

Preparation and Characterization of Green Tea & Brahmi RSM Based Bilayer Tablet Formulation for Treatment of CNS Improvement

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Abstract: Most of the ayurvedic medicines are in the form of powder and they may have some kind of unacceptable or bitter taste and have problem of patient compliance. Medicines in powder form have problem of administration of accurate dose with due to their fine particulate nature. These Ayurvedic powders are taken with water for administration and chances of spoilage and waste are more for using powder formulation especially bulk powder. The botanical name of Brahmi: *Bacopa monnieri* (Family- Plantaginaceae) & The botanical name Green tea: *Camellia sinensis* (Family- Theaceae) powder- (wtf 10.0.1) RSM made a bilayer tablet by the direct compression method. Brahmi is derived from word "Brama", the mythical creator in the Hindu pantheon. Or other hand, Brahmi is derived from word 'Brahman', the diety responsible for creation of universe. In mythology, Goddess Saraswati takes Brahmi in deity for learning. This is because the herd is useful in improving learning skills & intelligence. Micromeritic properties are within desired range. F9 formulation is the best batch among total 9 batches and the cumulative % drug release of F9 is tends to 99%.

Keyword: Green tea, Brahmi, MCC, PVP, Response surface methodology.

1. INTRODUCTION

Now a day most of the human diseases are cured by the plant extract or formulated crude drug, as the crude drug contains the active constituent in pure and original form. It may produce better pharmacological action with minimum toxic manifestation or side-effect. Obesity, diabetes and arthritis problem are national problem or major problem of human kind in India or 3rd world country. This can be treated or well manage by applying various herbal drug. For this reason my choice of herbal are Brahmi and green tea for managing to some extant problem mentioned above. Most of the ayurvedic medicines are in the form of powder and they may have some kind of unacceptable or bitter taste and have problem of patient compliance. Medicines in powder form have problem of administration of accurate dose with due to their fine particulate nature. These Ayurvedic powders are taken with water for administration and chances of spoilage and waste are more for using powder formulation especially bulk powder. So to avoid the drug adherence issue, carrying drug, bitter taste and various other disadvantages which arise due to powder nature of ayurvedic formulation, there is a need to convert these powders formulations into suitable modern dosage form. Active constituent present in those drug are normally use for releasing the anxiety which is the main reason for obesity and diabetes associated with the obesity. The botanical name of Brahmi: *Bacopa monnieri* (Family- Plantaginaceae) & The botanical name Green tea: *Camellia sinensis* (Family- Theaceae) powder made a bilayer tablet by the direct compression method. Brahmi is derived from word "Brahma", the mythical creator in the Hindu pantheon. Or other hand, Brahmi is derived from word 'Brahman', the diety responsible for creation

of universe. In mythology, Goddess Saraswati takes Brahmi in deity for learning. This is because the herd is useful in improving learning skills & intelligence. The history of human civilization, man has selected three important non-alcoholic beverages from nature's resources, namely tea, coffee & cocoa. Among these, tea is the most widely consumed beverage. It is consumed by half of the World's population for its attractive aroma, taste & health benefits. It is a safe & easily affordable drink for all sections of society throughout the World & there is considerable evidence that consumption of tea is one of the most important ways to prevent a number of human ailments. Scientific research has validated the positive effects of tea on health, especially green tea, & shifted its reputation from being "the cup that cheers" to "the cup that heals". Widely accepted, custom size, shape and appearance, lower the cost and deliver the large amount of dose. Tablets are more suitable formulation.

2. MATERIAL USED:

Table 1. MATERIAL USED

SL NO	INGREDIENTS	COMPANY NAME(SUPPLIER)
1	Brahmi	HER-BALL HILLS ISHA AGRO DEVELOPERS PVT.LTD
2	Green tea	HEAP -WILL JAPANESE MATCHA TEA
3	Microcrystalline cellulose	LOBA CHEMIC PVT.LTD
4	Hydroxy Propyl Methyl Cellulose	CIPT & AHS
5	Hydrochloric acid	RANKEM, RFCL LIMITED
6	Polyvinylpyrrolidone	CIPT & AHS
7	Magnesium Stearate	CIPT & AHS

- 1. Preparations** The formulations were done by applying Wet granulation technique under the guidance of my respected sir Dr. Rabindranath pal.
- 2. Experimental Design** The optimization of bilayer tablets was done by using Central composite Design (center point 3), [lack of fit 0], DESIGN EXPERT SOFTWARE BY STAT EASE (**Design Expert® Software WTF (Windows trial file) 7.0 trial version**). **Table 2**

Table 2. formulation table

		Factor 1	Factor 2	Response 1	Response 2
Std	Run	A:MCC	B:PVP	Drug Release	Entrapment
		mg	mg	%	%
7	1	600	2	91	50
2	2	900	2	86	55
6	3	900	2.5	92	65.36
3	4	300	3	93	71.34
1	5	300	2	93.5	40.25
5	6	300	2.5	96	60.24
8	7	600	3	95.7	53.28
4	8	900	3	97.35	68.31
9	9	600	2.5	99	76.23

Design-Expert® Software
 Trial Version
 Factor Coding: Actual

Drug Release (%)
 ● Design Points
 86 99

X1 = A: MCC
 X2 = B: PVP

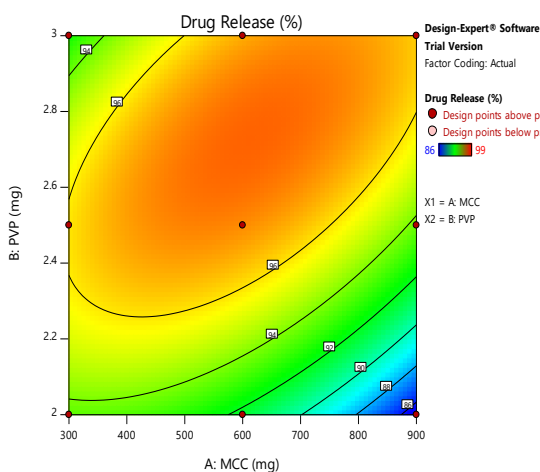


Fig. 1.1. Contor diagram of %dee

Design-Expert® Software
 Trial Version
 Factor Coding: Actual

Drug Release (%)
 ● Design points above predicted value
 ○ Design points below predicted value
 86 99

