



Preformulation Studies of Rapid Dissolving Tablets of Doxylamine

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ABSTRACT

Rapid release dose forms have become popular as an alternative to oral dosing forms in order to get around these problems. After administration, rapid drug release dosage forms dissolve more quickly and dissolve at a faster pace. The current study's objective is to formulate and produce Doxylamine succinate fast-dissolving tablets using the direct compression method in order to increase their dissolution rate. In this experiment, the super disintegrating agent was used in an effort to speed up the release of the drug from the oral tablets. Precompression properties were applied to the manufactured rapid dissolving tablets, and their hardness, weight variation, friability, wetting time, and disintegration time were measured. Doxylamine succinate rapid dissolving tablets were created via the direct compression process in order to boost the dissolve rate.

Keywords: Rapid release dose forms, oral dosing, doxylamine succinate, fast-dissolving tablets

1. INTRODUCTION

The purpose of immediate release tablets is to dissolve and release the medication without the need for any regulating elements like coating or additional formulation methods. After swallowing the solution containing the active ingredients, the target is reached and the intended effect is produced by the active chemicals being absorbed via the gastrointestinal epithelium. (Shyamala, B. & Narmada, G. Y. 2002)

The term "immediate release" refers to dose forms that dissolve quickly and release the medication. (Nyol Sandeep, Dr. M.M. Gupta 2013). A suitable pharmaceutically acceptable diluent or carrier can be used to facilitate immediate release; nevertheless, it

should be noted that these substances do not significantly slow down the rate of drug release and/or absorption. (**Utsav Patel, Khushbu Patel, Darshan Shah, Rushabh Shah 2012**). Formulations that are modified, controlled, sustained, protracted, extended, or delayed in their release of the medication are not included in this phrase. (**Dedhiya**).

Quick release One can categorize solid oral dose forms based on how quickly or slowly they dissolve. (**R.Natarajan, Rohit Vaishnani, and NN. Rajendran 2011**). Dosage forms labeled as immediate release dissolve at least 85% of the contents in less than 30 minutes. The only thing stopping the medicine from releasing from immediate release pills is the basic erosion or disintegration stage, which takes less than an hour to complete on average. Disintegration is a crucial step in the process of improving any drug's dissolving and, consequently, its bioavailability from rapid release tablets. Commercially available super-disintegrants include croscarmellose sodium, crospovidone, and SSG. (**Srinivas Pannala, Mahalaxmi Rathnanand 2011**).

At least 85% of the contents of dosage forms designated for immediate release dissolve in less than 30 minutes. The basic erosion or disintegration stage, which typically takes less than an hour to complete, is the only thing preventing the medication from releasing from instant release pills. Improving a drug's ability to dissolve and, as a result, increase its bioavailability from rapid release tablets requires disintegration. Super-disintegrants that are sold commercially include croscarmellose sodium, crospovidone, and SSG. (**A.K. Tiwari, H. Shah, A. Rajpoot, Manmohan Singhal 2011**). The goal of the current study is to create teneligliptin orodispersible tablets by utilizing various super disintegrants to increase the drug's solubility and disintegration and increase its bioavailability.

Oral administration is the most commonly utilized approach due to its ease of consumption, pain prevention capabilities, versatility (accepting different types of medication candidates), and most importantly, patient compliance. Furthermore, because they don't require sterile conditions, the production of solid oral delivery systems is less expensive. Several novel technologies for oral distribution have recently become available to address the physicochemical and pharmacokinetic aspects of drugs and to increase patient compliance. (**Allen LV1996**)

For elderly people, the ideal formulation is one that is simple to handle and swallow. A fast-dissolving tablet has been attempted to be developed with these requirements in mind. Such a pill dissolves in a small amount of water in the oral cavity, making it easily swallowed by any patient, regardless of age or location. For example, someone who doesn't have easy access to water can carry it with them wherever they go, whenever they choose. It's also easy to dose bedridden patients, elderly people, and babies who have trouble swallowing pills and capsules. Recently, a lot of companies have been researching and developing fast-disintegrating dosage form technologies, which can accommodate various pharmacokinetic, pharmacodynamic, and physicochemical characteristics of drugs. (**Biradar SS 2006, Lachmann L 1998**)

2. Preformulation Studies

Preformulation testing's main goal is to produce data that will be helpful in creating a stable, bioavailable formulation. Additionally, using preformulation parameters increases the likelihood of creating a product that is stable, effective, safe, and acceptable. Studying the physicochemical characteristics of the bulk medication, such as its description, solubility, identification test, melting point, and molecular weight, is required

before formulating any medicinal ingredient into a dosage form.(Cooper J Gunn C, Carter SJ 1986)

a. Organoleptic evaluation:

