

RESEARCH ARTICLE

Formulation and Evaluation Of Hard Gelatin Capsules Containing *Bacopa Monnieri*

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ABSTRACT

Introduction: The present work deals with the formulation of hard gelatin capsules containing granules of Brahmi (*Bacopa monnieri*). *Bacopa monnieri* is used in Traditional Ayurvedic medicine to improve memory and to treat various ailments. The project aims to achieve the immediate release of drug from the dosage form to achieve therapeutic efficacy and patient compliance. Hard gelatin capsules offer rapid drug release and protection from atmospheric oxygen.

Materials and methods: In this work, we have prepared the granules of Brahmi and filled into the empty hard gelatin capsule shells. The hard gelatin capsules were then evaluated for dissolution studies, disintegration study, drug content, and weight variation.

Results and Discussion: After the dissolution study, it was found that 93.46% of Brahmi was released within 90 min. The kinetics of drug release was also studied, and it was found to follow the Korsmeyer Peppas model.

Keywords: Brahmi, Granules, Hard gelatin capsule, Kinetic release profile

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INTRODUCTION

The present work deal with the preparation and evaluation of Brahmi botanical name, *Bacopa monnieri* (Family- Plantaginaceae) extract powder granules hard gelatin capsule. The leaves of this plant are succulent, oblong, and 4–6 mm (0.16–0.24 in) thick. Leaves are oblanceolate and are arranged oppositely on the stem. The flowers are small, actinomorphic, and white, with four to five petals. Its ability to grow in water makes it a popular aquarium plant. It can even grow in slightly brackish conditions. Propagation is often achieved through cuttings. *Bacopa monnieri* is used in Traditional Ayurvedic medicine to improve memory and to treat various ailments. Preliminary clinical research found that

Bacopa minnieri may improve cognition. *Bacopa monnieri* increase antioxidant/detoxification enzyme activity in the spleen, brain, heart, thymus, and mesenteric lymph nodes thereby showing neuroprotection. The best-characterized phytochemicals in *Bacopa monnieri* are dammarane-type triterpenoid saponins known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units. Bacosides comprise a family of 12 known analogs.^{1,2} Other saponins called bacopasides I–XII have been identified more recently. The alkaloids brahmine, nicotine, and herpestine have been catalogued, along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacin and plantainoside B.

Capsules are the solid dosage form in which the drug substance is enclosed in a water-soluble shell. A capsule shell is made of gelatin. The capsules are available both as hard capsules and soft capsules. Hard gelatin capsules are used for the administration of solid medicaments. The capsules shell is prepared from gelatin, color, and titanium dioxide to make it opaque. Soft gelatin capsules are used for the administration of liquid medicaments. Soft gelatin capsules are available in round, oval, and tube-like shapes. They are used to enclose liquid medicaments-oils, suspensions, food concentrates and ophthalmic products.⁵ The drugs having unpleasant odor and taste can be administered by enclosing them in a tasteless shell of capsules. Capsules are smooth, become very slippery when moist and can be easily swallowed.

Granulation is a process whereby small particles gathered into large, permanent masses in which the original particles can still be identified. Granulation is joining particles within a given granulation process that will improve flow and compression characteristics, reduce segregation, improve content uniformity, and eliminate excessive amounts of fine particles. The results of granulation are improved yields, reduced tablet defects, increased productivity, and reduced downtime. Granulation is a process of collecting particles together by creating bonds between them and these bonds are formed by compression or by using a binding agent. Particles-particles bonding mechanisms involved in adhesion and cohesion of particles. Several forces that can be act are van der waals forces and electrostatic forces. In wet granulation method the powder or powder mixture is moistened and then pass the resulting paste through a screen of the mesh size to produce the desired

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size of granules. The granulation liquid (fluid) contains a solvent which must be volatile so that it can be removed by drying, and be non-toxic. Typical liquids include water, ethanol and isopropanol either alone or in combination. The granules are placed on drying trays and are dried by air or under heat. The granules are periodically moved about on the drying trays to prevent adhesion into a large mass.^{3, 4}

MATERIALS AND METHODS

Materials used

Organic Brahmi (Cultivator Natural Products Pvt. Ltd.), Methanol (Finar Ltd.), Potassium chloride (Central Drug House Pvt. Ltd.), Hydrochloric acid (RFCL Ltd.) and Distilled water, sodium chloride, disodium hydrogen phosphate, potassium dihydrogen phosphate

Drug analysis

Determination of absorption maxima

A solution of Brahmi (10µg/ml) in 1.2pH acidic buffer was scanned between 200-400nm using Chrom One spectrophotometer. The scanned λ_{max} compared with literature value.

