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Formulation and Estimation of Floating Tablets of *Eclipta alba* Extract

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ABSTRACT

Eclipta alba Hassk. (Bhringaraja, Fam: Compositae) is a perennial shrub which grows widely in moist tropical countries. Different uses have been reported for this shrub. It is used as anthelmintic, expectorant, antipyretic, antiasthmatic, tonic, deobstruent in hepatic and spleen enlargement, in skin diseases and as a substitute for Taraxacum (a popular liver tonic). It has been reported to be useful in liver ailments and has been shown to possess hepatoprotective activity against carbon- tetrachloride induced liver cell damage in animals. The aim of the present study was to design and estimate gastro retentive floating tablet of selected hepato-protective herbal drugs to increase the efficacy and stability of the drug. The floating tablet of extract of *Eclipta alba* was prepared by using kollidon SR as floating and release retarding polymer. The effect of various additive excipient was also studied to alter the floating behaviour and drug release from the floating tablet.

Keywords: GRDDS, floating tablet, *Eclipta alba*, Hepatoprotective.

INTRODUCTION

Herbal medicine also called botanical medicine or phytomedicine refers to using a plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Herbalism has a long tradition of use outside of conventional medicine. Its use is becoming more prominent in treating and preventing disease as there are improvements in analysis and quality control along with advances in clinical research, which shows the value of herbal medicine[1]. The liver is the most important organ in the body. It plays a pivotal role in regulating various physiological processes. It is also involved in several vital functions, such as metabolism, secretion and storage. It has great capacity to detoxicate toxic substances and synthesize useful principles. It helps in the maintenance, performance and regulating homeostasis of the body. It is involved with almost all the biochemical pathways to growth, fight against disease,

nutrient supply, energy provision and reproduction[2]. In addition, it aids metabolism of carbohydrate, protein and fat, detoxification, secretion of bile and storage of vitamins. The role played by this organ in the removal of substances from the portal circulation makes it susceptible to first and persistent attack by offending foreign compounds, culminating in liver dysfunction. Liver diseases remain one of the major threats to public health and are a worldwide problem. They are mainly caused by chemicals like acetaminophen (in large doses), excess consumption of alcohol, infections and autoimmune disorders. Most of the hepatotoxic chemicals damage liver cells mainly by inducing lipid peroxidation and other oxidative damages[3]. Acetaminophen, an analgesic and antipyretic drug, developed in the last century, causes serious liver necrosis in humans and in experimental animals if taken in large doses[4-7]. While alcohol is one of the main causes of end stage liver disease worldwide, alcoholic liver disease is the second most common reason for liver transplantation in the United States[8]. Due to increased frequency of drinking and change of diet construction, such as the increase of fat content, the incidence of liver diseases has increased in China, becoming another important risk factor for morbidity and mortality in addition to viral hepatitis.

A large number of plants and formulations have been claimed to have hepatoprotective activity. Nearly 160 phytoconstituents from 101 plants have been claimed to possess liver protecting activity[9]. In India, more than 87 plants are used in 33 patented and proprietary multi-ingredient plant formulations[10]. Inspite of the tremendous advances, no significant and safe hepatoprotective agents are available in modern therapeutics. Therefore, due importance has been given globally to develop plant-based hepato-protective drugs effective against a variety of liver disorders[10].

Rapid gastrointestinal transit can prevent complete drug release in the absorption zone and reduce the efficacy of administered dose since the majority of drugs are absorbed in stomach or the upper part of small intestine. Dosage forms that can be retained in the stomach are called gastroretentive drug delivery systems (GRDDS). GRDDS can improve the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site thus ensuring its optimal bioavailability[11].

Eclipta alba Hassk. (Bhringaraja, Fam: Compositae) is a perrenial shrub which grows widely in moist tropical countries. Different uses have been reported for this shrub. It is used as anthelmintic, expectorant, antipyretic, antiasthmatic, tonic, deobstruent in hepatic and spleen enlargement, in skin diseases and as a substitute for Taraxacum (a popular liver tonic)[12]. It has been reported to be useful in liver ailments and has been shown to possess hepatoprotective activity against carbon- tetrachloride induced liver cell damage in animals[6].

