IJPSR (2019), Volume 10, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 June 2018; received in revised form, 10 December 2018; accepted, 10 February 2019; published 01 March 2019

DESIGN AND DEVELOPMENT OF ANTI-DIABETIC TABLET FORMULATION CONTAINING SPRAY DRIED EXTRACT OF MULBERRY LEAVES

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Keywords:

Diabetes Mellitus, Mulberry, Spray dryer, Alloxan monohydrate

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ABSTRACT: Diabetes is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia in diabetes is associated with long term damage, dysfunction, failure of kidney, nerves and blood vessel. Nowadays, herbal treatments available for diabetics are eroding the share of allopathic formulations. Currently, the spray drying technique has been widely used for improving processability, biopharmaceutical performance as well as modifying the physical form of various phyto-extracts. Extract of mulberry being sticky may find difficulty in its formulation to tablet dosage form. Across the world, mulberry has been used for its medicinal importance. Looking at its availability and medicinal prospects spray dried mulberry extract was prepared and which is finally assembled into a tablet dosage form. Inert excipients are used to deal with processability, amorphous form and bioavailability issues. Spray drying of the mulberry extract was carried out by using carrier maltodextrin. Results obtained shows excellent/good flowability, compressibility, and compatibility. The dissolution profile of spray dried extract tablet shows a better result. In animal studies, the spray dried extract formulation group had a significant decrease in blood glucose level when compared to the powder formulation group on the 28th day. Successful completion of this work will revolutionize the herbal market of anti-diabetic formulations available till date. The cost-effective formulation will be available to the patients.

INTRODUCTION Diabetes mellitus (DM) is a type of metabolic disorders consisting of chronic hyperglycemic condition due to abnormal insulin secretion, insulin action or both [1]. Diabetes has been an important public health problem. Both the number of cases and the prevalence of diabetes have been steadily increased over the past few decades.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.10(3).1501-09

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(3).1501-09

In 2015, 489 million were suffering from diabetes. Globally, it has been calculated that 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population. This reflects an increase in associated risk factors such as being overweight or obese [9].

Type 1 Insulin Dependent Diabetes Mellitus (IDDM): Worldwide approximately 20 million people are affected by type 1 diabetes. The occurrence of type 1 diabetes is rising [2]. Type 1 diabetes occurs most frequently in children and young adults, although it can occur at any age.

Type 2 Non-insulin Dependent Diabetes Mellitus (NIDDM): It is a metabolic disorder caused by the deficiency of insulin hormone secreted by the pancreatic beta cells. Type 2 diabetes is much more common and accounts for 90-95% of all diabetes [3]. Type 2 diabetes primarily affects adults; however recently type 2 has begun developing in children. There is a strong correlation between type 2 diabetes, physical inactivity, and obesity.

Patients are required to control their blood glucose with medications or by adhering to an exercise program and a dietary plan. Insulin therapy by injection is given to those with type 1 DM and also to some patients with type 2 DM when oral hypoglycaemic drugs fail to lower blood glucose. Due to the modernization of lifestyle, non-insulin dependent diabetes mellitus is becoming a major health problem in developing countries.

In herbal medicine, a various number of conditions are treated by using fruits, leaves, flowers, stems, bark, and roots. As per ancient literature, more than 800 plants have been reported to have antidiabetic activity. About 1200 species of organisms have been used ethnopharmacologically or experimentally to treat symptoms of diabetes mellitus. Ayurvedic antidiabetic herbs improve digestive power, increase one of the Rasas (gastric secretions); being Laghu, get easily digested in the body; and being Ruksha, decrease the output of overall body fluids, *e.g*. urine, sweat, *etc*. [7]

Mulberry (*Morus alba* L.): Mulberry is one of the herbs which is used in medicines from centuries ago due to its active chemical components and pharmacological functions [4]. Mulberry belongs to the family Moraceae. The genus *Morus* contains a variety of species some of them includes *Morus alba*, *Morus nigra*, *Morus rubra*, *Morus indica*, *Morus australis*, *Morus cathayana*, *etc*. *Morus alba* Linn. which is also known as white mulberry [5].

These plants show the beneficial effect in lowering serum glucose and blood cholesterol level; these properties are due to the presence of many active components such as flavonoids, alkaloids, polyphenols, terpenoids in the plant. Different parts of the plant show antioxidative, hypolipidemic, antihyperglycemic, anticancer, anti-inflammatory effect [2, 7].

Spray Drying of Extract: For the herbal processing industries, to obtained standardized dried natural extracts development of new technologies is an important subject. The improvement of the dried extract over conventional one are higher concentration, the stability of active components and lower storage costs. The spray drying method is largely used in the pharmaceutical industry in the production of the bulk (raw) drug and recipients in the microencapsulation process. This method transforms liquid feed into a dry powder in a one-step continuous particle processing operation and can be applied to a wide variety of materials [6].

