Research Article

Development and Evaluation of Herbal Fast Dissolving Tablets of *Tectona grandis* Linn

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ABSTRACT

Fast dissolving Tablets are disintegrating and/or dissolve rapidly in the saliva without the need for water. FDTs are convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, to achieve better patient compliance. Fast disintegrating tablets have been formulated for pediatric, geriatric, and bedridden patients. FDTs can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method. Herbal drugs comprise of a major share of all the officially recognised systems of health in India. The popularity and usefulness of the formulation resulted in development of several FDT technologies. The herbal extract of *Tectona grandis* Linn is used in this formulation. The aim of this study was to formulate FDTs with sufficient mechanical integrity and to achieve faster disintegration in the oral cavity without water. To achieve this goal, MCC is used as diluent and sodium saccharin as sweetening agent for the formulation of tablets. Attempts were made to enhance dissolution rate along with faster disintegration using superdisintegrants like Crospovidone, Sodium starch glycolate (SSG)and mixture of crospovidone and sodium starch glycolatein the formulation of tablets. The tablets were subjected to weight variation, drug content uniformity, hardness, friability, wetting time, *In vitro* dispersion time,*In vitro* drug release studies and *In vivo* studies. *In vivo* studies showed that formulation F1 has antidiabetic activity.

Keywords: Crospovidone (CP), Fast dissolving tablets (FDTs), microcrystalline cellulose (MCC), Sodium starch glycolate (SSG)

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INTRODUCTION

Now-a-days, Fast dissolving drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, Fast dissolving tablets (FDTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles. FDTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. New FDT technologies address many pharmaceutical and patient needs, ranging from enhanced life-cycle management to convenient dosing for paediatric, geriatric, and psychiatric patients with dysphagia. This has encouraged both academia and industry to generate new Fast dissolving formulations and technological approaches in this field (1).

Fast dissolving tablets dissolve or disintegrate instantly on the patient tongue or buccal mucosa. It is suited for tablets undergoing high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to minimize side effect and make it more cost effective. This study was aimed, which can disintegrate or dissolve rapidly once placed in the oral cavity (1).

Herbal drugs comprise of a major share of all the officially recognised systems of health in India viz. Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy, except Allopathy. More than 70% of India's 1 billion populations still use these non-allopathic systems of medicine. Currently, there is no separate category of herbal

drugs or dietary supplements, as per the Indian Drugs Act. However, there is a vast experiential-evidence base for many of the natural drugs. This offers enormous opportunities for Observational Therapeutics and Reverse Pharmacology. Evidence-based herbals are widely used in the diverse systems and manufactured, as per the pharmacopoeial guidelines, by a well-organised industry. Significant basic and clinical research has been carried out on the medicinal plants and their formulations, with the state-of-the-art methods in a number of Institutes/Universities (2).

Indian medicinal plants also provide a rich source for antioxidants that are known to prevent/delay different diseased states. The antioxidant protection is observed at different levels. The medicinal plants also contain other beneficial compounds like ingredients for functional foods (2).

The aim of this study was to formulate FDTs with sufficient mechanical integrity and to achieve faster disintegration in the oral cavity without water. To achieve this goal, MCC is used as diluent and sodium saccharin as sweetening agent for the formulation of tablets. Attempts were made to enhance dissolution rate along with faster disintegration using superdisintegrants like Crospovidone, Sodium starch glycolate (SSG) and mixture of crospovidone and sodium starch glycolate in the formulation of tablets. The herbal extract of Tectona *grandis* Linn used in this formulation. It is a herbal formulation prepared for diabetis. Diabetes mellitus is a group of metabolic diseases characterized by hyperglycaemia, hyper-triglyceridaemia and hypercholestero-laemia. The synthetic hypoglycemic agents have serious side effects like haematological effects, disease of liver, kidney and coma etc. Plant derived drugs are mostly considered to be less toxic and with fewer side effects. Therefore, search for more effective and safer herbal antidiabetic agent has become an area of active research (3).