X1 = A: MCC
 X2 = B: PVP

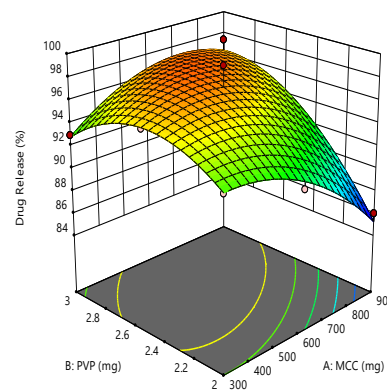


Fig. 1.2. 3d plot of %dee

Fig. 1. Drug release pattern of MCC and PVP

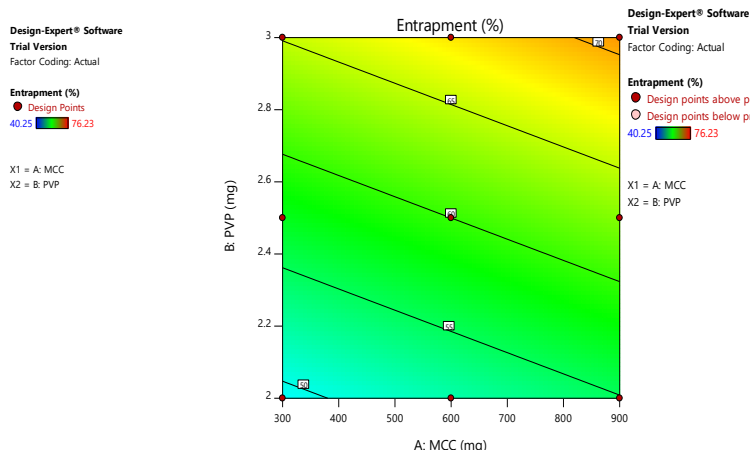


Fig. 2.1. Contor diagram of % cdr

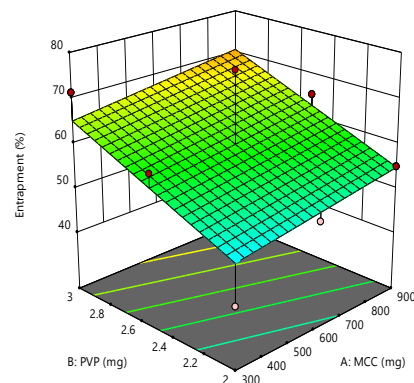


Fig. 2.2. 3d plot of % cdr

Fig. 2. Entrapment Efficiency of MCC and PVP

3. PREFORMULATION STUDY:

3.1 Angle of Repose: Angle of repose of granules was measured by fixed funnel standing method. The accurately weighed granules were taken in a funnel, the height of the funnel was adjusted in such a way that the tip of the funnel just touch the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured. Angle of repose was calculated using the following equation-

$$\text{Eq.(1). } \theta = \tan^{-1}h/r$$

- 1) θ = angle of repose
- 2) r = the radius of the base the pile
- 3) h = height of the pile

3.2 Bulk density of powder blend: Both loose bulk density (LBD) and tapped density (TBD) were determined. A quantity of 2gm of powder from each trial formulation, previously lightly shaken to break any agglomerates formed, was introduced into a 10ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5cm at 2second intervals. The tapping was continued until no further change in volume was noted. LBD and TBD were calculated using the following formulas-

$$\text{Eq.(2). TBD} = \frac{\text{weight of the powder}}{\text{volume of the packing}}$$

$$\text{Eq.(3). LBD} = \frac{\text{weight of the powder}}{\text{volume of the packing}}$$

3.3 Carr's Index Of Powder: Compressibility index is an indication of the Carr's index of a powder. It is calculated by the formula, Where is the freely settled volume of a given mass of powder, and VT is the tapped volume of the same mass of

powder. The Carr's index is frequently used in pharmaceuticals as an indication of the flow ability of a powder. A Carr's index greater than 25 is considered to be an indication of poor flow ability and below 15, of good flow ability. But Carr's index 20-40 shows reasonable flow property.

$$\text{Eq.(4). Carr's index (\%)} = [(1-VT/VB) \times 100]$$

$$\text{Eq.(5). Carr's index (\%)} = [(1-\rho B/\rho T) \times 100]$$

Where ρB is loose bulk density ρT is tapped bulk density.

3.4 Hausner Ratio Of Powder Blend: Hausner ratio was determined by using the ρB is loose bulk density and ρT is tapped bulk density. Hausner ratio is greater than 1.25 is considered to be an indication of poor flow ability.

$$\text{Eq.(6). Hausner ratio} = \rho T / \rho B$$

3.5 Tablet Thickness: The thickness of tablet was measured by using screw gauge. The thickness variation should be within $\pm 5\%$ limit.

3.6 Tablet Hardness: In this experiment Monsanto hardness tester determined hardness of tablets. It has a graduated scale, which gives the reading in kg/sq cm. the tablet to be tested was placed between the spindle and anvil. The desired pressure needed to hold the tablet in position moved so that the indicator was fixed zero. The pressure was then applied till the tablet broken. The reading was noted, which indicate the pressure which was needed to break the tablet.

3.7 Measurement Of Tablet Friability: The friability of tablets was determined by Roche friabilator. This device subjected a number of tablets to combined effects of abrasion and shock by utilizing a plastic chamber that revolved at 25rpm, dropping the tablets a distance of six inches with each revolution. 4tablets were weighed and placed in the

friabilator it was operated for 100 revolutions. The tablets were then dusted and reweighed. For the calculation,

Eq.(7). %weight loss = initial weight of tablet (W¹) – final weight (W²)/ W¹ x 100

3.8 Weight Variation Test Of Tablet: For each batch 20 tablets were selected randomly and their average weight was determined. Weight of the individual tablet was also determined.

3.9 Disintegration Test: The drug release process from tablets often includes a step at which the tablets disintegrate into smaller fragments. In our experiment the disintegration test was done by using USP disintegration test apparatus. To test the disintegration test 3 tablets of each batch was placed in 3 glass tubes and the basket rack was positioned in the beaker containing 900 ml 0.1 N HCL solution maintained at 37±2°c. The disintegration time was recorded using mobile phone stop watch.

3.10 Dissolution studies: The drug deliver from the dosage form is studies by using the in vitro release test. The purpose of an in vitro release study is to provide a fast, easily performed and inexpensive method that correlates with the performance of a dosage form in human subjects. In vitro release profile, Tablet preparations was examined in 0.1 N HCL solutions from 0 to 7 hours using USP-II dissolution rate test apparatus (rotating paddle type) at 100 rpm. One tablet accurately weighed, was placed in the 900 ml of dissolution medium and maintained at 37± 0.5°c. 5ml aliquot of was withdrawn from dissolution media periodically at intervals of 1 hour by manual sampling, and same volume of fresh medium was replenished immediately to maintain the sink condition automatically. Withdrawn samples were further diluted properly with fresh medium. The diluted samples were analyzed spectrophotometrically at wavelength of maximum absorbance (λ max) 254 nm. Concentration of drug in solution was than determined from the calibration curve and cumulative percent release was calculated.

4. FOURIER-TRANSFORM INFRARED SPECTROSCOPY (FTIR):

FTIR is a technique used to obtain an infrared spectrum of absorption or emission of a solid, liquid

or gas. An FTIR spectrometer simultaneously collects high-spectral-resolution data over a wide spectral range. This confers a significant advantage over a dispersive spectrometer, which measures intensity over a narrow range of wavelengths at a time.

