The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 19-09-2013
Accepted: 21-10-2013

Vol. 2 No. 10 2013
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Development of Pharmaceutical Excipient from *Vigna mungo* husk Powder

Sandeep M. Ambore[1*], Ambar A. Gangale[1], Mukesh M. Gavit[1], Swapnil G. Patil[1]

1. School of Pharmacy, SRTM University Nanded.
[Email: ambore.sandeep@gmail.com, Tel: +91-9822916966]

Excipients are the vital part of the pharmaceutical formulations, as these are important for drug release, pharmacokinetic and pharmacodynamics properties of dosage form. Thus it is difficult to prepare the formulations without any excipient. In current study we explore the chances of natural waste material i.e. *Vigna mungo* husk powder for its excipient properties and compared with marketed formulation to check its efficacy. The results showed that the current formulation have good disintegrating property and passes the different Pharmacopoeial parameters viz. powder char acteristics, post formulation evaluation tests etc.

Keyword: *Vigna mungo* Husk Powder, Natural Disintegrant, Excipient From Waste.

1. Introduction

1.1 Excipient[1]

Excipient is the major part of the final formulation (dosage form) which may be used for human use or veterinary use. Excipients are the substances other than the Active Pharmaceutical Ingredient, which have been appropriately evaluated for safety and are intentionally included in a drug delivery system. Like active drug, excipients are also obtained from natural sources or are synthesized chemically or by other way. They may be simple, highly characterized, organic or inorganic molecules. As we all know that in earlier days the excipients were not as important as, they are considered now in drug formulation. But as pharmaceutical scientists study on different properties of the excipients it is observed that the excipients may show different application in the final dosage form which may enhance quality, safety and efficacy of the drug substance(s) in the dosage form. Characteristics of an ideal excipient are pharmaco-toxicologically inactive, high fluidity, Chemically and physically inert to drug & other formulation ingredients, colorless, high compressible and tasteless, well characterized by suppliers, i.e., master file, easy to store & lot-to- lot reproducible, performance consistent with the specific dosage form[2].

1.2 Traditional concept of the excipient[3]

The biological and analytical study requires origin of the excipient and active principle, whether of natural or synthetic origin. This is found to be always been at the center of pharmaceutical industries and health authorities attention. Now it's increasing demands and expectations with regard to quality have stimulated the development of new excipients characterized by higher assay and lower content of impurities. Quality of formulation does depend on the quality of excipient. Some factors outside the pharmaceutical area, such as the supply sources, quality of the material, the manufacture and marketing of raw materials justify the attention paid to the matter of excipients up to a few years ago.

An US FDA has issued a guideline about the safety testing required for the novel excipients[4]. It is also given in IPEC in their IPEC new excipient evaluation guidelines dated Octomber 1996[5], which were the basis for the USP-NF 26 General Chapter Excipient Biological Safety Evaluation Guidelines[4]. These documents gives the information which is useful for the assessing the safety of a chemical for use as an excipient. The IPEC Europe Safety Committee has published similar guidelines[5]. The manufacture of the new or novel excipient should develop the safety information recommended in these guidelines for their appropriate use[6]. This information provides the basis for establishing the suitability of the material for use as an excipient in a specific type of dosage form.

2. Material and Method:

2.1 Procurement and Authentication Of Sample[7]

Mung Dal husk sample was collected from Balaji Dalmill (Nanded) in October 2011. It was well dried and greenish in color. Herbarium sheet is prepared according to the instructions given by Botanical Survey of India.

2.2 Physicochemical Characterization Of Mung Dal Husk Powder Sample[8-15]

The different sample grades were evaluated for properties like swelling index, moisture content, Carr's index, Hausner's ratio, solubility and angle of repose. The evaluation was carried out as per procedure reported.

2.3 Prefomulation Studies[16]

A. UV Spectroscopy (Determination of lambda max.): UV light absorption spectrum in the range 200 to 400 nm of 0.0025% w/v solution of drug in 0.1 N HCl $_{(aq.)}$ is studied. The different peaks are observed according to the drug sample, which will give the lambda max of that drug sample.

B. FTIR[17]

The FTIR spectrum gives the idea regarding sample powder composition. For the same IR testing is done by using KBr as background. The KBr and sample are kept in small motor-pestle and triturated it. After the proper mixing small quantity is taken in IR crucible and IR spectra is obtained. From this spectrum the composition of sample can be evaluated.

C. DSC (Differential Scanning Calorimetry) [18, 19]

The DSC was used to measure the occurrence of exothermal or endothermal changes with increase in temperature. The DSC because of its sensitivity and accuracy has been extensively used to study the phase transition of polymer. Differential Scanning Calorimetry (DSC) measures the temperature and heat in the material time function and temperature in a controlled atmosphere.

