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Research Article

Formulation and optimization of water soluble granules of *Withania Somnifera*

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Abstract

Herbal medicines have great demand in the treatment of various kinds of illness. Ayurvedic system of medicine has consisted of many herbal sources in which ashwagandha one of them which are the very popular herbal sources. Many literature surveys suggest that ashwagandha is used as an immunomodulator, tranquilizer, antioxidant, antidiabetic, and nootropic activity. Present research work explored the potential benefit of ashwagandha by designing suitable granules of its water extract. Further, it is characterized by various parameters and *In-vitro* drug release

Keywords: Immunomodulator, Tranquilizers Ayurvedic, Ashwagandha, Granules

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INTRODUCTION:

Herbal drug treatments and their arrangements have been broadly used historically, for the lots of years in developing and developed nations owing to its herbal origin and lesser aspect outcomes or dissatisfaction with the consequences of synthetic pills. One of the characteristics of oriental herbal medicine arrangements is that all the natural drugs, both presenting as single herbs or as collections of herbs in composite formulae¹. The traditional arrangements comprise medicinal plant life, minerals, natural be counted, and so forth. Herbal capsules represent in particular the ones traditional drugs which usually use medicinal plant arrangements for therapy² India is referred to as the "Emporium of Medicinal flowers" because of availability of numerous thousands of medicinal plant life inside the one-of-a-kind bioclimatic zones³. Medicinal vegetation continues to provide valuable therapeutic retailers, each in contemporary medication and in traditional structures of medicine. Attention is being centered on the research of efficacy of plant based capsules used inside the conventional medication due to the fact they are economy, have a touch facet results and in keeping with WHO, about 80% of the world populace depend specially on herbal remedies⁵. The World Health Organization has these days defined traditional medication (which include natural capsules) as comprising healing practices that have been in existence, regularly for masses of years, before the improvement and unfold of present day medicinal drug and are nevertheless in use. The

points of concept are why not unusual humans divert to apply the Ayurvedic, Chinese and other herbal medicines? Though it's miles used all over the international, in India, its use is much greater due to their clean accessibility, no expert consultation required, are considered safe to use and also due to the fact number one fitness care services fall brief of peoples" want both in qualitative and quantitative phrases. We have to make these kind of without difficulty advertised ayurvedic, and other herbal drug treatments FDA accepted and growth public attention approximately professionals and cons of their makes use of. The common place notion that something herbal is safe isn't accurate.

MATERIALS AND METHODS:

Roots of *withania somnifera* collected nearby Bhopal, Petroleum ether, Mayer"s reagent Wagner"s reagent methanol, Sodium Starch glycolate (SSG), Croscarmellose sodium (CCS), and Lactose.

Preparation of extract

Roots of *withania somnifera* collected nearby Bhopal shade dried and powdered roots then extracted. For extraction defatted the coarsely powdered drug with petroleum ether by maceration method and then extracted with water. The extract was evaporated above their boiling points. Finally, the percentage yields were calculated of the dried extracts.

Qualitative phytochemical tests: The extracts obtained by solvent extraction were subjected to various qualitative tests to detect the presence of plant constituents.

Estimation of total phenolic content: Total Phenolic content estimation Principle: The total phenolic content of the extract was determined by the modified Folin-Ciocalteu method.

Preparation of Standard: 50 mg Gallic acid was dissolved in 50 ml methanol; various aliquots of 5-25µg/ml were prepared in methanol Preparation of Extract: 10 mg extract dissolved in 10 ml methanol and filtered. Two ml (1mg/ml) of this extract was for the estimation of phenol.

Procedure: 2 ml of extract or standard was mixed with 1 ml of Folin-Ciocalteu reagent (previously diluted with distilled water 1:10 v/v) and 1 ml (7.5g/l) of sodium carbonate. The mixture was vortexed for 15 sec. and allowed to stand for 15min for colour development. The absorbance was measured at 765 nm using a spectrophotometer.

Estimation of total flavonoid content:

Principle: Determination of total flavonoid content was based on aluminum chloride method

Preparation of standard: 10 mg quercetin was dissolved in 10 ml methanol, and various aliquots of 5- 25µg/ml were prepared in methanol.

Preparation of extract: 10 mg of dried extracted dissolve in 10 ml methanol and filtered. Three ml (1mg/ml) of this extract were taken for the estimation of flavonoid.

Procedure: 1 ml of 2% AlCl₃ methanolic solution was added to 3 ml of extract or standard and allowed to stand for 15 min at room temperature; absorbance was measured at 420 nm

Preparation of Granules: Granules were prepared by using wet granulation technique. Extract (powder) and citric acid were mixed in a mortar. This was followed by subsequent addition of starch, Sodium Starch glycolate (SSG), Croscarmellose sodium (CCS), and Lactose. Sufficient quantity of distilled water was added to form a lumpy mass which was then passed through sieve no. 22 to form granules. Granules were dried in the hot air oven. Magnesium stearate was added at the end ⁶.