*Tectona grandis*Linn (Verbenaceae) is a large deciduous tree. Branchlets are quadrangular, channeled and stellately tomentose. The tree is growing in higher situations, native to central India, Konkan, Western Deccan peninsula, South India and Burma. Teak is a hardwood species of worldwide reputation. Leaves are 30-40 by 15-30cm, elliptic or obvate, acute or acuminate. Upper surface of leaf is rough but usually glabrous and the lower clothed with dense stellate grey. Flowers are shortly pedicellate withlanceolate bracts at the forks. Fruits are 1-3 cm indiameter, subflobose; pericarp is soft with densefelted stellate hairs (4).

EXPERIMENTAL DESIGN:

Materials:

The plant *Tectona grandis* Linn was collected from western ghats. The roots were collected, dried and powdered. Crospovidone, Sodium starch glycolate and microcrystalline cellulose were obtained as gift sample from Loba Chemie Pvt Ltd Mumbai 40002.All other chemicals and reagent was of analytical grade.

Method:

Preparation of *Tectona grandis* Linn extract:

The Barks of the plant *Tectona grandis* Linn are collected. Dried under roof & then powdered. This Powder is then placed in the soxhlet Apparatus for extraction process. 250gm of powder is placed in packing column & extraction is carried out by mixture of water & alcohol (1:1).The extraction process is continued upto 8 cycles for 24hrs. Then the extract is dried at room temperature. This powdered extract is used for preparation of the tablet (5).

Preparation of fast dissolving tablet:

Herbal Fast dissolving tablets were prepared by direct compression method using various formulation additives in varying concentrations. All the ingredients were powdered separately in a clean and dry porcelain mortar and then they were passed through # 60 mesh sieve. The extract and β- cyclodextrin were complexed (kneading method) and then all the additives were mixed thoroughly in an inflated polyethylene pouch in a geometric ratio of their weight. Then the powder mixture was compressed in to the tablets of 500 mg weight (6).

Table 1: Composition of Herbal fast dissolving tablets

Ingredients (mg/ tab)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Extract	200	200	200	200	200	200	200	200	200
β-cyclo dextrin	200	200	200	200	200	200	200	200	200
crospovidone	15			15			15		
SSG		20			20			20	
Mixture of CP + SSG			25			25			25
MCC	65	60	55	65	60	55	65	60	55
Sodium saccharin	10	10	10	10	10	10	10	10	10
Mg.sterate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
TOTAL	500	500	500	500	500	500	500	500	500

CP– Crospovidone , SSG – Sodium starch glycolate

Characterization of fast dissolving tablets

FTIR studies (7).

Pure drug, formulation (F1) were subjected for FTIR analysis using Fourier transformer infrared spectrophotometer (8600, Shimadzu Corporation, Japan). The samples were prepared on KBr-press (Spectra Lab, India) and scanned over wave number range of 3500 to 350 cm -1. Spectra were analyzed for drug interactions and functional groups.