D. SEM (Scanning Electron Microscopy)[20]

The scanning electron microscope (SEM) uses a focused beam of high-energy electrons to generate a variety of signals at the surface of solid specimens. The signals that derive from electron reveal information about the sample including external morphology (texture), chemical composition, and crystalline structure and orientation of materials making up the sample.

2.4 Preparation Of Fast Disintegrating Tablets of Ondansetron Hydrochloride by Direct Compression Method [21]

The fast disintegrating tablets of Ondansetron hydrochloride were prepared by direct compression method. The Table No: 2.1 given below shows the composition of each fast disintegrating tablet formulation.

Mixing of powders was carried out using a pestle and mortar. Mixing was continued for 3min. Finally, 200 mg of each mixture was weighed and fed manually into the die of a single punch tablet machine (Karnavati, India), equipped with 9 mm flat punches to produce the desired tablets. The hardness of the tablets was adjusted at 3--3.5 kg/cm^2 using a Monsanto hardness tester (Monsanto Chemical).

The compressed tablet of each formulation batch was then evaluated for tablet characteristics such as thickness, hardness, weight variation, friability

and drug content.

Table 2.1: Composition of Ondansetron hydrochloride tablet

Ingredients (mg)	Formulation Code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug	0	0	0	0	0	0	4	4	4	4
MD Sample	5	10	15	5	10	15	10	15	10	15
Ethyl Cellulose	5	5	5	5	5	5	5	5	5	5
Mannitol	5	5	5	5	5	5	5	5	5	5
Lactose	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total weight(mg)	200	200	200	200	200	200	200	200	200	200

2.5 Evaluation Of Prepared Tablets

A. Hardness

Although hardness test is not an official, tablet should have sufficient handling during packing and transportation. Hardness of tablet was measured using Monsanto hardness tester. It is the pressure required to fracture diametrically placed tablets by applying the force. The hardness of 3 tablets, from each batch was determined and mean hardness was taken into account, which was expressed in kg/cm^2.

B. Weight variation test

Weighed 20 tablets individually, calculated the average weight and comparing the individual tablet weight to the average USP weight variation test. As given below shows the weight variation tolerance for uncoated tablets.

Average Weight of Tablet (mg) Deviation Allowed	Max. %
130 mg or less	10
130 mg to 324 mg	7.5
More than 324 mg	5

C. Friability

Friability test was performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Pre-weighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and re-weighed. Compressed tablets should not lose more than 1% of their weight.

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100 \quad \ldots\ldots \quad (Eq^n \text{ no: } 2.8)$$

Where, % F = friability in percentage, W_o= Initial weight of tablet, W= weight of tablets after revolution

D. Thickness

The thickness of the tablet was measured using Vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

E. Content Uniformity

To check content uniformity 30 tablets were randomly selected. Out of 30 tablets, 10 tablets were crushed into fine powder and assayed individually; the tablet should be within 90% to 110% of the labeled claim.

F. Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$dl/dt = r\Upsilon\cos\theta/(4\eta l) \quad \ldots\ldots(Eq^n \text{ no: } 2.9)$$

Where, l is the length of penetration, r is the capillary radius, Υ is the surface tension, η is the liquid viscosity, t is the time and θ is the contact angle.

G. In-vitro drug release

In-vitro drug release studies of Ondansetron hydrochloride was carried out using USP type II Dissolution Testing Apparatus (6 vessel assembly, Paddle type II) at 50 rpm. The dissolution medium consisted of 900 ml of phosphate buffer (pH 6.8) solution. Temperature maintained at 37±0.5 ^{0}C. Aliquots of 1 ml were withdrawn at five min time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. Aliquots were filtered through whatmann filter paper, suitably diluted using Phosphate buffer (pH 6.8) soln. and analyzed spectrophotometrically at 248 nm.

Dissolution conditions used in the study are indicated as:

Speed of Rotation: 50 rpm
Weight of Tablet tested: 200 mg
Temperature: 37±0.5 °C
Time: 30 min

Test Medium: Phosphate buffer 6.8
Vol. of Sample taken: 1 ml
Vol. of Test Medium: 900 ml in each vessel.

H. Modified disintegration test

A petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully kept in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

I. Water absorption Ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation:

$$R=10(Wa/Wb) \quad \ldots\ldots\ldots\ldots(Eq^n \text{ no: } 2.10)$$

Where, Wb & Wa is weight of tablet before & after water absorption

3. Result And Discussion

3.1 Authentication of plant

Plant Authentication of plant is done from Botanical Survey of India, Pune. This Authentication of plant proved that plant specimen is *Vigna mungo* (mung plant).