5. RESULTS

5.1. Uv-analysis

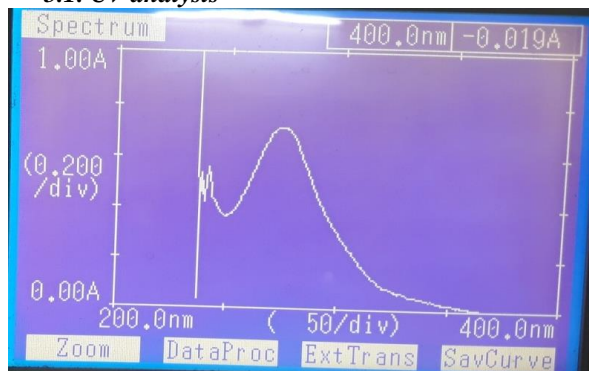


Fig. 3. Highest λmax of Green tea

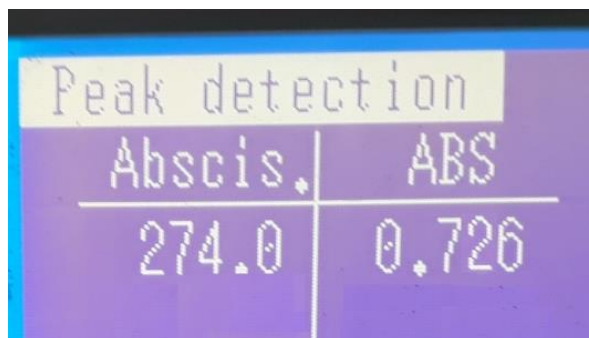


Fig. 4. Peak value of highest λmax of Green tea

Table 3. Absorbance vs Concentration table of green tea

Green tea	
Concentration	Absorbance
0.1	0.232
0.2	0.346
0.3	0.47
0.4	0.608
0.5	0.726

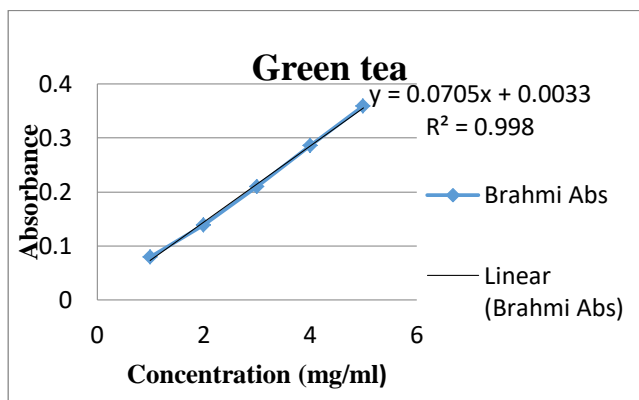


Fig. 5. Absorbance vs Concentration graph of Green tea



Fig. 6. Highest λ_{max} of Brahmi

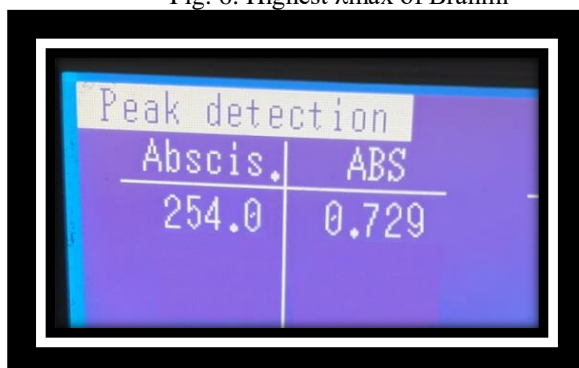


Fig. 7. Peak value of highest λ_{max} of Brahmi

Table 4. Absorbance vs Concentration table of Brahmi

Brahmi	
Concentration	Absorbance
2	0.139
4	0.286
6	0.425
8	0.573

10	0.729
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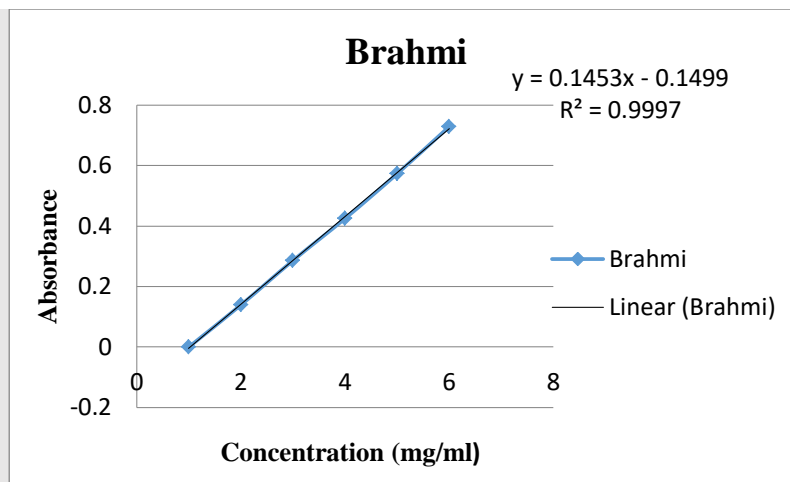


