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Design, Development and Characterization of Poly Herbal Antidiabetic Tablet Glucomap

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ABSTRACT

Plants are very useful to mankind. Many of them are used exclusively for medicinal purposes. According to the World Health Organization (WHO), "a medicinal plant is a plant which, in one or more of its organs, contains substances that can be used for therapeutic purposes, or which are precursors for chemo-pharmaceutical semi-synthesis." Such plants are in great demand by pharmaceutical companies for their active ingredients. The present study deals with the in-house formulation of herbal antidiabetic tablet Glucomap. Various evaluation parameters of tablets were evaluated and were compared with standard drug glucomap.

Keywords: Herbal antidiabetic tablet, Glucomap, In-house formulation.

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INTRODUCTION

Diabetes mellitus is one of the most common disorders affecting almost 6% of the world population and the dynamics of the diabetes are changing rapidly in low- to middle-income countries.[1] According to International Diabetes Federation's (IDF) estimates, 80% of the world diabetic population will be from low and middle income countries in 2030. As per IDF 2011 report, China, India, and the United States of America have a diabetic population of 90.0, 61.3, and 23.7 million, which may be increased up to 129.7, 101.2, and 29.3 million, respectively, in 2030.[2]Globally, diabetes is one of the six major causes of death and also causing various systemic complications. Diabetes mellitus is treated by hormone therapy (insulin) or by administering glucose-lowering agents such as alpha-glucosidase inhibitors, sulfonylureas, biguanides, and thiazolidinediones. Development of an adverse event is one of the complications in the treatment of any systemic disorder; hence, many of the research institutes and pharmaceutical companies are involved in drug development to find the molecules with good therapeutic potential and less adverse events.[3]In the USA, 10-25% of patients experience an adverse drug reaction and these adverse drug reactions are responsible for 3.4-7.0% of hospital admissions[4]. In traditional systems of medicine, many plants have been documented to be useful for the treatment of various systemic disorders. Many of the traditional/indigenous systems of medicine are effective than the modern system of medicine, but they suffer from lack of complete standardization which is one of the important challenges faced by the traditional system of medicine. The concept of polyhedral formulation is well documented in the ancient literature. Compared to the single herb, the polyherbal formulation has better and extended therapeutic potential. Hence, the present study was planned to formulate and standardize a polyherbal formulation using a plant having known antidiabetic activity.

MATERIALS AND METHOD

Selection, Collection and Authentication of Plant Material

The herbs viz., *Enicostamalittorale* Blume. (whole plant), *Phyllanthusniruri* Linn. (bhooamala), *Eugenia jamboloma* Linn.(seeds), *Eugenia jamboloma*Linn.(leaves), *Azadirachtaindica*A. Juss. (leaves), *Terminaliaarjuna*(bark), *Aeglemarmelos* L. Correa (leaves), *Momordicacharantia*Linn. (fruits) were collected in the months Jan 2014 to August 2014 from the in and around local areas of Indore District of M.P. and identified & authenticated by Dr. S.N. Dwivedi, Professor & Head Dept. of Botany, Janata PG College, APS University, Rewa, M.P., and were deposited in Laboratory, Voucher specimen No. JC/SS/01 to 08were assigned.

Formulation of polyherbal formulation (PHF)

Herbal tablets were prepared separately by direct compression process using different proportions of drugs. The composition of various formulations was given in Table 1. All the ingredients were passed through mesh no. 100. The micromeritic properties were determined for all the mixtures. The powder mixtures possess good flow properties and good packing ability. Thus, the mixtures were directly compressible. Tablets were compressed each of 500 mg weight on a 10-station Mini Press-I rotary tablet compression machine fitted with 6-mm flat-shaped punches. No manufacturing defects were observed in tablets like capping, lamination and chipping.[5]

Table1: Formulation of poly herbal anti-diabetic tablets

S/No.	Ingredients	Quantity
1.	Enicostamalittorale	33.33
2.	Phyllanthusniruri	33.33
3.	Eugenia jamboloma-L	33.33
4.	Eugenia jamboloma-S	133.33
5.	Azadirachtaindica	33.33
6.	Terminaliaarjuna	33.33
7.	Aeglemarmelos	133.33
8.	Momordicacharantia	0.03
9.	Asphaltum	66.66
	Total Weight	500 mg

All quantities are in mg

Scanning and determination of maximum wavelength (λmax)

In order to ascertain the wavelength of maximum absorption of the extracts/drug, 100 mg of PHF extract were dissolved in suitable solvent (water)to prepare the stock solution of 1000 µgm/ml. From this various concentration of 10, 20, 30, 40 and 50 µgm/ml were prepared and were scanned using spectrophotometer within the wavelength range of 400-200 nm against water as blank and the wavelength corresponding to maximum absorbance was noted to determine the λmax.