3.2 Grinding and Sieving

Dried husk of Mung Dal sample was grinded well and sieved to have desired particle size of sieve number #44, #60, #72 in Indira College of Pharmacy Sahayog Campus, Vishnupuri, Nanded.

3.3 Physicochemical Properties of mung dal husk powder

Parameter	Inference
State	Solid
Colour	Green (Faint)
Odour	Odourless
Taste	Tasteless
Nature	Amorphous

3.4 Melting range by using Capillary method:

By Capillary method it was observed that, Mung Dal husk degraded between 75-80 ^{0}C, which was characterized by gradual charring of powder.

3.5 Powder Characteristic

Such as, bulk density, Hausner's ratio, angle of repose, compressibility index as compressibility of Mung Dal husk are given in table no: 3.1.

3.6. The pH

The pH of mung dal husk powder was found to be slightly acidic 6.53.

3.7. Loss on Driying

LOD was determined to be 0.9% which is within limits. This enable the use of mung dal husk powder as pharmaceutical excipient.

Table 3.1: Powder Characteristic of *Vigna mungo* Husk Powder

Sr. No.	Properties/ Sieve No.	Sieve No #44	Sieve No # 60	Sieve No # 72
1.	Bulk Density	0.4762 gm/ml	0.5 gm/ml	0.4878 gm/ml
2.	Tapped Density	0.588 gm/ml	0.601 gm/ml	0.599 gm/ml
3.	% Porosity	19.04	30	31.70
4.	Carr's Index (%) Remark	**19.05** **Fair**	**16** **Good**	**19** **Good**
5.	Hausner's Ratio Remark	**1.2347** **Good Flow Property**	**1.202** **Good Flow Property**	**1.227** **Good Flow Property**
6.	Angle of Repose Remark	**28º 96'** **Good Flow Property**	**28º 88'** **Good Flow Property**	**29º 65'** **Good Flow Property**
7.	Moisture Content (%)	0.15	0.25	0.15

3.8 Phytochemical Analysis

Mung dal husk powder was tested for presence of carbohydrates, steroid, amino acid, tannins. It gives positive test for carbohydrate as:

Parameter	Result
Carbohydrate	*Present*
Steroids	*Absent*
Amino acid	*Absent*
Flavonoids	*Absent*
Tannins	*Absent*

A. Total ash and acid insoluble ash

Ash value can be used as the quality standard for powder. Total ash value and acid insoluble ash was determined. It was observed that total ash value is 3.5% and there is negligible acid insoluble ash. These are given as:

Type of Ash	Ash value
Total Ash	3.5±0.1 %
Acid insoluble Ash	99.8±0.01 %
Water soluble Ash	4.2±0.1 %

3.9 Instrumental Analysis of Ondansetron Drug and Vigna mungo Powder

A. By UV Spectroscopy

UV Analysis of Ondansetron hydrochloride in 0.1 N HCl

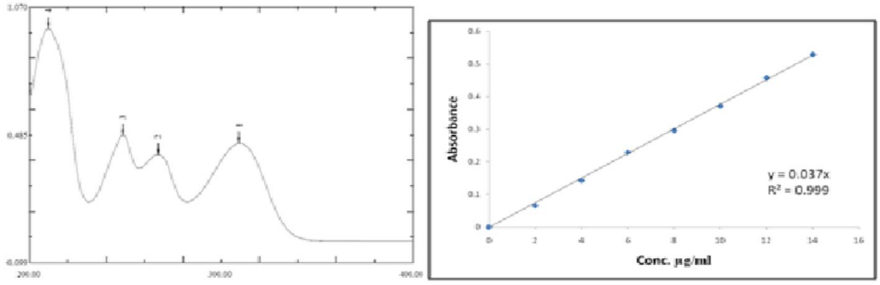


Fig 3.1: a) UV Spectra of Ondansetron b) Standard Calibration Curve of Ondansetron hydrochloride

By checking UV spectra of Ondansetron four peaks were observed at the range 200 to 400 nm of 0.0025% w/v solution of drug in 0.1 N $HCl_{(aq.)}$. It exhibits four peaks at about 210, 248, 266, 310 nm.

The IR spectrum shown in Figure no.3.2 the band at 3410 $cm^{-1}$was assigned to the O-H stretching of water. The absorption band at 1638 cm^{-1}Indicated amine and carboxy group in six membered ring. The sharp band at 1531cm^{-1} is characteristics of C=C aromatic group. While peaks at 1458 and 1479 cm^{-1} associated with methyl group in the compound. Whereas, peak at 756 cm^{-1} is due to the o- distributed benzene group which make up the gross structure of carbohydrate which is interpreted in Table no 3.2.

