European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 11 Issue 5, 2024

DOI: 10.53555/ejmcm/2024.11.05.17

FORMULATION AND EVALUATION OF RAPID DISSOLVING TABLETS OF DOXYLAMINE

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ABSTRACT

Doxylamine, a histamine H1 antagonist, has potent sedative properties. It has also antiemetic, hypnotic, and allergy properties. An antihistaminic that is commonly used to treat and prevent nausea and vomiting is doxylamine succinate. It comes in the shape of quickly dissolving pills. Giving the patient a more conventional manner to take their medication gave rise to the concept of fast-dissolving drug administration. The direct compression approach was used to manufacture fast-dissolving tablets containing doxylamine succinate. Evaluation criteria for the produced fast-dissolving tablets included weight variation, hardness, friability, disintegration time, drug content, wetting time, and short-term stability investigations. It was found that the % weight variation and drug content uniformity of all the formulations were within the approved range. Friability and hardness, two evaluation measures, demonstrated that every formulation's tablet had good mechanical resistance.

1. INTRODUCTION

Any drug delivery system's 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**).

Because of their ongoing development and application of creative ideas to address the fundamental flaws in the current formulations, tablets continue to be the most widely used and acceptable dosage forms. The tablets and capsules are said to be the most often used oral dose forms, with advantages that have been demonstrated for decades. However, there are certain disadvantages, such as swallowing difficulties, as dysphasia is more common in bedridden, elderly, and pediatric patients. The idea for the rapid dispersible drug delivery system was born out of the need to give patients a traditional way to take their medications.

The oral route of administration has gained popularity recently due to its simplicity of consumption, ability to avoid pain, variety, and most significantly, patient compliance. (**Ghosh et al. 2005**). Because of this, a novel method of drug delivery called "fast dissolving," "disintegrating," or "melt-in-mouth" tablets is becoming more and more popular. These tablets are made to be absorbed through the esophagus and buccal mucosa as saliva enters the stomach. In the latter instance, a drug's bioavailability from rapidly dispersible and/or dissolving formulations may be considerably higher than it is in oral dose forms that are traditionally used. (**Anil et al. 2012**).

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2. METHODOLOGY

2.1 Formulation of Doxylamine Succinate Tablets

In this work, the formulation development of Doxylamine succinate tablets that dissolve quickly was attempted using the direct compression method with the assistance of superdisintegrants. There are 10 mg and 20 mg dosages of Doxylamine succinate tablets on the market. A dosage of 20 mg has been used for this investigation. (Udupa N, Venkatesh, Mutalik S, Venugopal K.2001).

The kind and concentration of polymers as well as the characteristics of the medication were the primary determinants in the formulation development of the current investigation. (Badhan AC, Mahajan HS, Kuchekar BS 2004) Several polymers were utilized in varying concentrations (5%, 7.5%, and 10%) to produce tablets with favorable physical characteristics

Table 2.1 Formulation of Doxylamine succinate rapid dissolving tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Doxylamine succinate	20	20	20	20	20	20	20	20	20
SSG	5	7.5	10	-	-	-	-	-	-
Crosscarmellose	-	-	-	5	7.5	10	-	-	-
Crospovidone	-	-	-	-	-	-	5	7.5	10
Aspartame	5	5	5	5	5	5	5	5	5
Raspberry flavour	3	3	3	3	3	3	3	3	3
Talc	12	12	12	12	12	12	12	12	12
Magnesium state	5	5	5	5	5	5	5	5	5
MCC(q.s)	100	100	100	100	100	100	100	100	100

Nine formulations (F1 to F9) of doxylamine succinate rapid dissolving tablets were formulated with the tablet's total weight (100 mg) remaining consistent throughout. The #60-sieve was used to filter both the medication and the excipients. The medication and excipients, with the exception of magnesium stearate, were weighed and manually combined for 20 minutes in a polybag using the geometric addition method. After that, the mixture was further mixed with magnesium sterate (#60-sieve) to lubricate it. After flavoring the mixture and drying it at 40 to 45 degrees Celsius to remove moisture, the powder blend was compressed using flat-faced puncablets on a 10-station rotary punching machine.Round punches measuring 8 mm diameter were used for compression of tablets. **(Modasiya MK, Smith RD, Michel JH. 2009)**