In spray drying application, different drying aids and carrier material are used to obtain good product recovery and stability. Nowadays maltodextrin using as a drying carrier is a popular method. Maltodextrins have many functionalities including usage as wall material, dispersing aid, carrier and bulking agent. Carriers are majorly used in the materials that are difficult to dry such as fruit juices, flavorings, and to reduce stickiness, thereby improving the product stability. The extract obtained would be converted into the amorphous form by spray drying and solubility will increase which in turn enhance the bioavailability.

METHODS AND MATERIALS: Mulberry (*Morus alba* Linn.) leaves were collected from the Botany Department (Shivaji, University, Kolhapur, Maharashtra), Plant authentication voucher specimen number (AKP-01). Leaves were dried under shade by spreading in thin layer aluminum trays for 10-15 days. Leaves were turned upside down repeatedly during the process of drying to achieve complete drying. The dried leaves of *Morus alba* Linn. were powdered using an electric grinder and sieved through a 40 mesh screen. Mulberry leaves powder preserved properly in an airtight container.

25 g powder of *Morus alba* Linn. leaves was used for extraction. 70% of ethanol was selected as an extracting solvent. Extraction was carried out at slightly above the boiling point of the solvent. The solvent was collected and filtered through Whatmann filter paper to remove traces of powder and solvent recovered on evaporating bath. After completion of the process, the extract was dried on

a water bath for 3 h at 45 ºC. The extract was kept in the deep freezer until the use. Avicel pH 102, sodium starch glycolate, povidone k-30, magnessium strearate, croscarmellose sodium colloidal silicon dioxide, maltodextrine.

Drying of Extract by Spray Drying Method: A laboratory-scale Mini Spray Dryer Model LU-122 Advance, Labultima was employed for mulberry leaves spray-dried extract production. A one-fluid nozzle with a cap orifice diameter of 0.5 mm was used and the air atomizing pressure. Spray drying was carried out at the operating condition to obtain a mulberry leaves extract powder with appropriate flow properties and stability attributes. The best set of operating conditions were: drying inlet temperature 60 ºC, feed volumetric flow rate 10% (expressed as % of the maximum pump rate, equal to 10 ml/min), air outlet temperature 55º, aspiration 60. The mulberry leaves spray-dried extract was obtained by spray-drying a dispersion of the fluid plant extract and maltodextrin. The proportion of extract: maltodextrin was 1:0.5. This dispersion was mixed for 10 min before the atomization, and during the spray drying process, magnetic stirrer bar rotating at 100 rpm was used to keep the mixture homogenized.

TABLE 1: FORMULATION TABLE FOR ALL FOUR BATCHES OF SPRAY DRIED EXTRACT FORMULATION

Ingredient (mg)	Tablet (650 mg)			
	B1	B2	B3	B4
Herbal leaves powder	500	500	500	500
Avicel PH 102	102.75	117.5	89	98
Povidone K 30	19.5	6.5	19.5	19.5
Sodium starch glycolate	-	-	22.75	19.5
Croscarmellose sodium	19.5	13	-	-
Colloidal silicon dioxide	3.25	6.5	13	19.5
Magnesium stearate	6.5	6.5	6.5	6.5

Preparation of Tablet Containing Granules of Powder: Initially powder, avicel pH 102, sodium starch glycolate, croscarmellose sodium, colloidal silicon dioxide were mixed then solution of povidone K-30 added into mixture until damp mass occurred, sieved through an 18-mesh sieve to produce granules. The granules were dried in a hot air oven at 50 ºC for 30 min. The dried granules were sieved all over again a 20-mesh sieve, and magnesium stearate was added and mixed. Then, the granules were compressed into tablets by using Rimek Minipress-I. The granules were evaluated by preformulation studies and post-compression study.

Preformulation Study:

Bulk Density: Apparent bulk density was determined by pouring a weighed quantity of blend into the graduated cylinder the bulk volume, and weight was determined:

LBD = Weight of the powder/volume of the packing

Tapped Density: It was determined by placing a graduated cylinder, containing a known mass of drug excipient blend. The cylinder was tapped for a fixed time. The minimum volume occupied by powder blend after a fixed number of tapping in the cylinder and weight of the blend was measured:

TBD = Weight of the powder / Vol. of the tapped packing

The angle of Repose: It was determined by using the funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap or head of blend. The drug excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured, and the angle of repose was calculated:

$$\tan \theta = h / r$$

Where the h= height of powder cone formed, the r = radius of the powder cone formed.

Angle of Repose θ in degree	Flow
< 25	Excellent
25-30	Good
30-40	Passable
>40	Poor

Compressibility Index: Carr's compressibility index determined the Compressibility index of the blends.