B. By FTIR Spectroscopy

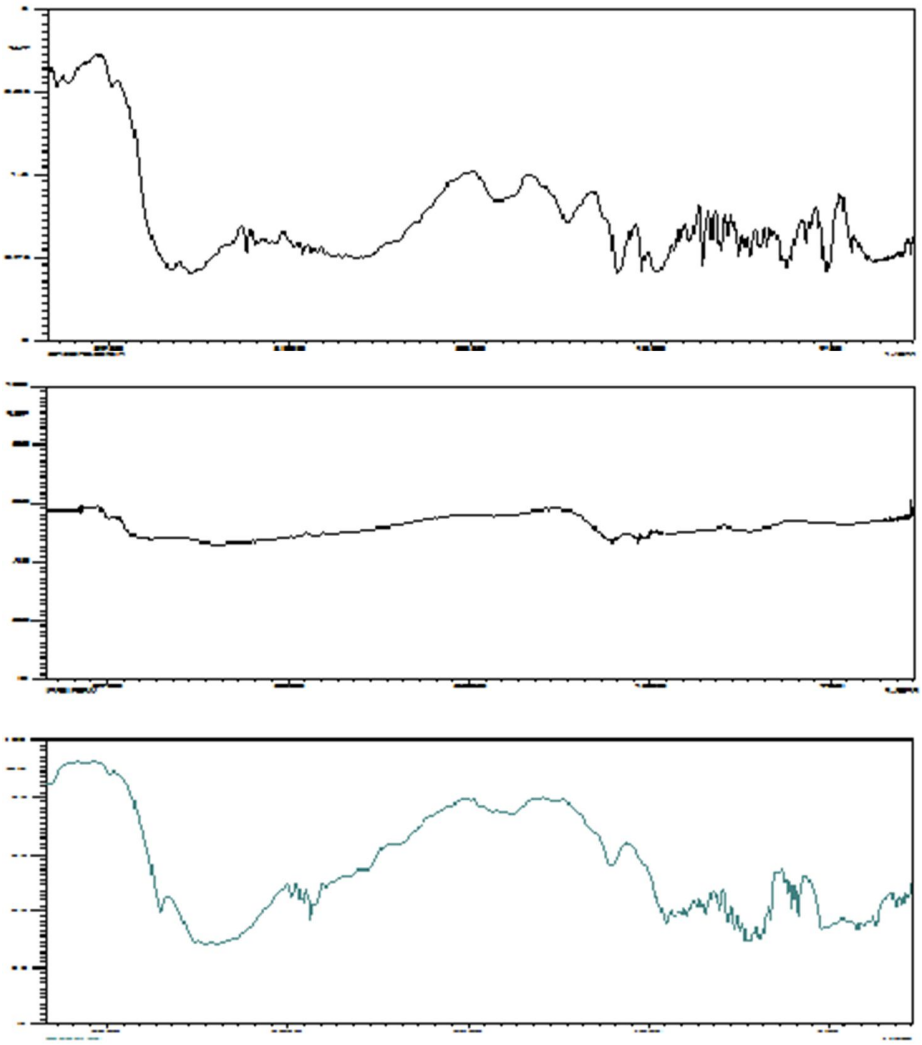


Fig 3.2: a) FTIR Spectra of Ondansetron drug b) FTIR Spectra of *Vigna mungo* c) FTIR Spectra of Ondansetron with excipient

Table 3.2: FTIR Interpretation of pure drug and *Drug + Vigna mungo*

Ondansetron Drug FTIR Interpretation		***Drug + Vigna mungo* FTIR Interpretation**	
Characteristic Peak Observed	**Groups present in drug**	**Characteristic Peak Observed**	**Groups present in drug**
3410	O-H Group in H_2O	3738	O-H, N-H groups
1638	C=N ,C=O, in six member ring	3294	O-H Group in H_2O
1531	C=C aromatic	1656	C=N ,C=O, in six member ring
1458 and 1479	CH_3	1466	CH_3
756	o-distributed benzene	856	o-distributed benzene

The *Vigna mungo* husk sample does not give the sharp peaks, but the peaks obtained show presence of different groups, which are given in the Table No- 3.2.

C. By DSC Spectroscopy

The DSC thermogram for *Vigna mungo* (mung dal) husk powder is shown in figure below and corresponding parameters are tabulated as well. The DSC shows that mung dal husk powder has onset occurred at 73.86 ^{0}C, while the peak temp was at 99.74 ^{0}C. The onset, peak and conclusion temperatures of base transition were observed to be moderate. The knowledge of glass transition Tg is essential in production processes and storage.