EVALUATION PARAMETERS[6-8]

General appearance (Organoleptic Properties)

The compressed tablets were examined for their color and appearance. The color, odor, taste were observed and noted down.

Tablet Hardness

The crushing strength Kg/cm^2 of prepared tablets was determined for 10 tablets of each batch by using Monsanto tablet hardness tester. The average hardness and standard deviation was determined.

Friability

Twenty tablets were weighed and placed in the Electrolab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula.

% F = {1-(W_t/W)} ×100

Where, % F = friability in percentage, W = Initial weight of tablet, W_t= weight of tablets after revolution.

Weight Variation

The tablets were evaluated as per I.P., 1996 for weight variation (n = 20) using 1mg sensitivity balance. Randomly selected twenty tablets were individually weighed and the average weight was calculated. From the average weight of the prepared tablets, the standard deviation was determined. The percentage deviation were presented in table 2.

Table 2: Percentage deviation allowed under weight variation

Percentage deviation allowed under weight variation test.	
Average weight of tablet (X mg)	***Percentage deviation***
X < 80 mg	10
80 < X < 250 mg	7.5
X > 250 mg	5

Disintegration Time

Disintegration time of the tablet was measured in water (37^0C) using USP disintegration test apparatus. A glass of plastic tube 80-100 mm long with an internal diameter of about 28 mm and external diameter 30-31 mm fitted at the lower end with a disc of rust proof wire gauge. Six tablets were placed in the tube, raise and lower the tube in such a manner that the complete up and down movement is repeated 28 to 32 per minute. The tablets are disintegrated when no particles remains above the gauge, which readily pass through mesh (10 mesh screen).

Content Uniformity

Five randomly selected tablets were weighed and powdered. The powdered tablet equivalent to 100 mg drug in one tablet was taken and transferred in a 100 ml flask containing 100 ml of 0.1 N HCl pH 1.2. The flask was shaken on a flask shaker and was kept for few hours for the sedimentation of un-dissolved materials. The solution is filtered through Whatman filter paper. 10ml of this filtrate was taken and appropriate dilution was made. The samples were analyzed at specific wavelength using UV visible spectrophotometer. The drug content was determined from the standard curve prepared at optimum λ max.

***In-Vitro* Dissolution Studies (Drug Release)**

Drug release was assessed by dissolution test under the following conditions: n = 6 (in triplicate), USP type II dissolution apparatus (Lab India, DISSO 2000) at 50 rpm in 900 ml of 0.1N HCl pH1.2 maintained at 37 ± 0.5^{0}C. The tablet was allowed to sink to the bottom of the flask before stirring. Special precaution was taken not to form air pockets on the surface of the tablet. Five milliliters of the sample was withdrawn by using a syringe filter at regular intervals and replaced with the same volume of pre warmed (37 ± 0.5^{0}C) fresh dissolution medium. The drug content in each sample was analyzed after suitable dilution using UV spectrophotometer method at respective maximum wave length.

Modeling of Dissolution Profiles

In the present study, data of the *in vitro* release were fitted to different equations and kinetic models to explain the release kinetics from the matrix tablets. The kinetic models used were a Zero order equation, First order, Hickson-Crowell, Higuchi release and Korsmeyer-Peppas models. The dissolution release kinetics and result of best fit model among the preparations were also compared.[9]

Stability Studies

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile.

The optimized formulation of the drug was subjected to accelerated stability studies at specified conditions of temperature and relative humidity of 25^{0}C/60% RH, 30^{0}C/60% RH and 40^{0}C/75% RH for 3 months. After the completion of three month the samples were analyzed visually for any color changes due to physical and chemical interaction within excipients and with the drug. The percentage drug content in all the tablets was determined after specified period.[10]

RESULTS AND DISCUSSION

Scanning for λmax

For UV scanning for λmax, about 100 mg of formulated and standard drug were weighed, powdered and transferred to a 100ml volumetric flask containing water solution and was shaken to dissolve and volume was made to 100 ml. Then 10 ml of this solution was diluted to 100ml to obtain a solution of 100 µg/ml and further diluted to obtain 10, 20, 30, 40 and 50 µg/ml and scanned for λmax determination. From the curve, peaks for the drugs were determined. Maximum absorption was shown to be 224 (Graph 1 & 2) for both formulated and standard drug.

