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Der Pharmacia Lettre, 2016, 8 (5):170-183
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Development and evaluation of herbal formulation from *Polyalthia longifolia, Tabernaemontana alternifolia, Benincasa hispida* plant extracts

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ABSTRACT

Today's age has anticipated the importance of herbal formulations in the treatment of various diseases comprising from major to minor ailments. The importance of these herbal development industries has immensely gained momentum due to the underlying side effects associated with allopathic medicines ranging from minor problems such as ulcerations to major life threatening problems such as growth retardation. In the present research studies the aim was to develop oral herbal tablets from Polyalthia longifolia (PL), Tabernaemontana alternifolia (TA), Benincasa hispida (BH) plant extracts and perform its evaluation as per ICH guidelines. PL and TA leaves were extracted by cold extraction at room temperature and BH fruit peels was extracted by petroleum ether using soxhlet extraction process. Wet granulation method was used for the development of oral herbal tablets. The developed herbal tablets were evaluated by paramaters such as general appearance, hardness, friability, disintegration time and dissolution profile as per ICH guidelines at different temperatures and humidity. The developed herbal tablets showed decent elegance and palatability followed by good hardness, friability, disintegration time and dissolution characteristics. Thus, article discusses and encompass the readers vision that in future local plants developed formulations could be probable prove to be equipotent with medicinal plants formulations useful for various therapeutic purposes.

Keywords: *Polyalthia longifolia, Tabernaemontana alternifolia, Benincasa hispida, Carbapol, Microcyrstalline cellulose*

INTRODUCTION

Plants have been the basis of many traditional medicinal systems for thousands of years and continue to provide mankind with new remedies for each and every disease. Use of plants as a source of medicine has been inherited and regarded as an important component of the health care system in agricultural like India [1]. Local plants are euipotent to medicinal plants and useful in the management of various diseases comprsing microbial infections and immunosystem related disorders [2,3].

Polyalthia longifolia (PL) is one of the most important indigenous medicinal plants in Indian medicinal literature which is found throughout Malaysia and widely used in traditional medicine as febrifuge and tonic. Almost all parts of this plant are used in Indian traditional system for the treatment of various ailments. PL leaves have been used in pyrexia as well as menorrhagia [4]. *Bennicasa hispida* commonly known as Ash gourd belongs to Cucurbitacae

family, which is a single species of tender annual vine, believed to have originated in Java. It is valued for its medicinal properties and widely studied by Ayurvedic practioners. It has special potency as nervine tonic. It alleviates nausea (*Vatta*) and acidity (*pitta dosha*). The properties of fruit changes according to stage of ripening. It is interesting to note that the tender fruits alleviates acidity, medium ripened fruit alleviates cough, where as fully ripened fruit alleviates all of them. BH fruit juice is used in syrup and anti-anxiety tablets with combination of drugs [5]. *Tabernaemontana alternifolia* is used as antihementic for many years to treat tape worms in children with milk or curd as well as as pain relievers [6]. The selected local plants namely *Polyalthia longifolia*, *Tabernaemontana alternifolia*, *Benincasa hispida* are widely known due to its uniqueness to exert ethnopharmacological activities comprising analgesic, anti-oxidant, anti-inflammatory, antibacterial which have well cited by the researchers in the studies [7-12].

Herbal drugs constitute a major part of therapeutics in all the traditional systems of medicines like ayurveda, siddha, unani. Plants have been the basis of many traditional medicinal systems for thousands of years and continue to provide mankind with new remedies for each and every disease. Use of plants as a source of medicine has been inherited and regarded as an important component of the health care system in agricultural country like India. Most practitioners formulate and dispense their own recipes, which necessitates proper documentation and with utmost attention to research oriented services[1,13].

Across the world, the use of herbal medicines is steadily growing to treat medical illnesses comprising of major and minor ailments. Augmented incidence of the adverse reactions of synthetic drugs in humans and economic burden of the modern system of medicine on government has paved the interest in development of traditional medicine from local plants. It is estimated that approximately one quarter of prescribed drugs contain plant part derived extracts or active ingredients obtained from whole plants. Below are few examples of a plant derived drugs such as atropine, artimesinin, colchicine, digoxin, ephedrine, morphine, physostigmine, pilocarpine, quinine, quinidine, reserpine, taxols, tubocurarine, vincristine and vinblastine which proved its potential in important pharmacological categories [14].

Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing; however in many cases immediate onset of action is required than conventional therapy. To overcome these drawbacks, immediate release pharmaceutical dosage form has emerged as alternative oral dosage forms. There are novel types of dosage forms that act very quickly after adminstration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymelhylcellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone), starch 1500 etc. which provide instantaneous disintegration of tablet after administration. The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, a wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs can be considered candidates for this dosage form [15].

The objective of present study was to make immediate release herbal tablets which would contain a plant material equivalent to that found in traditional dosage form that would meet conventional pharmaceutical standards. Tablets are chosen as dosage form because they are easy to handle,patient compliance and show immediate action.

MATERIALS AND METHODS

Part A: Collection, authentication and extraction

Fresh leaves of *Polyalthia longifolia*, *Tabernaemontana alternifolia* and *Benincasa hispida* fruit peels were collected from Mumbai local market in month of April-May and shade-dried. The leaves were authenticated by Agarkhar Research Institute, Pune. A voucher specimen (No.3/187/2013/Adm.1692) was deposited in the botany department of Agharkar Research Institute, Pune. Further, they were subjected to extraction procedure as follows:

Methanol was used as solvent for the extraction of Polyalthia longifolia and Tabernaemontana alternifolia. Fresh leaves were air- dried. The leaves of the plants were grounded into powder passed through sieve no. 40 to obtain fine powder. The powder was soaked in methanol for 24 hours with simultaneously shaking on orbital shaker at 50 rpm. Further they were filtered through Whatman filter paper no.1, the collected filtrate was evaporated to dryness using rotary evaporator at 40 ° C to obtain an alcoholic extract stored in amber colored air tight bottle in refrigerator until further use.