The aim of the present investigation was to design and evaluate gastro retentive floating tablet of selected hepato-protective herbal drugs to increase the efficacy and stability of the drug.

MATERIALS AND METHODS

Selected Plant

Eclipta alba

Polymers used in GRDDS

Kollidon SR
Stearic Acid
Lactose
Dicalcium phosphate (DCP)
Cetostearyl alcohol

Instruments and equipments

UV/Vis
Double Beam Spectrophotometer
Analytical Balance
Rotary Tablet Machine
Dissolution Test Apparatus
Modified Beaker Apparatus
Monsanto Hardness Tester
Roche Friabilator
Rota Sieve Shaker

METHODOLOGY

Extraction of powdered plant

The coarsely powdered drug was extracted with 50% ethanol [12]by cold maceration (I.P. 1985). The solvent was removed at low temperature & reduced pressure and extract was stored in a refrigerator. The dried mass of the extract was stored air tight container.

Analytical method development

It is very important to establish a accurate and reproducible method development to estimate the drug release of the extract. Hence estimation of extract was developed using UV Spectroscopic method.

λ Max determination by uv spectrum

Accurately weighed dry extract of drug equivalent to 100 mg was dissolved in 100ml solvent and prepared 1000 mcg/ml stock solutions. And from that 10 mcg/ml solution was scanned from 200 to 400 nm by using UV spectroscopic method.

Preparation of calibration curve of drug extract by using uv spectroscopic method

Accurately weigh amount was dissolved in solvent and prepare 1000 mcg/ml solution as stock solution. Further dilutions were made in the range of 0, 25, 50, 100, 200, 300 and 400 mcg/ml solutions and scanned for absorbance at 207 nm by using UV spectroscopic method. By using Microsoft excel calibration curve was developed. The absorbance of solutions was measured against blank. Then plotted absorbance versus concentration and further regression analysis carried out.

Estimation of active in the extract by HPLC

Standard preparation

Weight accurately 3.0 mg reference standard and transfer it in to the eppendroff tube and make stock solution with suitable diluents , from the stock solution prepare the linearity solution 10 ppm, 20 ppm, 30 ppm, 40 ppm and 50 ppm with suitable diluents.

Sample preparation

Weight accurately 5 gm herbal extract and transfer it in to the 100 ml volumetric flask make the volume with suitable diluents.

Diluents

0.5 % Acetic acid : Methanol (45:55 v/v)

Chromatographic parameter

Column	:	Kromasil C18 (250 x 4.6 mm) 5µ
Mobile phase	:	0.5 % Acetic acid: Methanol (45:55 v/v)
Retention time	:	About 16 min
Run time	:	25 min
Wavelength	:	254 nm
Column Temperature	:	25°C
Injection Volume	:	20 µl

Formulation studies

For the present investigation, 100 mg dose of dried *Eclipta alba* extract was selected for the formulation of the tablet. To select the amount of kollidon SR, three batches were prepared consisting of drug to kollidon SR ratio of 1:1, 1:2, and 1:3.

The influences of various excipients were studied and the compositions of the batches are given in the Table 1.

The calculated amount of stearic acid and lactose were mixed homogenously and heated to 75^0 C i.e. above the melting point of stearic acid. The mixture was cooled to room temperature and passed through 30 # seive. Each tablet containing the 100 mg powdered extract of *Eclipta alba* and the excipients were punched in the rotary tablet press by direct compression using 10 mm flat punches with the hardness of not more than 3.5 and not less than 3.0.