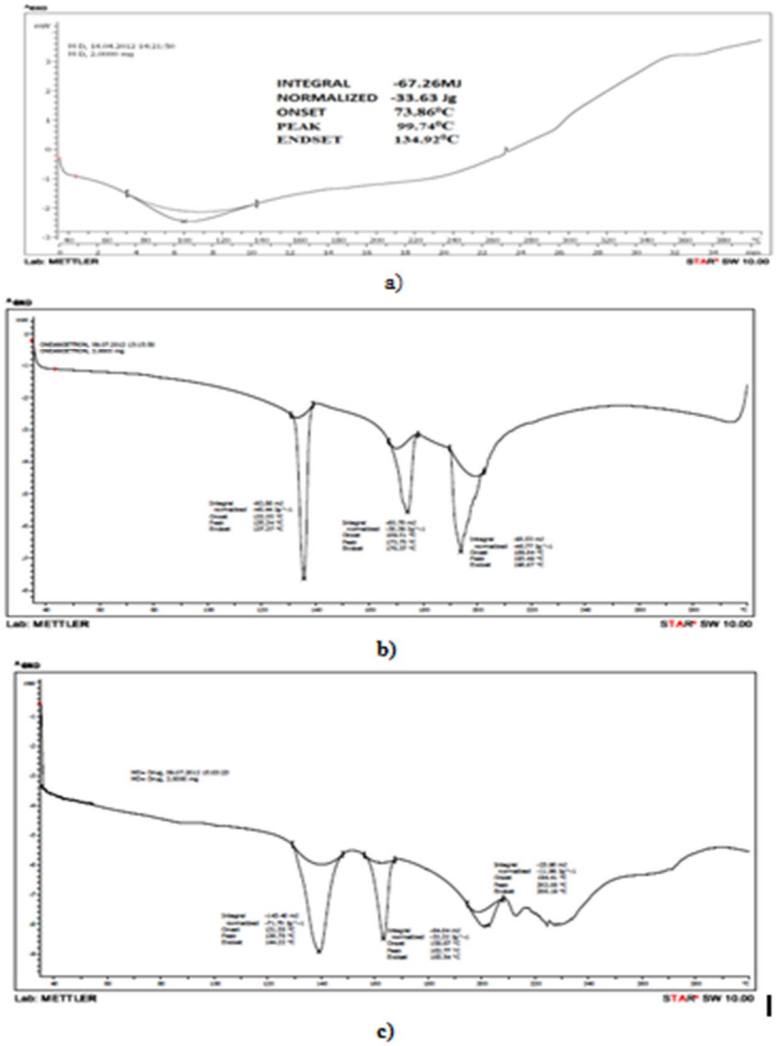


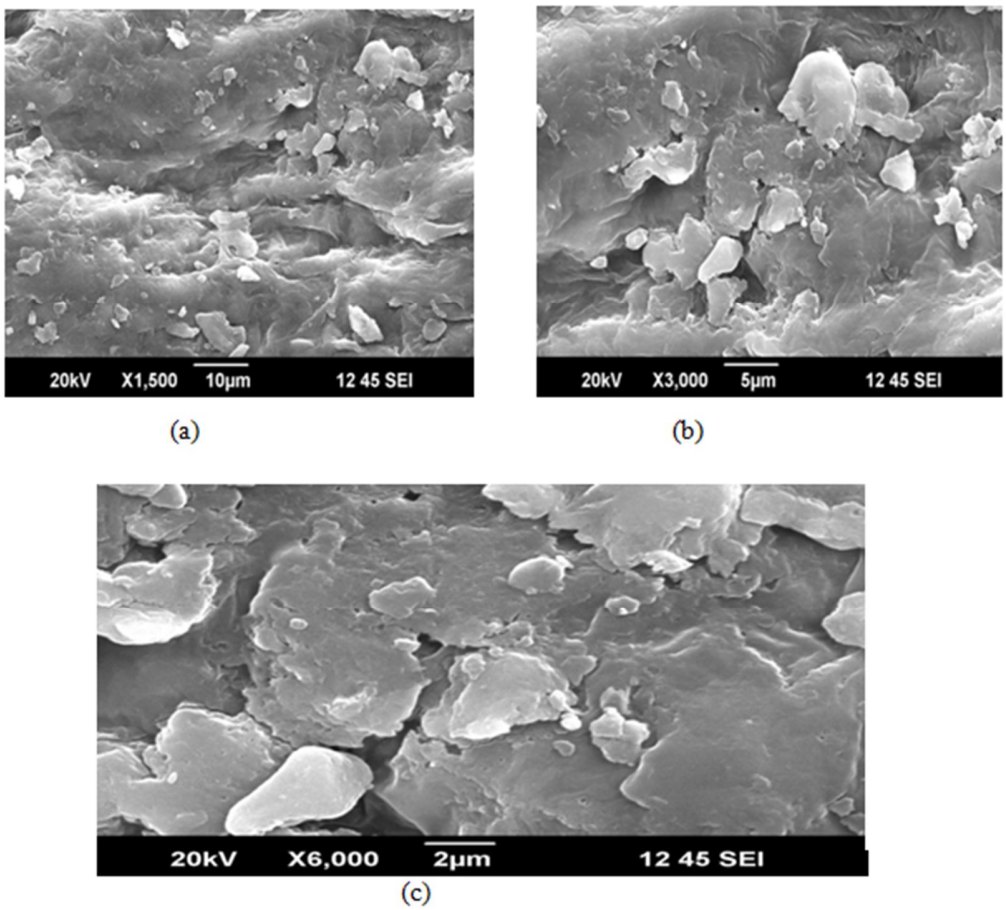
Fig 3.3: a) DSC Thermogram of *Vigna mungo* husk powder b) DSC Thermogram of Ondansetron drug c) DSC of drug with excipient