Table 1: Composition of fast disintegration granules

Ingredients	Formulation code						
	F1	F2	F3	F4	F5	F6	In house Granules*F7
Granules (mg)	125	125	125	125	125	125	125
Starch (mg)	50	50	50	50	50	50	50
Sodium Starch glycolate (mg)	10	15	20	-	-	-	-
Cross-carmellose sodium (mg)	-	-	-	10	15	20	-
Lactose (mg)	34	29	24	34	29	24	44
Talc (mg)	5	5	5	5	5	5	5
Magnesium stearate (mg)	6	6	6	6	6	6	6
Total weight	230	230	230	230	230	230	230

* In house Granules= without disintegration

Characterization of Herbal granules

1. Flow property: The angle of repose of powder blend was determined by using funnel method. The accurately weighed 5 gm powder blend was taken in the funnel. The powder blend was allowed to flow through the funnel freely on to the surface⁷. The diameter of the powder cone was measured & angle of repose was calculated using the following formula:-

Angle of Repose (θ) = \tan^{-1} (h/r) Where, h and r are the height and radius of the powder cone

Further Hausner's Ratio, Compressibility index (Carr's Index) were also determined by using tapped density & poured density.

Content Uniformity: Granules were 1 gm weighed and then powdered by pestle in a mortar. 100 mg of powdered sample was taken in a beaker containing 20 ml of methanol to dissolve it. The content of the beaker were sonicated for 10 min to extract and dissolve out the flavonoid from granules. The solution was centrifuged at 3000rpm for 10 min and the supernatant react with 2% AlCl₃ and was analyzed after suitable dilution at 420 nm using UV spectrophotometer.

The mean percent flavonoid content was calculated as an average of three determinations.

In-vitro Disintegration Time: In-vitro disintegration time of formulated herbal granules was determined by using digital disintegration test apparatus. In-vitro disintegration test was carried out at 37±0.5°C in 0.1N HCl, 10 mg of granules were placed in each of the six tubes of disintegration test apparatus. The time required for complete disintegration of granules in each tube was noted.

In-vitro Drug Release: Study In-vitro dissolution studies of prepared granules were carried out using USP Paddle type dissolution test apparatus. To determine the dissolution, 900 ml of 0.1N HCL was taken as dissolution media and filled in vessel and temperature was maintained at 37±0.5°C. Granules were dropped in vessel and paddle was rotated at speed of 50 rpm at 37±0.5°C. 2 ml of samples were withdrawn at suitable time intervals (1, 5, 10, 15 min) and filtered with pre weighted whatman filter paper. The samples were analyzed using UV spectrophotometer at λ max 420 nm for determination of flavonoid content. Equal amount of fresh dissolution medium was replaced after each withdrawal.

RESULTS AND DISCUSSION

Table 2: Result of percentage yield of extract of *Withania somnifera*

S. No.	Solvents	Percentage Yield
1.	Aqueous	4.2 %

Table 3: Results of phytochemical screening of aqueous extract of *Withania somniferae*

S. No.	Constituents	Aqueous extract
1.	Alkaloids	-
2.	Flavonoids	+
3.	Diterpenes	+
4.	Phenolics	-
5.	Amino Acids	+
6.	Carbohydrate	+
7.	Proteins	+
8.	Saponins	+
9.	Glycosides	-

Presence = (+) absence = (-)

Phytochemical analysis of the plant extracts were done to determine the presence of various bioactive constituents according to standard methods. The phytochemical screening revealed the presence of Flavonoids, Diterpenes, Proteins, Amino Acids, Carbohydrate and Saponins compounds in the aqueous extract of roots of *Withania somnifera*.

Total Flavanoid Content estimation (TFC)

The content of total flavanoid compounds (TFC) content was expressed as mg/100mg of quercetin equivalent of dry extract sample using the equation obtained from the calibration curve: $Y = 0.06X + 0.019$, $R^2 = 0.999$, where X is the quercetin equivalent (QE) and Y is the absorbance.

Calibration Curve of Quercetin

Table 4: Preparation of calibration curve of Quercetin

S. No.	Conc. (µg/ml)	Absorbance
0	0	0
1	5	0.352
2	10	0.61
3	15	0.917
4	20	1.215
5	25	1.521

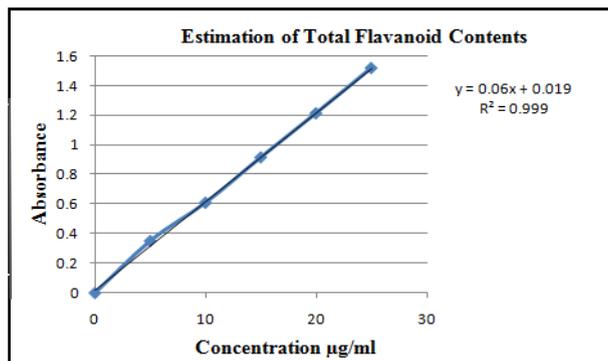


Figure 1: Graph of estimation of total flavanoid content

The flavonoids content was determined by aluminium trichloride method using Quercetin as reference compound. The total flavanoid content in crude extract were evaluated in the present study. The amount of flavanoid present in root of *Withania somnifera* was 1.010 mg of QE/mg of crude extract.