Stability study of tablets of promising batch

This is a requirement in most of the countries and is stipulated by the regulatory agencies of those countries. These studies would very quickly identify the need, if any, to stabilize the active substance or the formulation, and save invaluable time and effort from being spend on an unmarketable formulation. With the recent trend towards globalization of manufacturing operation, it is imperative that the final product be sufficiently rugged for marketing worldwide under various climatic conditions including tropical, subtropical and temperate. In order to determine the change in performance of dosage form on storage, stability study of optimised batch was carried out at 40°C in a humidity jar having 75 % RH according to ICH. Samples were withdrawn after three month and evaluated for change in buoyancy characteristics and drug release pattern. The similarity factor (f_2) was applied to study the effect of storage on batch S6. Batch S6 evaluated for the floating lag time, total floating time.

RESULTS AND DISCUSSIONS

Analytical method development

An accurate and reproducible analytical method development is very important to evaluate the performance of the formulation. Hence for extract of *Eclipta alba* reliable and accurate method was developed by using UV spectroscopic method.

Determination λ max by uv spectrum and preparation of standard curve

To reduce the complexity in estimating the drug release from the dosage foam standard curve of extract was prepared rather then to find concentration of active in the release extract. As described in the methodology section drug extract λ max was determined as 207 nm by using UV spectroscopic method as depicted in Figure 1. The R^2 value of 0.999 indicated good correlation between absorbance and concentration of the extract.

Estimation of active in the extract by HPLC

Chromatogram obtained from HPLC analysis is shown in Figure 3 and data for the potency of herbal extract is shown in Table 2. From the above HPLC analysis for the herbal extract wedelolactone was found to be 3.923 % w/w.

Formulation study

All the preliminary batches for the selection of ratio of kollidon SR floated without any lagtime and remained floated till the end off dissolution as batch P_3 exhibited. Significant decrease in the drug release, 1:3 drug to polymer ratio was selected for further study to investigate effect of other additives on drug release and floating behaviour of dosage form.

Physicochemical properties of various formulations of S batches are shown in Table 4. Comparative dissolution profile for S batches are shown in Figure 5 and Table 5. From the above dissolution profile it can be observed that PEG 6000 (S5 batch) exhibited maximum.

Release from the kollidon SR matrix. It may be due to high solubility and hydrophilicity of PEG 6000. Lactose and aerosol also exhibited faster release in case S1, S2 and S3, S4 respectively. It may be due to soluble characteristic of lactose leading to channel formation while in case of aerosil,

tablet displayed surface erosion leading to the drug release. Aerosil being fluffy and hydrophilic in nature may also contribute to the increase drug release from the tablet. Batch S6 containing dicalcium phosphate as added excipient is insoluble and therefore resist the drug release from the tablet. Batch S7 and S8 containing stearic acid and cetostearyl alcohol respectively shows the slower drug release because of the lipophilicity. Cetostearyl alcohol suppresses the drug release more than that of stearic acid due to its sticky nature. Aerosil when added in combination with the cetostearyl alcohol retards the overall drug release which may be due to adherence of aerosil particle on to the fatty excipients. The tablets of the all the batches floated from initial time to till the end of the dissolution except batch S6 which sink at the bottom of the dissolution jar. Hence DCP was discarded from the further study due to its high density.

From this study it was decided to select lactose and stearic acid as an added excipients in the kollidon SR tablet of *Eclipta alba* to control the extract release from the floating tablet of *Eclipta alba.*

STABILITY STUDY

Figure 6 Shows the drug release data after 3 month of stability studies. The value of dissimilarity factor (f_1) was found to be 3.71 and similarity factor (f_2) was found to be 80.33 for dissolution profile of tablets after three month of storage compared with the dissolution profile of freshly prepared formulation. The tablets had no floating lag time and total floating time obtained was more than 12 hr which indicated no change in buoyancy characteristic upon storage.