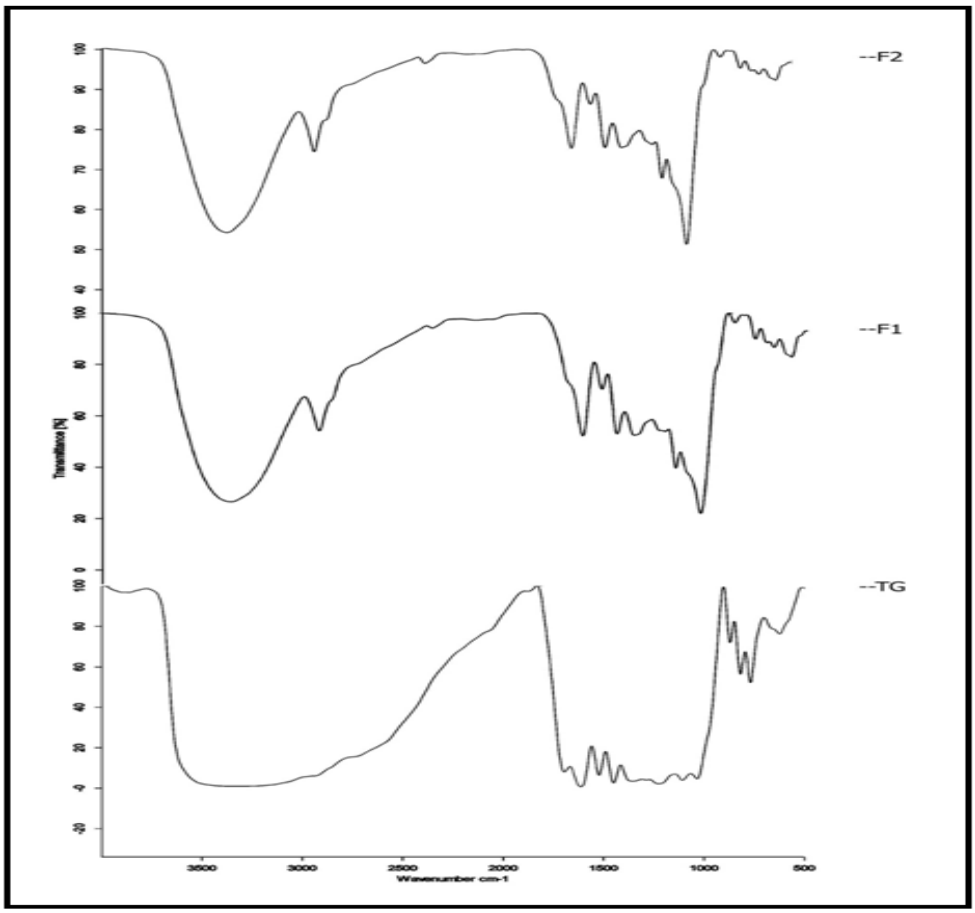

Figure 1: IR spectra of *Tectona grandis* Linn

DSC Studies (7).

The pure extract of *Tectona grandis* Linn and formulation F1 were subjected to differential scanning calorimeter equipped with an intra cooler. Indium/Zinc standards were used to calibrate the DSC temperature and enthalpy scale. The samples (Pure drug, and F1) were sealed in aluminum pans and heated at a constant rate of 10^0C/ min over a temperature range of 50 to 400^0C.