The interpretation of the above DSC thermogram is given as following Table No: 3.3

Table 3.3: DSC Interpretation of Drug & *Vigna mungo*

Sr. No.	Parameter	Drug	*Vigna mungo*
1.	Onset temperature	169.51 ^{0}C	73.86 ^{0}C
2.	Peak temperature	173.73 ^{0}C	99.74 ^{0}C
3.	Endset temperature	176.37 ^{0}C	134.92 ^{0}C

D. By Scanning Electron Microscopy (SEM)



Fige 3.4: SEM Analysis of *Vigna mungo* powder
a) 10 µm; b) 5 µm; c) 2 µm

From the above SEM result it is observed that the *Vigna mungo* husk powder sample is amorphous in nature. Physically it looks like the flakes, which have the irregular shape. The number of flakes are aggregated together to form big flake which varies in particle size.

E. By FTIR Spectroscopy

Peaks in FTIR spectra of Ondansetron were observed and by comparing peaks in both FTIR spectra of drug and Ondansetron along with excipient. From the spectra we can conclude that stretching shown by respective group were not changed. The O-H stretching at 3410 cm^{-1}, amine group at 1638 cm^{-1}, C=C group at 1531 cm^{-1} and O-distributed benzene at 756 cm^{-1} is same as that of pure drug. Therefore the study indicates that no interaction between the Ondansetron drug and excipient *Vigna mungo* husk powder.

F. Compatibility Study by DSC

From the Figure 3.3 of pure Ondansetron drug and Ondansetron with *Vigna mungo* excipient, the compatibility of Ondansetron drug is checked. The melting point of pure drug is in the range of 178-179 ^0C. The above thermogram of pure drug shows three peaks. The thermogram of Ondansetron along with the excipient shows comparatively same peaks at same onset and peak temperature as that of the pure Ondansetron drug. Hence from Fig. No 3.3 of DSC thermograms we can conclude that the *Vigna mungo* sample is compatible with the Ondansetron drug.

3.10 Formulation of Ondansetron Fast Disintegrating Tablet

The fast disintegrating tablets of Ondansetron hydrochloride were prepared by direct compression method. The formulation of each fast disintegrating tablets composed of mung dal husk powder as a disintegrant. The other excipients used were mannitol, ethyl cellulose for binding property, Lactose for its diluent property. The weight of tablet was adjusted to 200 mg and each tablet contains 4 mg of Ondansetron hydrochloride. Total 10 batches (F1-F10) were prepared; out of this F7-F10 are optimized batches. These optimized batches are selected from F1-F6 on the basis of their good tablet properties given in Table No: 3.4.

3.11 Evaluation of Ondansetron Fast Disintegrating Tablet

A. Hardness test

The hardness is the resistance of the tablet during handling, transportation, breakage and storage. The hardness of the batches from F1-F10 are given in Table No: 3.4. The hardness of all these batches was found to be in the range of 2.1-3.5 kg/cm^2 which is acceptable in case of fast disintegrating tablets.

B. Friability test

Friction and shocks are the forces which generally cause damage to the tablet. The friability test is done to evaluate the withstand capacity of the tablet in packaging, handling and shipping. The batches formed gives friability in the range from 0.25-1.49. from this passing batches are selected and used as optimized batches. The friability results are given in Table No: 3.4.

The optimized batches shows good friability tolerance and passes the limit of below 1%, hence these batches can be useful for their commercial application to formulate the fast disintegrating tablets.