Compressibility index (%) = (TBD-LBD) × 100 / TBD

Compressibility index (%)	Flow
5-12	Excellent
12-16	Good
18-21	Fair
23-35	Poor
33-38	Very poor
>40	Very very poor

Hausner's Ratio: It is determined by using the following formula:

Hausner's ratio= TBD / LBD

Hausner's ratio	Flow
1.25	Excellent
1.5>	Good
1.5<	Poor

Kawakita: The powder blend was weighed accurately and transferred into a graduated cylinder. The number of tapping as 2, 4, 6….. 12 was taken, and the volume reduction against it was noted. The noted value of individual tapping was put in software and values of 'a' and 'b' were determined.

Heckel's: The granules were kept for tableting, tablets of different pressure 0.5, 1, 1.5, 1.7, 2 were selected. Then the individual tablets were subjected to weighing. They are further evaluated for thickness and diameter by using Vernier caliper. The hardness by using Monsanto hardness tester. The value obtained above were put in Heckel software, and Myp (compressibility) was determined.

Leuenberger:

Compatibility (σ t max): Compressibility is defined as the ability of a powder to decrease in volume under pressure, and compatibility as the ability of the powdered material to be compressed into a tablet of specified strength.

Compression Susceptibility (γ): The term 'compressibility' was defined as the ability of a powder to decrease in volume under pressure.

Evaluation of Tablets:

Hardness and Thickness: The hardness of the tablets was tested by using calibrated hardness tester (Monsanto). The thicknesses of the tablets were evaluated by Vernier calipers.

Weight Variation: 20 tablets were selected randomly, and the average weight was determined. Then the individual tablet was weighed, and its weight was compared with average weight. Not more than two of individual weight should deviate from the average weight.

Dosage form	Average weight	% Deviation
Uncoated tablets	Less than 80 mg	10
	80 mg to 250 mg	7.5
	More than 250 mg	5

Friability Test: The friability test for tablets was carried out to determine weight loss due to friability by using Roche Friabilator. The friability is expressed in percentage (%). Ten tablets were initially weighed and transferred into friabilator. The friabilator was operated at 25 rpm for 4 min or run up to 100 revolutions. The tablets were weighed again. % Friability of tablets less than 1% is considered acceptable.

Disintegration: The *in-vitro* disintegration time was determined by the disintegration test apparatus. Disintegration test was performed using USP Disintegration test apparatus, (model ED-2L, Electrolab, Mumbai, India) using 0.1 N HCl as a disintegrating media at 37 ± 2 ºC. Six tablets were placed in each of the six tubes of the apparatus, and one disc was added to each tube.

Drug Content: 20 tablets were weighed and average weight and powder. The quantity of powder equivalent to 10 mg of mulberry extract was weighed and dissolved in 20 ml portions of distilled water and filtered through Whatmann 41 filter paper into 100 ml volumetric flask and volume adjusted with distilled water, 1 ml of above filtrate was diluted up to 10 ml with distilled water. The concentration of drug was determined by measuring absorbance at 275 nm by UV spectrophotometer.

***In-vitro* Dissolution Study:** The 900 ml of 0.1N HCl was used as dissolution medium for 2 h and also pH of the medium was adjusted to 6.8 for 2 h at 37.5 ± 0.5 ºC. The paddles were rotated at a constant speed of 100 rpm. Each time 5 ml of samples were withdrawn at the interval of 15 min for 2 h until the end of dissolution study. The same amount of fresh 0.1 N HCl and phosphate buffer, pH 6.8 was used to replace the amount withdrawn for respective dissolution media. The withdrawn samples were analyzed by UV- spectrophotometer at the respective wavelength.

Animals: Healthy adult Albino rats (180-250 g) were obtained from the animal house of Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India for the study. Rats were housed in polypropylene cages and fed on standard pellet diet and water, and the room maintained under controlled condition (12 h light-dark cycle at 22 ± 2°C). Animals were allowed to acclimatize for 7 days before experiments being carried out.

All animals were taken care of under ethical consideration as per the guidelines of CPCSEA. Institutional ethics committee permission was obtained as per CPCSEA guidelines (Approval no: BVCPK/CPCSEA/IAEC/01/09/2016-2017) for carrying out the study on animals. Animals were used for anti-diabetic activity in alloxan-induced diabetic rats.

Procedure: Hyperglycemia will be induced in the experimental rats by single intraperitoneal (i.p.) injection of 150 mg/ kg body weight of alloxan monohydrate in saline solution. After 7 days, rats with moderate diabetes, having hyperglycemia (plasma blood glucose level > 130 mg/dL) can be used for the experiment. The four groups of three rats each were grouped as follows:

Group I: The Saline solution to diabetes-induced rat.
Group II: Ethanolic spray dried extract granules suspension to the diabetes-induced rats.
Group III: Mulberry leaves powder granules suspension to diabetes induced rats.
Group IV: Standard miglitol solution to diabetes-induced rats.