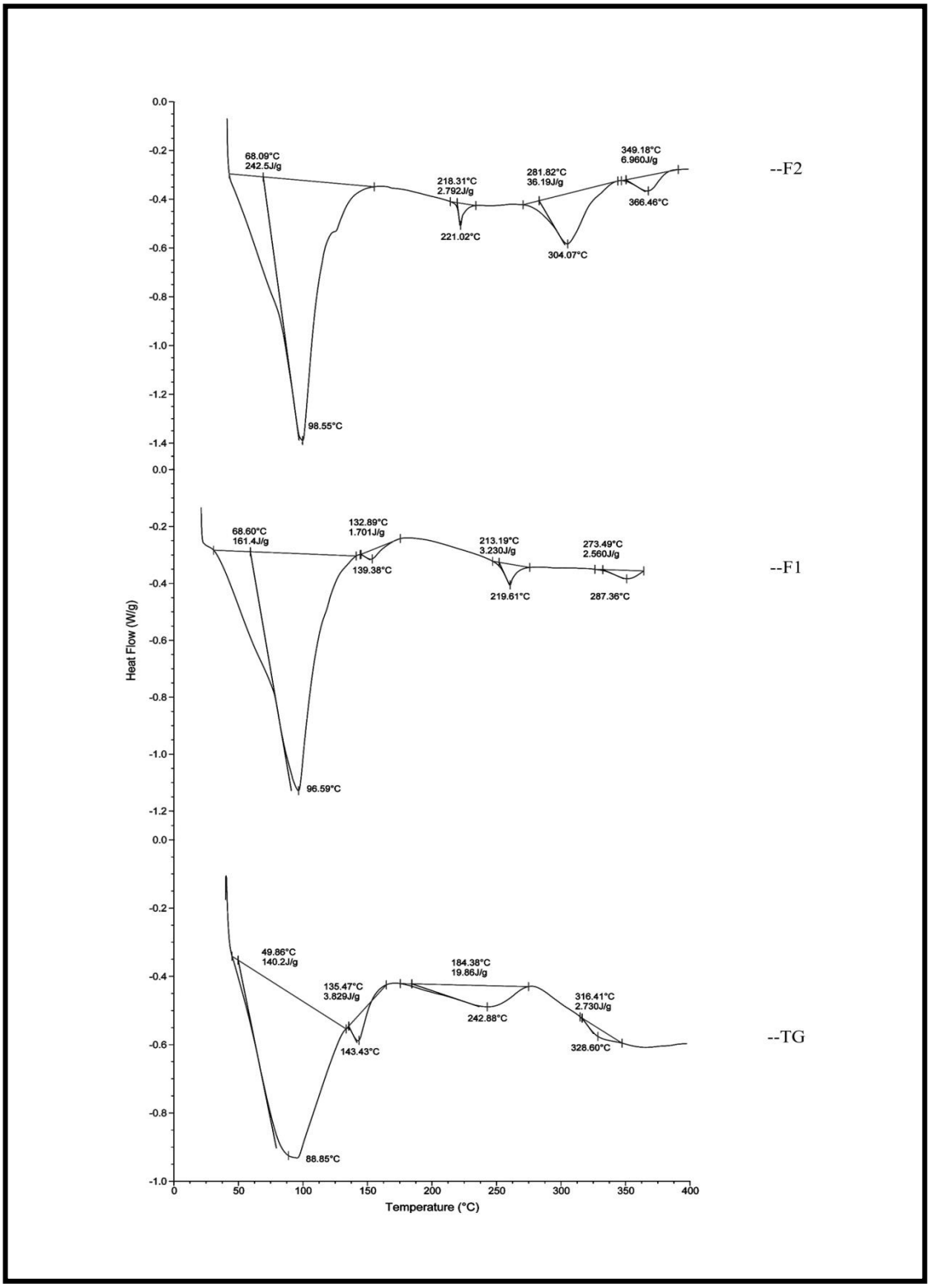

Figure 2: DSC of *Tectona grandis* Linn

XRD studies (7). The PXRD patterns of pure *Tectona grandis* Linn were recorded using X-ray diffractometer with a copper tube anode over the interval 20 to 90^0 $2\theta^{-1}$.

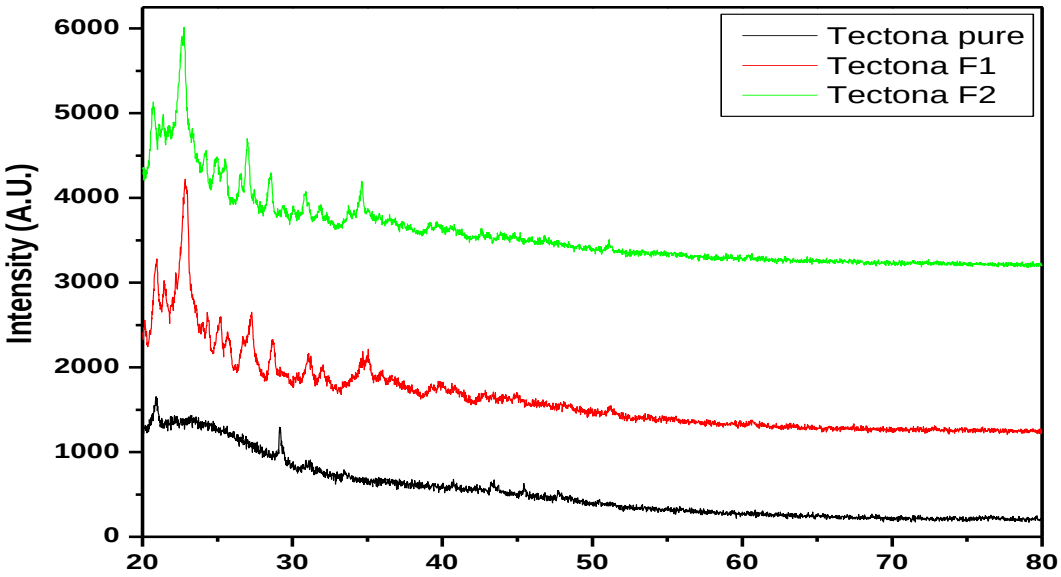

Figure 3: XRD of *Tectona grandis* Linn

Evaluation of tablets

The tablets from all the batches were evaluated for different parameters as follows:

Appearance

Tablets were evaluated for organoleptic properties.

Weight Variation (8).

Ten tablets were selected and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight.

Friability (8).

Pre-weighed sample of tablets was placed in the Roche Friabilator tester, which was then operated for 100 revolutions. Tablets were deducted and reweighed; tablets should not lose more than 1% of their initial weight.

Despersion time (8).

Two tablets were placed in 100 ml of *water* and stirred gently until completely dispersed. A smooth dispersion was obtained which passes through a sieve screen with a nominal mesh aperture of 710 µm.

Wetting Time (8).

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish containing 10 ml of water. Containing Eosin, a water soluble dye, was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper and allowed to wet completely. The time required for water to reach upper surface of the tablet was noted as a wetting time.

Disintegration Time (8).

The disintegration time of tablet was measured in water (37 ^{0}C) according to USP Disintegration test apparatus.

Hardness (9).

Tablets were selected at random from each formulation and hardness was checked using Monsanto Hardness Tester.

Drug content (10).

Drug content of all the batches was determined. Six tablets were weighed and crushed with pestle in a small glass mortar. The fine powder was weighed to get 500 mg, and transferred to 250 ml conical flask containing 100 ml of Distilled water stirred for 45 min in ultra sonicator. Solution was filtered and the filtrates obtained were analyzed UV spectrophotometrically and drug content was determined.

***In-vitro* Dissolution** (11).

The in vitro dissolution study was performed in the USP apparatus type II Aliquot equal to 5 ml of dissolution medium

was withdrawn at specific interval and replaced with fresh medium for maintaining sink condition. Sample was filtered and absorbance of filtered solutions determined by UV spectroscopy. Dissolution rate was studied for all formulations.

Stability studies (11).

Stability is defined as the ability of particular drug or dosage form in a specific container to remain with its physical, chemical, therapeutic and toxicological specifications. In any rational design and evaluation of dosages forms for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection. During the stability studies the product is exposed to normal condition of temperature and humidity. However the studies will take a longer time and hence it would be convenient to carry out accelerated stability studies, were the product is stored under extreme condition of temperature and humidity. In the present study, stability studies were carried out on optimized formulation under the following condition for one month period as prescribed by ICH guidelines for accelerated study at 40 ± 2 ^{0} C and RH 75 % ± 5 %.

The tablets were withdrawn after a period of 30 days and analyzed for physical characterization, dissolution and drug content.

***In vivo* Studies** (5, 12).

Formulation F1 having less disintegration time and satisfactory *in vitro* drug release has been selected for *in vivo* studies. The study was done to compare *in vivo* antidiabetic effect of prepared formulation F1 and results are presented in Table no-24. In-vivo evaluation studies for Herbal Tablets were performed on Albino rats weighing 170 to 200 gm. A single intra-peritoneal injection of 120mg/kg body wt of alloxan monohydrate will be employed to induce diabetes. After 72h, animals with serum glucose levels higher than 250mg/dl were considered diabetic and were included in the study. Animals will be divided into four groups including six rats each. Group I normal rats (no alloxan treatment) and Group II diabetic rats were given 1 ml of distilled water. Groups III–IV will be given *Bauhinia variegate* Linn and, *Tectona grandis* Linn in the form of tablet given orally on the 3rd day after the induction of diabetes. Rats will be fasted overnight and blood samples will be collected from the tail vein on the 3rd day of alloxan treatment prior to and at 5min, 10min, 15min, 30min, 45min and 60 min intervals after the administration of the extract. Glucose level is estimated by using glucometer.