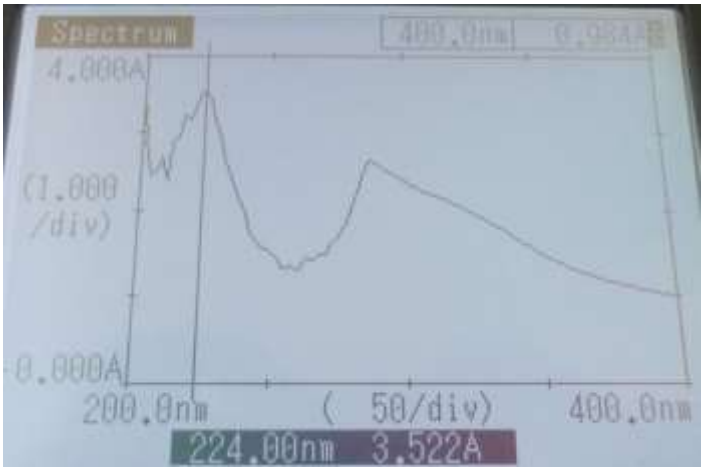


Figure 1: UV Scan of standard drug

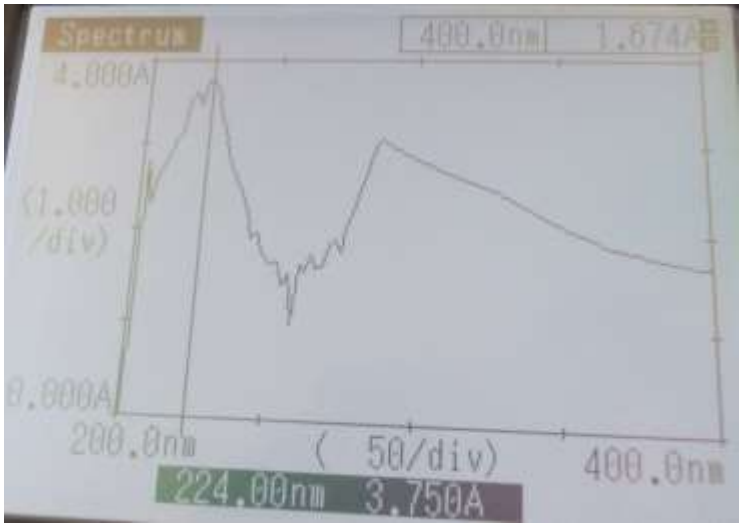


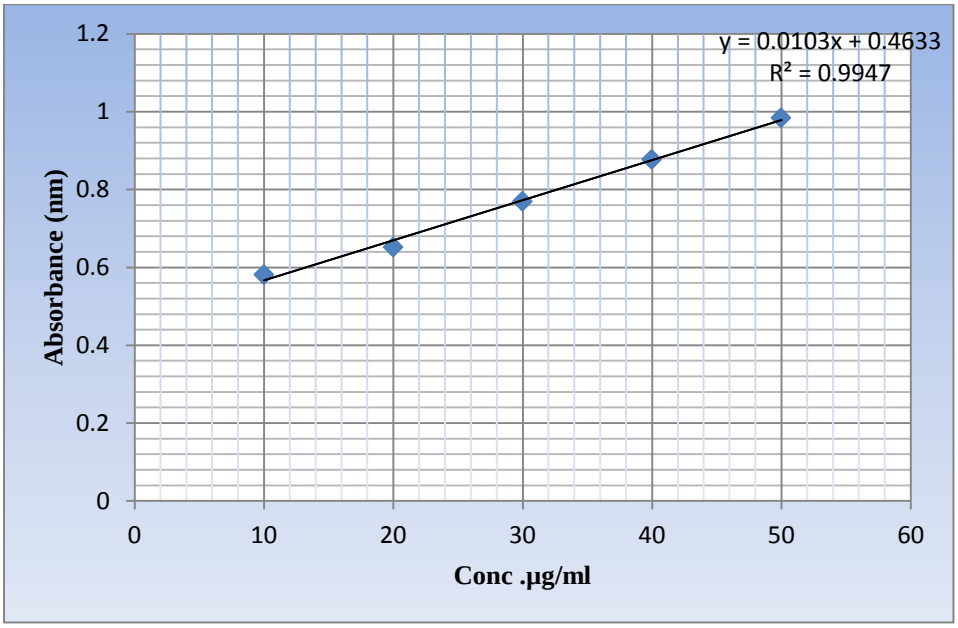
Figure 2: UV Scan of formulated drug

Standard curve of drug

Standard calibration curve of standard and formulated drug were determined by plotting graph between absorbance v/s concentration on double beam U.V. spectrophotometer using λmax at 224 nm, it follows the Beer's law. Straight line was obtained after plotting absorbance on X axis and concentration on Y axis. The line of equation was Y= 0.010X+0.463 & Y= 