Table 5: Total flavanoid content of aqueous extract of *Withania somnifera*

S. No.	Total flavanoid (QE) (mg/100mg)
1.	1.010

Table 6: Results of pre-formulation parameters of Herbal granules

Formulationcode	Parameters				
	Bulk density (gm/ml)	Tapped density(gm/ml)	Carr's Index (%)	Hausner'sRatio	Angle ofRepose
F1	0.38±0.05	0.45±0.02	15.556±0.12	1.184±0.012	29°25
F2	0.39±0.01	0.44±0.03	11.364±0.15	1.128±0.011	30°25
F3	0.38±0.04	0.46±0.02	17.391±0.11	1.211±0.010	29°36
F4	0.39±0.03	0.45±0.02	13.333±0.12	1.154±0.013	31°26
F5	0.38±0.02	0.45±0.02	15.556±0.11	1.184±0.014	29°15
F6	0.37±0.02	0.46±0.03	19.565±0.14	1.243±0.010	29°36
F7	0.38±0.03	0.46±0.01	17.391±0.13	1.211±0.014	30°36

Prepared granules of herbal extract shows Carr's index in the range 11.364±0.15 to 17.391±0.11, Hausner's ratio in the range of 1.154±0.013 to 1.184±0.012 and the angle of repose

in the range of 29°36 to 31°26. The values of these parameter found within the limit which shows good flow property of prepared granules.

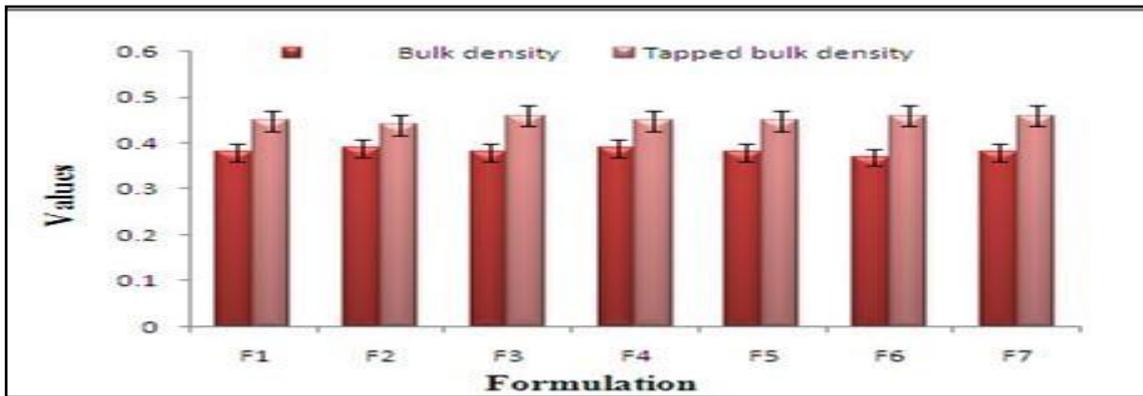


Figure 2: Graph of pre- formulation parameters (Bulk density and Tapped density)