Petroleum ether was used as primary solvent for the extraction of Benincasa hispida. The peels of the fruits were removed and air dried. The extraction was carried out at 40-60 ° C till the solution became colourless. Then it is flitered through Whatman filter paper no.1and further macerated with ethanol for 8 days,the extracted material obtain was evaporated to dryness an alcoholic extract stored in amber colored air tight bottle in refrigerator until further use.

Part B: Formulation development of Herbal tablets : [16-20]

Herbal tablets were prepared separately by wet granulation using different proportions of various exicipents and denoted as TA 1-TA 10, PL1-PL6 and BH1-BH4. The procedure is described as below:

- ***Sieving***: All exicipents used were passed through 60# sieve along with lubricant and glidant.
- ***Mixing :*** The steps are described as follows:

1. All the weighed exicipents were taken in the motar pestle, weighed amount of extract is added as depicted in tableno.1, the mixture wastriturated till you get fine freely flowing powder form.
2. PVP in IPA was added to get dough, passed through sieve mesh no. 8# and after drying finally through sieve mesh no. 20 #.
3. Magnesium streate was added and allowed to lubricate for 10 mins, followed by determination of micrometric properties for all the formulation are checked and compressed.
4. % of disintegrants used and MCC was changed in the developed herbal formulation.

- All three plants extracts of PL, TA and BH were subjected to the uniformity of the procedure described above.

The composition of the developed herbal tablets is described in Table no.1,2,3.

Table no. 1- Composition for *Tabermontana alternifolia* (TA) tablet

Ingredient In (mg/tablet)	TA1	TA2	TA3	TA4	TA5	TA6	TA7	TA8	TA9	TA10
Plant extract TA	100	100	100	100	100	100	100	100	100	100
Lactose	104	-	90	110	116	110	116	107	104	117
MCC	-	154	62	60	60	60	60	63	60	35
Starch	30	30	15	-	-	-	-	-	-	-
Cp	-	-	-	12	6	-	-	-	-	-
SSG	-	-	-	-	-	12	6	-	-	-
Starch 1500	-	-	-	-	-	-	-	9	15	15
PVP in IPA	q.s	q.s	q.s	q.s	q.s	qs	q.s	q.s	q.s	q.s
Magnesium strerate	3	3	3	3	3	3	3	3	3	3
Total	300	300	300	300	300	300	300	300	300	300

Table no.2- Composition of *Polyalthia longifolia* (PL) tablet

Ingredient in (mg/tablet)	PL1	PL2	PL3	PL4	PL5	PL6
Plant extract PL	100	100	100	100	100	100
Lactose	92	116	116	105	104	117
MCC	60	60	60	65	60	35
Starch	15	-	-	-	-	-
Cp	-	6	-	-	-	-
SSG	-	-	6	-	-	-
Starch 1500	-	-	-	9	15	15
PVP in IPA	q.s	q.s	q.s	q.s	q.s	q.s
Magnesium strerate	3	3	3	3	3	3
Total	300	300	300	300	300	300

Table no.3- Composition of *Benincasa hispida* (BH) tablet

Ingredient In (mg/tablet)	BH1	BH2	BH3	BH4
Plant extract BH	100	100	100	100
Lactose	92	116	107	117
MCC	60	60	63	35
Starch	15	-	-	-
Cp	-	6	-	-
SSG	-	-	6	-
Starch 1500	-	-	9	15
PVP in IPA	q.s	q.s	q.s	q.s
Magnesium strerate	3	3	3	3
Total	300	300	300	300

- ***Compression :*** The developed herbal formulation was subjected to compression for formulating into effective oral tablet form. Herbal Tablets were prepared comprising each of 300 mg on single punch tablet machine having 10-mm concave-shaped punches.

Part C: Evaluation of developed herbal tablets: [22]

I. Precompression Parameters:

a) Untapped Bulk Density

Powder weighing 10 g was placed into 100 ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and bulk density was calculated by the following equation:

$$\text{Untapped Bulk Density} = \frac{\text{Mass of bulk drug}}{\text{Volume of bulk of drug}}$$

The experiment was done in triplicate.

b) Tapped Bulk Density

Powder weighing 10 g was placed into 100 ml measuring cylinder. The cylinder was then subjected to a fixed number of taps (~100 times) until the powder bed volume had reached the minimum level. The final volume was recorded and the tap density was calculated by the following equation:

$$\text{Tapped Bulk Density} = \frac{\text{Mass of bulk drug}}{\text{Volume of bulk drug on tapping}}$$

The experiment was done in triplicate.

c) Compressibility

Compressibility of the drug was found out using the following formula:

$$\% \text{ Compressibility} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

d) Hausner Ratio

Hausner of the drug was found out using the following formula:

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

e) Angle of Repose:

The angle of repose gives an indication of the flow ability of the substance. Funnel was adujusted such that the stem of the funnel lies 2cm above the horizontal surface. The drug powder was allowed to flow from the funnel under the gravitational force till the apex of the pile just touched the stem of the funnel, so the height of the pile was taken as 2cm. Drawing boundary along the circumference of the pile and taking the average of six diameters determined the diameter of the pile. These values of height and diameter were then substituted in the following equation:

$$\text{Angle of Repose } (\theta) = \tan^{-1} \frac{[2h]}{d}$$

Where, h - Height of the pile and
d - Diameter of the pile.
The experiment was done in triplicate.

II. Post Compression Parameters:

1. Weight Variation

20 tablets were selected randomly from the lot and weighed individually to check for any weight variation. Weight variation was checked as per specification of I.P. is shown in Table.4

2.Hardness
Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It was expressed in kg/cm2.

3.Friability Test
Friability of the tablet was determined using Roche friabilator. The device subjects the tablet to combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping tablet at height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula:

$$F = \frac{W_{Initial} - W_{final}}{W_{Initial}} \times 100$$

4.Determination of Thickness of Tablets
The thickness of tablets were determined by using Vernier caliper instrument.