CONCLUSION

Floating extended release formulation of the herbal extract like *Eclipta alba* is need of the day so as to control the extract release thereby improving the therapeutic effect specifically for the hepatic disorders. Kollidon SR was successfully employed as a floating and extended release polymer in the drug to polymer ratio of 1:3 to extend the release of extract of *Eclipta alba.* From the various excipient added in the formulation it was found that combination of lactose and stearic acid give desire drug release as well as floating time with zero lag time.

Floating time of this tablet was found to be sensitive to compression force and hardness. Hardness of the tablet more than four adversely effected the floating ability of the extract of *Eclipta alba* tablet.

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Table 1. Composition of batches to investigate the influence of excipients

Ingredients	S1	S2	S3	S4	S5	S6	S7	S8	S9
Eclipta alba Extract	100	100	100	100	100	100	100	100	100
Kollidon SR	260	240	260	240	260	260	260	260	240
PEG 6000					40				
Lactose	40	60							
Aerosil			40	60					30
Di-calcium Phosphate						40			
Stearic acid							40		
Cetostearyl alcohol								40	30

Table 2. Data for the potency of herbal extract

Conc. in mcg/ml	Area
0	0
10	67131
20	144780
30	226348
40	327273
50	444227
Extract	326970

Table 3. Data for P1, P2 and P3 dissolution profile

Time (hr)	P1	P2	P3
0	0.00	0.00	0.00
0.5	42.56	26.33	21.28
1	64.36	39.67	27.36
2	69.62	46.82	32.25
3	78.45	57.30	37.68
4	90.47	70.14	45.51
6	99.65	89.65	58.64
8		99.35	66.13
12			79.57

Table 4. Physicochemical properties of various formulation of S batches

Batches	Hardness Kg/cm2 (n=3)	% Friability	Average Weight of tablet(n=20)	% extract per tablet
S1	3.2±0.4	0.39	382	96.88±0.12
S2	3.8±0.9	0.56	388	97.13±0.31
S3	4.1±0.6	0.41	401	100.2±0.22
S4	3.8±0.2	0.78	410	102.73±0.62
S5	4.2±0.9	0.64	411	103.33±0.46
S6	5.6±0.9	0.25	392	98.01±0.49
S7	3.3±0.7	0.37	395	97.91±0.49
S8	3.5±0.1	0.46	415	99.45±0.54
S9	3.3±0.4	0.39	412	98.65±0.87

Table 5. Comparative dissolution profile of S batches

Time (hr)	S1	S2	S3	S4	S5	S6	S7	S8	S9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
0.5	20.24	22.41	17.22	18.24	26.55	13.98	13.98	14.12	16.72
1	28.40	29.07	23.04	27.24	40.69	20.19	15.54	16.70	20.96
2	31.86	36.00	31.25	39.83	56.23	23.31	17.18	18.11	22.26
3	39.07	44.60	41.89	48.58	64.60	27.77	19.30	19.28	24.01
4	52.00	55.86	47.06	61.30	75.28	35.19	23.25	21.32	27.37
6	70.77	79.02	60.61	72.68	92.49	45.17	30.20	26.04	34.62
8	81.87	91.35	70.88	82.35		52.51	38.40	34.65	39.40
12	100.74		86.49	92.04		66.20	51.11	45.85	51.07

