Journal of Pharmaceutical and Biological Research

Journal Home Page: www.pharmaresearchlibrary.com/jpbr

Research Article   **Open Access**

Design, Development & Evaluation of Domperidone Dispersible Tablet

Shilpi Singh*

Department of Pharmaceutics, Llyod Institute of Pharmacy, Greater Noida, India

A B S T R A C T

"The present study was aimed to prepare dispersible tablet of domperidone by using dried mucilage (DM, i.e. Mucilage isolated from seed of *Ocimum basilicum*) as novel disintegrant & to confirm the mechanism of disintegration of DM, ie. Mucilage isolated from seed of *Ocimum basilicum*". There are several technologies that produce commercially available DTs. ZydisR (Cardinal Health, Dublin, Ohio), OraSolvR /Dura Solv R (Cima Labs, Eden Prairie, Minnesota) and WOWTABR (Yamanouchi Pharma Technologies, Norman, Oklahoma) are widely known technologies. Although these technologies meet the special requirements for DTs to some extent, none has all the desired properties. The technologies are usually grouped according to the method used in making DTs, such as freeze drying, molding, and compression. Compression is the most widely used method for making DTs. Some methods are focused on unique granulation methods, such as spray-drying and flash-heating, to make shear form formulations; some are focused on selecting specific excipients such as water-insoluble calcium salt, specific disintegrant combination, and specific sugar combination; and some are focused on special treatment after compression, such as sublimation, sintering, and humidity treatments. *In-vitro* release study showed 75-80 % drug release from formulations of factorial batches within five to ten min. Formulation F3 disintegrated rapidly as compared to other factorial batches and hence taken further for stability studies and was found stable at the end of stability testing conducted as per the ICH guidelines. The dissolution profile of optimized batch F3 was compared with the dissolution profile of marketed formulation. There was no significant difference in the profile when compared statistically by applying t test at p<

Keywords: Domperidone, Dispersible tablet, Antiemetic, Dysphagia

A R T I C L E   I N F O

CONTENTS

*Corresponding Author
Shilpi Singh
Department of Pharmaceutics,
Llyod Institute of Pharmacy,
Greater Noida, India
Manuscript ID: JPBR3100

PAPER-QR CODE

1. Introduction

The oral route of drug administration is the most common and preferred route of drug delivery due to safest, most convenient, economical route and ease of ingestion. The tablet is the most widely used dosage form because of its convenience in terms of self administration, compactness, and ease in manufacturing. However, it has been reported that Dysphasia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. This leads to poor patient compliance. [1] According to a study dysphasia is common in about 35% of the general population, as well as an additional 30–40% of elderly institutionalized patients and 18–22% of all persons in long-term care facilities. Common complaints about the difficulty in swallowing tablets in the order of frequency of complaints are size, surface, form, and taste of tablets. Geriatric and pediatric patients and traveling patients who may not have ready access to water are most in need of easy swallowing dosage forms. [2]Solid dosage forms that can be dissolved or suspended with in less amount water and available in the form of smooth paste or suspension in mouth for easy swallowing are highly desirable for the pediatric and geriatric population, as well as other patients who prefer the convenience of readily administered dosage forms. [3].

The DTs is also known as fast melting, fast disintegrating, rapid dissolve, rapid melt, and/or quick disintegrating tablet. The disintegration time for good DTs varies from several seconds to about a minute. [4]. The advantages of Dispersible tablets are the ODTs do not need water for swallowing unlike conventional dosage forms. This is very convenient for patients who are travelling or do not have immediate access to water, and thus, provide improved patient compliance. [5] .Rapid drug therapy intervention is possible. [6] .Many techniques have been reported for the formulation of dispersible tablets [7] are Freeze drying / lyophilisation ,Tablet Moulding, Spray drying, Sublimation, Direct compression and Mass extrusion.

Mode of action of domperidone tablets

Domperidone acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. Antiemetic: The antiemetic properties of domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood brain barrier, which - among others - regulates nausea and vomiting. [8]

2. Material and methods

Domperidone as gifted sample from Lloyd School of Pharmacy Greater Noida (UP),   and Lactose, Saccharine, PVP K30, Magnesium stearate purchased from central drug house. All other reagents and chemicals used were of analytical grade.