5.Disintegration Test (DT)
DT test was carried using disintegration apparatus. Distilled water at 37 ± 2°C was used as a disintegration media and the time in minutes was taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus which was measured in minutes.

6. Drug Content
5 tablets were randomly selected and weighed. Tablets were powdered in a glass mortar. Powder equivalent to 100mg was weighed and dissolved in 0.1N HCL in 50 ml of volumetric flask to obtain a stock solution of 1000 µg/ml. It was filtered and 1 ml was pipetted out and diluted with 0.1N HCL to 10 ml in each case, so as to get 100 µg/ml. The absorbance of this solution was noted at 254, 273 and 280 nm in each case.

7. In-Vitro Drug Release
Dissolution test protocol : This dissolution protocol of all PL, TA and BH tablets were similar but their detection was done at 254, 273 and 280 nm

Dissolution apparatus : USP Type II (Paddle)
Temperature : 37 ± 0.50 C
Paddle speed : 50 rpm
Tablet strength : 100 mg of tablets
Dissolution medium : 0.1 N HCL
Volume of dissolution : 900 ml medium
Volume of sample removed : 10 ml
Sampling profile : 5, 10,15,20,30,45 and 60 min intervals.
Dissolution limit : Not less than 80% at the end of 60 min.

Every time the volume of sample withdrawn, was replaced by fresh dissolution medium maintained at the same temperature. The sample removed was diluted and analyzed by UV-spectrophotometry.

III.Stability Studies
In our research studies, batch T1, T3 and T4, PL1 and PL 3 and BH2 showed burst release in 5mins so the batch was discarded. Tablets of the optimized formulation (T8, PL4 and BH3) were tested for stability under two conditions for a period of three months. All the tablets were packed in blister type strip package. The tablets stored in stability chambers maintained at 40^0C/ 75% RH and 25^0C/ 60% RH, were evaluated for their physical characteristics, *in vitro* drug release and content of active ingredient at the end of 0 day, 15 days, 30 days, 60 days and 90 days of storage period. They were subjected to various parameters as follows:
1. **Physical characteristics**
Various parameters evaluated were appearance, thickness, diameter, hardness and friability using the method described earlier.

2. **Uniformity of weight**
Twenty tablets were randomly selected from stability batches and weighed individually to check for weight variation and results were compared with IP specification.

3. **Drug content, disintegration, dissolution test** were carried out as described in post compression parameters.
IV Drug release kinetics:
Different kinetic models were studied from dissolution profile of the final optimized formulation (BH4, PL5 and TA8) as shown in table no.8

RESULTS AND DISCUSSION

Herbal drugs are now a days receiving greater momentum and attention in finding as the alternative as well as the new source of promising drugs for the treatment and cure of various ailments. As stated in our research studies, batches T1, T3 and T4, PL1 and PL 3 and BH2 showed burst release in 5mins, hence the batches were discarded. The pre compression (optimized batches) and post compression results were depicted in Table no.4.

Table 4: Precompression Parameters of Optimized Batch

Batch	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Loss on drying
TA8	0.46	0.54	14.81	1.17	26.5	2.5
PL4	0.45	0.52	16.67	1.2	35.7	2.2
BH4	0.44	0.53	16.98	1.2	31.6	2.3

Table no.5: Post Compression Parameters and disintegration Time

Formulation code	Weight variation of Tablets (gms)	Thickness (cm)	Drug content (%)	Hardness Kg/cm^2	Friability (%)	Disintegration Time
TA1	0.289	3.3	98.4	3.5	0.72	10min 10 sec
TA2	0.301	3.4	96.5	4	0.85	8 min 45 sec
TA3	0.297	3.2	97.4	4	0.78	6 min 21 sec
TA4	0.295	3.6	98.56	4	0.68	3 min 25 sec
TA5	0.300	3.7	99.56	4	0.76	7 min 12 sec
TA6	0.309	3.8	99.45	5	0.83	8 min 12 sec
TA7	0.289	3.4	97.56	4	0.72	6 mins 18 sec
TA8	0.300	3.5	98.76	5	0.74	3 min 40 sec
TA9	0.299	3.8	96.56	4	0.69	1 min 33sec
TA10	0.245	3.7	97.78	5	0.58	1 min 18 sec
PL1	0.304	3.5	98.35	4	0.86	1 min5 secs
PL2	0.295	3.5	97.56	4	0.56	14 min 34sec
PL3	0.302	3.8	97.67	4	0.67	11 min45sec
PL4	0.30	3.6	99.87	5	0.78	3 min 56 sec
PL5	0.301	3.5	99.5	5	0.78	1 min 48 sec
PL6	0.299	3.7	98.66	5	0.65	1 mins 55 sec
BH1	0.304	3.4	97.76	5	0.67	10min 54 sec
BH2	0.289	3.8	98.78	5	0.79	8 min 10 sec
BH3	0.296	3.5	99..67	5	0.76	11min 25 sec
BH4	0.304	3.6	98.98	5	0.89	3 min 30 sec

Batch T1 was formulated using lactose as diluent along with starch as disintegrant and T2 was formulated using MCC as diluent along with starch as disintegrant showed release in 60 mins i.e 30.5 and 45.85 in 60 min and disintegration time 10 min 10 sec and 8 min 45 sec so the batch is discarded. Batch T3, PL1 and BH1 was formulated using starch as an disintegrant along with lactose and MCC as diluent showed release in 60 mins i.e 40.5 %, 42.35 %and 3% DT 6 min 21 sec, 1 min 5 sec and 10min 54 sec so batches were discarded. Batch TA4, TA 6, PL 2, PL3, BH 2, and BH3 72 was formulated using only crospovidone and SSG which showed DT 5 min 14 sec and 11min 12 sec, 14min 34 sec and 11min 45 sec, 12 min 54sec and, 8min 10 sec, drug release 54.34% and 60.45%, 50.45% and 40.5%, 60% and 48.4% with very less drug release in 60 min. TA 9, TA10, PL5 and PL6 was formulated using 5% Starch 1500 with different concentration of lactose and MCC showed burst release in 5mins i.e 88.1% and 90.45%, 84.1% and 93.45% and disintegration time 1 min 33 sec and 1 min 18sec, 1min 48 sec and 1 min 55 sec. In order to attain desired dissolution rate, DT batches – TA8, PL4 and BH4 were taken using 3% Starch 1500 showed disintegration time 3min 40 sec, 3 min 56 sec and 3 min 30 sec of which drug release was found to be 95%, 91.7 %and 94 % respectively. Batch TA 8, PL4 and BH4 was showing acceptable properties hence it was

considered as optimum batch and kept for accelerated stability studies for three months. (Table no.5,6 and Fig.no. 1-7)

