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INVESTIGATIONS ON PREFORMULATION OF DOXYLAMINE RAPID DISSOLVING TABLETS

[*1]Harish Kumar Singh and [2]Ashish Manigauha

[1]Research Scholar, Faculty of Pharmacy, Mansarovar Global University Sehore (M. P.).

[2]Professor, Faculty of Pharmacy, Mansarovar Global University Sehore (M. P.).

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***Corresponding Author**
Harish Kumar Singh
Research Scholar, Faculty of Pharmacy, Mansarovar Global University Sehore (M. P.).

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 disintegranting 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 have become popular as an alternative to oral dosing forms in order to get around these problems.

1. INTRODUCTION

Any drug delivery system's (DDS) main objective is to offer a human being a treatment that is both effective and safe. For a long time, oral medication distribution has dominated the global pharmaceutical industry's market. It is growing every day as a result of its appeal as a drug administration route. (Tiwari et al.2008). The production of tablets is now a science thanks to numerous advancements in pharmaceutical technology. In recent times, tablets have been the most advantageous form when compared to other conceivable dosage forms. (Rasenaket al. 2002). This dosage form's ease of manufacture, ease of administration, high dose precision, stability, and safety are its main selling points. Many techniques, including

direct compression, dry granulation, and wet granulation, are frequently employed in the production of tablets. (Shangraw, 1989; Rudnic et al. 2005).

To create a suitable tablet, a medicine might be combined with a variety of excipients. The crucial elements are the excipients' chemical and mechanical characteristics. The majority of contemporary tablets have the following features: easy swallowing; ideal size, shape, and color for identification; and mechanical strength suitable for coating, packing, and transportation. Tablets eventually have to meet USP requirements for drug content, release rates, stability, and 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).

The phrase "immediate release" describes dosage forms that release the drug rapidly after dissolving. [Dr. M.M. Gupta, Nyol Sandeep, 2013]. Although immediate release can be facilitated by the use of a suitable and pharmaceutically acceptable diluent or carrier, it should be emphasized that these substances do not considerably slow down the rate of drug release and/or absorption. [Darshan Shah, Rushabh Shah, Khushbu Patel, and Utsav Patel 2012]. This phrase excludes formulations that release the medication in a modified, regulated, sustained, prolonged, extended, or delayed manner.

2. Preformulation Studies

The primary objective of preformulation testing is to generate information that will aid in the development of a stable, bioavailable formulation. Furthermore, the use of preformulation parameters raises the possibility of producing a stable, safe, effective, and palatable product. Before incorporating any medicinal substance into a dosage form, it is necessary to examine the bulk medication's physicochemical properties, including its description, solubility, identification test, melting point, and molecular weight. **(Cooper J Gunn C, Carter SJ 1986).**

a. Organoleptic evaluation

Using descriptive language, the drug's organoleptic properties—such as color, smell, and taste—were observed.

b. Melting point

The melting point of pure Doxylamine succinate was determined using the open capillary technique. Doxylamine succinate was repeatedly added to the capillary tube after it had been taped shut at one end by fusing. The capillary tube was maintained in place by a digital melting point apparatus. Medication was powdered fine and put into a glass capillary tube with a previously sealed end. Prior to being ignited, the thermometer is connected to the capillary tube and placed within the Thieles tube. The temperature at which the powder will melt was observed.

c. pH Range

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

d. Solubility: A little amount of the medication (about 1-2 mg) was placed in a test tube alone, and 5 ml of the solvent (water, acetone, methanol, benzoene, and chloroform) was added. The mixture was shaken vigorously and allowed to sit for a while to assess the drug's solubility. Take note of the drug's solubility in various solvents. (at room temperature) (IP, 2007).