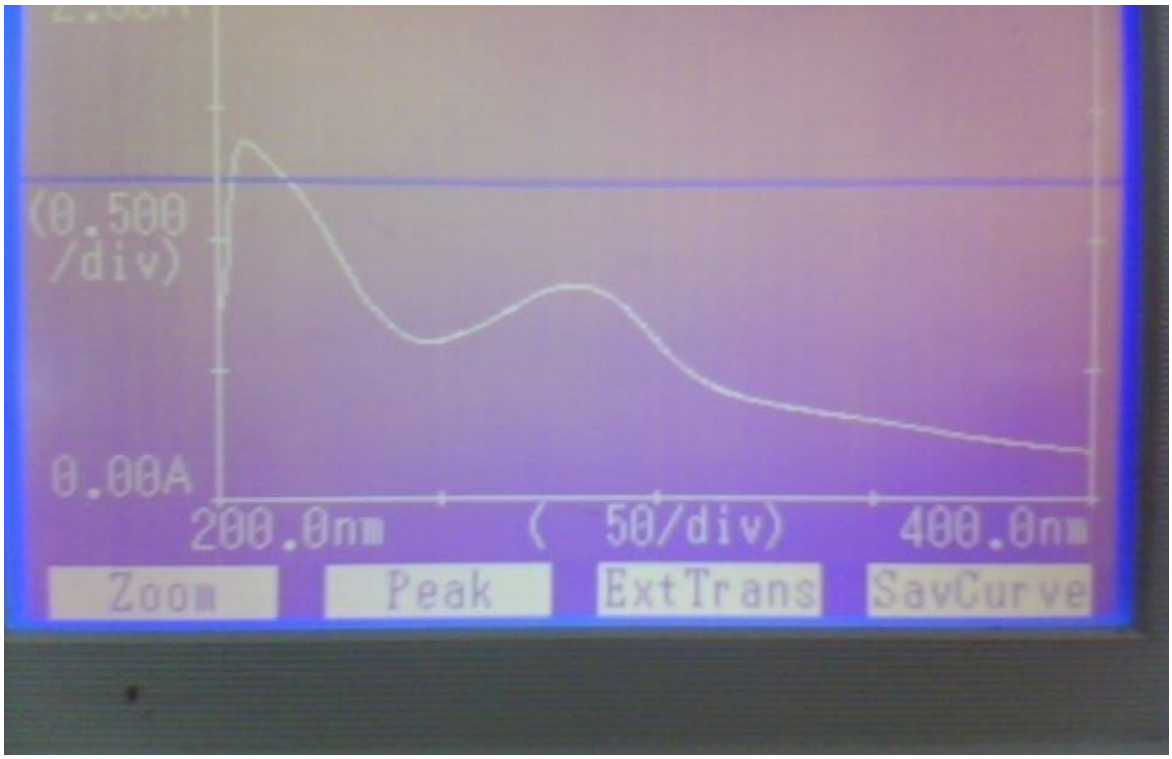

Figure 1. UV spectrum of *Eclipta alba*

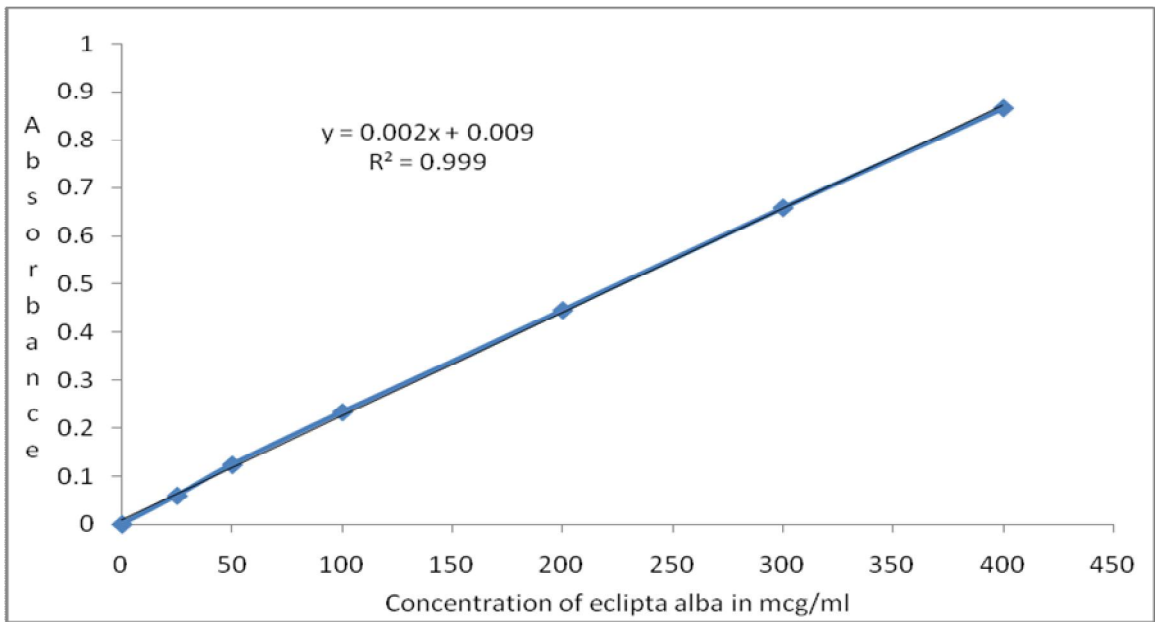