Table no.6: Drug release studies of tablets

Formulations	% Cumulative release in 5 mins	% Cumulative release in 10 mins	% Cumulative release in 15 mins	% Cumulative release in 20 mins	% Cumulative release in 30 mins	% Cumulative release in 45 mins	% Cumulative release in 60 mins
TA1	4.67	10.23	10.4	4.67	10.23	10.4	4.67
TA2	10.67	17.76	16.8	10.67	17.76	16.8	10.67
TA3	13.5	20.65	23.4	13.5	20.65	23.4	13.5
TA 4	13.65	22.34	28.45	38.45	43.45	47.69	54.34
TA5	10.13	19.38	25.2	30.13	38.12	40.12	45.4
TA6	12.34	24	30	36.45	46.35	55.45	60.45
TA7	13.54	20	27	34	42.17	45.14	50.12
TA8	55	68	75.23	82	86	90	95
TA9	82.1	72	76	69.5	72.6	86	87
TA10	90.45	79.45	68.45	53.34	46.45	38.38	28.67
PL1	16.35	21.23	27.45	37.67	36.36	40.34	42.35
PL2	13.5	20	27.73	30.91	41.7	45.64	50.45
PL3	10.4	16.8	23.4	27.9	30.2	35.4	40.5
PL4	48.2	55.1	60.12	68.23	75.96	85.34	91.7
PL5	84.1	75	77	69.5	73.6	85	88
PL6	93.45	78.45	66.45	55.34	42.45	35.38	25.67
BH1	5	10	18	22	28	30	36
BH2	8	17	25	32	43	52	60
BH3	11.23	18.38	26.2	32.13	36.12	45.12	48.4
BH4	53	65.4	72.23	80	84	88	94