Fig. 8. Absorbance vs Concentration graph of Brahmi

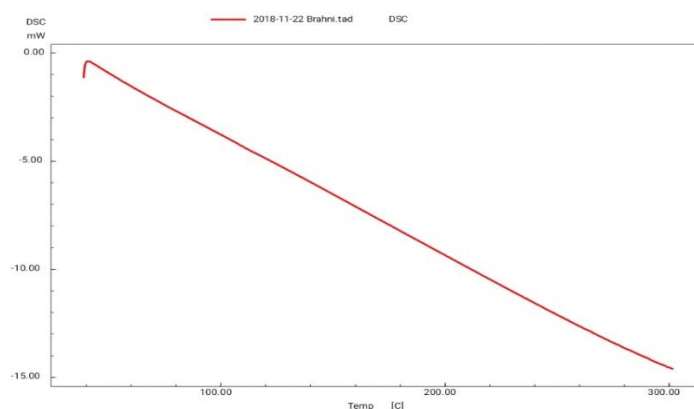


Fig. 9. DSC (Differential Scanning Calorimetry) graph of Brahmi

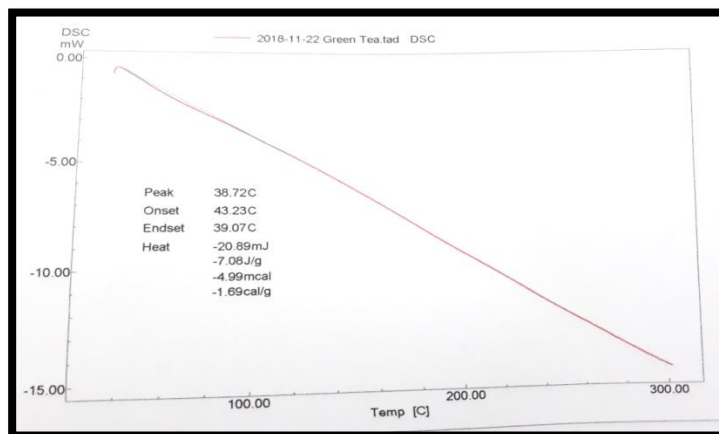


Fig. 10. DSC (Differential Scanning Calorimetry) graph of Green tea

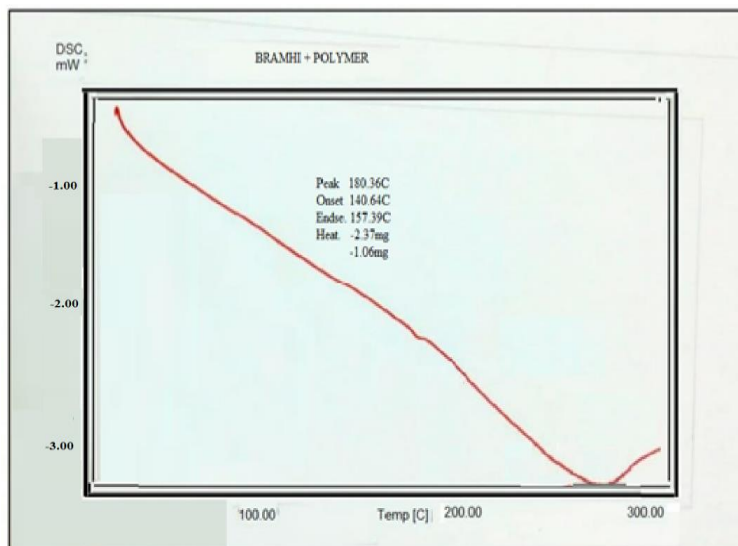


Fig. 11. DSC (Differential Scanning Calorimetry) graph of Brahmi+Polymer

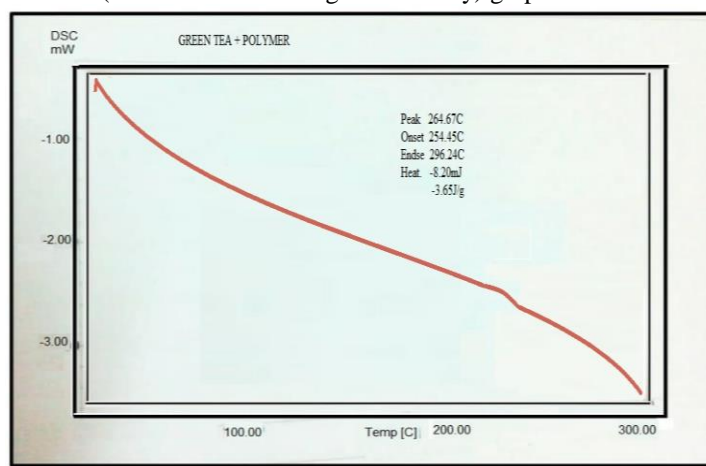


Fig. 12. DSC (Differential Scanning Calorimetry) graph of Green tea+Polymer

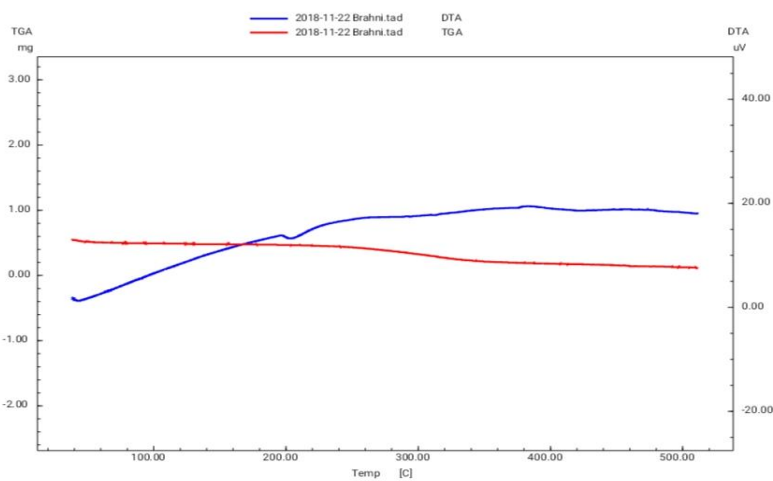


Fig. 13. TGA (Thermal gravimetric analysis)+ DTA (Differential thermal analysis) graph of Brahmi

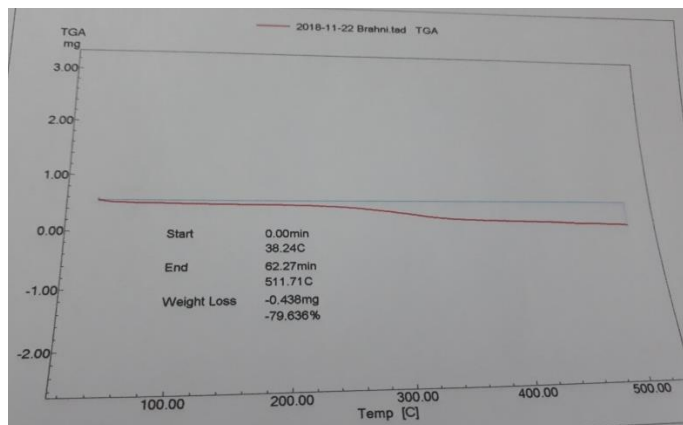


Fig. 14. TGA (Thermal gravimetric analysis) graph of Brahmi

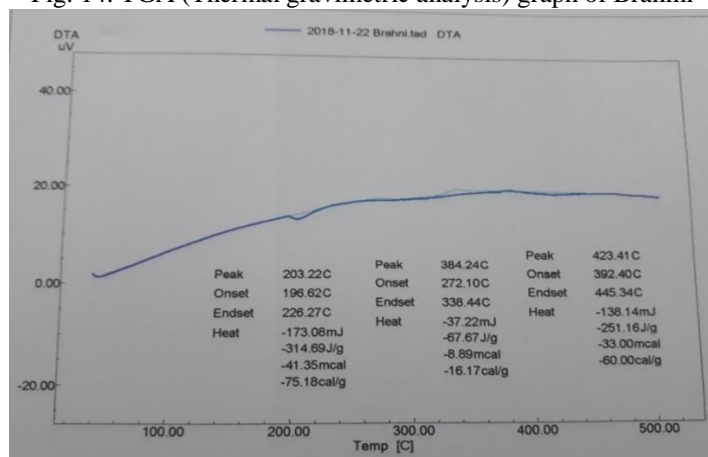


Fig. 15. DTA (Differential thermal analysis) graph of Brahmi

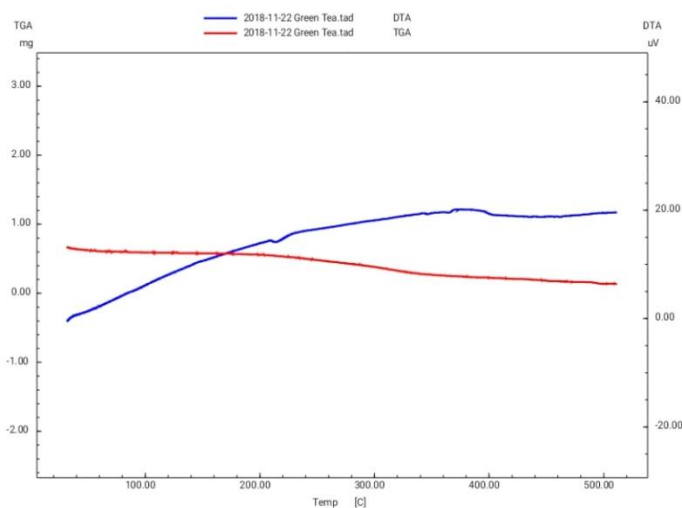


Fig. 16. TGA (Thermal gravimetric analysis)+ DTA (Differential thermal analysis) graph of Green Tea