Figure 2. Calibration curve of *Eclipta alba* at 207 nm

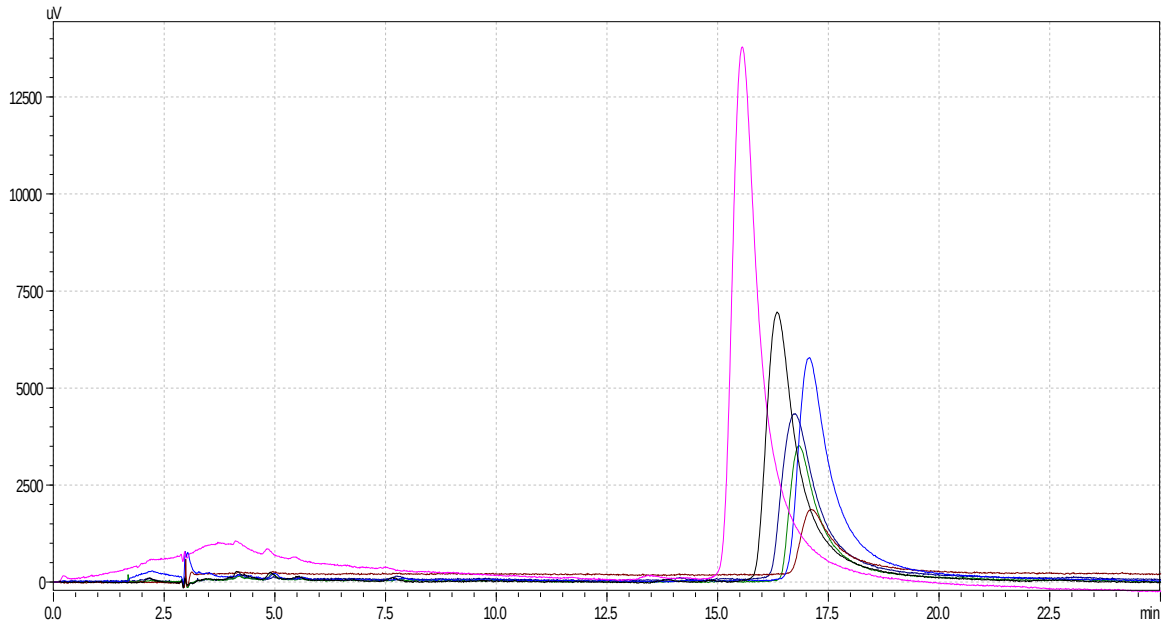

Figure 3. Overlay peaks from HPLC

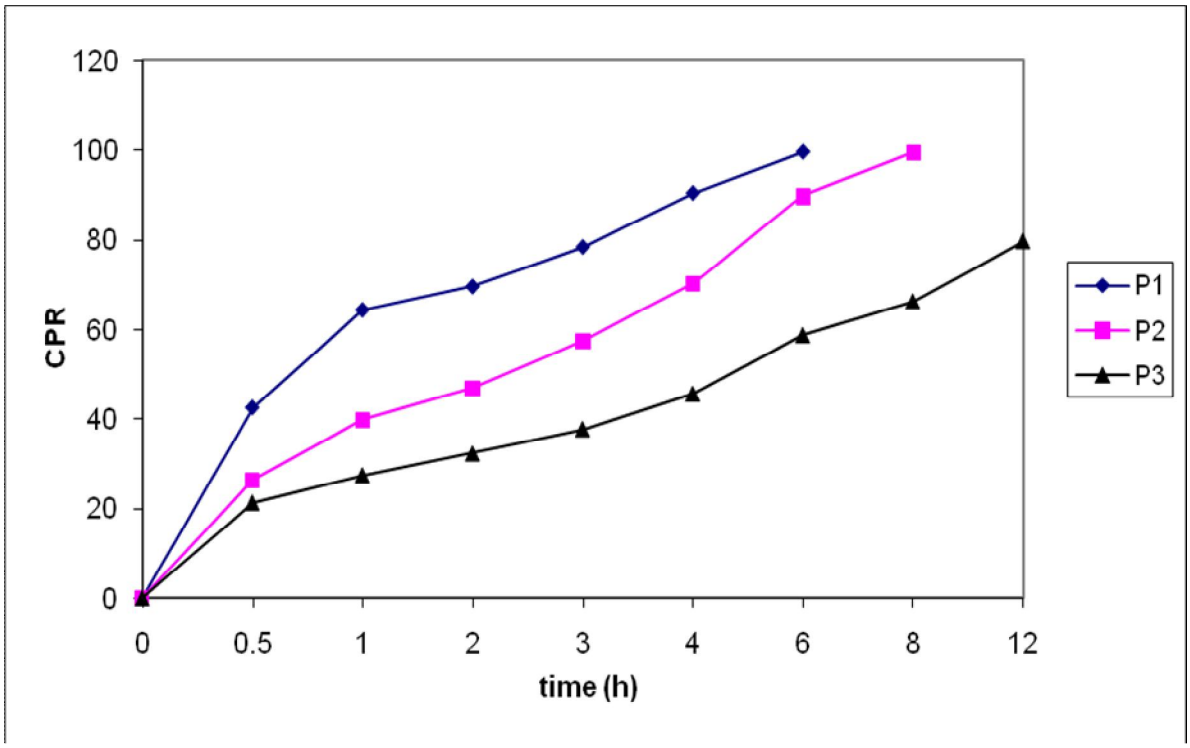

