ISSN-2249-5746

International Journal Of Ayurvedic And Herbal Medicine 2:1 (2012) 128:134

Journal Homepage http://interscience.org.uk/index.php/ijahm

Formulation And Evaluation Of Antidepressant Matrix Tablet Of 5-Hydroxy Trytophan Derived From Griffonia Simplicifollia

Raghuwanshi Prakash*[1], Patidar Deepak[1], Chourasiya Deepak[1], Jatav Rajesh[1]

Corresponding Author: - Mr. Deepak Patidar Central India Institute of Pharmacy, Indore – Dewas Bypass Road, Arandiya, Indore - 452016 (M.P.), India Email: prakash_dws@yahoo.co.in

Griffonia Simplicifollia is an Antidepressant drug which is water soluble. The matrix tablets have best for water soluble drug in sustained release. Matrix tablet of Griffonia Simplicifollia for its very useful formulation. Griffonia Simplicifollia 5HTP is a safe way to boost Serotonin levels. Serotonin is a neurotransmitter useful for proper brain function it also increases melatonin and endorphin levels. Serotonin deficiency has been implicated in anxiety, depression food Cravings, Insomnia, headaches, muscle and joint pain, panic disorder and hyperactivity. Clinical studies in Europe and Japan have exhibited equal result to pharmaceutical antidepressants. The present study is to lay down an efficient approach to develop a suitable herbal matrix tablet formulation a large number of excipients are screened of the excipients for the final formulation on the basis of the derived properties of granules like, angle of repose, Carr's index, Hausner's ratio as well as on the basis of their effect on the physical characteristics of the tablets. The evaluation study was performed such as Weight Variation, Thickness, Hardness, Friablity and in-Vitro study and stability study.

Key word: -- Matrix Tablet, Griffonia Simplicifollia, HPMC, DCP and Aerosil.

INTRODUCTION:

Oral route is the most preferred route for administration of drugs. Tablets are the most popular oral formulations available in the market and preferred by the patients and physicians alike. In long-term therapy for the treatment of chronic disease conditions, conventional formulations are required to be administered in multiple doses, and therefore have several disadvantages. Controlled release (CR) tablet formulations are much desirable and preferred for such therapy because they offer better patient compliance, maintain uniform drug levels, reduce dose and side effects, and increase safety margin for high potency drugs[1].

Increased complications and expense involved in marketing of new drug entities has focused greater attention on development of sustained release (SR) or controlled release (CR) drug delivery systems [2].

Sustained or controlled release delivery systems can achieve predictable and reproducible release rates, extended duration of activity for short half - life drugs, decreased toxicity, and reduction of required dose, optimized therapy and better patient compliance[3,4,] Matrix type sustained delivery systems are popular because of their ease of manufactures. It excludes complex production procedure such as coating and pellitization during manufacturing and drug release from the dosage form. It is controlled mainly by the type and proportion of the polymers used in the preparation. Hydrophilic polymer matrix is widely used for formulating a sustained release dosage form [5, 6,]

Depression is the most common of the affective disorder (defined as disorders of mood rather than disturbance of thought or cognition); it may range from a very mild condition, bordering on normality, to severe (psychotic) depression accompanied by hallucinations and delusions. Worldwide, depression is a major cause of disability and premature death. In addition to the significant suicide risk, depressed individuals are more likely to die from other cause, such as heart disease or cancer[7, 8, 9]

A natural antidepressant made from the seeds of the Griffonia Simplicifollia plant. 5 –HTP is a precursor to neurotransmitter, serotonin and as a result increase Serotonin levels. This herbal remedy primarily comes in capsule form. Some small studies indicate that 5-HTP may be useful in treating depression, but further research is needed. Side effects appear to be fewer and severe than usual antidepressants[10].

MATERIALS AND METHOD:

Materials:
Griffonia Simplicifollia was provided by Plethico Pharma ltd. Indore. HPMC, DCP, Aerosil and all other chemicals used were of analytical reagent grade and double distilled water was used throughout the experiments.

Experimental work:

Identification of Drug: Identification of drug was done by its FT-IR spectra. The infrared spectral assignment of Griffonia was obtained from Choksi lab, Indore by FT-IR Shimadzu in the wave number region of 4000-400cm^{-1}.