Determination of solubility

Solubility studies of drug were carried out in distilled water, methanol and 1.2 pH acidic buffer. An excessive amount of drug was added in screw capped vial using 10ml distilled water, 10ml methanol and 0.1 N HCl respectively. The saturated solution then filtered through Whatmann filter paper and was analyzed on UV Spectrophotometer at λ_{max} of each solvent.

Preparation of standard plot

Standard plot of Brahmi was prepared in 1.2 pH acidic buffer. 50 mg of Brahmi was dissolved in small volume of methanol in 100ml volumetric flask and volume was made up to 100ml with methanol to get a concentration of 500 µg/ml. From this stock solution, aliquots of 0.4ml, 0.8, 1.2ml, 1.6ml and 2ml were withdrawn into a series of 10ml volumetric flask and volume was methanol to get a concentration ranging from 20-100 µg/ml. The absorbance of resulting solution was then measured at 254 nm using UV spectrophotometer against parent solvent as a blank.

Formulation of granules of Brahmi^{7,8}

Granules of Brahmi were prepared by wet granulation method. 250 mf of Brahmi was weighed and required quantity of water drop wise incorporated to the blend. Wet granules will be passed through sieve #10 & air dried for 15 minutes. The dried granules will then be passed through sieve #22. Required quantity of magnesium

stearate & talc were added to the granules. The prepared granules were then added to the Size #3 empty hard gelatin capsule.

Evaluation Parameters

Flow property⁶

Flow properties of granules are generally assessed by determining the angle of repose.

Angle of repose is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane. The angle of repose is determined by allowing powder to flow freely through an orifice from a certain height and form a conical heap on the horizontal plane.

The angle which the heap forms with the horizontal surface is the angle of repose and is determined by the formula:

$$\tan \theta = \frac{h}{r}$$

Where,

θ is the angle of repose,

h is the height of heap of powder and

r is the radius of the base of heap of powder.

Generally, powders with Angle of Repose more than 50 have unsatisfactory flow properties.

Weight Variation⁹

The average weight of capsule along with length and diameter was determined by weighing. Randomly 20 filled capsules were selected and weighted all 20 capsules collectively, and find out average weight.

$$\text{Average weight } \theta = \frac{\text{weight of 20 capsules}}{20}$$

Then weighted each 20 capsules one by one and note down their respective weights then find out percentage weight variation for each capsule with using formula-

$$\% \text{ Average weight} = \frac{\text{Real weight}-\text{Average weight}}{\text{Average weight}}$$

Drug Content

Drug content was determined by measuring absorbance of prepared solution of extract powder, using UV Spectroscopy and determined the value using regression line of calibration

Disintegration Time

The disintegration test was performed under a given set of condition for six randomly selected capsules to disintegrate into particles which will pass through a 10 mesh screen with in the apparatus using 6.8 pH (simulated

saliva fluid) and assembly at maintained temperature $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$ as disintegration media.

In Vitro dissolution Studies^{10,11}

The dissolution test was performed for capsule using capsules basket type USP dissolution apparatus. The 900 ml of the 1.2 pH acidic buffer dissolution medium was introduced into the vessel of the apparatus at the speed of 50 rpm for two hrs. After each 15 min a 10 ml specimen was withdrawn. For each of the capsule tested, the amount of dissolved active ingredient in the solution was calculated as a percentage dissolved in 1.5 hrs.

Release Kinetics^{12,13,14}

In vitro drug release study were fitted with various kinetic equations like zero order (cumulative percent drug released vs. Time), first order (Log cumulative percent drug retained vs. Time), Higuchi (cumulative percent released vs. T), Peppas (log of cumulative percent drug released vs. log Time). The kinetic model that best fits the dissolution data was evaluated by comparing the regression coefficient (r) values obtained in various models. Peppas model used 'n' value to characterize different release mechanisms. The values of n = 0.5 for Fickian diffusion, between 0.5 to 1.0 for non-Fickian diffusion and n = 1 for zero order.

RESULT AND DISCUSSION

Absorption maxima

The absorption maxima of Brahmi in 1.2 pH acidic buffer was found to be 254 nm.

Solubility

The solubility of Brahmi in distilled water, methanol and 1.2 pH acidic buffer is shown in Table 1.

Flow Property

The angle of repose of granules of Brahmi was found to be 20.55 which is acceptable flow for preparing a formulation.

$$\text{Average} = \frac{\text{Trial 1} + \text{Trial 2}}{2}$$

$$\text{Average} = \frac{20.80 + 20.30}{2}$$

$$\text{Angle of repose} = 20.55$$

Standard Curve

Standard curve of Brahmi was prepared in 1.2 pH acidic buffer at their λ_{max} using UV spectrophotometer

Weight variation of capsules

The weight variation was found in the range of -4.40% to +4.89%. The data of weight variation is tabulated in Table 4.