e. Determination of bulk density and tapped density

This measurement is used to determine the amount of medicine in milligrams per milliliter before and after tapping, as well as to describe the manner the particles are packed. The loose bulk density (LBD) and tapped bulk density (TBD) of the tablet mixtures and Doxylamine succinate were determined using a bulk density instrument. 5 g of the drug or 25 g of carefully weighed polymers were stored in a 100 ml graduated measuring cylinder. It was stated what the initial volume was. Initially, 200 taps were made at a distance of 14 ± 2 mm from the cylinder. The tapped volume was measured to the nearest graded unit. Two hundred additional taps were made. Once again, the nearest graded unit was used to quantify the tapped volume. A precisely weighed amount of powder (W) was carefully poured into the graduated cylinder, and the volume (Vo) was measured. After that, the graduated cylinder was put into the density measuring apparatus and covered with a lid. The volume (Vf) was measured after the density apparatus had been set for 500 taps, and the procedure was

repeated until the two consecutive 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 flow characteristics are measured using the angle of repose. Inappropriate powder flow is caused by frictional forces between the particles. These frictional forces are measured using the angle of repose. The angle of repose is the maximum angle that can occur between the surface of a powder pile and a horizontal plane. The angle of repose was determined using

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

the fixed funnel technique. **(Syed azeem, Shawetsharma 2011)**

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.

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

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 flow characteristic of the powder is determined by dividing the tapped density by the bulk density.

Table No. 2.3: Hausner Ratio Properties.

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

i. Sieve analysis

Finding the different drug particle sizes that are present is the main objective of sieve analysis. Standard sieves were arranged sequentially, with the bottom sieves having more sieve numbers and the top sieves having wider holes (fewer 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

Following a month at 60°C, the drugs and excipients were kept in the recommended storage conditions, and the combination underwent physical changes.

3. RESULTS AND DISCUSSION

a. Organoleptic character of Doxylamine succinate

After much investigation, it was shown that the whole organoleptic nature of doxylamine succinate satisfies USP standards.

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

Doxylamine succinate's melting point was determined to be 106^0C.

c. pH Range

pH range of Doxylamine succinate found between 4.9-5.1.

c. Solubility

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

d. Bulk & Tapped Density

The assessment and report results for each pre-compression parameter are shown in Table No. 8.7. Good flow qualities were shown by the Doxylamine succinate powder blend batch's overall bulk density of 0.58g/cm3 to 0.65g/cm^3 and its total tapped density of 0.70g/cm3 to 0.77g/cm^3.

e. Flow Properties

The angle of repose of the excipients and the medication was measured. Each formulation's total powder mix's angle of repose ranged from 25.74 to 29.96, indicating that the blend had acceptable flow characteristics. Therefore, it is confirmed that each blend exhibits good flow qualities by being able to flow freely.

f. Compressibility

Carr's index is an additional technique for measuring free-flowing powder. The Carr's indices for each formulation, which vary from 12.83 to 14.15, demonstrate that the mixtures have a reasonable flow character.

g. Hausner Ratio

The Hausner ratio between the drug and the excipient was computed in accordance with procedure. The hausner ratio of the entire powder mix for each formulation ranged from 1.13 to 1.27, suggesting that the mixture is free flowing. Therefore, it is confirmed that each mix may flow freely.

h. Sieve Analysis

A mechanical sieve shaker was used to determine the particle size or conduct a sieve analysis. Notably, 78% of drug particles were retained on sieve number 50 and around 22.0% of drug particles were retained on filter number 18. As a result, the particles went through sieves 50 and 18. The drug's particle sizes range from 287 µm to 1 mm.

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 results are given, and the drugs and excipients were kept in the proper storage conditions.

Table No. 3.4: Drug – Excipient stability profile.

S. No	Items	1 Month/Control	1Month/ 60^{0}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 ºC, no physical changes were seen in the mixture.

CONCLUSION

Due to a constantly increasing demand, the medication delivery pharmaceutical business is now undergoing rapid innovation and fierce rivalry. Fast-dissolving tablets are one such innovative and unique medication delivery technique that is rapidly gaining traction in the field of rapid dissolving technology. The oral route is preferred because of its ease of use, versatility, patient compliance, and accurate dosage. It is not advised to provide medication orally to those who have dysphasia, a condition that causes difficulty swallowing. Furthermore, many pediatric and elderly patients may not find oral administration to be the best option. In this sense, pills that dissolve quickly provide a useful alternative. When rapid-disintegrating tablets come into touch with saliva, they rapidly break down and release the drug.

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