Table 2: Evaluation of *Tectona grandis* Linn tablet

Batch	Hardness (kg/cm^2)	% Weight variation	% Friability	Disintegration time	Wetting Time	Drug Content
F1	3.2±0.06	1.89±0.0020	0.60±0.090	17 sec	42sec	**102.15**
F2	3.4±0.07	2.15±0.0021	0.61±0.083	50 sec	1 min 3sec	100.85
F3	3.6±0.09	2.56±0.0025	0.64±0.086	1 min 9 sec	1 min 8sec	99.17
F4	3.6±0.078	2.48±0.0020	0.63±0.091	1 min 38 sec	2 min 3sec	98.54
F5	3.8±0.09	2.20±0.0020	0.65±0.068	1 min 58 sec	3min 6 sec	98.91
F6	3.3±0.08	2.31±0.0021	0.62±0.051	2 min 12 sec	3min	100.30
F7	3.4±0.06	2.11±0.0031	0.67±0.081	1 min 22 sec	1 min5 sec	100.96
F8	3.6±0.065	2.23±0.0020	0.69±0.081	1 min 12 sec	3min 2sec	101.52
F9	3.5±0.09	2.56±0.0020	0.68±0.075	1 min 7 sec	3 min	99.74

Table 4: Drug Release Profile for *Tectona grandis* linn

Time in min	F1 %CDR	F2 %CDR	F3 %CDR	F4 %CDR	F5 %CDR	F6 %CDR	F7 %CDR	F8 %CDR	F9 %CDR
2	4.64	1.85	3.71	0.92	0.92	2.78	4.64	0.92	1.85
4	22.97	12.06	10.00	21.35	10.00	17.64	11.04	22.97	22.97
6	30.33	30.33	32.49	29.71	32.49	30.33	32.49	32.49	28.41
8	38.60	38.99	49.20	43.64	44.57	38.60	40.85	38.60	38.60
10	49.21	56.64	56.02	55.38	53.70	51.99	50.14	49.21	55.60

15	67.78	71.49	67.78	65.93	64.07	66.85	72.08	64.07	65.90
20	76.13	77.06	73.35	72.43	68.71	75.21	77.06	78.92	77.06
25	82.63	82.63	78.92	76.13	77.06	79.86	82.63	82.63	84.49
30	88.20	86.34	84.49	82.63	83.57	83.57	86.34	86.34	88.20
45	91.00	88.20	87.28	87.28	88.70	89.14	89.14	91.00	91.00
60	97.49	91.90	91.00	94.71	94.71	91.90	93.78	94.70	94.70