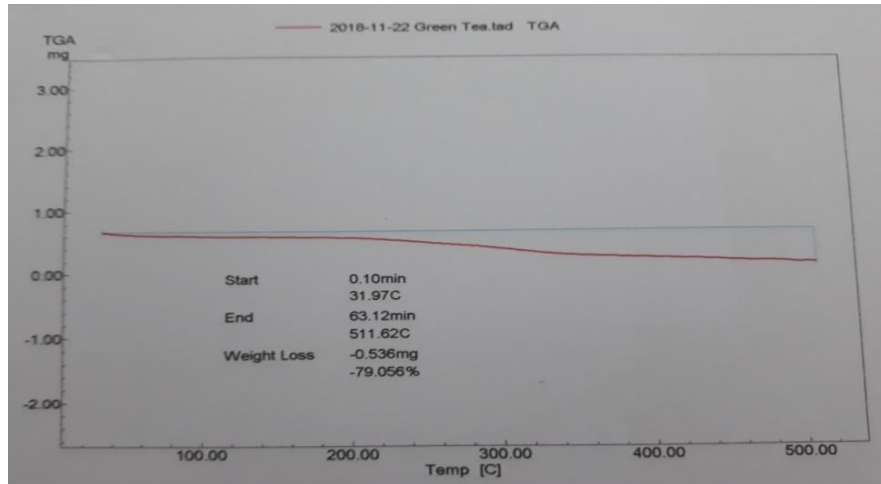


Fig. 17. TGA (Thermal gravimetric analysis) graph of Green tea

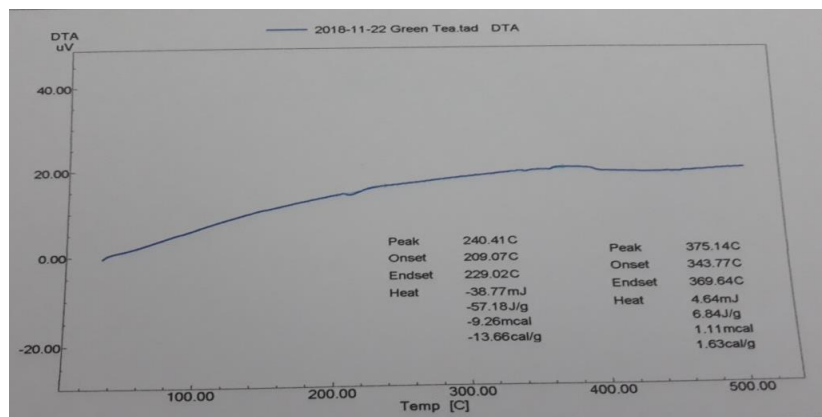


Fig. 18. DTA (Differential thermal analysis) graph of Green tea



Sample ID: BRAHMI
 Sample Scans: 12
 Background Scans: 12
 Resolution: 8
 System Status: Good

User: admin
 Date/Time: 12-03-2018 12:20:22 PM
 Range: 4500 - 450
 Apodization: Happ-Genzel

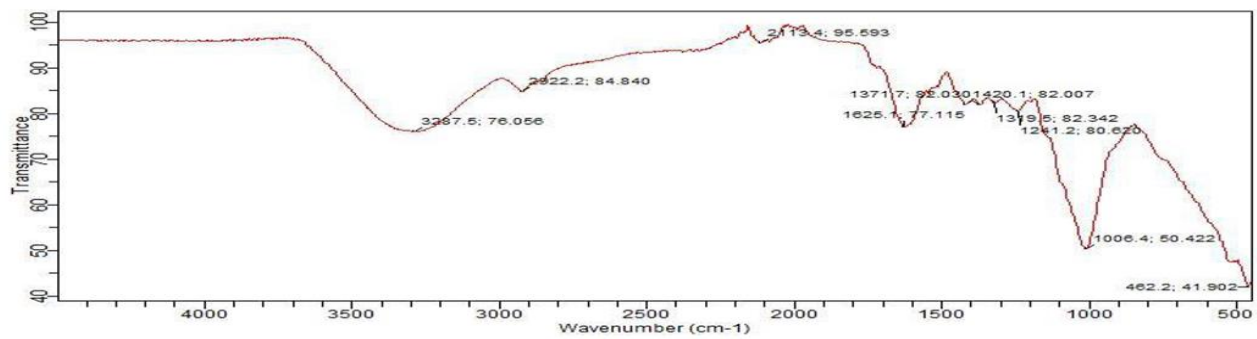


Fig. 19. FTIR (Fourier-transform infrared spectroscopy) of Brahmi



Sample ID: GREEN TEA
Sample Scans: 12
Background Scans: 12
Resolution: 8
System Status: Good

User: admin
Date/Time: 12-03-2018 12:17:04 PM
Range: 4500 - 450
Apodization: Happ-Genzel

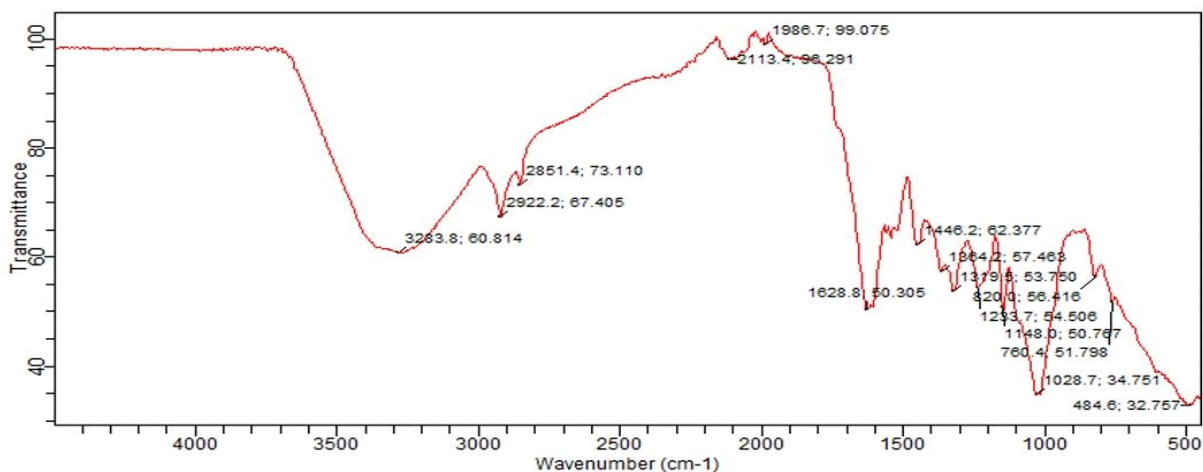


Fig. 20. FTIR (Fourier-transform infrared spectroscopy) of Green tea



Sample ID: GREEN TEA + POLYMER
Sample Scans: 12
Background Scans: 12
Resolution: 8
System Status: Good
File Location: C:\Users\Public\Documents\Agilent\MicroLab\Results\GREEN TEA + POLYMER
POLYMER_2019-02-19T16-38-06.a2r