C. Weight variation

The weight variation is obtained in the range of 2-5% and the weight values ranges from 196-206 mg. This shows that all the batches formed lies within the standard limit of 7.5% weight variation. It was obtained that not more than two tablets differ from average weight by more than 5% and no tablet differs by more than double the relevant percentage. The values are given in Table No: 3.4.

Table 3.4: Evaluation of Initial Batches & Marketed formulation of Ondansetron Drug Tablet

Batch No.	Evaluation Parameter Of Tablets					
	Weight Variation(mg)	Friability (%w/w)	Hardness in (kg/cm^2)	Thickness (nm)	Disintegration time (sec)	Wetting time (sec)
F1	199±1.1	1.49±0.05	2.5±0.12	2.1±0.14	1 min. 15 sec	1min 34 sec
F2	198±0.6	0.45±0.03	2.1±0.32	2.4± 0.07	55 sec	55 sec
F3	200±1.3	0.74±0.04	2.8±0.41	2.1±0.46	40	42
F4	197±1.4	1.75±0.09	2.5±0.75	2.3±0.23	55	45
F5	201±056	0.61±0.01	2.8±0.08	2.2±0.19	48	52
F6	199±2.3	0.58±0.07	3.2±0.56	2.3±0.34	42	47
F7	197±1.7	0.35±0.04	3.2±0.12	2.3±0.20	28	49
F8	199±0.9	0.78±0.07	3.5±0.43	2.2±0.17	32	55
F9	201±1.8	0.64±0.01	3±0.34	2.4±0.23	53	45
F10	197±1.2	0.87±1.2	2.5±0.51	2.3±0.14	45	53
F11	200±0.23	0.65±0.09	3.1±0.7	2.1±0.29	31	34

D. Thickness

Thickness is an important property of the tablet, which depend upon the compression force applied during the punching of tablet. It also depend on the speed of tablet compression. Thickness was found to be in the range of 2±0.11 to 2.5±0.04 mm. Tablet thickness was within ±55 variation of standard value, hence these are within the limit. The thickness values are given in Table No: 3.4.

From the Table No: 3.4 four batches F2, F3, F5 and F6 are having good tablet properties. Hence these batches are optimized as F7-F10 and used along with the Ondansetron drug. These optimized batches are again evaluated and are given in Table No: 3.4.
In Table No: 3.4, the F11 batch is marketed formulation of Ondansetron drug. This marketed Ondansetron tablet (Vomikind ODT) is evaluated for its various tablet specifications and the optimized batches are compared with this marketed formulation.

E. In Vitro Drug Release Study

The *in-vitro* drug release was studied using dissolution apparatus. At different time interval was withdrawn and cumulative percent drug release was calculated. The *in-vitro* drug release of Ondansetron fast disintegrating tablet is within standard limit of 90-110%. The % cumulative drug release of optimized and marketed formulation is given as follows.

Table 3.5: Comparison of bathes F7-F10 with Marketed formulation

Sr. No.	Batch code	Water absorption ratio	Modified disintegration time (Sec)	% CDR
1.	F7	30.17%	46	96.33
2.	F8	30.52%	30	98.25
3.	F9	25.92%	32	97.26
4.	F10	28%	26	99.13
5.	F11	31.14%	27	96.43

The percent cumulative drug release of batches F7, F8, F9 and F10 is 96%, 98%, 97% and 99% respectively, which is within the desired limit of 90-110 % of drug content. The comparison with the marketed formulation can be given as:

4. Summary

In the present study the husk powder of *Vigna mungo* was investigated for its physicochemical properties and its application in pharmaceutical industry. The well dried, sieved husk powder has been studied for its physicochemical properties like organoleptic properties, melting point, loss on drying, ash value, bulk and tapped density, angle of repose etc. This husk powder was compared with the other official excipients, which was followed by preformulation study and formulation of orally disintegrating tablet of Ondansetron HCl as a model drug. Then different batches were prepared and evaluated official and un-official tests.

5. Conclusion

In the present work, efforts have been made to evaluate disintegrating property of *Vigna mungo* husk powder by formulating fast dissolving tablets of Ondansetron with the use of lactose as a diluent by direct compression technique. The results revealed that the 0.5% of disintegrant husk powder shows good cumulative drug release rate. Release profile of F10 was found to have maximum release of 99.43% at the end of 5 minutes.
The drug release from all batches was found to be concentration and particle size dependant. The fast disintegrating tablets (FDT) found to have excellent physical characters. The disintegrant and sweetening agent were also found to be compatible with the other excipients of the formulation as well as with drug, which is evident from the drug release. Hence the formulation of F10 fulfills the objective of the present study.

6. Acknowledgment

This dissertation would not have been possible without the guidance and the help of several individuals. First and foremost, my utmost gratitude to Dr. S. G. Gattani, Director of School of Pharmacy, SRTM University whose sincerity and encouragement I will never forget.