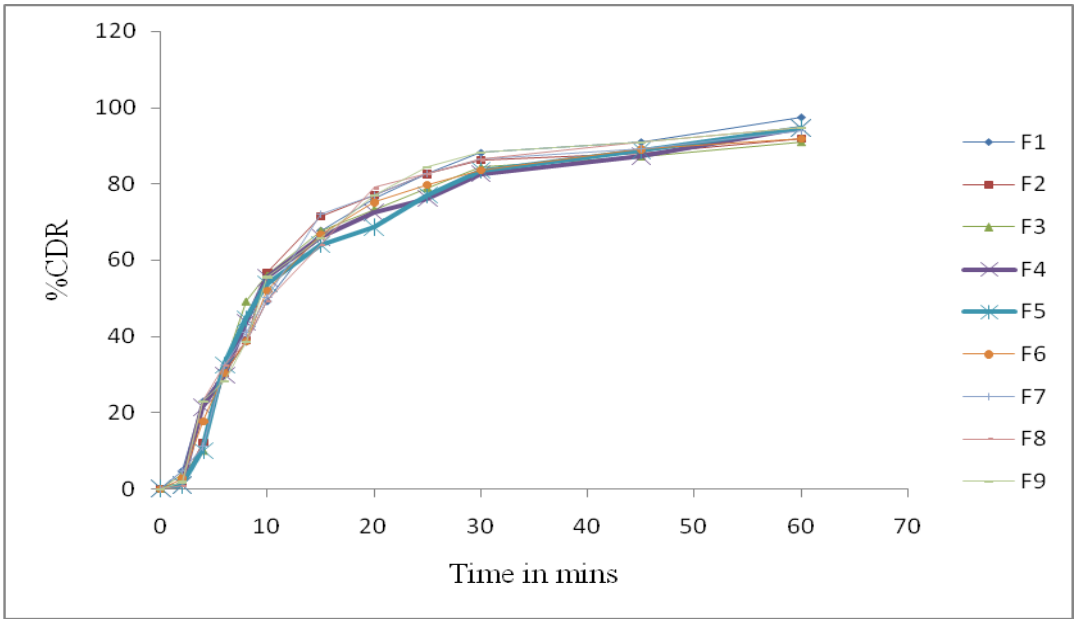

Figure 4: Drug release of *Tectona grandis* linn

Table 5: Determination of Blood Plasma concentration in different groups

N =6	Treatment	Blood Glucose concentration (mg/dl) (mean ± S.E.M) 5 min	10 min	15 min	30 min	45 min	60 min
I	**Normal control**	89±2.3	90±1.9##	85±2.2##	93±2.4##	91±1.8##	92±2.3##
II	**Diabetic Control**	298±3.5	284±4.2*	291±3.9*	267±4.6*#	263±5.1*	277±4.4*
III	**BV tablet**	295±5.7	284±4.2*	262±3.2*#	249±4.6*##	246±3.5*##	239±4.9*##
IV	**TG Tablet**	302±5.0	291±5.2*	261±4.5*#	251±5.2*##	245±4.8*##	241±4.2*##

Table 6: Plasma concentration V/s time profile

Time in mins	Plasma concentration of *Tectona grandis* Linn extract (µg/ml)	Plasma concentration of Formulation F1 (µg/ml)
5	5.4	13.7
10	6.9	15.4
15	10.4	18.7
30	7.1	10.1
45	3.6	6.6
60	1.4	3.2

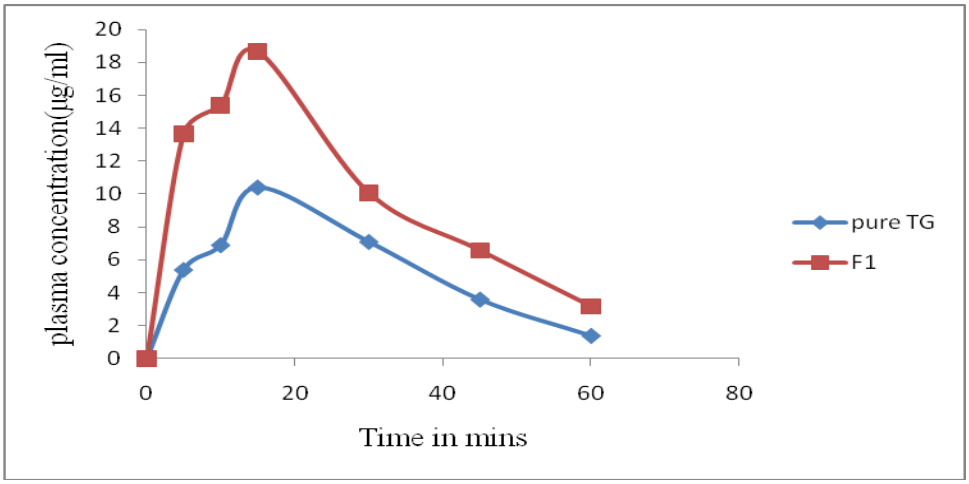

Figure 5: Plot of Plasma concentration of Pure *Tectona grandis* Linn extract and Formulation F1 V/s Time