User: admin
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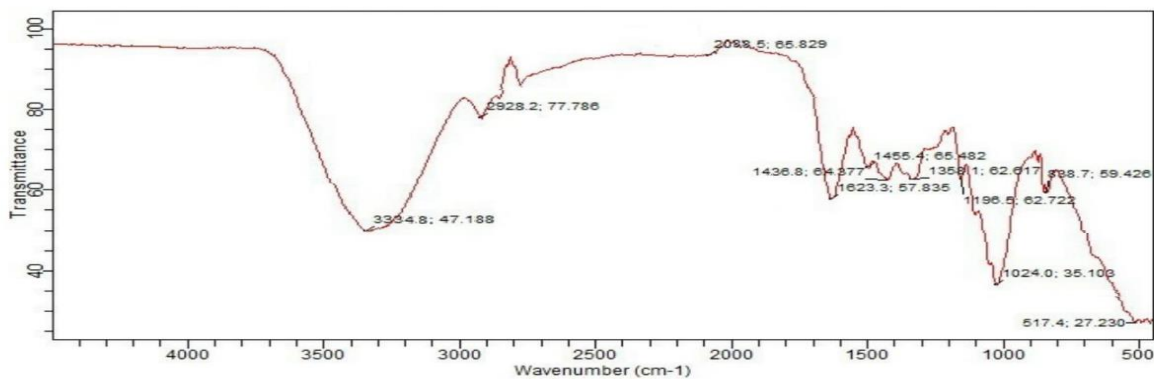


Fig. 21. FTIR (Fourier-transform infrared spectroscopy) of Green tea+Polymer



Sample ID:BRAMHI+POLYMER

Sample Scans:12

Background Scans:12

Resolution:8

System Status:Good

File Location:C:\Users\Public\Documents\Agilent\MicroLab\Results\BRAMHI+POLYMER

POLYMER_2019-02-19T16-12-03.a2r

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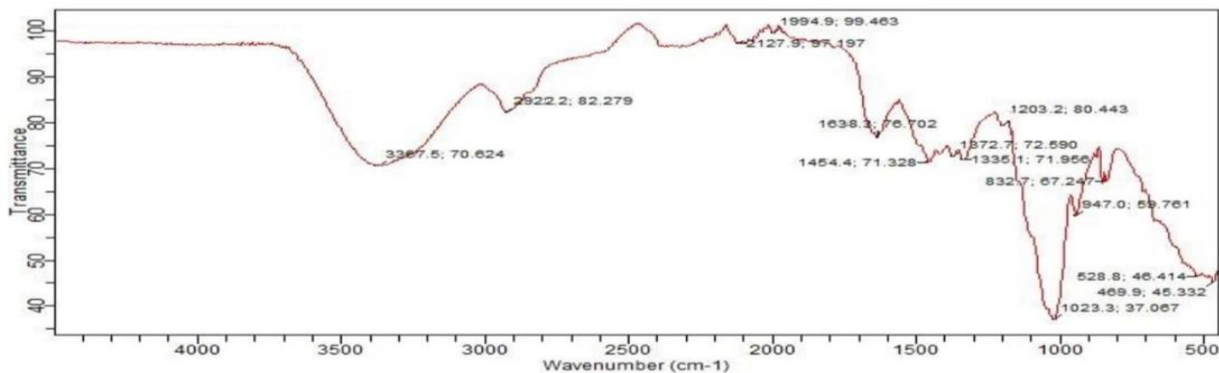


Fig. 22. FTIR (Fourier-transform infrared spectroscopy) of Brahmi+Polymer



Sample ID:GREEN TEA+BRAMHI+POLYMER

Sample Scans:12

Background Scans:12

Resolution:8

System Status:Good

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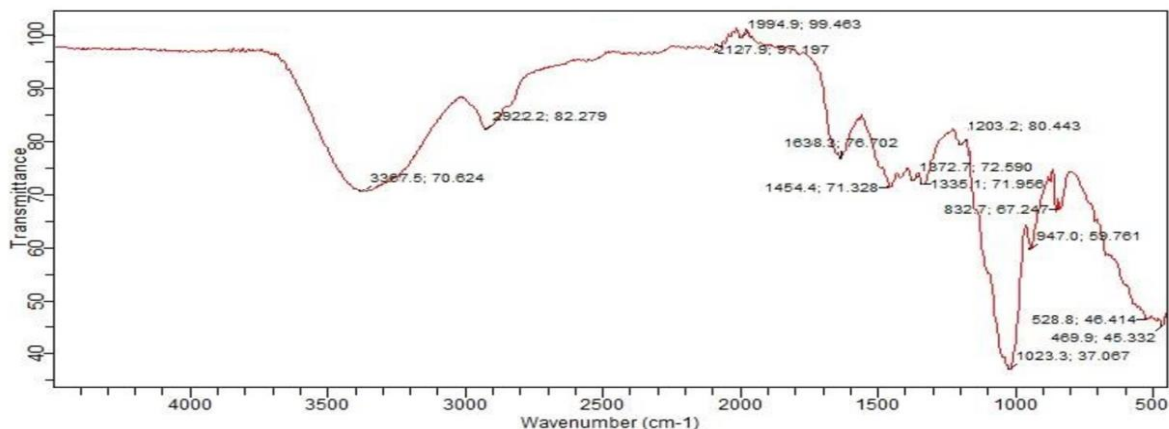


Fig. 23. FTIR (Fourier-transform infrared spectroscopy) of Green tea+Brahmi+Polymer

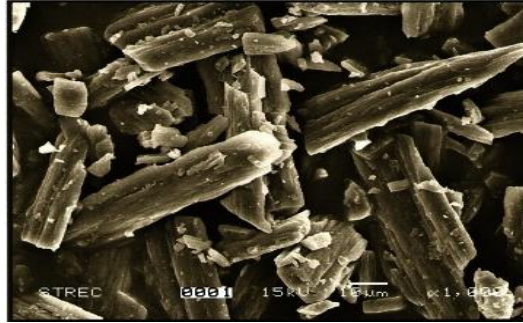


Fig. 24. GREEN TEA POWDER (PURE GREEN TEA POWDER)