Fig. no 1: Drug Release of *Tabermontana alternifolia* tablets

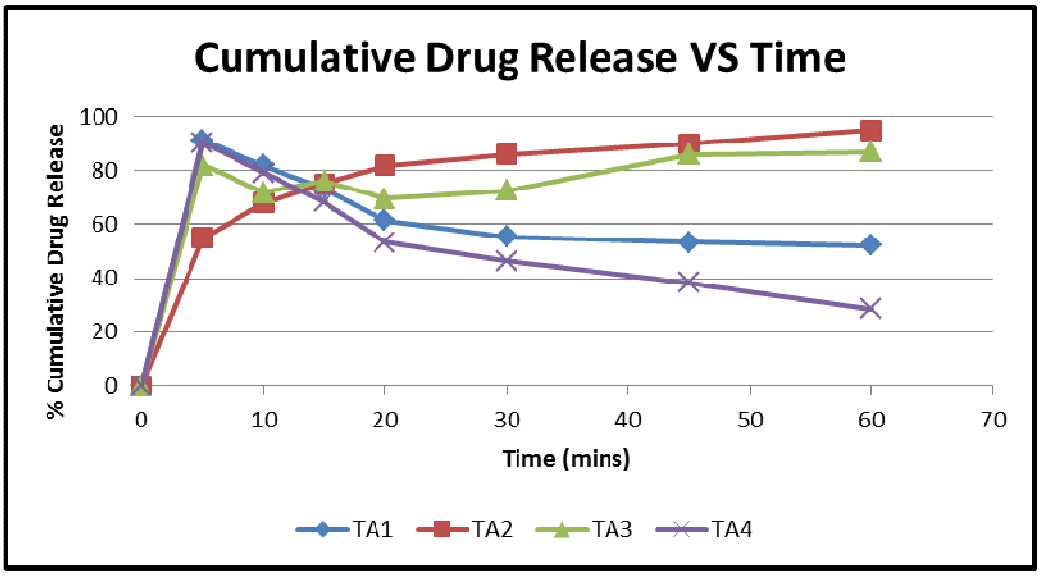


Fig. no. 2: Drug release of *Polyathia longifolia* tablets

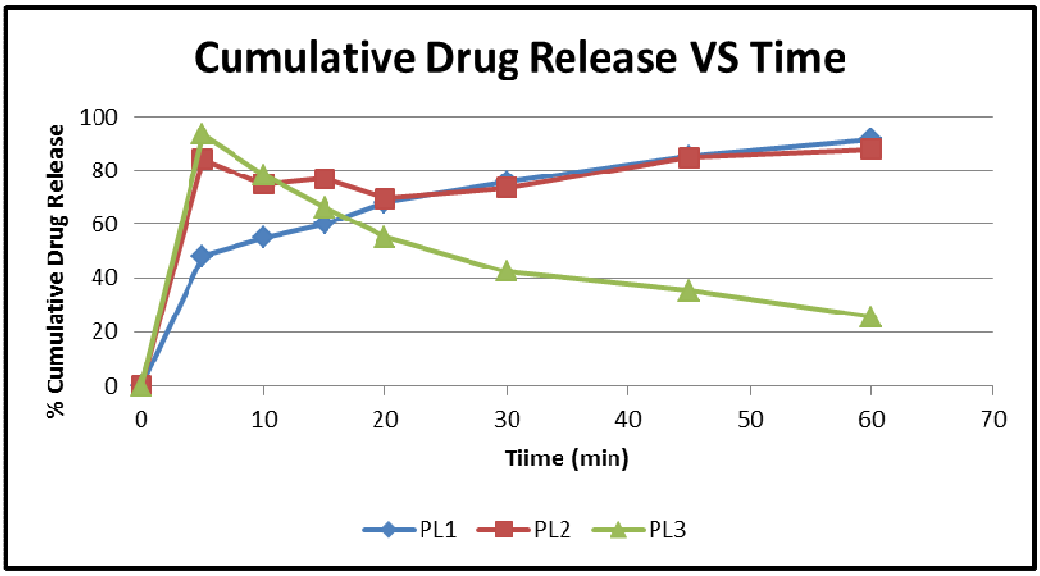


Figure no 3: Drug release of *Benincasa hispida* tablets

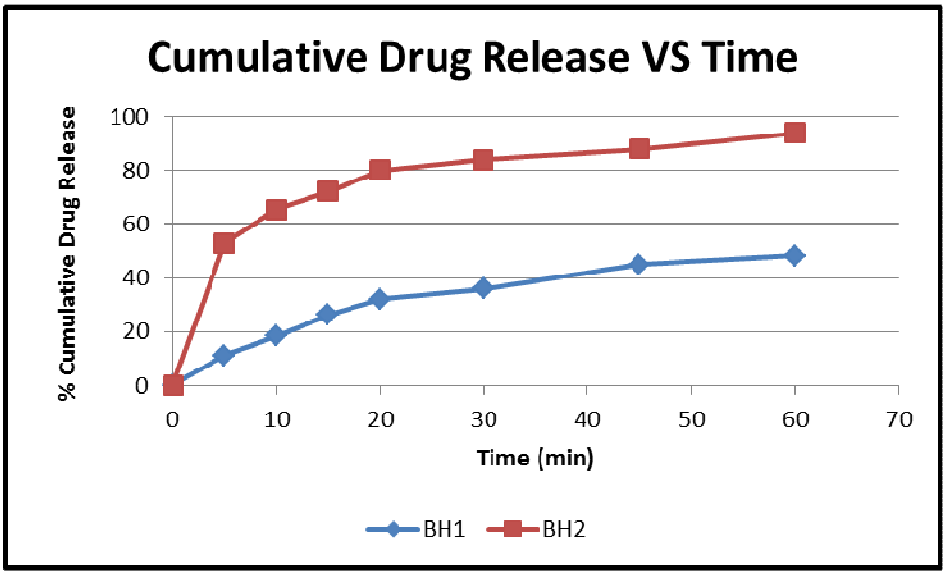


Fig.no. 4 : Cumulative drug release of *Tabermontana alternifolia* tablets

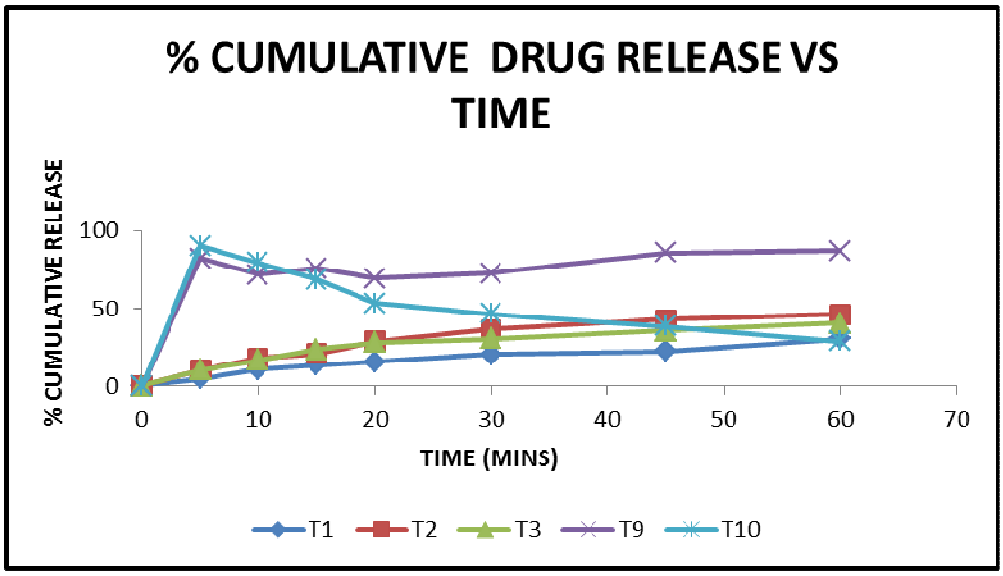


Fig.no.5: Cumulative drug release of *Tabermontana alternifolia* tablets

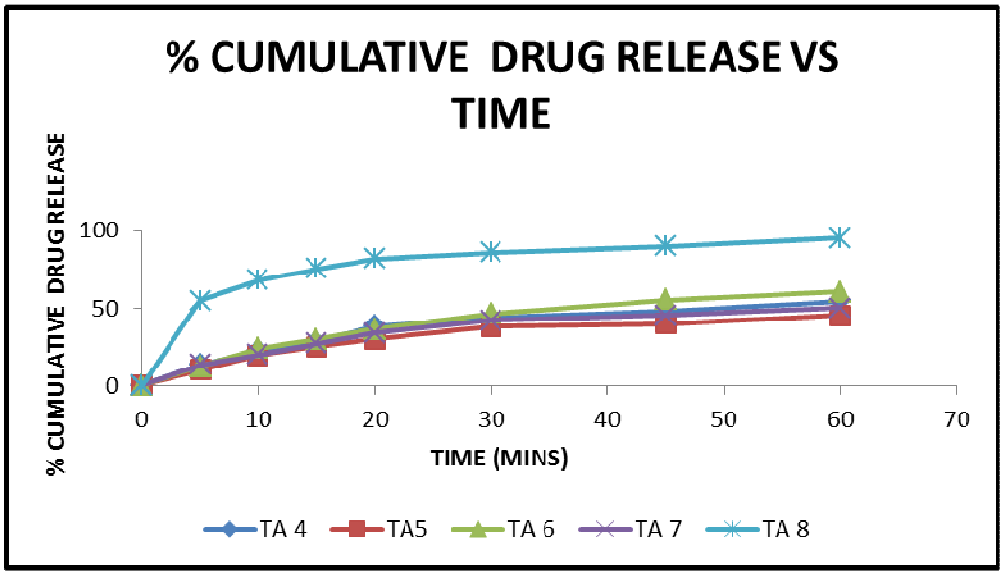


Fig.no.6: Cumulative drug release *of Polyalthia longifolia* tablets

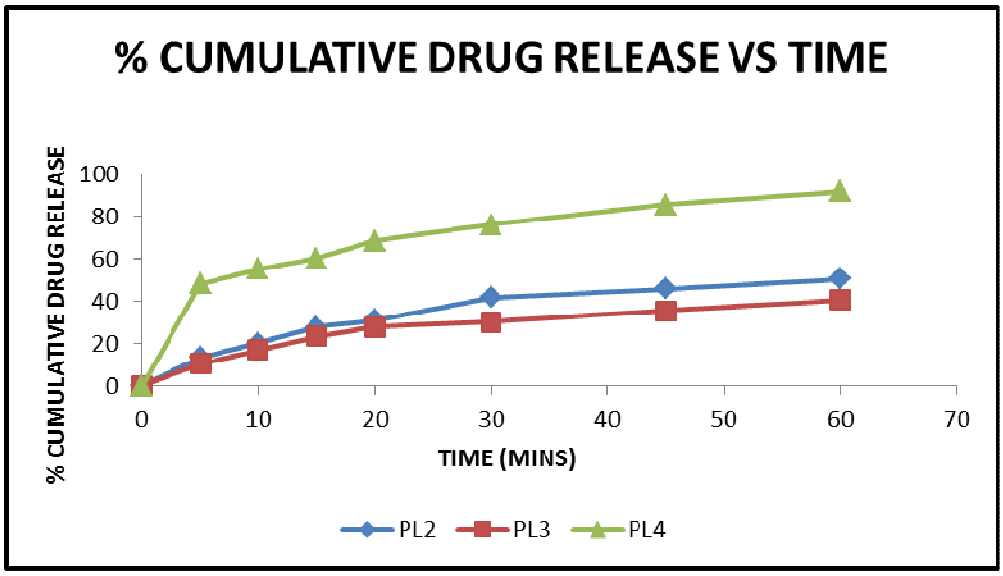
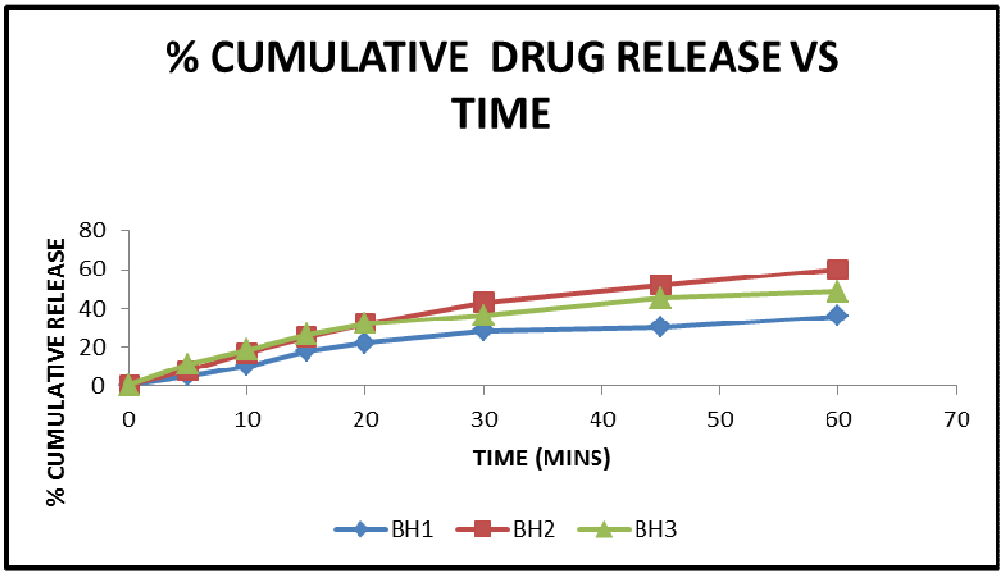


Fig.no.7: Cumulative drug release of *Benincasa hispida* tablets



In any rational design and evaluation of dosage forms, 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 conditions of temperature and humidity. However, the studies will take a longer time and hence it would be convenient to carry out the accelerated stability studies where the product is stored under exacerbated conditions of temperature tablets were evaluated for various physical parameters such as hardness and friability. Formulations were evaluated for disintegration time, assay and *in vitro* drug release. The optimized batch TA8,PL4 ad BH3 was subjected to stability study at 25°C/ 60% RH and 40°C/ 75% RH for three months.(Table no.7 and Fig.8-11).