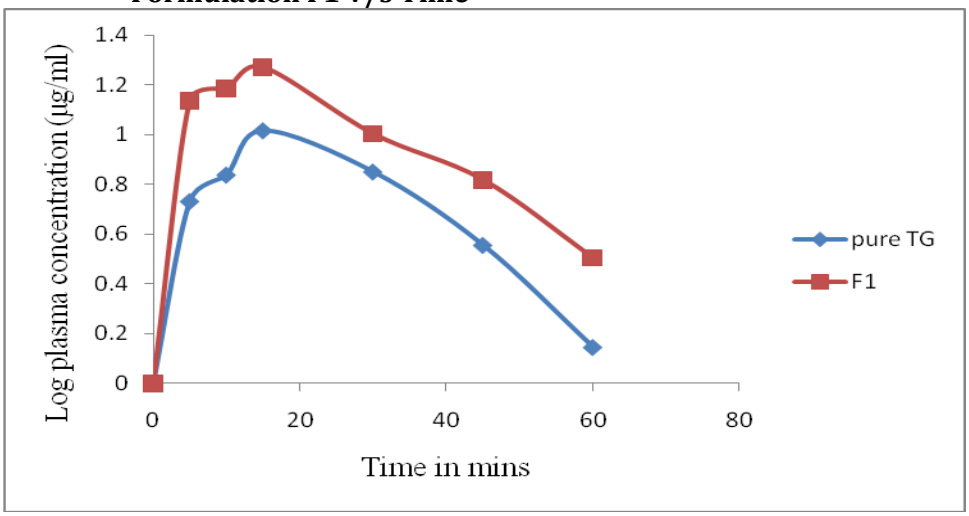

Figure 6: Plot of Log Plasma concentration of Pure *Tectona grandis* Linn extract and Formulation F1 V/s Time

RESULT AND DISCUSSION

Physicochemical evaluation of tablets

The results of physicochemical evaluation of tablets are given in Table 2. As the material was free flowing, tablets were obtained of uniform weight due to uniform die filling. Hardness of tablets was between 3.2-3.7 kg/cm^2 for all the formulations. Friability was found in between 0.62-0.69%. The friability value below 1% was an indication of good mechanical resistance of the tablet. The drug content was found to be 98.18- 102.50% which was within the acceptable limits. The disintegration time is shorter with quick wetting properties at the core of the tablets. The wetting time/dispersion time decreases with increase in the concentration of superdisintegrants. FTIR Studies IR-spectroscopic studies indicate that there are no drug–exipients interactions.

DSC Studies

In the DSC thermogram of pure *Bauhinia variegata* Linn the melting point of drug was shifted from 88.57^{0}C to 101.55^{0}C for F1 and 99.64^{0}C for F2 and in case of *Tectona grandis* Linn the melting point of drug was shifted from 88.85^{0}C to 96.59^{0}C for F1 and 98.55^{0}C for F2 indicating no interaction of the drug and other excipients.

XRD Studies

X-ray diffraction patterns showed that pure extract was amorphous in nature. Whereas Formulation F1 and F2 shows sharp intense peak. These suggest that the amorphous nature of drug changed to crystalline form.

In vitro release study

Formulations F1, F4 and F7 which contains 3% superdisintegrants releases 97.43%,

91.00% and 93.75% drug respectively at the end of 60 min (Fig 4). An increase in the drug release was observed when 3% superdisintegrants used in formulations. The rapid drug dissolution might be due to easy breakdown of particles and rapid absorption of drug into the dissolution medium..

Stability studies

The stability studies were carried out for selected tablets at 40°C ±2 °C / 75 % RH ± 5 % for a month. The orodispersible tablets were evaluated by their drug content, wetting time, water absorption ratio, dispersion time, disintegration time and *in vitro* drug release. The studies indicated that, there were no significant changes found in the tablet properties.

***In vivo* Studies**

The study shows antidiabetic effect in albino rats.

CONCLUSION

The prepared herbal fast dissolving tablets shows good disintegration property and dissolution rate. The comparative study of several superdisintegrants yielded a conclusion that Crospovidone at 3% concentration are suitable for the preparation of Herbal fast dissolving tablets which will satisfy all the criteria and official limits.

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