Drug content

The data of drug content is tabulated in Table 5. Drug content is found be ranging from 96.22% to 99.25%.

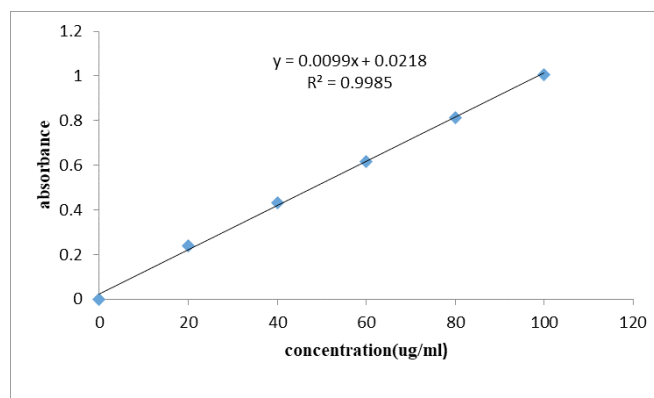


Figure 1: Calibration Curve of Brahmi in 1.2 pH acidic buffer

Table 1: Solubility of Brahmi in various solvents

S.NO.	Solvents	Solubility ($\mu\text{g/ml}$)
1	Methanol	72.13 ± 0.52
2	Distilled water	15.11 ± 0.75
3	Acidic buffer	30.52 ± 0.42

Table 2: Angle of repose

Trial 1					Trail 2				
Diameter (cm)	Radius (cm)	height (cm)	h/r	$\theta = \tan^{-1} h/r$	Diameter (cm)	Radius (cm)	height (cm)	h/r	$\theta = \tan^{-1} h/r$
14.2	7.1	2.7	0.38	20.80°	13.2	6.6	2.5	0.37	20.30°

Table 3: Calibration data of Brahmi in 1.2pH acidic buffer

S.No.	Concentrations ($\mu\text{g/ml}$)	Absorbance
1	20	0.2401
2	40	0.4298
3	60	0.6147
4	80	0.8144
5	100	1.007

Table 4: Data of weight variation

S.No	Weight of individual capsule content (mg)	Average weight	Difference in weight	% Weight variation (%)
1	251	250.3	0.7	0.279664
2	253	250.3	2.7	1.078706
3	249	250.3	-1.3	-0.51938
4	250	250.3	-0.3	-0.11986
5	250	250.3	-0.3	-0.11986
6	248	250.3	-2.3	-0.9189
7	249	250.3	-1.3	-0.51938
8	250	250.3	-0.3	-0.11986
9	250	250.3	-0.3	-0.11986
10	249	250.3	-1.3	-0.51938
11	248	250.3	-2.3	-0.9189
12	250	250.3	-0.3	-0.11986
13	250	250.3	-0.3	-0.11986
14	250	250.3	-0.3	-0.11986
15	253	250.3	2.7	1.078706
16	251	250.3	0.7	0.279664
17	250	250.3	-0.3	-0.11986
18	250	250.3	-0.3	-0.11986
19	252	250.3	1.7	0.679185
20	251	250.3	0.7	0.279664

Table 5: The data of drug content

S.No.	Drug Content (%)	S.No.	Drug Content (%)
1	97.42	11	97.20
2	96.22	12	98.42
3	97.40	13	97.18
4	98.20	14	97.50
5	97.60	15	98.00
6	98.50	16	99.18
7	97.20	17	98.17
8	97.80	18	97.20
9	98.20	19	98.16
10	97.28	20	99.25

Disintegration Time

The data of disintegration time is depicted in Table 6.
Average Time = 4min 6 second

Dissolution Study

The results of dissolution study is depicted in Table 7.

Drug Release Kinetics Data Analysis

Kinetics and mechanism of drug release from Brahmi Capsule was evaluated on the basis of Zero Order, First Order, Higuchi equation and Peppas model. The R^2 values are reported in Table 8. The of 'n' for Korsmeyer Peppas

Table 6: The data of disintegration time

S.No.	Trial 1	Trial 2
1	4 min 3 seconds	4 min 9 seconds

Table 7: Data of Dissolution study

Time (t) hrs	\sqrt{t}	Log t	Cumulative % Release	Log Cumulative % Release	Cumulative % Retained	Log Cumulative % Retained
0	0	0	0	0	100	2
15	3.872983	1.96799	15.09091	1.178715	84.90909	1.928954
30	5.477226	2.340347	22.67131	1.355477	77.32869	1.888341
45	6.708204	2.59002	35.37063	1.548643	64.62937	1.81043
60	7.745967	2.783158	46.40291	1.666545	53.59709	1.729141
75	8.660254	2.942831	77.39697	1.888724	22.60303	1.354167
90	9.486833	3.08007	93.46776	1.970662	6.532242	0.815062