0.014X+0.315 respectively for standard and formulated drug. The R^2 value found was 0.994 & 0.979 respectively. The results were shown in table 3 & 4and graph 1&2.

Table 3: Data of standard curve for standard drug at λmax at 224 nm

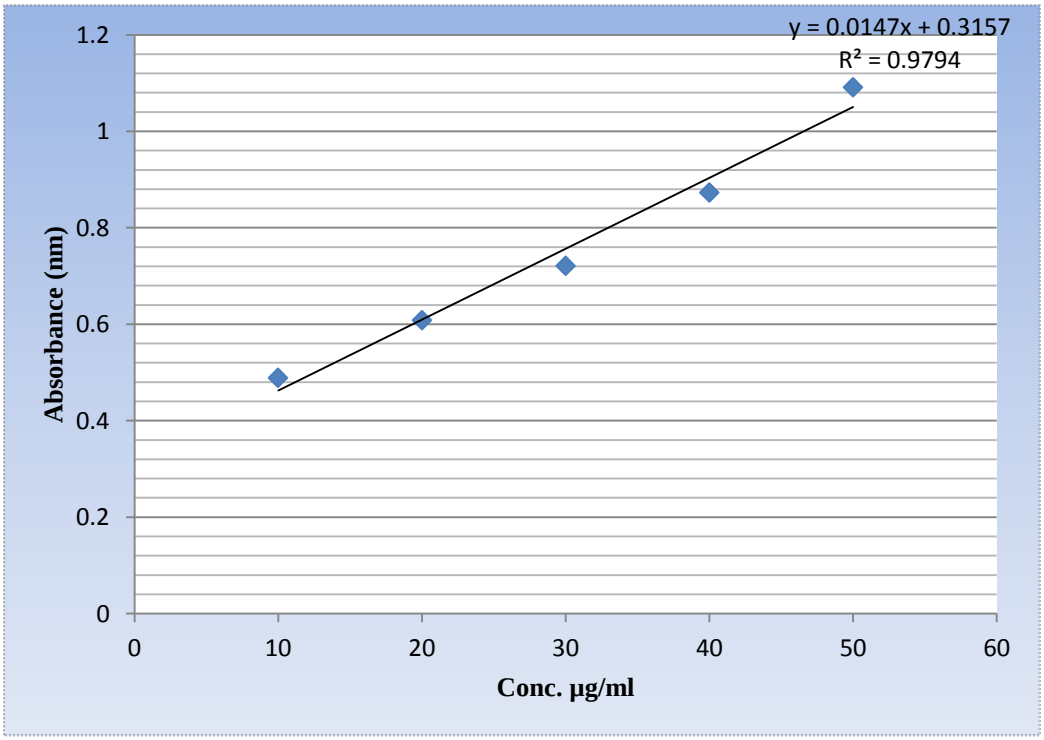
S/No	Conc. (µg/ml)	Absorbance
1	10	0.581
2	20	0.652
3	30	0.769
4	40	0.877
5	50	0.984



Graph 1: Standard curve for standard drug at λmax at 224 nm

Table 4: Data of standard curve for formulated drug at λmax at 224 nm

S/No	Conc. (µg/ml)	Absorbance
1	10	0.489
2	20	0.608
3	30	0.721
4	40	0.873
5	50	1.091