Figure 4. Comparative dissolution profile P1, P2 and P3

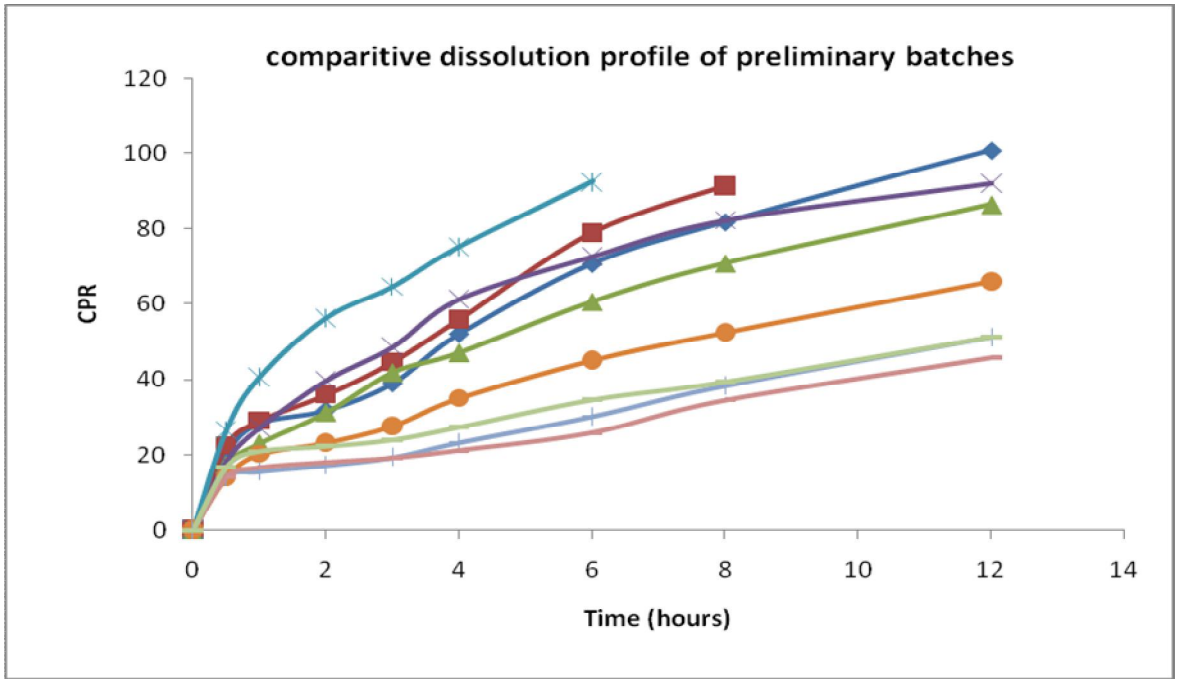

Figure 5. Comparative dissolution