Table 8: Kinetics of drug release from Brahmi capsule

S.No.	Zero Order	First Order	Higuchi	Korsmeyer Peppas	Best Fit Model
1.	0.961	0.786	0.960	0.991	Korsmeyer Peppas Model

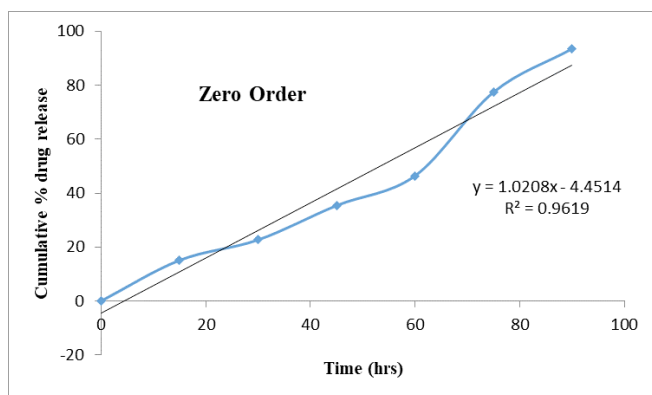


Figure 2: Zero order curve

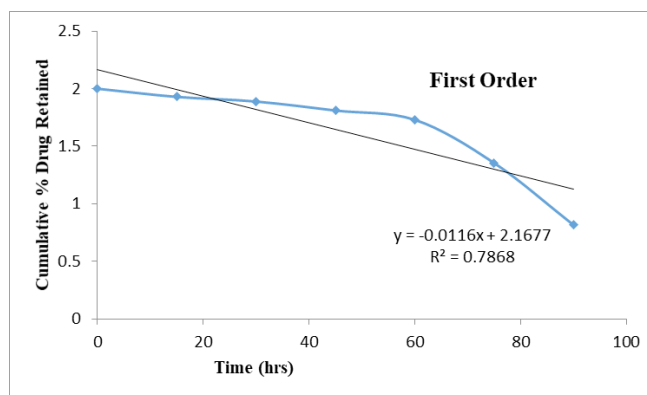


Figure 3: First Order curve

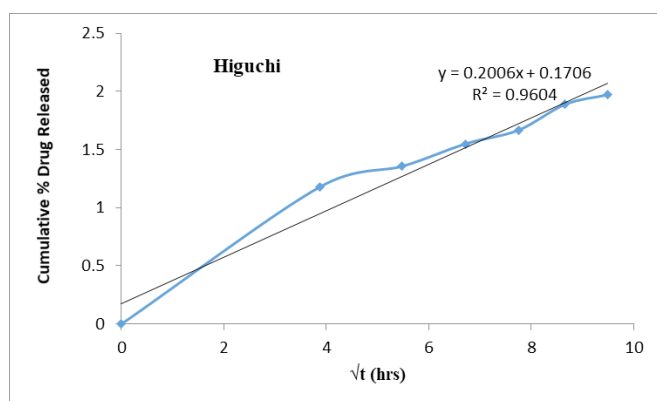


Figure 4 : Higuchi curve

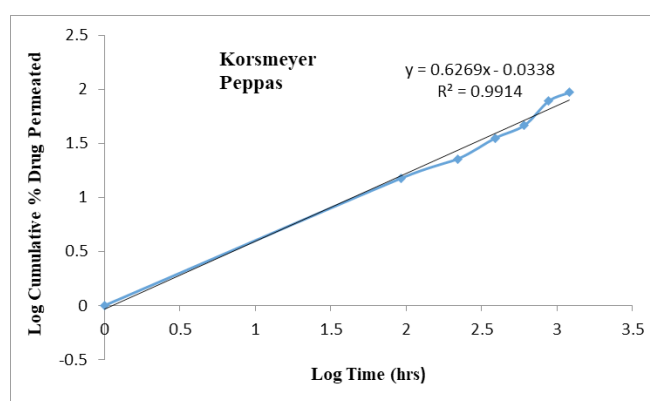


Figure 5: Korsmeyer Peppas curve

model was found to be 0.626 and its value is obtained from slope of Korsmeyer peppas curve.

CONCLUSION

Brahmi is the best Nutraceutical diet and supplements for the women's and children's. Brahmi strengthen the memory enhancement and brain capacity, and avoids a lot of nervous system problems. Dissolution Study drugs complete release time is 90 min. and found to maximum drug release 93.5%. The best fit model for release kinetics is found to be Korsmeyer peppas, where non-fickian transport is predominated in the formulation.

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