Drug's organoleptic characteristics, such as color, smell, and taste, were noticed using descriptive terminology

b. Melting point

Using the open capillary method, the melting point of pure Doxylamine succinate was found out. The capillary tube was repeatedly taped shut at one end by fusion, and then repeatedly filled with Doxylamine succinate. A digital melting point equipment held the capillary tube. A glass capillary tube with an end that had been previously sealed was filled with finely ground medication. The thermometer is attached to the capillary tube, and it is inserted into the Thieles tube before being set on fire. It was noted what temperature the powder will melt at.

c. pH Range :

pH of a 0.10 g/mL solution in water devoid of carbon dioxide R, 4.9–5.1

d. Solubility: Solubility of the drug was determined by taking a few quantity of drug (about 1-2 mg) in the test tube singly and added the 5 ml of the solvent (water, Acetone, methanol, Benzene, Chloroform) Shake strongly and kept for some time. Note the solubility of the drug in a variety of solvents (at room temperature) (IP, 2007).

e. Determination of bulk density and tapped density

It is a measurement used to characterize the way particles are packed and to calculate the volume of medication in milligrams per milliliter both before and after tapping. Using a bulk density device, the tablet mixes and Doxylamine succinate's loose bulk density (LBD) and tapped bulk density (TBD) were calculated. A 100 ml graduated measuring cylinder held 5 g of the medication or 25 g of polymers that had been precisely weighed. The starting volume was noted. At first, 200 taps were made on the cylinder at a distance of 14 ± 2 mm. To the closest graded unit, the tapped volume was measured. There were two hundred more taps made. The volume that was tapped was once more measured to the closest graded unit. The graduated cylinder was carefully filled with a precisely weighed quantity of powder (W), and the volume (V_o) was determined. The graduated cylinder was then sealed with a lid and placed within the density measurement equipment. After setting the density apparatus for 500 taps, the volume (V_f) was measured, and the process was repeated until the 2 successive readings were equal.. (Beeckett AH, Stenlake JB. 2003)

The tapped density & bulk density were calculated using the following formula:

$$\text{Bulk density} = W / V_o$$

$$\text{Tapped density} = W / V_f$$

Where,

W = weight of the powder

V_o = initial volume

V_f = final volume

f. Flow Properties

The angle of repose is used to measure the flow qualities. Frictional forces between the particles cause improper powder flow. The angle of repose is used to quantify these frictional forces. The greatest angle that can exist between a powder pile's surface and a horizontal plane is known as the angle of repose. The fixed funnel method was utilized to ascertain the angle of repose. (Syed azeem, Shawetsharma 2011)

$$\tan \theta = h/r \quad \theta = \tan^{-1} h/r$$

Where,

h=height of pile.

r= radius of the base of pile.

θ =angle of repose.

Table No. 2.1: Relationship belongings angle of repose and powder flow

S. NO	Angle of repose (θ)	Flow
1	<25	Excellent
2	25-30	Good
3	30-40	Passable
4	40 & Above	Very Good

g. Compressibility Index

From the particle density, compressibility was computed using the following formula.:

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

Where,

TD – Tapped density

BD – Bulk density

Table No. 2.2: Compressibility Index range

S. No	Percentage Compressibility Index	Flow ability
1	5-15	Excellent
2	12-16	Good

3	18-21	Passable
4	23-35	Poor
5	33-38	Very poor
6	<40	Very Very poor

h. Hausner Ratio:

The ratio of the tapped density to the bulk density is used to measure the powder's flow characteristic.

Table No. 2.3: Hausner Ratio Properties

Hausner Ratio	Properties
0-1.2	Free flowing
1.2-1.6	Cohesive powder

i. Sieve analysis

The primary goal of sieve analysis is to identify the various drug particle sizes that are present. Standard sieves were placed one on top of the other in a sequence so that the top sieves had larger pores (fewer sieve numbers), while the bottom sieves had greater sieve numbers.

Table No. 2.4: Relationship belongings Nature of sample and different particle size.

S. No	Nature of Sample	Result of Determination
1.	Coarse powder	NMT 40% passes through 36#, and NLT 95% of the sample mass passes through 14#.
2.	Moderately coarse Powder	NMT 40% passes through 60#, and NLT 95% of the sample mass passes through 25#.
3.	Moderately fine powder	NMT 40% passes through 40#, and NLT 95% of the sample mass passes through 36#.
4.	Fine powder	NMT 40% passes through 150#, whereas NLT 95% of the sample mass passes through 100#.
5.	Very fine powder	NMT 40% passes through 200#, whereas NLT 95% of the sample mass passes through 150#.
6.	Super fine powder	NLT 95% based on fewer than ten particles

j. Physical Stability of the Admixture

After a month at 60 °C, the medications and excipients were stored under the prescribed conditions, and physical changes were noticed in the mixture.