Solubility (at room temp): Solubility studied according to Indian pharmacopoeia.

Loss on drying: Loss on drying directly measuring by IR moisture balance. Firstly calibrate the instrument by knob then 5.000 gm sample (powder) was subjected in bottle and set the temp at 100º C to 105º C for 5 minutes and set the parameters and check % moisture.

Determination of pH (1% w/v solution in water): 1gm of the extract was taken and dissolved in 100 ml of distilled water with sonication and filtered, pH of the filtrate was checked with standard glass electrode by pH meter.

Compatibility Studies: In the compatibility testing program, blends of drug and excipients are prepared by triturating the drug with individual excipients. Realistic ratios of excipients to drug were based on a dosage form containing 200 mg of Griffonia Simplicifollia extract with a target average weight of 665 mg tablet. Binary/tertiary blends of extract and excipients were prepared and transferred to inert glass vials. The mouths of the vials are covered with rubber closures followed by the aluminum seal caps. Binary/tertiary blends of extract and excipients, Griffonia Simplicifollia extracts neat and excipients were stored at 4ºC (refrigerator) as control; and at 40ºC/75%RH for accelerated stability studies for 4 weeks. The visual observation (color, flow, & sticking) were recorded for initial and at the end of the first, second, third and fourth week. FT-IR spectra for drug and excipients mixture shown in figure 2.

Formulation of tablets: Granulation done by slug formation, drug and polymer were mixed together and forms the slug by roller compacter. The Slug passed through the 20# sieve to get granules. After sieving lubrication of granules was done and mix them uniformly. Tablet compressed by Ganson single rotatory (Punch size 9.5*19.5) machine. Composition of Matrix Tablets of Griffonia Simplicifollia is represented in

Table 1: Composition of Matrix Tablets of Griffonia Simplicifollia

Ingredient	F1	F2	F3	F4	F5	F6
HPMC K15M	80 mg	100 mg	120 mg	-	-	-
HPMC K35M	-	-	-	55 mg	57.5 mg	60 mg
MCC102	91mg	91 mg	91 mg	91 mg	91 mg	91 mg
DCP Dihydrate	241 mg	221 mg	201 mg	266 mg	263.5 mg	261 mg
Stearic acid	26 mg	26 mg	26 mg	26 mg	26 mg	26 mg

Aerosil-200	18.5mg	18.5mg	18.5 mg	18.5 mg	18.5 mg	18.5 mg
Magnesium Stearate	8.5mg	8.5mg	8.5mg	8.5mg	8.5mg	8.5mg
Total weight	**665 mg**	**665 mg**	**665 mg**	**665 mg**	**665 mg**	**665 mg**

*Each formulation contains 200 mg 5HTP-naturally derived Griffonia Simplicifollia.

Evaluation of granules:

Angle of repose (θ): The frictional forces of granules can be measurement by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.[11]

$$\tan\theta = h/r$$

Where, the θ is the angle of repose, h = height, r = radius

Bulk density: Both loose bulk density (LBD) and tapped density (TBD) were determined. The accurately weighted amount of sample taken in a 25 ml measuring cylinder of Borosil measurement/recorded the volume of packing recorded and LDB and TBD calculated by following[12].

$$\text{LBD (loose Bulk Density)} = \frac{\text{Mass of Powder}}{\text{Bulk Volume of Powder}}$$

$$\text{TAB (tapped bulk density)} = \frac{\text{Mass of Powder}}{\text{Tapped Volume of Powder}}$$

Hausner's ratio: Flow properties of granules were determined by Hausner's ratio calculated by following formula:

$$\text{H} = \frac{\text{Tapped bulk density}}{\text{Lose bulk density}}$$

A Hausner ratio greater than 1.25 is considered of poor flow ability.

Carr's Index: Percentage compressibility of granules was determined by carr's compressibility index calculate by following formula[13].

$$\text{Carr's Index} = \frac{\text{TBD - LBD}}{\text{TBD}}$$

Evaluation of Tablets:

Physical characteristics of tablets: Thickness and diameter were measured using a calibrated dial caliper. Ten tablets of each formulation were evaluated.