Table no.7 Stability studies of tablets

Physical Parameter	Tablets	Batch no	0 day	15th day	30th day	60th day	90th day
Appearance	40°C/75% RH	BH3	+++	+++	+++	+++	+++
		Pl4	+++	+++	+++	+++	+++
		TG 8	+++	+++	+++	+++	+++
	25°C/60% RH	BH3	+++	+++	+++	+++	+++
		Pl4	+++	+++	+++	+++	+++
		TG 8	+++	+++	+++	+++	+++
Thickness (mm)	40°C/75% RH	BH3	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2
		Pl4	3.6 ± 2	3.6 ± 2	3.6 ± 2	3.6 ± 2	3.6 ± 2
		TG 8	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2
	25°C/60% RH	BH3	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2
		Pl4	3.6 ± 2	3.6 ± 2	3.6 ± 2	3.6 ± 2	3.6 ± 2
		TG 8	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2	3.5 ± 2
Hardness (Kg/cm2)	40°C/75% RH	BH3	5	4	5	4	5
		Pl4	5	4	5	4	5
		TG 8	5	4.5	4	4.5	5
	25°C/60% RH	BH3	5	4.5	5	4.5	5
		Pl4	5	4	4.5	4	5
		TG 8	5	5	4	4.5	5
Friability (%)	40°C/75% RH	BH3	0.74	0.75	0.78	0.81	0.85
		Pl4	0.78	0.79	0.82	0.84	0.86
		TG 8	0.76	0.78	0.83	0.85	0.87
	25°C/60% RH	BH3	0.74	0.75	0.72	0.75	0.76
		Pl4	0.78	0.79	0.75	0.72	0.8
		TG 8	0.76	0.78	0.8	0.74	0.78
Uniformity of weight (mg)	40°C/75% RH	BH3	300 ±10	300 ±10	300 ±10	300 ±10	300 ±10
		Pl4	302±10	302±10	302±10	302±10	302±10
		TG 8	304±10	304±10	304±10	304±10	304±10
	25°C/60% RH	BH3	300 ±10	300 ±10	300 ±10	300 ±10	300 ±10
		Pl4	302±10	302±10	302±10	302±10	302±10
		TG 8	304±10	304±10	304±10	304±10	304±10
Drug content (%)	40°C/75% RH	BH3	99.67	98.56	97.47	95.65	96.75
		Pl4	99.87	98.72	96.67	95.36	95.99
		TG 8	98.76	98.68	97.74	97.57	96.66
	25°C/60% RH	BH3	99.67	98.86	97.58	97.69	96.75
		Pl4	99.87	98.88	96.67	96.82	95.67
		TG 8	98.76	97.57	97.29	97.38	97.89
Disintegration time (mins)	40°C/75% RH	BH3	11min 25 sec	12 mins 30 sec	13 mins 12 secs	13 mins 40 secs	14 mins 10 sec
		Pl4	10 min 56 sec	11 mins 15 secs	11 mins 35 secs	12 mins 40 secs	13mins 13 secs
		TG 8	12 min 40 sec	13 min 25 sec	14 min 14 sec	14 min 40 sec	15min 12secs
	25°C/60% RH	BH3	11min 25 sec	12 mins 20 sec	13 mins 32 secs	13 mins 45 secs	14 mins 18 sec
		Pl4	10 min 56 sec	11 mins 8 secs	11 mins 30 secs	12 mins 45 secs	13mins 19 secs
		TG 8	12 min 40 sec	13 min 20 sec	14 min 12 sec	14 min 30 sec	15min 20secs

Fig.no.8: Cumulative drug release of *Benincasa hispida* tablets

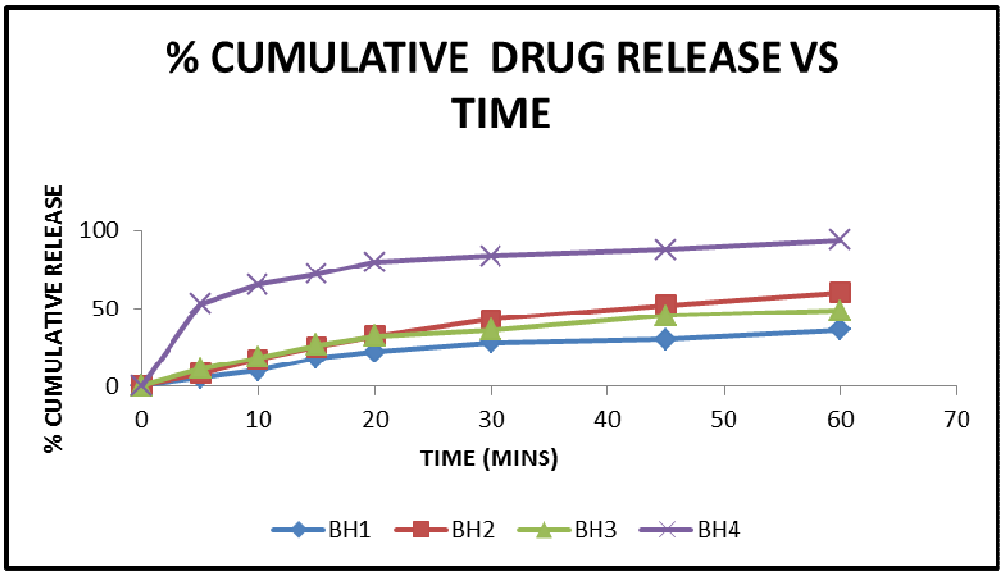


Fig.no. 9: Drug release from stability batch of *Benincasa hispida* at 40^{0}C/ 75% RH

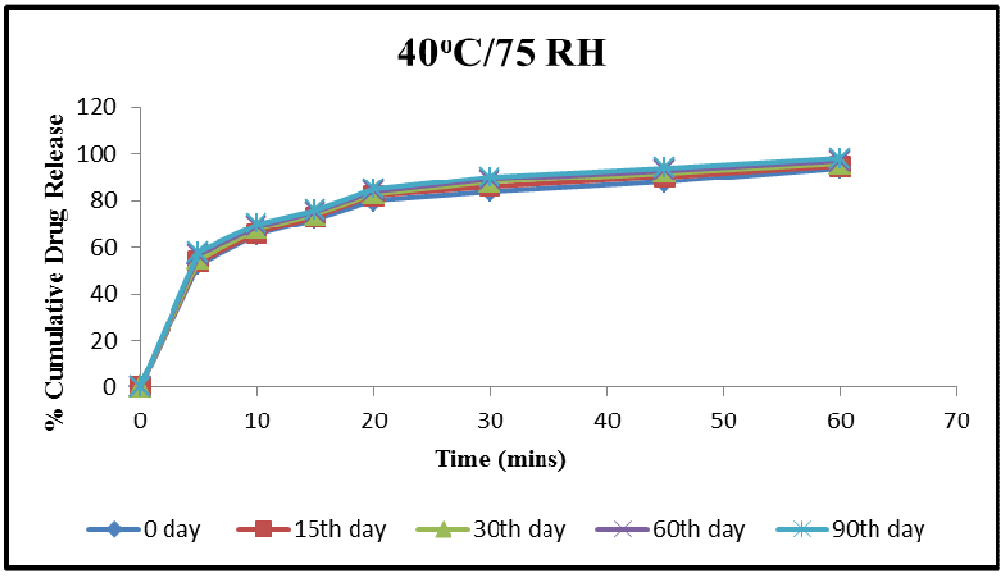


Fig.no.10: Drug release from stability batch of *Polyalthia longifolia* at 40^{0}C/ 75% RH