Method:

Preparation of domperidone dispersible tablet

Procedure for preparation of granules: Powder blend was prepared by mixing all the ingredients (excluding Magnesium stearate) mentioned in table 1. In this powder blend sufficient amount of 10% PVP **K30** in IPA was added till cohesive mass is obtained. This cohesive mass was passed through the sieve no #30. Then the prepared granules are subjected to drying and tablet of granules was compressed with magnesium stearate at pressure 3 tons by using rotary tablet machine. Fast dispersible tablets containing 100 mg of domperidone were prepared by direct compression method and the various formulae used in the study are   shown   in   [Table 1]   All   the ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. The prepared powder blend was evaluated for variousparameters like bulk density, tapped d ensity, angle of repose, compressibility index and Hausner r atio. After evaluation of powder blend the tablets were compressed with a ten-station rotary punch-tableting machine (Rimek Mini Press-1) using 7mm flat puches set.

Evaluation of Domperidone Dispersible Tablets

Bulk Density (Db):

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$Db = M/ Vb$$

Where, M is the mass of powder, Vb is the bulk volume of the powder

Tapped Density (Dt):

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$Dt = M / Vt$$

Where,

M is the mass of powder, Vt is the tapped volume of the powder

Carr's index (or) Compressibility index

It indicates powder flow properties. It is expressed in percentage and is give

$$CI = \frac{TD - BD}{TD} \times 100$$

Where, TD is the tapped density of the powder and BD is the bulk density of the powder. The compressibility index (CI) was calculated by using the equation.

Hausner's ratio

Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner ratio = TD/BD

Where, TD is the tapped density. BD is the bulk density.

Angle of repose

The friction forces in a loose powder can be measured by the angle of repose ( ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane

Tan ( ) = h / r

= tan-1 (h / r)

Where,

 is the angle of repose. h is the height in cms r is the radius in cms.

Friability of Tablets

Friability is measured of mechanical strength of tablets. Roche friabilator is used to determine the friability

$$Friability\ (\%) = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

The results are reported in **Table no 2**

Weight Variation of Tablets

According to I.P. procedure for uniformity of weight, twenty tablets are taken and their weight is determined individually and collectively on an electronic weighing balance. The average weight of one tablet was determined from the collective weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the table and none deviates by more than twice that percentage. The weight variation test would be a satisfactory method of determining the drug content uniformity. The results are reported in **Table no 2**

In-vitro disintegration time.

This test determines whether dosage forms disintegrate within a prescribed time when placed in a liquid medium under the prescribed experimental conditions. The results are reported in Table no 2

Drug content

Ten tablets were weighed accurately. The average weight was determined and then ground to a fine powder. A quantity equivalent to 10 mg of domperidone was transferred to a 100 mL volumetric flask. The contents was ultrasonicated for 10 min with methanol, made to volume and filtered through Whatmann filter paper No.41. The solution was further diluted with methanol to give concentrations of 10mcg/mL. Absorbances of these solutions were measured at 287 nm and concentrations of drug in the sample was calculated using equation (8.8) and

Results of the analysis of the tablet formulations are reported in Table no 2. [9]

A= abc

Where A is absorbances of sample solution at 287

Uniformity of content: The test for uniformity of content of single-dose preparations is based on the assay of the individual contents of active substance(s) of a number of single-dose units to determine whether the individual contents are within limits set with reference to the average content of the sample.

Results are reported in Table no 2

Wetting time and water absorption ratio

Wetting time of dosage form is related to with the contact angle. Five circular tissue papers of 10cm diameter are placed in a petridish. Ten milliliters of dye solution is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time. Results are reported in Table no 2.

In-vitro Drug Release

The in vitro release tests were performed using the USP XXIV type II (paddle method) dissolution test apparatus (ElectrolabTDT-08L, India). The tablets were placed in dissolution vessel containing 900ml of buffer (pH 0.1 N HCL) maintained at 37 ± 0.5°C. The paddle rotation speed was kept at 50 rpm. Samples were diluted and filtered through a Whatman filter paper no.41 and assayed by UV spectrophotometry at 283 nm. Cumulative percentage of drug released from the tablets were calculated and plotted as a function of time. Results are reported in Table no 3 and shown in fig. 1

3. Results and discussion

Wet granulation is method of choice for drug that is hydrophobic in nature. Binder which was added during wet granulation method imparts compressibility to the powder bulk as well as improved wettability of the drug and hence its dissolution. Domperidone tablet were prepared in present study by using PVP K30 as a binder using its 5%, 10% and 15% solution in isopropyl alcohol though starch is supposed to be first choice as a binder. As its disintegration property is also reported, it not used as binder in study because the present work is aimed to investigate the disintegration ability of 'Dried mucilage' as novel disintegrants.