7. References

1. John S, Louie-Helm W, Markey J, Micheline. Extending the duration of drug release within the stomach during the fed mode U.S. Patent US 6340475; 1999.

2. Rouge N, Allemann E, Gex-Fabry M. Comparative pharmacokinetic study of a floating multiple-unit capsule, a high-density multiple-unit capsule and an immediate-release tablet containing 25 mg atenolol. Pharm Acta 1998; 73(2):81-87.
3. Vasir JK, Tambwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. Int J Pharm 2003; 255:13–32.
4. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating Drug Delivery Systems: A Review. AAPS PharmSci Tech 2005; 6(3):47:372-390.
5. Nayak AK, Ruma M. Gastroretentive drug delivery systems: a review. Asian Journal of Pharmaceutical and Clinical Research 2010;3(1):1-10.
6. Gurnany E, Singhai P, Soni A, Jain R, Jain SK, Jain A. Gastro Retentive Drug Delivery System- A Review. Journal of Pharmacy Research 2011; 4(6)1899-1908.
7. Rapolu K, Dharani S, Yamsani M R. Preparation and evaluation of multiple-unit gastro retentive floating drug delivery system for ondansetron hydrochloride based on gas formation technique. Int J Pharm 2012; 2(1):46-54.
8. Goswami L, Mukhopadhyay S, Durgapal S. Formulation and evaluation of combined floating bilayer tablet of metformin and pioglitazone. Journal of Pharmacy Research 2011, 4(3):645-646.
9. Singh B, Ashu R, Babita, Ahuja N, Rishi K. Formulation Optimization of Hydrodynamically Balanced Oral Controlled Release Bioadhesive Tablets of Tramadol Hydrochloride. Scientia Pharmaceutica 2010; 78:303–323.
10. Reddy SN, Mahendra Kumar CB, Ramesh A, Chandrashekhar MS. Development and *In vitro* Evaluation of Gastro retentive matrix tablets: an approach using natural gums and polymers. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2011; 2(1):90-107.
11. Mohammed M, Ali S. Development of famotidine buoyant drug delivery system using natural polymers. International Journal of Biopharmaceutics 2012; 3(1):17-21.
12. Yadav A, Jain D K. Formulation development and in vitro characterization of bilayer and floating-bioadhesive tablets of propranolol hydrochloride. Asian Journal of Pharmacy & Life Science 2011; 1(1):1-12.
13. Chavanpatil M, Jain P, Chaudhari S, Shear R, Vavia P. Development of sustained release gastroretentive drug delivery system for ofloxacin: *In vitro* and *in vivo* evaluation. International Journal of Pharmaceutics 2005; 304(1-2):178-184.
14. Kouchaka M, Atyabib F. Ion-exchange, an Approach to Prepare an Oral Floating Drug Delivery System for Diclofenac. Iranian Journal of Pharmaceutical Research 2002; 2:93-97.
15. Bandari S, Chandra ME, Thadishetty A, Yamsani M R. Formulation and evaluation of multiple tablets as a biphasic gastroretentive floating drug delivery system for fenoverine. Acta Pharm 2010; 60:89–97.
16. Patil P, Rao SB, Kulkarni SV, Basavaraj, Surpur C, Ammanage A. Formulation and *In Vitro* Evaluation of Floating Matrix Tablets of Ofloxacin. Asian J Res Pharm Sci 2011; l(1):17-22.
17. Rajinikanth PS, Balasubramaniam J, Mishra B,. Development and evaluation of a novel floating in situ gelling system of amoxicillin for eradication of *Helicobacter pylori*. International Journal of Pharmaceutics 2007; 335:114–122.
18. Sungthongjeen S, Sriamornsak P, Puttipipatkhachorn S. Design and evaluation of floating multi-layer coated tablets based on gas formation. European Journal of Pharmaceutics and Biopharmaceutics 2008; 69:255–263.
19. Streubel A, Siepmann J, Bodmeier R. Floating matrix tablets based on low density foam powder: effects of formulation and processing parameters on drug release. European Journal of Pharmaceutical Sciences 2003; 18(1):37-45.
20. Srikanth MV, Srinivasa Rao N, Sunil SA, Sharma GS, Uhumwangho MU, Ramana MKV. Formulation and Evaluation of Gastro retentive Floating Drug Delivery System of Ofloxacin. Drug Invention Today 2011; 3(3):7-9.
21. Sharma N, Agarwal D, Gupta MK, Khinchi M. A Comprehensive Review on Floating Drug Delivery System. International Journal of Research in Pharmaceutical and Biomedical Sciences 2011; 2(2):428-440.