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Formulation and Evaluation of an Orodispersible Tablet of Diazepam: A Review

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ABSTRACT

The present study was to analyze the prepared orodispersible tablet of Diazepam using different super disintegrant and evaluate them to enhance bioavailability as well as their quick onset of action. Orodispersible tablet of diazepam was prepared through various super disintegrant by direct compression technique and evaluated for hardness, thickness, weight variation, friability, the content of uniformity, wetting time, *in-vitro* dispersion time, in vitro disintegration time and dissolution studies. The disintegration time of prepared tablets was found to be in the range of 18 to 31 sec. The drug release studies were found to be 99.92% in 10 minutes for the prepared F2 formulations. These studies indicate that the application of an orodispersible tablet was more convenient and more impactful as compared to the conventional tablet to achieve rapid treatment.

INTRODUCTION

The most convenient and acceptable route of administration among the various other delivery system is the oral route of administration. There are more than 70% of drugs that are available in the market, present in the form of an oral drug delivery system to avoid pain as well as versatility (1)**.** The most well-known solid dosage forms are tablets and capsules. Although, various people are facing many difficulties regarding swallowing tablets as well as hard gelatin capsules. These phenomena are considered as dysphasia. These types of difficulties are mostly found in all groups of patients, but mainly with pediatric and geriatric people. Therefore, the conventional dosage form results in a high risk of objection or disagreement and inadequate for pediatric and geriatric patients concerning swallowing(2)**.** Orally disintegrating tablets are also known as orodispersible tablets, Rapid disintegrating tablets, quick-dissolving tablets, Melt in mouth tablets, rapid melts, and Freeze-dried wafers(3)**.** Orally disintegrating dosage forms can serve as an effective alternative mode of drug delivery in a disease like conditions such as motion sickness, sudden episodes of attacks of coughing and repeated emesis where swallowing conventional dosage forms became difficult. When these ODTs enter the mouth, they begin to disintegrate immediately to release the drugs. Further, this dosage form dissolves with saliva and gets dispersed. As the saliva moves down, the drug often gets absorbed through the esophagus or GIT secretions which further enhances bioavailability(4)**.** The tablet dispersibility and their slow release of drugs with the use of super disintegrates are measured through various technological parameters (5)**.**

Advantages of orodispersible dosage form:

- Ease of administration.
- Improved patient compliance.
- It should be relevant for Sustained-release or controlled release targets.
- Long shelf-life.
- Less expensive.
- Less disintegration and Dissolution time due to the immediate release of the drug.

- Dose accuracy.
- These dosage forms have greater bioavailability.
- It should be more effective in lower concentrations (6).

Limitations of orodispersible tablets:

- Careful handling required because of the tablets which have inadequate mechanical strength.
- If tablets are not formulated then it may provide unpleasant taste as well as lumps in the mouth(7).

An ideal characteristic of orodispersible tablet:

- No need for water for oral administration
- Excessive drug loading
- It should have satisfying Taste.
- Insensitive to environmental condition
- The drug must have better solubility as well as stability in water.
- Ability to permeate the oral mucosal tissue(8).

Diazepam belongs to an important member of the benzodiazepine family. A benzodiazepine with anticonvulsants, anxiolytic, muscle relaxant, and amnesic properties with long duration of action. They are mostly insoluble in water. Diazepam is regarded as one of the most prescribed medications worldwide. Diazepam is recommended by the World Health Organization (WHO) as a basic medicine for the treatment of various diseases such as anxiety, seizures, alcohol withdrawal syndrome, and insomnia. Its actions are mediated through the enhancement of gamma-aminobutyric acid activity(9). Comparing to other benzodiazepines, diazepam (DZP) has specific physicochemical and pharmacological properties. The IUPAC naming of diazepam is 7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2H-1, 4-benzodiazepine-2-one. It has excess lipid solubility with a long elimination half-life that further aid its use in intranasal therapy(10).

MATERIALS AND METHODS

MATERIALS:

Diazepam was received as a gift sample from Ronak Pharmaceuticals Pvt Ltd., Patan. Chitosan, magnesium stearate, talc, orange flavor, sodium carboxymethylcellulose (sodium CMC), alginic acid, microcrystalline cellulose (MCC), crospovidone and sodium starch glycollate (SSG) were purchased from Central Drug House (P) Ltd., New Delhi.

METHOD:

A tablet of diazepam was prepared by the direct compression technique. Weighed quantities of diazepam were mixed with different super disintegrant in a pestle mortar according to their compositions. Further, the blend was weighed and passed through sieve no. 60 and compressed the powder blend using 6 mm flat-faced round-shaped punches at a weight of 138 mg by direct compression method. The prepared tablets were further evaluated (11)**.**

EVALUATIONS PARAMETERS

Orodispersible tablets of Diazepam were evaluated for hardness, weight variation, thickness, friability, disintegration time, drug content, and in vitro drug release(12)**.**

Tablet thickness

Tablet thickness is determined by the diameter of the tablet. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Thickness was recorded using a micrometer and vernier caliper. It is mainly determined for 10 tablets(13)**.**

Weight variation

The weight of the prepared tablets was determined by using an electronic balance in which 20 tablets were taken and weighed individually. Lastly, the average weight was calculated(14)**.**

Hardness

Monsanto hardness tester was used to determine the hardness of prepared tablets and measured in terms of kg/cm^2 (15)**.**

Friability

Friability tests are called “Drop Test” or “Abrasion test” in which 20 tablets were randomly taken and weighed accurately (w1) by using a friability tester. These testers were adjusted for 100 rotations at 25 RPM, after which tablets were re-weighed and accurately weighed (w2). Friability % was calculated using the following equation.