profiles of *Eclipta alba* formulation batches

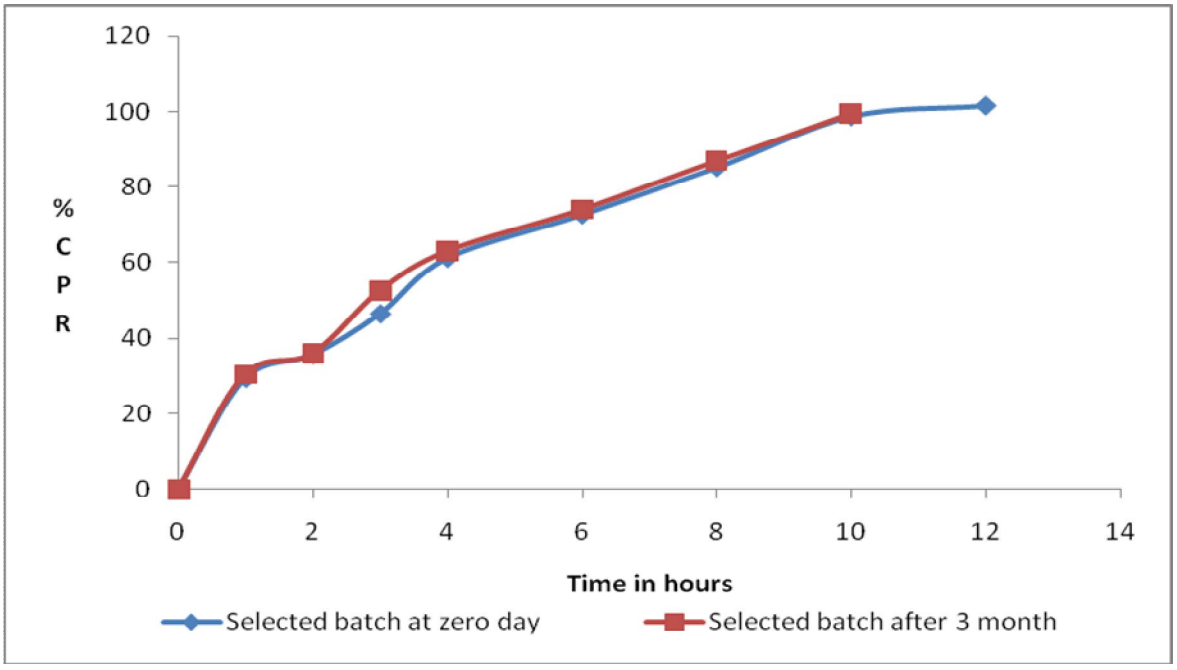

Figure 6. Drug release data after 3 month stability study