Blood samples were drawn on days 7, 14, 21 and 28 from retro-orbital plexus of rats under ether anesthesia using capillary glass tube. Then blood glucose level will be estimated by Glucometer (Accu-Chek).

RESULTS:

FTIR Spectra of Mulberry Leaves Extract Show Presence of Peaks at Various Wave Numbers: The spectra of extract shows the peaks for N-H stretch, = CH_2, C-O stretch and N=O stretch, C-H Deformation, etc. at wave number 3334 cm^{-1}, 2923 cm^{-1}, 2853 cm^{-1}, 1620 cm^{-1}, 1376 cm^{-1} respectively.

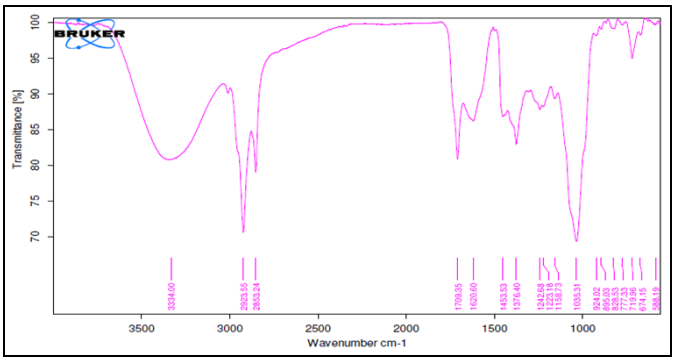

FIG. 1: FTIR SPECTRA OF MULBERRY LEAVES EXTRACT

The appearance of the above peaks in **Fig. 1**, confirms the presence of alkaloid like DNJ and flavonoids like rutin, quercitin, *etc*. The observed frequencies for the presence of different groups in extract have been given in **Fig. 1** and **Table 2**.

TABLE 2: FTIR SPECTRA ANALYSIS

S. no.	Observed frequency (cm^{-1})	Functional group
1	3334	N-H stretch
2	2923	=CH_2
3	2853.24	=CH_2
4	1709	C=O stretch
5	1620	C-O stretch
6	1453	N-O stretch
7	1376	N=O stretch
8	1223	N=O stretch
9	1128	C-O stretch
10	1035	C-O stretch
11	924.02	C-H Deformation
12	777	C-H(Out of plan)

Evaluation of Solid Dosage Forms Containing Spray Dried Extract of Mulberry Leaves:

Pre-compression Evaluation of Spray Dried Extract of Mulberry Leaves Tablet: The derivated powder property values such as bulk density and tapped density was found to be 0.345 ± 0.020 to 0.436 ± 0.040 gm/ml and 0.427 ± 0.020 to 0.427 ± 0.020 gm/ml respectively. From the density Angle of repose was found to be 32 ± 0.57 to 34 ± 0.790, % cars index was found to be 8.66 ± 0.95 and 8.66 ± 0.95% and Hausner's ratio was found to be below 1.12 indicating in well acceptable limits. Hence indicates good flowability.

Kawakita Plot, Heckel plot, and Leuenberger Analysis: Kawakita plot, gives two constants, constant 'a' and 'b.' The 'a' value indicates a total reduction in the volume of spray dried extract, and 'b' value is inversely proportional to yield strength of spray dried extract. The Heckel plot analyzes the relation between pressure and relative density and thus gives an idea about mean yield pressure (MyP) which eventually demonstrates the consolidation potential of spray dried extract. Leuenberger equation has been used to study the compression susceptibility (γ) and compressibility (σ t max). From **Table 3** it was observed that values of 'a' is lower as compared to values of 'b,' which indicates good compressibility of all four batches. And the MyP of four batches were found to be 0.6812 to 0.7637 which indicates good compressibility. The compatibility data obtained from all the batches

were found to be 4.15 to 9.929 indicating good compressibility. The compression susceptibility of all batches was found to be 3.67 to 1.889 indicating good compression.