2.2 Evaluation Parameters

2.2.1 Thickness and diameter:

Vernier calipers were used to measure the tablet's diameter and thickness. It has a millimeter measurement. Depending on the tablet's size, a deviation of ± 5% can be permitted. **(Dollery C.)**

2.2.2 Hardness test:

A tablet's strength can be determined by its hardness. A Monsanto tester was used to measure the hardness. When being handled and transported, the tablet needs to be stable under mechanical strain. The various manufacturers and tablet varieties have differing degrees of hardness. **(Parrot, E. L. 1970)**

2.2.3 Weight variation test:

The official USP limits for tablet percentage variation are shown in the following table. (**Gupta et al**). The weight variation's percentage difference need to fall inside the allowed ranges (±7.5%). There were 100 mg of tablets in total that were formulated. The table below displays the % deviation for tablet weight uniformity according to IP limitations.

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$$PD = \frac{(W_{avg}) - (W_{initial})}{(W_{avg})} X\,100$$

Where,
PD = Percentage deviation,
W_{avg}= Average weight of tablet,
$W_{initial}$ =individual weight of tablet.

2.2.4 Friability test:

The tablets' friability was determined using the Roche friabilator. The allowed friability cap is one percent. The tablets' friability was assessed using a Roche friabilator. The tablets in the friabilator were subjected to rolling, which caused the tablets to fall freely (6 inches) inside the chamber. The speed at which it rotated was 25 rpm. The tablets were removed from the friabilator after 100 rotations, or 4 minutes, and their intact weight was once more determined collectively. **(Margret Chandira .R., Jaykar .B.,Chakrabarty B. L., 2010)**

The percentage of weight loss was calculated using the formula.

$$\% \text{ Friability} = \frac{(W1 - W2)}{W1} \times 100$$

Where,
W1= Weight of tablet before test
W2 = Weight of tablet after test

2.2.5 Wetting time

The dosage form's wetting time and contact angle are connected. The amount of time it took for water to reach the tablets' upper surface was known as the wetting time.

2.2.6 Disintegration Time

Disintegration happens when the unit being examined disappears from the instrument's screen, or if it does, it is reduced to pieces of the tablets' broken constituent parts, such as the insoluble coating, which is a gooey mess with an invisible core. Allow the machine to run for the designated amount of time after placing the assembly in the beaker containing the designated liquid. Take the assembly out of the fluid if none of the tablets or capsules break down, then the tablet or capsule passes the test. Repeat the test with 12 more tablets or capsules if any of the original 18 do not dissolve; at least 16 of the tested 18 pills or capsules should dissolve.

2.2.7 Drug content determination

The average weight of three randomly chosen uncoated tablets was determined. A precisely weighed quantity of tablet powder was extracted from the crushed mixture after the tablets were crushed in a mortar. Following that, the samples were moved into three 100 ml volumetric flasks and diluted with phosphate buffer (pH 6.8) solution to the appropriate level. The contents were shaken once a day for a whole day to allow the medicine to thoroughly dissolve. Using the standard calibration curve of Doxylamine succinate in phosphate buffer pH 6.8 solution, the amount of medication in each tablet was determined.

2.2.8 Stability study

Stability testing of drugs and medicinal products is essential to product quality at every stage of

development. Stability assurance is essential to drug product's safety and efficacy throughout its use and shelf life. **(Sheinin EB.1998)** For almost three months, stability tests were conducted in a thermal lab under a variety of settings, such as 40ºC/75% RH and 25ºC/60% H. In the first, second, and third months, samples were collected.

3. RESULT AND DISCUSSION

3.1 Evaluation Parameter

Doxylamine succinate tablets of various formulations were put through a battery of evaluation procedures, including ones that measured drug content, friability, hardness, thickness, and weight fluctuation. Table 3.1 displays the entire outcome.

3.1.1 Thickness & Diameter

The thickness of the tablets was measured with a Vernier Caliper; the uncoated tablets ranged in thickness from 2.9 to 3.8 mm. Hence, every formulation displayed consistent thickness.

3.1.2 Hardness test

Using a Monsanto hardness tester, the tablet's hardness was determined. Hardness tests on ten tablets from the sample revealed that their densities ranged from 3.6 to 4.3 kg/cm^2.

3.1.3 Weight variation test

For tablets having more than 250 mg, the pharmacopoeial limit for the percentage variance in a weight fluctuation is ±5%. Since each pill formulation's average percentage deviation fell within the allowed range, all formulations complied with the regulatory requirements for weight uniformity. The results of the Weight Variation Test showed that they varied from 98.6±0.17 to 102.3±0.41.