Hardness: Monsanto hardness tester was used to evaluate hardness of tablet. The force of fracture was recorded, and the zero force reading was deducted from it. Ten tablets of each formulation were evaluated.

Friability: The Friability of the tablet was determined using Roche friabilator. Weigh accurately 20 tablets and placed them in the friability test apparatus. Adjust the timer to 4 minutes. Operate the apparatus at 25 rpm and observe the tablets while rotating. The tablets were weighed again. The % friability was then calculated by:-

$$\%\quad \text{Friability} = \frac{(W_1 - W_2)}{W_1} \times 100$$

Where, W_1 = Initial weight of the tablets, W_2 = Final weight of the tablets.

Weight Variation: Twenty tablets were sampled randomly. Tablets were weighed individually and average weight was calculated. Then deviation of each tablet from average weight was calculated and percent deviation was computed. The deviation was compared with the pharmacopoeia limits[14].

Uniformity of Content: Five randomly selected tablets were weighed and powdered. The powdered tablet equivalent to 100 mg drug in tablet was taken and transferred in 100 ml volumetric flask of distilled water. It was shaken on a flask shaker for the sedimentation of undissolved materials. The solution is filtered through Whatmann filter paper (0.45µm). 1ml of this filtrate was taken and transferred in 100 ml volumetric flask of distilled water. 1ml of this solution was taken and an appropriate dilution was made. The samples were analyzed at 276nm using visible spectrophotometer (UV-1700 Shimadzu). The drug content was determined from the standard curve prepared at max 276 nm.

***In-Vitro* Dissolution Rate Studies:** In-Vitro dissolution study was carried out using USP I apparatus (basket apparatus) in 900 ml of 0.1N HCL (pH 1.2), for 12 hours. The temperature of the dissolution medium was kept at 37±0.5ºC and the basket was set at 50 rpm. 1ml of sample solution was withdrawn at λ_{max} 276 nm using UV visible spectrophotometer. Cumulative percentage of drug release was calculated[15].

Stability Studies for Formulation: stability studies were as per ICH guideline at 30°C/65% RH and 40°C/75% RH for 3 month and tablets were evaluated for their physical appearance, Hardness, Weight variation drug content and cumulative % drug release at specified intervals of time[16].

RESULT AND DISCUSSION

Identification test by FT-IR: Identification of 5-HTP (naturally) derived from Griffonia Simplicifollia by FT-IR Spectroscopy shown in figure

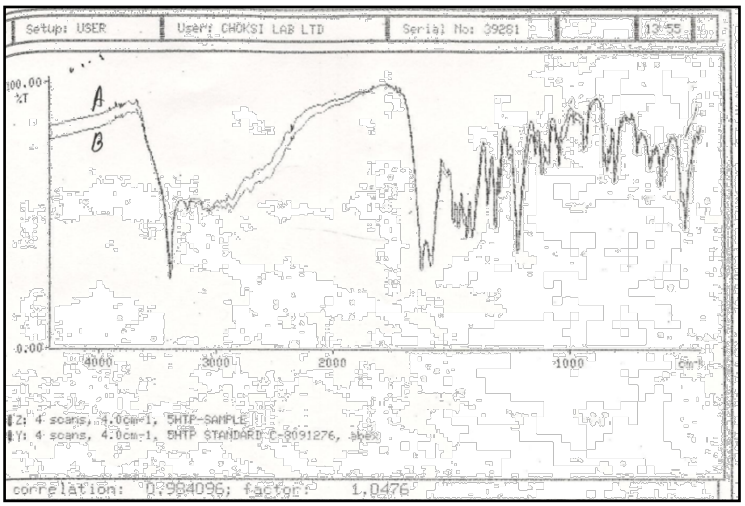

Fig1: IR spectra of (a) Standard (b) Drug sample.