TABLE 3: FLOW PROPERTIES OF GRANULES OF DIFFERENT FORMULATION BATCHES

Batch code	Bulk density (gm/mL)	Tapped density (gm/mL)	Angle of repose (θ)	Compressibility index (%)	Hausner's ratio
B1	0.390 ± 0.008	0.517 ± 0.010	33 ± 0.317	8.66 ± 0.95	1.02 ± 0.01
B2	0.436 ± 0.040	0.630 ± 0.028	34 ± 0.500	11.67 ± 0.57	1.3 ± 0.04
B3	0.345 ± 0.020	0.427 ± 0.020	32 ± 0.577	10.39 ± 0.84	1.12 ± 0.01
B4	0.352 ± 0.033	0.430 ± 0.034	34 ± 0.790	8.66 ± 0.95	1.08 ± 0.01

TABLE 4: KAWAKITA HECKEL PLOT AND LEUENBERGER ANALYSIS

Batch code	Kawakita Constant		Heckel	Leuenberger	
	Compactibility (a)	Cohesiveness (b)	MyP	Compactibility (σ t max)	Compression susceptibility (γ)
B1	0.3924	0.3928	0.7537	4.15	3.67
B2	0.5084	0.5267	0.7637	9.234	1.879
B3	0.2567	0.3333	0.6812	9.929	1.876
B4	0.2737	0.3593	0.7508	9.442	1.761

Post-Compression Evaluation of Spray Dried Extract of Mulberry Leaves Tablet:

Hardness, Thickness, and Weight Variation: Hardness of the tablets was found to be 4.7 ± 0.60 kg/cm^2 to 5.36 ± 0.56 kg/cm^2. The thickness was found to be between 3.44 mm to 3.68 mm. The weight variation of the tablets ranged between 648 ± 0.57% and 653 ± 1.15%. The obtained results indicated that the tablets were passed the friability test. The disintegration time was found to be below 15 min. The drug content of all the tablets was found to be more than 95%.

TABLE 5: HARDNESS, THICKNESS AND WEIGHT VARIATION OF DIFFERENT TABLET BATCHES

Batch Code	Hardness (kg/cm^2)	Thickness (mm)	Weight variation (mg)	Friability (%)	Disintegration time (min)	Drug content (%)
B1	4.85 ± 0.78	3.68 ± 0.09	648 ± 0.57	0.510 ± 0.027	8	96.18 ± 0.28
B2	4.7 ± 0.60	3.45 ± 0.02	650 ± 0.57	0.551 ± 0.035	9	96.19 ± 0.31
B3	4.83 ± 0.76	3.44 ± 0.01	653 ± 1.15	0.620 ± 0.026	10	98.17 ± 0.18
B4	5.36 ± 0.56	3.44 ± 0.01	649 ± 1.52	0.605 ± 0.042	12	95.65 ± 0.12

***In-vitro* Dissolution Study of Spray Dried Extract of Mulberry Leaves Formulation:** *In-vitro* dissolution study of spray dried extract tablets showed that drug was released in 0.1 N HCl as well as in phosphate buffer pH 6.8 within 0 to 120 min. time interval. From the dissolution study, it has been observed that drug release was more in 0.1N HCl than phosphate buffer pH 6.8.

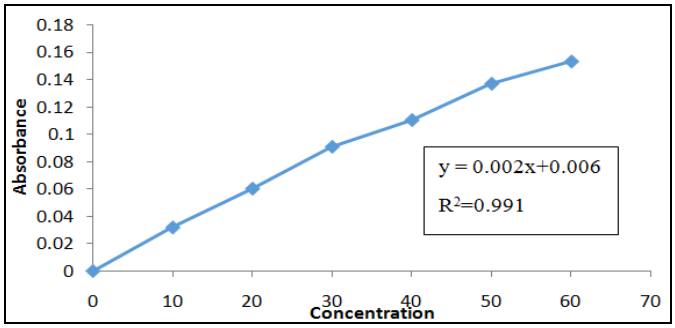

FIG. 2: CALIBRATION CURVE OF SPRAY DRIED EXTRACT IN 0.1N HCl

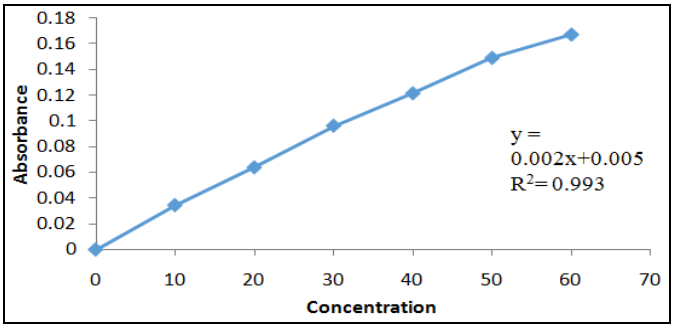

FIG. 3: CALIBRATION CURVE OF SPRAY DRIED EXTRACT IN PHOSPHATE BUFFER pH 6.8

TABLE 6: CALIBRATION CURVE PARAMETERS OF MULBERRY LEAVES SPRAY DRIED EXTRACT

S. no.	Parameters	0.1 N HCl	Phosphate buffer pH of 6.8
1	Slope	0.002	0.002
2	Intercept	0.006	0.005
3	R^2	0.991	0.993
4	λ_{max} (nm)	267	267