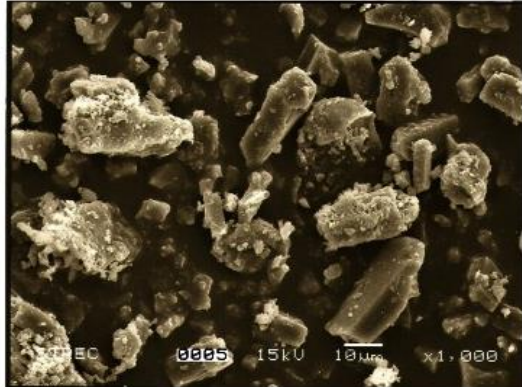


Fig. 25. GREEN TEA POWDER + POLYMER

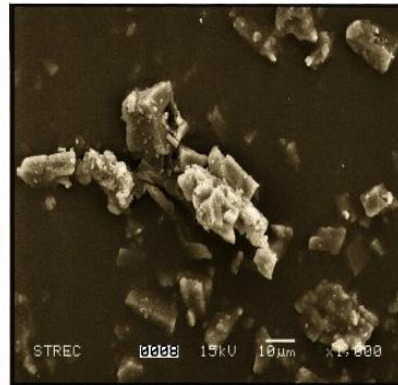


Fig. 26. BRAMHI POWDER (PURE BRAMHI POWDER)

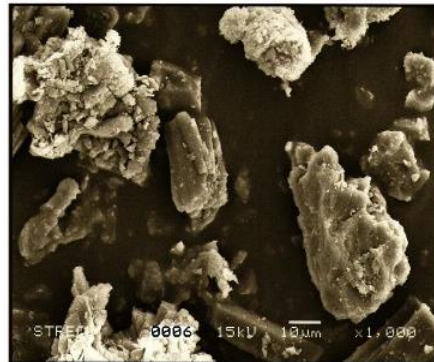
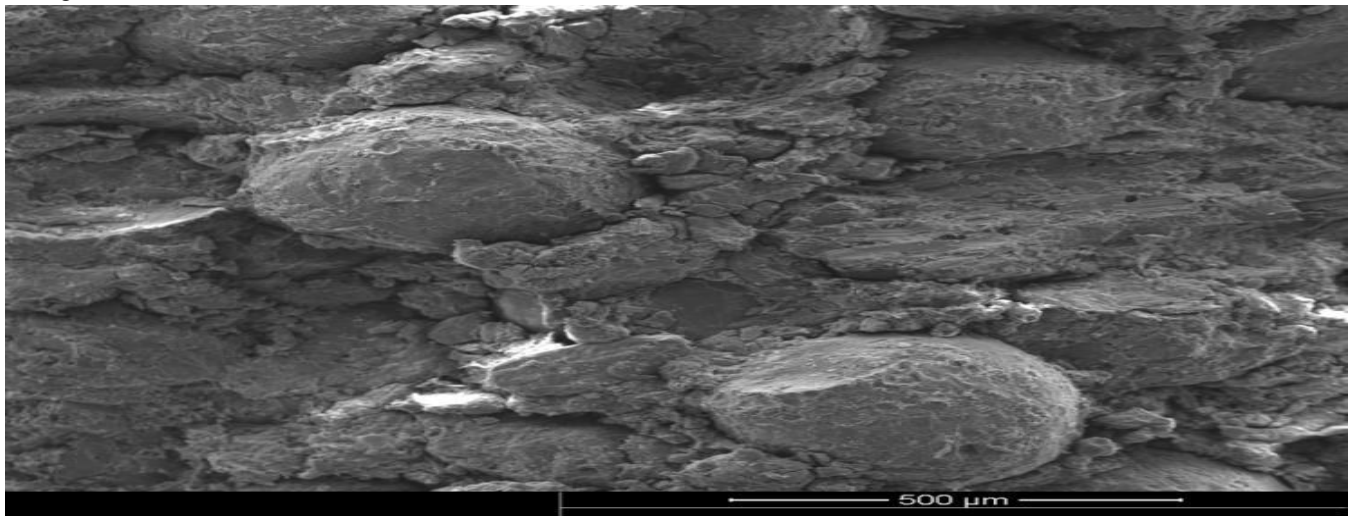


Fig. 27. BRAMHI POWDER+ POLYMER

Fig. 28. GREEN TEA POWDER + BRAMHI POWDER + POLYMER MIXED IN A TABLET WITH DISSOLUTION



(BUFFER) TABLET INNER SURFACE PHOTOGRAPH

Batch code	Hardness cm ²	Friability	Weight variation(mg)	Thickness mm
F1	6.12±0.02	0.32±0.01	480±0.3	5.21±0.02
F2	5.86±0.01	0.76±0.01	470±1.6	5.06±0.02
F3	5.96±0.003	0.49±0.01	480±0.3	5.15±0.02
F4	5.36±0.71	0.82±0.01	490±0.8	5.18±0.02
F5	6.20±0.03	0.49±0.01	480±0.3	5.01±0.02
F6	5.86±0.01	0.82±0.01	490±0.8	5.21±0.02
F7	5.76±0.02	0.59±0.01	490±0.8	5.15±0.02
F8	5.96±0.003	0.39±0.01	490±0.8	5.13±0.02
F9	6.23±0.03	0.59±0.01	480±0.3	5.09±0.02

Table 5. PROPERTIES OF BI-LAYER TABLET

Batch code	Angle of repose	Bulk density	Tapped density	Carr's index	Hauser ratio
F1	25.31±1.23	0.42±0.02	0.51±0.04	18.73±2.21	1.21±0.03
F2	26.30±0.08	0.47±0.04	0.57±0.04	17.54±1.21	1.21±0.02
F3	23.67±2.31	0.46±0.03	0.53±0.04	13.6±1.32	1.15±0.06
F4	24.37±1.72	0.47±0.02	0.55±0.05	15.34±1.62	1.17±0.04
F5	22.47±1.03	0.45±0.08	0.56±0.07	19.69±1.87	1.24±0.02
F6	26.51±1.88	0.42±0.02	0.51±0.04	18.73±2.21	1.21±0.03
F7	24.31±1.71	0.45±0.08	0.56±0.07	19.69±1.87	1.24±0.02
F8	26.56±1.9	0.46±0.03	0.53±0.04	13.6±1.32	1.15±0.06
F9	23.61±2.12	0.45±0.08	0.56±0.07	19.69±1.87	1.24±0.02