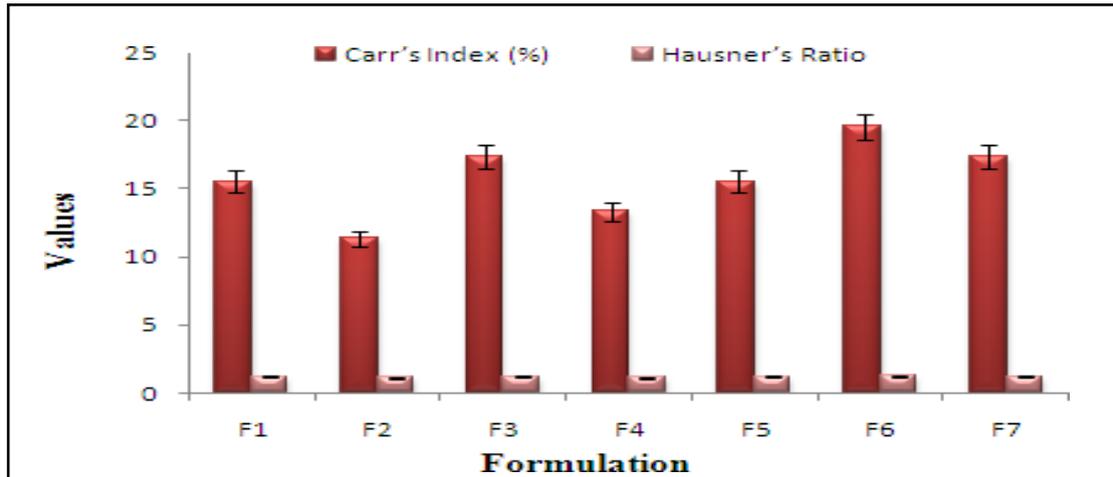


Figure 3: Graph of pre- formulation parameters (Carr's Index and Hausner's Ratio)

Table 7: Results of flavonoid content and *in vitro* disintegration Time

Formulation Code	Flavonoid content (%)	<i>In vitro</i> disintegration time (sec.)
		Mean ± SD
F1	95.23±0.11	42±1
F2	96.56±0.12	36±2
F3	95.12±0.21	32±1
F4	93.32±0.32	42±2
F5	95.54±0.45	36±2
F6	96.65±0.52	30±2
F7	95.45±0.12	14.25±2

Table 8: *In-vitro* Drug Release Study

Time (Min.)	% Drug Release						
	F1	F2	F3	F4	F5	F6	F7*
1	29.98	35.65	38.45	41.56	44.45	45.65	12.25
2	55.65	49.39	55.65	58.98	65.58	76.69	32.25
5	65.65	60.45	65.48	67.98	78.98	88.98	40.25
15	79.98	75.65	78.98	80.25	82.26	95.65	48.98

In vitro drug release study of flavonoid from herbal granules (*without super disintegrants)

In-vitro release studies of prepared herbal granules were performed in simulated fluid such as simulated gastric fluid pH 1.2. It was found that release of flavonoid was started

after 1 min. The drug release from F1, F2, F3, F4, F5, F6 and F7 was 29.98, 35.65, 38.45, 41.56, 44.45, 45.65 and 12.25 after 1min. In comparison to all formulation F7 Showed Slowest drug release because of absence of super disintegrants. Formulation F6 showed fastest drug release as compare to other formulation 95.65% after 15 min.

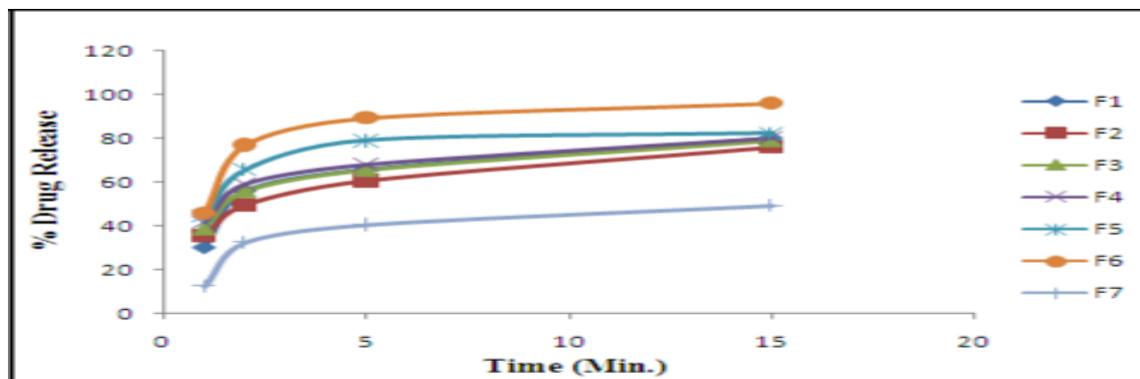


Figure 4: *In vitro* drug release study of flavonoid from herbal granules

CONCLUSION

Withania somnifera is considered to be one of the best rejuvenating agents in Ayurveda. Its roots, seeds and leaves are used in Ayurvedic and Unani medicines. *Withania somnifera* roots find an important place in treatment of rheumatic pain, inflammation of joints, nervous disorders and epilepsy. Dried roots are used as tonic for hiccup, cold, cough, female disorders, as a sedative, in care of senile debility, ulcers, etc. Leaves are applied for carbuncles, inflammation and swellings. Leaf juice is useful in conjunctivitis. Bark decoction is taken for asthma and applied locally to bed sores. *Withania somnifera* and its extracts are used in preparation of herbal tea, powders, tablets and syrups.

Upon above study we can conclude that designing of dosage form by using super disintegrating agent's changes the release pattern of constituents present in aswagandha extract, and this can helpful in management of dosage protocol and provide better patient compliance. Also this study guides the researcher to how to design the delivery of herbal extracts to get management of dosage regimen.

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Conflict of Interest

The author declares that no conflict of interest

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