TABLE 7: PERCENTAGE DRUG RELEASE OF DIFFERENT BATCHES OF SPRAY DRIED EXTRACT TABLET IN 0.1 N HCl

Time (min)	% Drug release			
	B1	B2	B3	B4
5	28.32 ± 0.28	28.54 ± 0.85	23.05 ± 0.75	20.99 ± 0.55
15	55.11 ± 0.47	53.85 ± 0.59	44.36 ± 0.82	42.51 ± 0.63
30	57.75 ± 0.56	57.58 ± 0.74	49.06 ± 0.39	46.69 ± 0.85
45	58.53 ± 0.14	58.95 ± 0.61	51.76 ± 0.57	49.66 ± 0.62
60	58.98 ± 0.39	60.26 ± 0.48	53.55 ± 0.65	50.56 ± 0.44
75	59.61 ± 0.31	61.40 ± 0.71	55.32 ± 0.44	52.30 ± 0.53
90	61.06 ± 0.19	63.13 ± 0.52	56.54 ± 0.57	54.41 ± 0.86
105	61.21 ± 0.27	64.03 ± 0.54	58.24 ± 0.32	58.14 ± 0.65
120	65.09 ± 0.85	64.80 ± 0.69	62.11 ± 0.16	60.53 ± 0.29

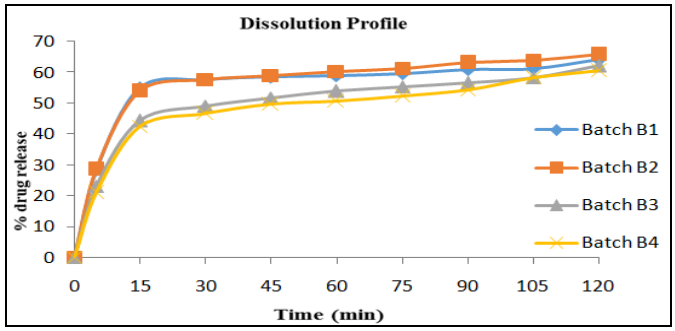

FIG. 4: PLOT OF % DRUG RELEASE *VS.* TIME (MIN) FOR DIFFERENT BATCHES OF SPRAY DRIED EXTRACT TABLETS

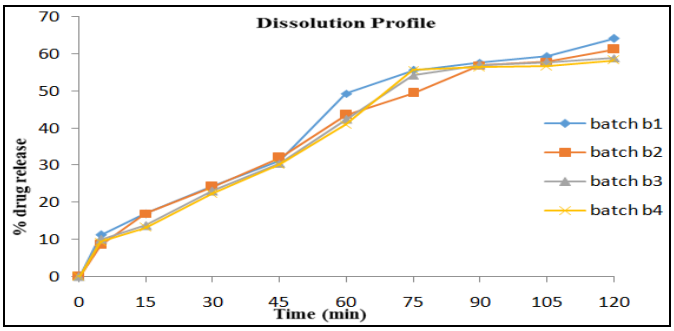

FIG. 5: PLOT OF % DRUG RELEASE *VS.* TIME (MIN) FOR DIFFERENT BATCHES OF SPRAY DRIED EXTRACT TABLETS

TABLE 8: PERCENTAGE DRUG RELEASE OF DIFFERENT BATCHES OF SPRAY DRIED EXTRACT TABLET IN PHOSPHATE BUFFER pH 6.8

Time (min)	% Drug release			
	B1	B2	B3	B4
5	11.30 ± 0.59	8.63 ± 0.85	10.03 ± 0.58	9.48 ± 0.54
15	17.01 ± 0.61	17.04 ± 0.64	13.81 ± 0.31	13.26 ± 0.58
30	24.38 ± 0.38	24.21 ± 0.94	23.09 ± 0.54	22.35 ± 0.33
45	31.21±0.85	32.12 ± 0.56	30.49 ± 0.49	30.19 ± 0.64
60	49.35 ± 0.39	43.60 ± 0.76	42.27 ± 0.21	41.02 ± 0.76
75	55.55 ± 0.48	49.42 ± 0.49	54.21 ± 0.67	55.71 ± 0.49
90	57.66 ± 072	56.92 ± 0.66	56.92 ± 0.59	56.42 ± 0.53
105	59.29 ± 0.68	57.89 ± 0.64	57.79 ± 0.34	56.64 ± 0.53
120	64.06 ± 0.55	61.16 ± 0.57	58.87 ± 0.48	58.24 ± 0.67

The **Fig. 4** represents % drug release of all four batches of spray dried extract tablets in 0.1 N HCl was found to be 65.09%, 64.80%, 62.11%, and 60.53%. The batch B1 showed highest drug release as compared to other batches. Hence, batch B1 was selected as an optimized batch.