Table 6. PROPERTIES OF GRANULES

5.2. In-Vitro Drug Release Profile:

Table 7. (Cumulative % of drug release vs time) zero order of green tea

time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	8.5±3.39	9±2.89	10±1.89	10.5±1.39	11±0.89	13.5±1.6 1	13.2±1.31	14.85±2.96	16.5±4.61
2	16±2.83	11.4±7. 43	17.5±1.33	18±0.83	18.5±0.33	21±2.17	20.7±1.87	22.35±3.52	24±5.17
3	23.5±2.83	18.9±7. 43	25±1.33	25.5±0.83	26±0.33	28.5±2.1 7	28.2±1.87	29.85±3.52	31.5±5.17
4	31±2.83	26.4±7. 43	32.5±1.33	33±0.83	33.5±0.33	36±2.17	35.7±1.87	37.35±3.52	39±5.17
5	38.5±2.83	33.9±7. 43	40±1.33	40.5±0.83	41±0.33	43.5±2.1 7	43.2±1.87	44.85±3.52	46.5±5.17
6	46±2.83	41.4±7. 43	47.5±1.33	48±0.83	48.5±0.33	51±2.17	50.7±1.87	52.35±3.52	54±5.17
7	53.5 ±2.83	48.9±7. 43	55±1.33	55.5±0.83	56±0.33	58.5±2.1 7	58.2±1.87	59.85±3.52	61.5±5.17
8	61±2.83	56.4±7. 43	62.5±1.33	63±0.83	63.5±0.33	66±2.17	65.7±1.87	67.35±3.52	69±5.17
9	68.5±2.83	63.9±7. 43	70±1.33	70.5±0.83	71±0.33	73.5±2.1 7	73.2±1.87	74.85±3.52	76.5±5.17
10	76±2.83	71.4±7. 43	77.5±1.33	78±0.83	78.5±0.33	81±2.17	80.7±1.87	82.35±3.52	84±5.17
11	83.5±2.83	78.9±7. 43	85±1.33	85.5±0.83	86±0.33	88.5±2.1 7	88.2±1.87	89.85±3.52	91.5±5.17
12	91±2.83	86.4±7. 43	92.5±1.33	93±0.83	93.5±0.33	96±2.17	95.7±1.87	97.35±3.52	99±5.17

Table 8. Zero order release kinetics of Brahmi

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	8.8±1.9	9.5±1.2	10.5±0.0 2	11±0.3	11.3±0.6	13.8±3.1	13.7±3	14.9±4.2	16.5±5. 8
2	16.3±3. 4	17±2.7	18±1.7	18.5±1. 2	18.8±0.9	21.3±1.6	21.2±1.5	22.4±2.7	24±4.3
3	23.8±3. 4	24.5±2. 7	25.5±1.7	26±1.2	26.3±0.9	28.8±1.6	28.7±1.5	29.9±2.7	31.5±4. 3
4	31.3±3. 4	32±2.7	33±1.7	33.5±1. 2	33.8±0.9	36.3±1.6	36.2±1.5	37.4±2.7	39±4.3
5	38.8±3. 4	39.5±2. 7	40.5±1.7	41±1.2	41.3±0.9	43.8±1.6	43.7±1.5	44.9±2.7	46.5±4. 3
6	46.3±3. 4	47±2.7	48±1.7	48.5±1. 2	48.8±0.9	51.3±1.6	51.2±1.5	52.4±2.7	54±4.3
7	53.8±3. 4	54.5±2. 7	55.5±1.7	56±1.2	56.3±0.9	58.8±1.6	58.7±1.5	59.9±2.7	61.5±4. 3
8	61.3±3. 4	62±2.7	63±1.7	63.5±1. 2	63.8±0.9	66.3±1.6	66.2±1.5	67.4±2.7	69±4.3
9	68.8±3. 4	69.5±2. 7	70.5±1.7	71±1.2	71.3±0.9	73.8±1.6	73.7±1.5	74.9±2.7	76.5±4. 3
10	76.3±3. 4	77±2.7	78±1.7	78.5±1. 2	78.8±0.9	81.3±1.6	81.2±1.5	82.4±2.7	84±4.3
11	83.8±3. 4	84.5±2. 7	85.5±1.7	86±1.2	86.3±0.9	88.8±1.6	88.7±1.5	89.9±2.7	91.5±4. 3
12	91.3±3. 4	92±2.7	93±1.7	93.5±1. 2	93.8±0.9	96.3±1.6	96.2±1.5	97.4±2.7	99±4.3

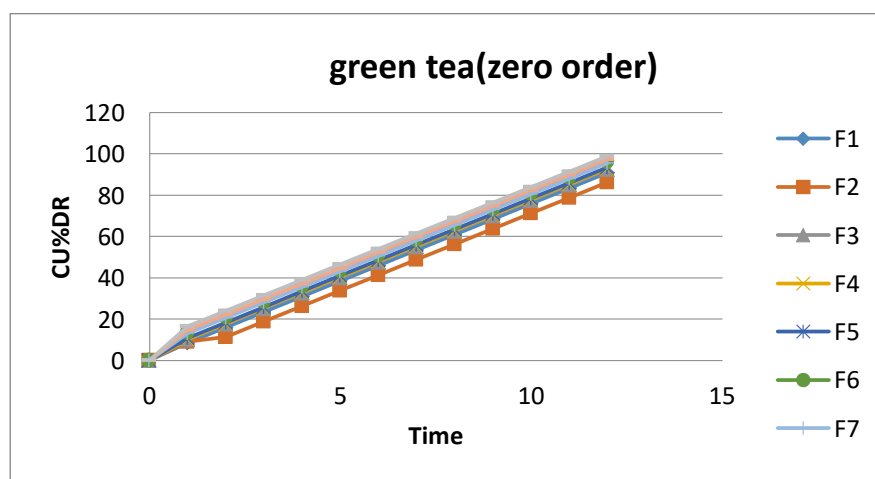


Fig. 29. Zero order drug release kinetic of batch F1-F9 of green tea

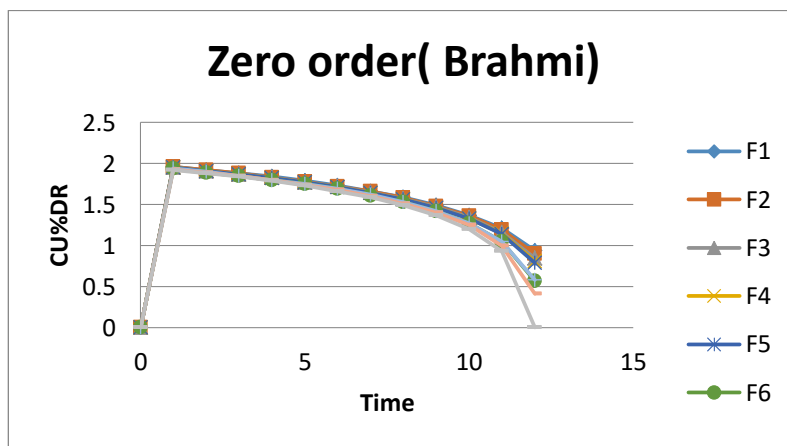


Fig. 30. Zero order drug release kinetic of batch F1-F9 of Brahmi

6. CONCLUSION:

The F9 batch is the best formulation and bilayer tablet follows Zero order release kinetics.

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