Hence inclusion of starch is avoided in preliminary batches. 5% were selected as the optimum concentration that showed minimal disintegration time of 30+2 seconds. It was observed that further increase in concentration of binder led to the increase in disintegration time. Such delay in disintegration may be because of the tight binding between molecules which ultimately slow down the water uptake by the tablets and thus Superdisintegrants do not get sufficient water to swell. Dispersible tablets of the composition B1 showing superior disintegration time with sufficient hardness as compared to B2 and B3 batch materials it might be due to high concentration of binder in B2 and B3 batch than B1 batch. Composition of batch B1 was selected for further study.
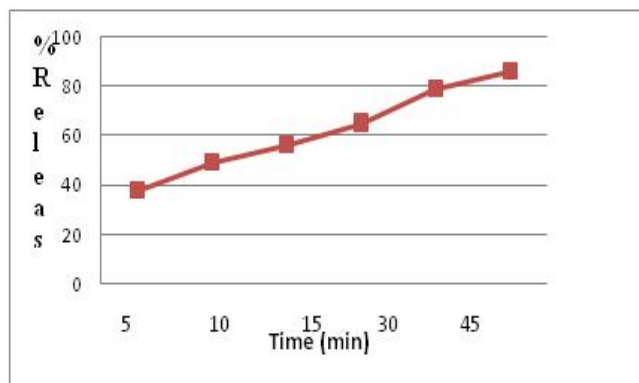
Figure 3: Dissolution data of fast dispersible Tablet prepared from batch B1 composition
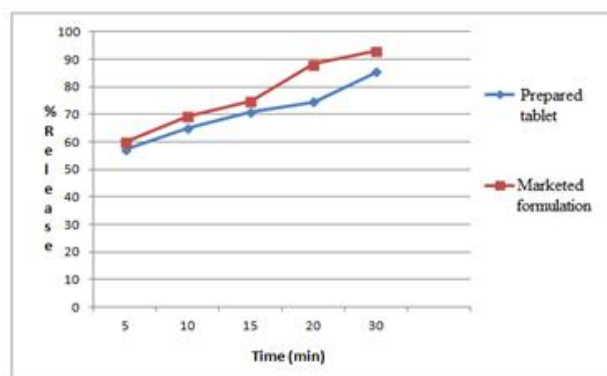

Figure 2: Comparison of dissolution profile of tablet of optimized batch with marketed formulation.

Table 2: Concentration and absorbance obtained for calibration curve of Fenofibrate In pH 6.8 Phosphate buffer

	Batch 1	Batch 2	Batch 3
Bulk density*	0.42 + 0.15	0.39 + 1.0	0.42 + 0.15
Tap density*	0.55 + 1.00	0.53 + 0.5	0.57 + 0.15
Compressiblity index.*	23.00+ 0.10	26.41 + 1	26.31 + 0.15
Housner's Ratio*	1.30 +0.00	1.35 +0.50	1.35 +0.1
Angle of repose*	18.0 +0.0	23.5+0.0	24.0 +1.0
Disintegration time (Seconds)	30+2	48 +5	68+2
wetting time (Seconds)	45+2	65 + 5	80 + 5
Hardness (kg/Cm2)	3.5 + 0.5	4.9 + 0.5	5.4 + 0.9

*All values are expressed as Mean ± SD, (n = 3)

Table 2: Physical tests of preliminary batches of B1 batch fast dispersible tablets.

S. No	Test	Observation	Specification
1	Friability (n=18)	0.40 ± 0.04%	Passes the test
2	Weigh variation(n=20)	300.0 + 2	Passes the test
3	Disintegration time (Seconds)	26 + 2.0	Passes the test
4	Drug content. (%)	90.66 + 0.91	Passes the test
5	Content uniformity	92.57±2.17	Passes the test
6	Wetting time (Seconds)	39 + 2	Passes the test

This table concluded that all the test performed were passes the test.
*All values are expressed as Mean ± SD

Table 3: Dissolution data of fast dispersible Tablet prepared from batch B1 composition

Time (mins)	% Cumulative release*
5	37.88 + 0.05
10	49.05 + 0.07
15	56.26 + 0.20
30	64.92 + 0.03
45	78.67 + 0.10
60	85.78 + 0.96

*All values are expressed as Mean ± SD, (n = 3)

Table 4 Characterization of tablet blends for various physical properties.