Friability % = Initial weighed-Final weighed/Initial weighed × 100(16)**.**

Content of uniformity

From each batch of the prepared tablet, ten tablets were randomly taken and each tablet was crushed and the active ingredient extracted with phosphate buffer (pH 7.4) in a 100 mL volumetric flask. The drug content in each tablet was determined by using a UV spectrophotometer at a wavelength of 284 nm (17)**.**

***In-vitro* disintegration time**

A disintegration test can be performed by using a disintegration tester in which 6 tablets of the prepared product were placed in six tubes of the basket. The operations were started using a buffer with maintained temperature and Ph for 30 minutes(18)**.**

Wetting time

The wetting time of the tablet was measured by placing a piece of tissue paper in a Petri dish of 10 cm in diameter. Then methylene blue which acquires 10ml of water was placed in the Petri dish. Put the prepared tablet on the upper surface of the tissue paper and the time required for the tablet to be wetted was recorded as wetting time(19)**.**

Dissolution studies

The dissolution studies were performed by using dissolution tester either paddle-type or model TDT-08L in which 900 ml buffer solution was placed by maintaining temperature 37 ± 0.5°C at 75 rpm. The prepared tablet was placed and after a one-minute time interval, the aliquotes were withdrawn and at the same time, the fresh buffer medium is placed in an apparatus. Finally, after following dilutions, the samples are assayed by using UV spectrophotometry at 274 nm (20)**.**

RESULTS AND DISCUSSION

RESULTS

Orodispersible tablets of diazepam were prepared by direct compression technique and evaluated for thickness, friability, weight variations, hardness, the content of uniformity, disintegration time, wetting time, and dissolution studies. The thickness was found to be in the range of 3.61±0.054 to 3.68±0.087 mm of the prepared tablet (21)**.** Friability of the prepared tablet was found to be below 1% which indicates a good mechanical resistance (22)**.** All the prepared tablets passed successfully the weight variation test. The weight was found to be uniform of all the tablets with low standard deviation values (23)**.** The hardness of the prepared tablet was found to be 3 to 4 kg/cm²(24)**.** The drug content of all the tablet was found to be in the range of 95 to 101%, within acceptable limits (25)**.** The wetting time was found to be 10.04±1.44 to 13.34±1.01 (26)**.** *In-vitro* disintegration time of all the tablets was found to be in the range of 18 to 31 seconds. % Cumulative drug release of the prepared tablet was found to be 99.92% in 10 minutes in F2 formulations shown in the given Table (27)**.**

Table No. 1: Post compression parameters

Sr. No.	Parameters	Formulations				
		F1	F2	F3	F4	F5
1	Weight variation	Passed	Passed	Passed	Passed	Passed
2	Thickness	3.22±0.004	3.60±0.002	3.61±0.054	3.63±0.066	3.68±0.087
3	Hardness	3.50±0.020	4.00±0.010	4.02±0.030	4.03±0.020	4.04±0.011
4	Friability	0.82±0.001	0.85±0.002	0.86±0.005	0.88±0.007	0.92±0.008
5	Content of uniformity	95.92±0.23	97.89±0.72	99.01±0.58	99.78±0.27	101.00±0.2
6	Wetting time	10.04±0.04	10.92±0.80	11.94±1.21	11.02±0.63	13.34±1.01
7	Disintegration time	18.00±0.01	18.00±0.00	28.00±0.00	30.00±0.01	32.00±0.02

Table No. 2: Cumulative % drug release

Time (min)	Cumulative % drug release				
	F1	F2	F3	F4	F5
0	00	00	00	00	00
2	22.74 ± 11.33	27.37 ± 6.54	37.85 ± 12.22	40.71 ± 5.53	41.81 ± 2.75
4	51.32 ± 3.83	46.24 ± 12.30	50.84 ± 13.13	58.69 ± 5.67	66.27 ± 10.00
6	71.68 ± 8.44	62.05 ± 2.78	70.76 ± 11.21	74.89 ± 17.55	89.19 ± 4.67
8	82.48 ±1 2.88	84.51 ± 10.89	81.05 ± 6.52	85.02 ± 2.88	88.14 ± 3.77
10	72.83 ± 3.78 9	99.92 ± 7.56	94.51 ± 22.78	97.14 ± 1.89	98.29 ±1.10

DISCUSSION

The Orodispersible tablet prepared by direct compression technique. Prepared tablets were applied for different evaluation parameters such as hardness, thickness, weight variation, friability, the content of uniformity, wetting time, disintegration time, and dissolution time. Prepared tablets disintegrate within a few seconds which further increases bioavailability and enhanced patient compliance. These formulations prepared and exhibit rapid disintegration used for the paediatric and geriatric population.

CONCLUSION

At present, orally disintegrating tablets are much efficient than any other conventional tablet. Such formulations play an important role in the treatment of pediatric and geriatric patients. These types of formulations develop the acceptability towards patients and contribute to improving their safety as well as efficacy. Orally disintegrating tablets developed to overcome the swallowing difficulty in different patients. Due to the various advantages of orally disintegrating tablets (ODTs), different pharmaceutical companies can make use of ODTs products for first-to-market products. With the continued development of ODTs, the emergence of more novel technologies may approach regarding in the future.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTEREST

Declared none

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