97	0.91	Zero order
F5	0.97	0.98	0.99	0.96	Zero order
F6	0.98	0.95	0.98	0.96	Higuichi
F7	0.99	0.88	0.97	0.92	Zero order
F8	0.98	0.97	0.97	0.92	Zero order

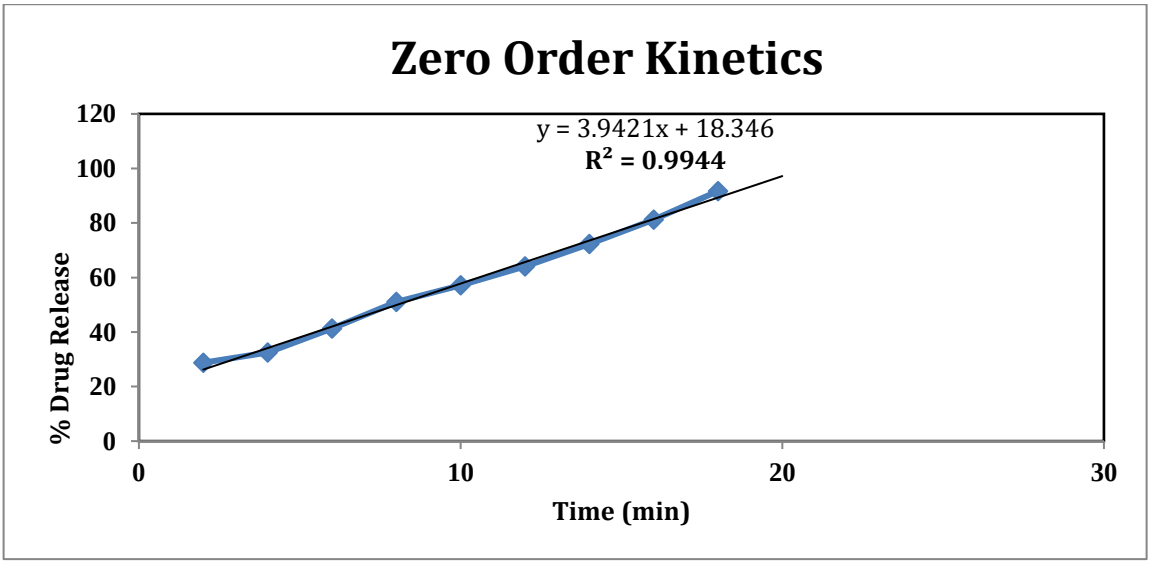

Fig 5: Zero order kinetics of *Withania coagulans dunal.*

3.5.2 Kinetics treatment of Dissolution profiles of formulations F1-F8 of *Hibiscus rosa sinesis*:
In the same way, the release kinetics of HRS from the antidiabetic tablets were examined by applying various kinetic equations to the release data. The data were analyzed by the method of regression coefficient and regression coefficient values (r2) of all batches were shown in Table 12. After examining the regression coefficient values of all batches, it became evident that Batch F1, 2, 3, 5, 6, 7, and 8 tablets displayed nearly zero-order kinetics Batch F4 tablets followed Higuichi model and F2 tablets followed first order kinetics. Results are shown in Table 12.

Table No.14: Kinetics treatment of Dissolution profiles of formulations F1-F8.

Batch	Zero order	First order	Higuichi	Korsemeyer Peppas	Best fitted
F1	0.99	0.94	0.93	0.86	Zero order
F2	0.95	0.99	0.95	0.96	First order
F3	0.99	0.93	0.92	0.95	Zero order
F4	0.97	0.98	0.99	0.96	Higuichi
F5	0.99	0.98	0.96	0.96	Zero order
F6	0.98	0.97	0.98	0.96	Zero order
F7	0.99	0.97	0.97	0.91	Zero order
F8	0.99	0.96	0.98	0.95	Zero order