Batches	Bulk density*	Tap density*	Compressiblity index.*	Housner's Ratio*	Angle of repose*
F1	0.37 + 0.89	0.50 + 0.00	26.00+ 0.00	1.35 +0.00	15+0.2
F2	0.37 + 0.78	0.51 + 0.00	27.00+ 0.00	1.37 +0.00	15+0.1
F3	0.31 + 0.02	0.34 + 0.00	20.00 + 0.00	1.09 +0.00	14.3+0.2
F4	0.30 + 0.00	0.41 + 0.00	26.82+ 0.00	1.36 +0.00	13.41+0.1

*All values are expressed as Mean ± SD, (n = 3)

The results of determination of bulk density, tapped density, compressibility index, Hausner ratio were summarized in below **Table 4.** The compressibility index and Housner's ratio of all the formulations was found to be in the range of 20 to 27 and 1.09 to 1.37 which indicated passable flow property of powder blend(U.S.Pharmacopoiea) .

Table 5: Comparison of dissolution profile of tablet of optimized batch with marketed formulation

Time (mins)	% Cumulative release of Prepared tablet	% Cumulative release of marketed formulation
5	57.08 $\pm$ 0.52	60.12 $\pm$ 0.24
10	64.88 $\pm$ 0.95	69.47 $\pm$ 0.42
15	70.85 $\pm$ 0.57	74.58 $\pm$ 0.83
20	85.31 $\pm$ 0.79	88.29 $\pm$ 0.54
30	89.30 $\pm$ 0.67	93.06 $\pm$ 0.13

*All values are expressed as Mean $\pm$ SD, (n = 3)

Comparison of dissolution profile of tablet of optimized batch (F3) with marketed formulation was statistically significant by applying 't'test (p<0.05)

4. Conclusion

In the present study dispersible tablet of domperidone were prepared by usind dried mucilage as superdisintegrants. The result obtained from pre-compression parametes such as angle of repose, carr's index, hausner ratio were found to be within acceptable pharmacopoeia range. Glidants was generally used to improve flow properties of all formulaions. The hardness and friability of prepared tablets indicated that the tablet is mechanically stable. Results of percent weight variation and drug content uniformity found within limits. The tablet formulated by using dried mucilage as a novel disintegrant, disintegrated within 27 $\pm$ 5 seconds. These tablets also exhibited excellent wetting time i.e. 37 $\pm$ 5 seconds. These results revealed that functionality of dried mucilage as a disintegrant. *In-vitro* release study showed 75-80 % drug release from formulations of factorial batches within five to ten min. Formulation F3 disintegrated rapidly as compared to other factorial batches and hence taken further for stability studies and was found stable at the end of stability testing conducted as per the ICH guidelines. The dissolution profile of optimized batch F3 was compared with the dissolution profile of marketed formulation. There was no significant difference in the profile when compared statistically by applying t test at p<.

5. Acknowledgement

6. References

[1] Lindgren S, Janzon L. Dysphagia: prevalence of swallowing complaints and clinical finding. Med Clin North Am ; 77:3–5

[2] Sastry SV, Nyshdham JR, Fix JA. Recent technological advances in oral drug delivery: A review. Pharmaceutical Science and Technology Today. 2000:3:138-45.

[3] Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. J Pharm Pharmacol. 1998: 50(4):375–382.

[4] Dobetti L. Fast Melting Tablets: Development and Technologies. Pharmaceutical Technology. 2001; 44- 50.

[5] Wagh MA, Dilip KP, Salunkhe KS, Chavan NV, Daga VR. Techniques used in orally disintegrating drug delivery system. Int J Drug Deliv. 2010: 2: 98-107.

[6] Manivannan R. Oral disintegrating tablets: A future compaction. Int J Pharm Res Dev. 2009: 1 (10): 1-10.

[7] Nayak AK and Kaushik M.Current developments in orally disintegrating tablet technology J Pharm Educ Res 2011; 2(1): 21-34

[8] Tripathi KD. Essencials of medical pharmacology, jaypee brother medical publisher pvt.ltd., 5th edition 2003.

[9] Ravi kumar P, Bhanu prakash P, Murali krishna M, yadav M, Deepthi C.Simultaneous Estimation of Domperidone and Pantoprazole in Solid Dosage Form by UV Spectrophotometry Department of Pharmaceutical Sciences Andhra University, E-Journal of Chemistry. 2006: 3(3):142-145