3.1.4 Friability test

Tablets need to be friable in order to withstand the compression force applied during tablet manufacture. Every formulation of Doxylamine succinate tablets was found to have friability ranging from 0.67 to 0.75%. The IP criteria stated that the friability of each formulation was less than 1%.

3.1.5 Wetting Time

The tablet's wetting time was measured, and the outcome was discovered in 38–44 seconds.

3.1.6 Disintegration Time

The breakdown After measuring the tablet's duration, the result was found to be between 34±0.69 and 52±0.73 seconds.

Table No. 3.1: Results of post compression parameters

Formulation code	Hardnesskg/cm^2)	Friability (%)	Weight variation Test (%) ±S.D	Thickness of Tablets (mm) ± D	Wetting Time (Seconds)	Disintegration Time (sec)± S.D	%Drug content
F1	3.8	0.67	101.3±0.51	3.1	40	47±0.68	98.17±0.75

F2	3.7	0.72	99.2±0.83	3.7	38	49±0.41	98.23±0.67
F3	4.1	0.69	100.3±0.28	3.2	43	52±0.73	96.81±0.24
F4	3.6	0.71	100.9±0.19	3.8	41	39±0.62	98.47±0.83
F5	3.8	0.73	101.1±0.39	2.9	39	47±0.79	98.69±1.4
F6	4.3	0.75	102.3±0.41	3.5	42	42±0.68	98.29±0.49
F7	4.4	0.72	100.2±0.47	3.8	44	39±0.45	99.34±0.27
F8	3.9	0.70	99.8±0.21	3.7	38	37±0.53	98.89±0.47
F9	3.8	0.68	98.6±0.17	3.7	37	34±0.69	99.75±0.57

3.1.7 Stability Study

A**.** Doxylamine succinate immediate-release tablet aging tests at 250°C and 60% relative humidity (2 month)

Table No 3.2: Stability studies of optimized formulation F9 at 25^0C/ 60% RH.

S. No	Evaluation Parameters	Observation		
		Initial	1 Month	2 Months
1	Physical Appearance	White	White	White
2	Weight variation (%)	98.6±0.17	98.8±0.58	98.9±0.43
3	Friability (%)	0.68	0.69	0.69
4	Thickness (mm)	3.9±0.072	3.8±0.072	3.8±0.023
5	Hardness (kg/cm^2)	3.80±0.86	3.71±0.27	3.72±0.64
6	Disintegeration Time (sec)	34±0.69	32±0.38	32±0.31
7	Drug content (%)	99.08±1.94	99.13±1.82	99.19±1.62

B. Doxylamine succinate immediate-release tablet aging studies at 400°C/75% relative humidity (2 month.)

Table No .3.3: Stability studies of optimized formulationF9 at 40^0C/ 75% RH.

S. No	Evaluation Parameters	Observation		
		Initial	1 Month	2 Months
1	Physical Appearance	White	White	White
2	Weight variation (%)	98.6±0.17	98.8±0.81	98.9±0.17
3	Friability (%)	0.68	0.70	0.70
4	Thickness (mm)	3.9±0.072	3.8±0.015	3.8±0.047
5	Hardness (kg/cm^2)	3.80±0.86	3.61±0.41	3.61±0.83
6	Disintegeration Time (sec)	34±0.69	31±0.49	31±0.57
7	Drug content (%)	99.08±1.94	99.12±0.72	99.15±0.46

CONCLUSION

The direct compression approach was used to create a rapid release tablet containing doxylamine succinate. The tablet broke down fast, and its friability and hardness are acceptable. Significantly improved medication solubility is seen in the in vitro drug release from the tablets. As a result, it

may be concluded that the Doxylamine succinate super disintegrant, which is based on an instant release tablet, would work rapidly after being given to treat emesis. Among the measures utilized to assess the tablets were studies on in vitro drug release, thickness, hardness, friability, wetting time, water absorption ratio, and percentage drug content. Based on the results, the formulation containing 10% crospovidone (F-9) was determined to be the most optimal and best of all the formulations made for Doxylamine succinate tablets. After 10 minutes, the best formulation of Doxylamine succinate fast dissolving tablets of F-9 was found to have an in vitro drug release of 99.08%.

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