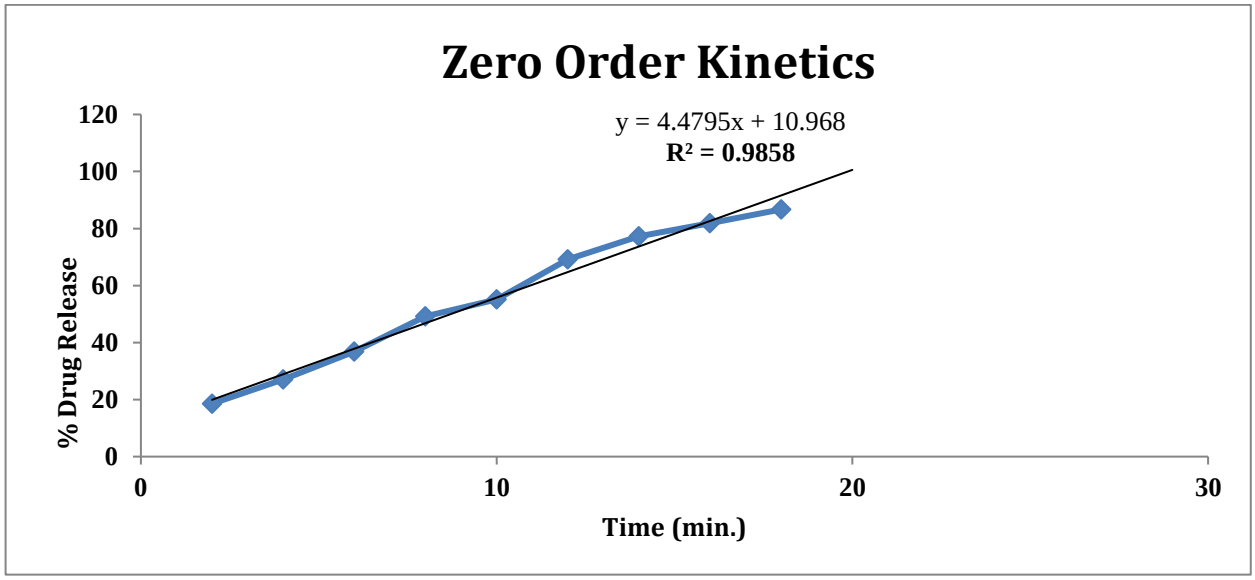

Fig: Zero order kinetics of *Hibiscus rosa sinesis.*

CONCLUSION

The aim of this study was to formulate and evaluate synergistic antidiabetic activity of *Withania coagulans dunal* and *Hibiscus rosa sinesis*. Preformulation studies on Withania coagulans dunal and Hibiscus rosa sinesis performed in accordance with the reported literature limits. The thickness and drug content of tablets were uniform and reproducible. HPLC studies indicated no chemical interaction. In vitro dissolution profile of *Withania coagulans dunal* and *Hibiscus rosa sinesis* formulation showing promising results. Dissolution studies results indicated that the *Withania coagulans dunal* and *Hibiscus rosa sinesis* release from formulated tablets was not generally similar and constant for all formulations as the concentration of *Withania coagulans dunal* was increased from 110 mg to 200 mg. These results indicate the optimized formulation. The formulation also shows significant antidiabetic activity.

FUTURE PERSPECTIVE

Future studies of stability for other dosage form applications, shelf-life determination, bioavailability and clinical investigations of the drug Withania coagulans dunal and Hibiscus rosa sinesis is possible. Further the following work can be recommended with Withania coagulans dunal and Hibiscus rosa sinesis

- Bioavailability studies (pre-clinical and clinical trials).
- *In vivo* studies.
- *In vivo-In vitro* correlation.
- Scale up studies of the optimized formulation.

REFERENCE

1. Kumar CR. Basic Pathology, Prism PVT. Limited Bangalore, 5th edition, 1992, 569-587.
2. Jun SK, Yoon YW. A new look at viruses in Type 1 diabetes, Diabetes/Metabolism Research and Reviews. 2002; 19:8-31.587.
3. Leonardo Jacob S, Pharmacology. The national medical series from Williams and Wilkins Bartiarco, Hong Kong, London, 3rd edition, 1987, 221-225.
4. Ross and Wilson. Anatomy and Pathophysiology in Health and Illness, Churchill Livingstone Elsevier, 11th edition, 2010, 227-229.
5. American Diabetes Association, Diagnosis and classification of diabetes mellitus, Diabetes Care, 2014, 1.
6. Aftab Ahmad Jan, Alamgir Khan, Causes, Complications and Management of Diabetes Mellitus, Chronicle Journal of Food and Nutrition,2017.
7. Chinmay D. Deshmukh, Diabetes Mellitus: A Review, INTERNATIONAL JOURNAL OF PURE & APPLIED BIOSCIENCE, Int. J. Pure App. Biosci. 3 (3): 224-230 (2015).
8. Muhammad Shahzad Aslam, Muhammad Syarhabil Ahmad, An Update Review on Polyherbal Formulation: A Global Perspective, Systematic Reviews in Pharmacy., 2016;7(1):35-41.
9. Matthew N. O. Sadiku, Tolulope J. Ashaolu, Traditional Indian Medicine, International Journal of Trend in Scientific Research and Development (IJTSRD) Volume: 3 | Issue: 2 | Jan-Feb 2019
10. Kaderkar Dattatray Shrikar, Tamboli Ashpak M., Review on Concept and Scope of Polyherbal Formulations. June 2020 | IJIRT | Volume 7 Issue 1 | ISSN: 2349-6002.
11. Vyas S.P and Khar R.K. Targetted and controlled Drug Delivery Novel carrier system1st Ed., CBS Publishers and distributors, New Delhi, 2002; 196-217.
12. Jain N.K., Progress in Controlled and Novel Drug Delivery Systems, 1st Ed. CBS Publishers and Distributors, New Delhi, 2004; 84-85.
13. Sanjay Thakur "Floating Drug Delivery System", Journal of Drug Delivery & Therapeutics. 2021;11(3-s):125-130.
14. Iannuccelli V., Coppi G., Bernabei M.T. and Cameroni R., Air compartment multiple unit system for prolonged gastric residence. Part I. Formulation study, Int.J.Pharm. 1998; 174: 47-54.
15. Garg, S and Sharma, S (2003), "Gastro retentive Drug Delivery System, Business Briefing", Pharmatech, 160-166
16. Chien YM. Novel Drug Delivery System, 3rd Ed. Vol. 1. New York: Marcel Dekker 1992; 139-96.
17. Patel DM, Patel MJ and Patel CN. Multi Particulate System: A Novel Approach in GastroRetentive Drug Delivery. Int J Ayurveda Pharm Res. 2011; 2(4): 96-106.