The **Fig. 5** represents % drug release of all four batches of powder tablets in phosphate buffer pH 6.8 it was found to be 64.06%, 61.16%, 58.87%, and 58.24%. The batch B1 showed the higher release as compared to other batches and this batch was optimized.

TABLE 9: PERCENTAGE DRUG RELEASE OF OPTIMIZED BATCH BEFORE AND AFTER STABILITY

Time (min)	% drug release in 0.1 N HCl		% drug release in phosphate buffer pH 6.8	
	B1	B1 AS	B1	B1 AS
5	28.32 ± 0.28	26.31 ± 0.51	11.30 ± 0.59	9.96 ± 0.61
15	55.11 ± 0.47	53.45 ± 0.63	17.01 ± 0.61	16.45 ± 0.54
30	57.75 ± 0.56	56.51 ± 0.25	24.38 ± 0.38	22.02 ± 0.25
45	58.53 ± 0.14	57.61 ± 0.41	31.21 ± 0.85	29.84 ± 0.84
60	58.98 ± 0.39	57.92 ± 0.36	49.35 ± 0.39	47.2 ± 0.24
75	59.61 ± 0.31	58.32 ± 0.82	55.55 ± 0.48	53.85 ± 0.16
90	61.06 ± 0.19	59.36 ± 0.64	57.66 ± 072	53.57 ± 0.38
105	61.21 ± 0.27	50.61 ± 0.95	59.29 ± 0.68	57.37 ± 0.42
120	65.09 ± 0.85	63.19 ± 0.12	64.06 ± 0.55	62.14 ± 0.65

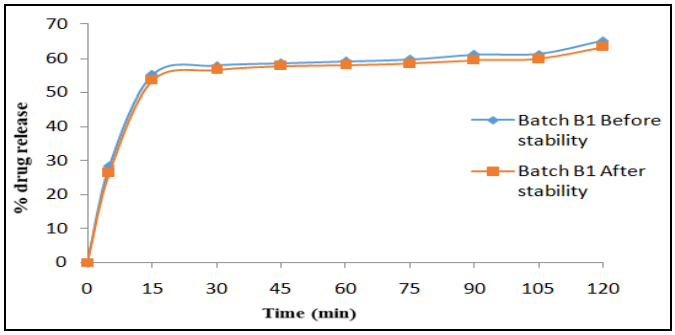

FIG. 6: PLOT OF % DRUG RELEASE *VS.* TIME (MIN) IN 0.1 N HCL FOR OPTIMIZED BATCH BEFORE AND AFTER STABILITY STUDY

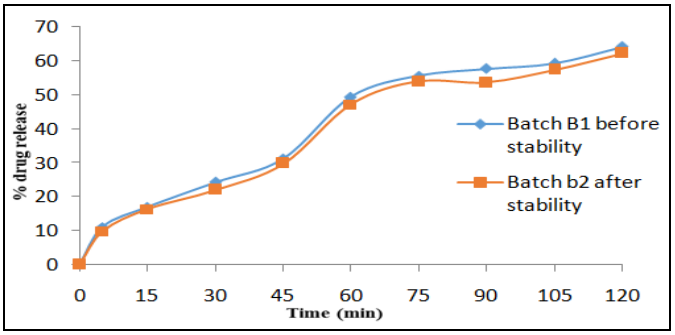

FIG. 7: PLOT OF % DRUG RELEASE *VS.* TIME (MIN) IN PHOSPHATE BUFFER PH 6.8 FOR OPTIMIZED BATCH BEFORE AND AFTER STABILITY STUDY

Stability Study of Optimized Batch of Extract Formulation: As compared to drug release of the optimized product at zero days with the product after stability showed no significant reduction in drug release. (B1 AS) Shows % drug release of 63.19% in 0.1N HCl and 62.14% respectively in phosphate buffer pH 6.8 at the end of 2 h, while tablet at zero-day shows 65.09% in 0.1N HCl and 64.06% in phosphate buffer pH 6.8 at the end of 2 h. So there is no major change seen in before and after stability. Hence, it indicates that spray-dried formulation is stable without causing any incompatibility.

Pharmacological Screening:

Effect of *Morus alba* L. on Blood Glucose Level in Diabetic and Non-diabetic Rats: Animals treated with alloxan (Group I, II, III and IV) (150 mg/kg intraperitoneally) a significant increase in blood glucose levels was observed on 7 days. Group-IV treated with the standard drug (miglitol-0.5 mg/kg i.p) showed a significant decrease in blood glucose level on 14, 21 and 28 days when compared to diabetic control group (G-I).