Solubility (At room temperature): Represented in table

Table 2: Solubility (At room temperature)

S. No.	Solvent	Solubility
1	Water	Soluble

2	Ethanol	Slightly soluble
3	Methanol	Slightly soluble
4	Acetone	Partial soluble
5	Chloroform	Slightly soluble
6	0.1 M HCL	Soluble
7	PH 6.8 buffer	Soluble
8	0.1 M NaoH	Slightly soluble
9	Propylene	Insoluble
10	Glycerol	Slightly soluble

Loss on Drying (LOD): The percentage of loss on drying was found to be 2.92% w/w.

Determination of pH (1% w/v solution in water): The pH of the 1% w/v solution in water found to be 6.56.

Evaluation of Granules: Various evaluation results represented in the table 3.

Table 3: Evaluation of Griffonia Simplicifollia tablet granules

S. No.	Parameter	Batch No.					
		F1	**F2**	**F3**	**F4**	**F5**	**F6**
1	Bulk density (gm/cc)	0.59	0.52	0.52	0.66	0.70	0.68
2	Tapped density (gm/cc)	0.68	0.65	0.62	0.74	0.78	0.75
3	Carr's index (%)	13.235	15.384	16.129	10.81	10.256	9.333
4	Hausner ratio	1.152	1.181	1.192	1.121	1.114	1.102
5	Angle of repose	55.007	48.81	36.86	33.69	45.00	38.65

Evaluation of tablets: All the tablet evaluation result represented in table 4.

Table 4: Parameters of Griffonia Simplicifollia Tablets

Batch	Av. wt. (mg)	Weight Variation (mg)	Hardness (kg/cm2)	Friability (%)	Drug Content	Thickness (mm)

F1	665	19.25 (3%)	6.8	0.64	97.22	6.7056
F2	655	19.25 (3%)	6.2	0.54	98.19	6.9088
F3	672	19.25 (3%)	6.8	0.48	97.08	6.731
F4	665	19.25 (3%)	6.6	0.38	98.17	6.8072
F5	664	19.25 (3%)	6.4	0.46	99.30	7.1374
F6	660	19.25 (3%)	6.2	0.42	98.16	6.9342

***In-Vitro* Dissolution Rate Studies:** Drug release profile of formulation F1-F6 graph shown in figure 3.

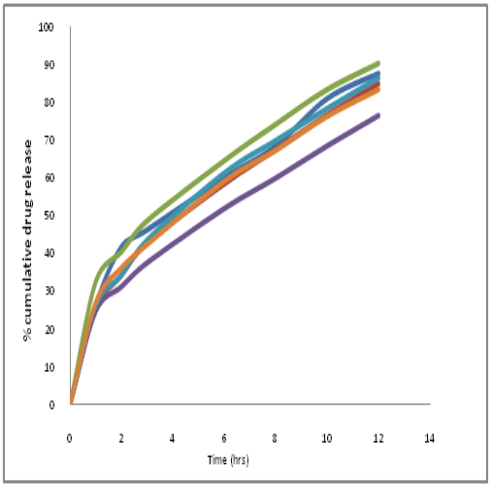

Fig 3 Drug release profile for formulation (F1-F6)

Stability Study: Stability studies shows no remark able changes in the physical properties of the tablets as well as no change in drug content and release profile.

CONCLUSION:

The present study was undertaken with an aim to formulate, develop and evaluate 5-HTP matrix tablets using different polymers by slugging method. Various formulations of sustained release tablets of Griffonia Simplicifollia were developed using various polymers viz, hydroxy Propyl methyl cellulose, MCC101, methyl cellulose in different proportions.

Results of in-vitro release profile indicated that extent of drug release from formulation F-5 was high as compared to other formulation. Stability study was conducted on tablets of batch F-5 stored at room temperature 40ºC and 2-8ºC for 3months.

Tablets were evaluated for moisture content (%w/w), Avg. wt. microbiological parameter, in-vitro release profile and drug content. After three months no significant changes were observed in any of the studied parameters during the study period. From the above results it concluded that formulation of matrix tablet of Griffonia Simplicifollia containing HPMC K35M and methyl cellulose batch F-5 can be taken as an optimized formulation of matrix tablets.

ACKNOWLEDGEMENTS:

The authors express deep thanks to Mr. Sanjay singh, Plethico pharma, Indore, India for providing facilities and guidance to carry out this work.

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