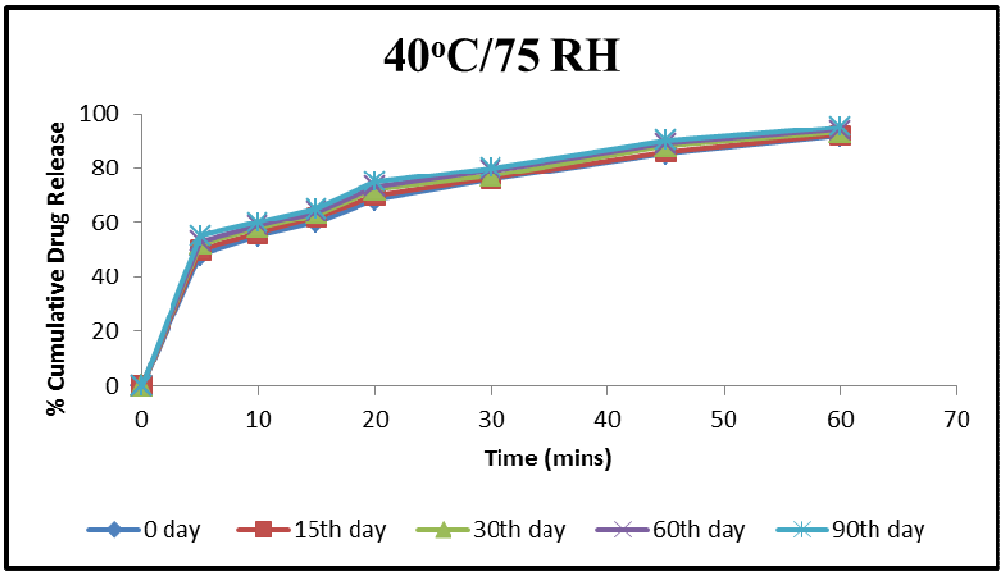
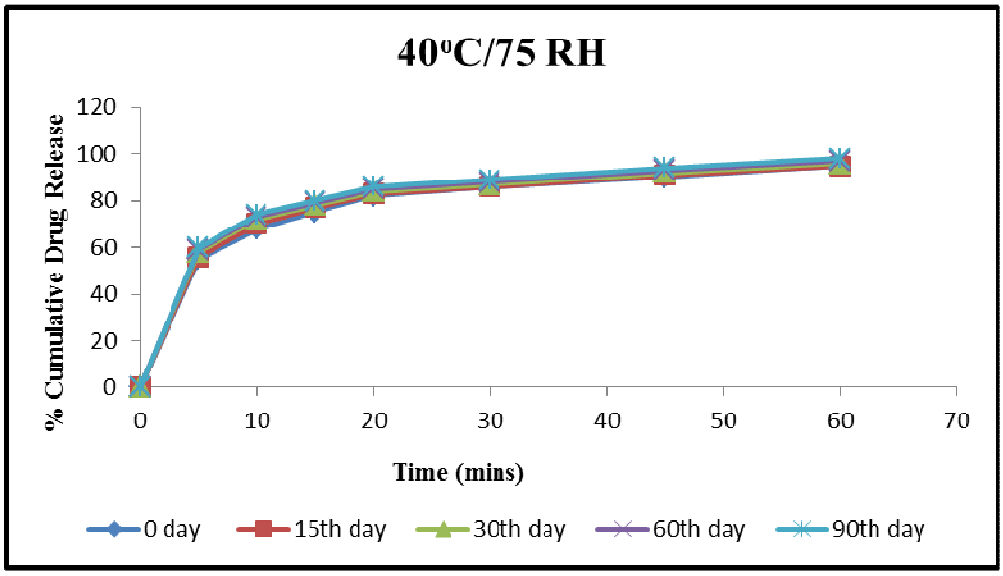


Fig.no.11.: Drug release from stability batch of *Tabermontana alternifolia* at 40^{0}C/ 75% RH



The physical parameters after 0 day, 15th, 30th, 60th and 90th day were as mentioned in table no.7**.** All the physical parameters were in the acceptable limits which showed that formulation was stable over the period of 90 days.The results of the physical parameters stability studies indicated that the IR tablet of *Benincasa hispida, Polyalthia longifolia and Tabermontana alternifolia* had reasonable stability. The stability studies of the optimized formulation (BH3, PL4, TA8) of Tablets revealed that:

1. There were no significant changes in the physical parameters when stored in accelerated temperature and humidity conditions hence no special storage conditions are required.
2. No significant reduction in the content of the active drug was observed over a period of three months. This indicated that the drug is stable in presence of excipients at elevated temperature and humidity conditions.
3. The optimized formulation did not show any significant change in the drug release profile.

It was observed that Hixson Crowel Cube Root Law was the dissolution model followed by the optimum batch PL4 and Korsmeyer- Peppas dissolution model was followed by BH4 and TA 8.(Table no.8)

Table no. 8: Drug release kinetics studies

Formulation	Zero order	First order	Hixson Crowel	Korsmeyer- Peppas	Higuchi model
BH4	0.7544	0.445	0.94	0.9677	0.8486
PL4	0.8382	0.325	0.9963	0.9894	0.9249
TA8	0.7349	0.287	0.9356	0.9604	0.8324

CONCLUSION

Thus, the formulation developed from *Benincasa hispida*, *Polyalthia longifolia and Tabermontana alternifolia* had reasonable stability and may be further be studied in details to prove its market utility.

Acknowledgement
We would like to acknowledge the college Management and Principal, Dr. Supriya Shidhaye who provided us all the facilities to carry out the research work.

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