Graph 2: Standard curve for formulated drug at λmax at 224 nm

Pre-Formulation Studies

The standard and formulated drug were blended and various pre-formulation studies such as bulk density, tapped density, carr's index, hausner's ration and angle of repose were recorded. The data were presented in table. It was found from the present investigation that all the studied parameters were within the limit. (Table 5)

Table 5: Preformulation studies and results of flow properties

S/No.	Parameters	Standard	Formulated
1.	Bulk Density	0.615	0.649
2.	Tapped Density	0.549	0.583
3.	Carr's Index	12.02	11.32
4.	Hausner's Ratio	0.892	0.898
5.	Angle of Repose	21.45	23.62

Evaluation

The tablets were prepared by direct compression technique and no any tablet defects were observed in all the batches. The organoleptic properties such as color, odor and taste for both ie., standard and formulated poly herbal tablets were noted down and presented in table 6. Various evaluation parameters of tablets such as hardness, friability, weight variations, disintegration time, drug content and dissolution profile were mentioned in table 7 & 8. The drug release was presented in graph 3. The stability studies at three temperature and RH were recorded and mentioned in table 9, 10 & 11. The data obtained from dissolution studies of different batches was analyzed using different mathematical model for the determination of release kinetics. The kinetic models used were zero order, first order, Korsmeyer-Peppas, Hickson-Crowell and Higuchi model. For both the batches, the best fit model with the highest correlation was shown by Korsmeyer-Peppas. (Table 12).

Table6: Organoleptic properties of poly herbal anti-diabetic tablets

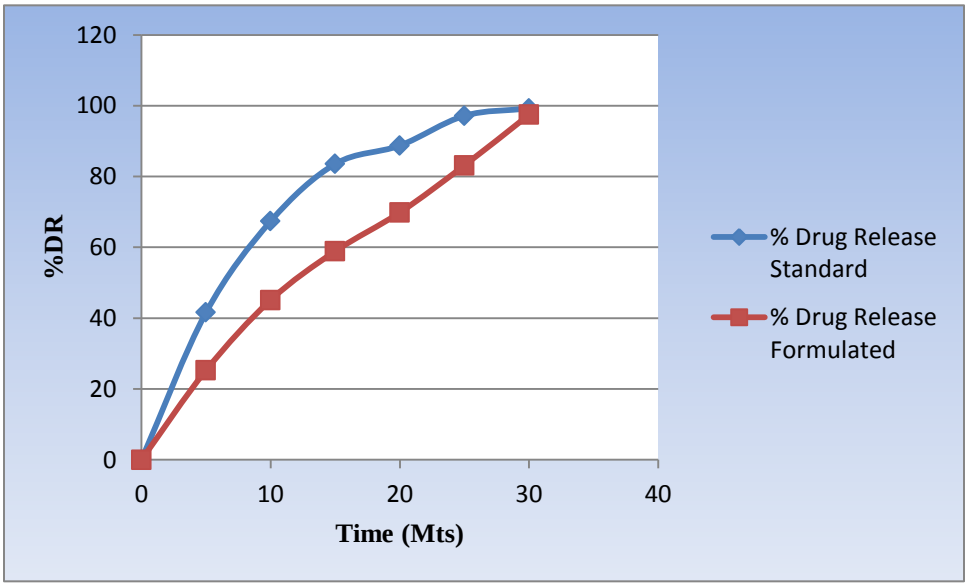
S/No.	Batch	Parameters		
		Color	Odor	Taste
1.	Standard	Light Brown	Characteristics	Slightly bitter
2.	Formulated	Light Brown	Characteristics	Slightly bitter

Table 7: Evaluation parameters of poly herbal anti-diabetic tablets

S/No.	Batch	Parameters				
		Hardness (kg/cm^2)	Friability (%)	Weight variations	DT (mts)	DC (%)
1.	Standard	5.8	0.63	500±4.7	37	98.47
2.	Formulated	4.3	0.71	500±3.2	32	96.41

Table 8: *In-Vitro* drug release of poly herbal anti-diabetic tablets

S/No.	Time (Mts)	% Drug Release	
		Standard	Formulated
1.	0	0	0
2.	5	41.61	25.29
3.	10	67.38	45.13
4.	15	83.56	58.93
5.	20	88.75	69.85
6.	25	97.15	83.16
7.	30	99.23	97.46