On administration of extract and powder formulation in groups (G-II, III), the blood glucose levels were decreased on day 14, 21 and 28 when compared to the control group G-I. The extract formulation group (G-II) had a significant decrease in blood glucose level when compared to the powder formulation group (G-III) on the 28th day.

These observations indicate the potential of *Morus alba* L. formulations in diabetic rats. Thus, formulations reduced blood glucose level and brought the glucose metabolism towards a normal level.

TABLE 10: EFFECT OF *MORUS ALBA* L. FORMULATION ON BLOOD GLUCOSE LEVELS IN DIABETIC RATS

Group	Treatment	Blood glucose level (mg/dL)				
		Day 0	Day 7	Day 14	Day 21	Day 28
I	Control	91.5 ± 1.70	355.5 ± 2.42	356 ± 7.60	356 ± 4.77	394.5 ± 2.47
II	Test 1	95.33 ± 1.14	407.66 ± 4.02	316.33 ± 3.29	309.66 ± 3.73	266.33 ± 4.4
III	Test 2	92 ± 0.33	361.66 ± 4.33	383.33 ± 4.83	330 ± 4.48	353 ± 1.13
IV	Standard	92.66 ± 3.00	267.33 ± 1.76	127.33 ± 2.34	94.33 ± 1.17	97.66 ± 4.11

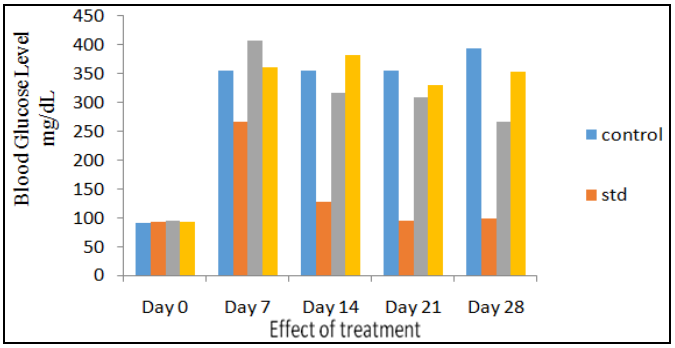

FIG. 8: EFFECT OF SPRAY DRIED EXTRACT TABLET AND POWDER TABLET FORMULATION ON BLOOD GLUCOSE LEVELS IN DIABETIC RATS

CONCLUSION: The safe and effective dose of ethanolic spray dried extract has been successfully formulated into tablet dosage form which exhibited an excellent anti-diabetic activity. Thus, the present plant holds a great future for its use as an anti-diabetic drug, alone or in the formulations thereof. Further, the work can be taken ahead for clinical trials, to check the efficacy of anti-diabetic tablets of *Morus alba* L.

ACKNOWLEDGEMENT: Authors are thankful to, Dr. N. R. Jadhav, Bharati Vidyapeeth College of

Pharmacy Kolhapur, for encouragement and support.

CONFLICT OF INTEREST: The authors declare that they have no conflict of interests.

REFERENCES:

1. Ozougwu J and Unakalamba C: The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. J of Physiology and Pathophysiology 2013; 4(4): 46-57.
2. Loghamni E: Diabetes mellitus: type 1 and type 2. Guidelines for Adolescent Nutrition 2005; 167-182.
3. Monan V and Sandeep S: Epidemiology of type 2 diabetes: Indian scenario. Indian Journal of Medical Research 2007; 125: 217-230.
4. Bajpai S: History and active pharmacokinetic principles of mulberry: a review. IOSR Journal of Pharmacy 2012; 2(4): 13-16.
5. Kohei K: Pathophysiology of type 2 diabetes and its treatment policy. Journal of the Japan Medical Association 2010; 53(1): 41-46.
6. Acosta-Esquijarosa J: Spray drying of aqueous extract of *Mangifera indica* L. (Vimang): Scale up for the process. World Applied Sciences Journal 2009; 6 (3): 408-412,
7. Marles R and Farnsworth N: Antidiabetic plants and their active constituents. Phytomedicine 1995; 2(2): 137-189.
8. Gallo L: Spray-dried *Cascara sagarada* extract for direct compression: Tablet formulation and a simple HPLC Method for Tablet Performance Evaluation. International Journal of Research in Pharmaceuticals and Biomedical Science 2013; 4(4): 1360-1370.
9. Joshi S and Das A: Current status of diabetes in India and the need for novel therapeutic agents. JAPI 2010; 58: 7-9.

How to cite this article:
Pujari AK and Jadhav NR: Design and development of anti-diabetic tablet formulation containing spray dried extract of mulberry leaves. Int J Pharm Sci & Res 2019; 10(3): 1501-09. doi: 10.13040/IJPSR.0975-8232.10(3).1501-09.