3. RESULTS AND DISCUSSION

a. Organoleptic character of Doxylamine succinate

After extensive research, it was discovered that Doxylamine succinate's entire organoleptic character meets with USP requirements.

Table No. 3.1: Characterization of Drug

Test	Specification	Result
Colour	White or powder	Confirms
Odour	Odourless	Confirms
Physical State	Crystalline Powder	Confirms

b. Melting point

Melting point of Doxylamine succinate found 106°C

c. pH Range

pH range of Doxylamine succinate found between 4.9-5.1

c. Solubility

Doxylamine succinate Extremely soluble in ethanol, benzene, and diethyl ether, soluble in water (1000 g/L at 25 °C); and soluble in chloroform.

d. Bulk & Tapped Density

Table No. 8.7 contains result of evaluation and report of all the pre-compression parameters. The Doxylamine succinate powder blend batch as a whole had a bulk density of 0.58g/cm³ to 0.65g/cm³, and its total tapped density was 0.70g/cm³ to 0.77g/cm³, indicating good flow properties.

e. Flow Properties

The drug's and the excipients' angle of repose was assessed. The angle of repose for the entire powder blend in each formulation was found to range from 25.74 to 29.960, suggesting that the blend had good flow qualities. Thus, it is verified that every blend has the ability to flow freely indicating good flow properties.

f. Compressibility

Another method for measuring free-flowing powder is to use Carr's index. All of the formulations' Carr's indices, which range from 12.83 to 14.15, show that the mixes have a fair flow character.

g. Hausner Ratio

According to protocol, the medication and excipient Hausner ratio was calculated. Each formulation's total powder mix's hausner ratio fell between 1.13 to 1.27, indicating that the mixes is free flowing. Thus, it is verified that every blend has the ability to flow freely.

h. Sieve Analysis

To perform a sieve analysis or ascertain the particle size, a mechanical sieve shaker was employed. The retention of approximately 22.0% of drug particles on filter number 18 and 78% of drug particles on sieve number 50 is noteworthy. Thus, the particles passed through sieves number 50 and number 18. The range of particle sizes for the drug is 287 μ m to 1mm.

Table No. 3.2: Results of Pre-compression parameters

Parameters	Bulk Density (g/cm ³)	Tapped density (g/cm ³)	Carr's Index (%)	Angle of Repose (θ)	Hausner Ratio
F1	0.61	0.74	13.31	25.74	1.27
F2	0.58	0.77	14.15	26.27	1.19
F3	0.59	0.73	13.96	27.32	1.16
F4	0.64	0.76	12.83	26.65	1.22
F5	0.62	0.74	13.19	28.42	1.17
F6	0.65	0.70	12.89	29.96	1.15
F7	0.61	0.73	13.74	25.07	1.13
F8	0.64	0.74	14.02	26.56	1.15
F9	0.66	0.76	14.29	27.60	1.17

Table No.3.3: Particle size determination of Doxylamine succinate

Sieve No	Microns	Wt of drug + sieve (g)	Wt of the drug retained (g)	% of drug retained	Cumulative % of drug (μ) retained
#18	1000	381.2	3.6	18.2	18.2
#50	282	357	18	80	98.2
#70	195	327.6	0.4	1.8	100
#120	118	339	0	0	0
#140	103	333	0	0	0
#170	82	322	0	0	0
#200	69	316	0	0	0
#200 Pass		448	0	0	0
			22	100	

i. Admixture Physical Stability

The medications and excipients were stored under the required conditions, and the outcomes are provided.

Table No. 3.4: Drug – Excipient stability profile

S. No	Items	1 Month/Control	1Month/ 60°C
1	API	No change	No change

2	API+ Crosscarmellose	No change	No change
3	API+ Crospovidone	No change	No change
4	API+ Talc	No change	No change
5	API+ Magnesium stearate	No change	No change

After a month at 60 °C, no physical changes were seen in the mixture.

Conclusion

The drug delivery pharma industry is currently experiencing intense competition and quick evolution due to an ever-growing demand. One such novel and distinctive drug delivery method that is quickly gaining popularity in the realm of rapid dissolving technology is the fast-dissolving tablets. Due to oral route's simplicity, adaptability, patient compliance, and precise dose, it is favored. For those with dysphasia a disorder that makes swallowing difficult, oral administration is not recommended. Additionally, oral delivery may not be the preferable method for many elderly and pediatrics patients. Rapid disintegrating tablets offer a helpful substitute in this regard. Rapid disintegrating tablets instantly breakdown upon contact with saliva, releasing the medication.

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