Graph 3: % Drug release of standard and formulated drug

Table 9: Evaluation parameters of at 25^{0}C ± 2^{0}C/ 60% ± 5% RH

S/No.	Evaluation Parameters	Formulation			
		Standard		Formulated	
		Initial	Final	Initial	Final
1.	Hardness	5.8	5.7	4.3	5.5
2.	Friability	0.63	0.65	0.71	0.78
3.	Weight variation	500±4.7	500±4.6	500±3.2	500±4.1
4.	Disintegration time	37	37	32	36
5.	Drug Content	98.47	98.42	96.41	96.12
6.	*In-Vitro* drug release	99.23	99.18	97.46	96.38

Table 10: Evaluation parameters at 30^{0}C ± 2^{0}C/ 65% ± 5% RH

S/No.	Evaluation Parameters	Formulation Code			
		Standard		Formulated	
		Initial	Final	Initial	Final
1.	Hardness	5.8	5.8	4.3	5.8
2.	Friability	0.63	0.64	0.71	0.79
3.	Weight variation	500±4.7	500±4.5	500±3.2	500±4.8

4.	Disintegration time	37	36	32	35
5.	Drug Content	98.47	98.38	96.41	95.89
6.	*In-Vitro* drug release	99.23	99.20	97.46	95.98

Table 11: Evaluation parameters at 40^0C ± 2^0C/ 75% ± 5% RH

S/No.	Evaluation Parameters	Formulation Code			
		Standard		Formulated	
		Initial	Final	Initial	Final
1.	Hardness	5.8	5.9	4.3	6.0
2.	Friability	0.63	0.66	0.71	0.84
3.	Weight variation	500±4.7	500±4.2	500±3.2	500±5.2
4.	Disintegration time	37	37	32	39
5.	Drug Content	98.47	98.20	96.41	94.98
6.	*In-Vitro* drug release	99.23	99.01	97.46	95.82

Table 12: Comparative release kinetics of formulations

Model		Batch	
Zero Order		Standard	Formulated
	R2	0.9908	0.9924
	K	2.1888	2.7763
	AIC	3.8075	2.3536
First Order	R2	0.9462	0.9229
	K	3.1474	4.9993
	AIC	4.1830	3.7317
Korsmeyer-Peppas	R2	0.9991	0.9967
	K	2.0559	7.9645
	AIC	3.3812	1.8502
Hickson-Crowell	R2	0.9823	0.9584
	K	4.2864	6.2708
	AIC	4.0433	3.3079
Higuchi	R2	0.9081	0.8869
	K	1.9775	1.4991
	AIC	3.4557	3.9710

Abbr.:R^2= Correlation coefficient; K=Constant; AIC= Akaike Information Criterion

REFERENCES

1. Adeghate E, Schattner P, Dunn E. An update on the etiology and epidemiology of diabetes mellitus. Ann N Y Acad Sci 2006, 1084:1–29.
2. Petchi RR, Parasuraman S, Vijaya C. Antidiabetic and antihyperlipidemic effects of an ethanolic extract of the whole plant of *Tridaxprocumbens* (Linn.) in streptozotocin-induced diabetic rats. J Basic Clin Pharm 2013, 4:88–92.
3. Parasuraman S, Kumar E, Kumar A, Emerson S. Free radical scavenging property and diuretic effect of triglize, a polyherbal formulation in experimental models. J Pharmacol Pharmacother 2010, 1:38–41.

4. Mandavi, D'Cruz S, Sachdev A, Tiwari P. Adverse drug reactions and their risk factors among Indian ambulatory elderly patients. Indian J Med Res 201;136:404–10.
5. Mishra US, Murthy P.N, Pasa G, Mishra D. Formulation development and evaluation of herbal tablet containing methanolic extract of *Butea frondosa*. Int J Inst Pharm and Life Sci 2011;, 1(3):1-15.
6. Lachman L, Liberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy, 3rd ed., Varghese publishing House Bombay 1999: 443-453.
7. Subrahmanyam CVS. Text Book of Physical Pharmaceutics, 2nded. New Delhi, Vallabh Prakashan 2001:253-261.
8. Aulton ME. Pharmaceutics: The Science of Dosage Form Design. 2nd ed. Churchill Livingstone, London 2002:322-334.
9. Costa P, Lobo J, Manuel S. Modelling and comparison of dissolution profile. Eur J of Pharm Sci 2001;13:123-133.
10. ICH guidelines. Stability testing of new drug substances and products, 27th October, 1993.