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Research Article

FORMULATE AND EVALUATE THE ORAL DISPERSIBLE TABLET OF ANTIDIABETIC DRUG TENELIGLIPTIN

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ABSTRACTS

Orodispersible tablets (ODTs) are novel drug delivery systems that have the potential to significantly affect conventional dosage forms in terms of patient compliance, convenience, bioavailability, and time to action. Despite the fact that significant research has gone into developing ODT formulations and technologies, in order to produce newer, more expense technologies and better items, more research is needed in these major destinations. Because of the availability of new technologies, as well as good market acceptance and patient compliance, the potential of dosage forms is attractive. Pharmaceutical companies can use ODTs for new product lines or first-to-market products, which is a factor in technology. With the continuing development of new pharmaceutical excipients, more unique ODT technologies are likely to occur soon. Method -For the orodispersible tablet optimized formulation, a direct compression method was used. Result: The pure dosage calibration curve was created by dissolving the medication in ethanol and measuring the absorbance with a UV spectrophotometer set at 243.5 nm. The value of the slope was 1.025. Light microscopy was used to predict the size of teneligliptin particles. The average length and breadth of drug particles were 2.10 µm and 1.14µm. In-vitro drug release study profile of formulation demonstrated around 71 % of the drug diffused in 60 min., while the formulation 85 % of the rug release in 60 min.

Keywords: Orodispersible tablets, hardness, dissolution test, disintegration test, wetting time

INTRODUCTION

One of the most prevalent methods for increasing bioavailability and patient compliance is to use an orodispersible drug delivery system. Due to better patient compliance stability, and solubility orodispersible tablets (ODT) have received more research in the last three decades than regular tablets and capsules. Because they contain medicinal compounds in a solid dosage form, orodispersible tablets breakdown quickly, usually in seconds, when placed on the mouth. Because it directly fulfills medicines and patient needs, for child, elderly, and neuropsychiatric patients with dysphagia, this revolutionary ODT technology improves patient life and enables a pleasant dosage plan. This technology stimulates academics and industry to produce novel orally disintegrating formulations and evaluation procedures that are appropriate for drug candidate prospects[1-3].

Most pharmacological dose forms designed for oral administration are intended for direct ingestion[1].A large range of treatments are administered orally since it is the most convenient mode of drug delivery to patients [4]. According to European Pharmacopoeia, an orodispersible tablet disperses in the mouth within 3 seconds [5]. The orodispersible tablet also called "ODTs" and it gets quickly disintegrates due to its porous and rapid melting nature [6]. Freezing and drying, tablet moulding, sublimation, and direct compression are the standard procedures that are utilized for the manufacturing of orally disintegrating tablets[3]. ODTs response time is very fast, and its disintegration time is few seconds to a minute. ODTs are a solid form drug with active ingredient and therapeutic material that dissolve rapidly in the mouth when placed over the tongue, according to the Food & Drug Administration of the U. S. (FDA). Because when ODTs come in contact with saliva it releases active drugs that provide maximum drug bioavailability in comparison to conventional dosage form due to which the tablet gets dispersed or disintegrate[4-7].

The hydrophilic nature of excipients is used in ODT technology and are selected based on physicochemical properties of the drug i.e., mainly hydrophilic or hydrophobic. In saliva, the active agent dissolves rapidly and no matter whatever membrane encounter unless it is protected by pre-gastric absorption. This study will also look at the evolution of ODT technology, as well as the long-term viability of drug candidates and their characterizations. Main objective orodispersible such as improve patient compliance; increase the bioavailability, enhance stability, for the hormone adjusting blood glucose level. Orodispersible tablets are made using a number of different technologies such as Direct compression, Sublimation, lyophilization or Freeze-drying, Tablet Molding Spray drying, Cotton candy process, Mass extrusion, Phase transition, Nano ionization fast dissolving films[8-12].

Teneligliptin is an antidiabetic drug that is used to treat type 2 diabetes in adults. For the best results, patients are encouraged to combine this drug with a rigorous diet and exercise routine. This drug should not be given to children. GLP-1 (glucagon-like peptide-1), which enhances pancreatic insulin production and regulates blood sugar levels by controlling glucagon release, is secreted from the alimentary canal in response to a meal. Teneligliptin reduces the activity of dipeptidyl peptidase-4 (DPP-4) and so increases the blood levels of active GLP-1, resulting in a hypoglycemic effect[13-15].

MATERIALS AND METHODS

Teneligliptin was received as a gift sample from Systopic Laboratories private limited, (Delhi). Magnesium Stearic acid, Microcrystalline, Sodium Starch glycolate, and Talc were obtained from Central Drug House (P) Ltd (New Delhi, India), Chitosan was obtained from Biochemical Laboratories (P)Limited (New Delhi, India), Crospovidone was obtained from Sigma-Aldrich Chemical (P) Limited (Bangalore)

Drug-excipients compatibility studies

Drug-excipients compatibility studies was analyzed using I.R spectroscopy. Pure drug and physical mixture of polymer pure drug was taken ratio 1:1. It was scanned 400 to 4500 cm^{-1}.

Preparation of Orodispersible[16]

The preparation of tablets is given step by step below.

- Teneligliptin was sorted through screen no.22 after being geometrically combined with microcrystalline cellulose and lactose.
- In a quick mixer granulator, this blend was combined with starch and ferric oxide yellow.
- The binder solution was made by dissolving hydroxypropyl methylcellulose in filtered water while stirring.
- Using the quick mixer granulator, this binder solution was added to the mixture.
- Dry granules were sifted through sieve no.30 using vibratory sifted.
- In a clean dry blender, the dried granules were mixed with hydroxypropyl methylcellulose and magnesium stearate.
- These lubricated granules were compressed to form tablets in a tableting machine.
- The tablet was coating with a coating pan.

Evaluation of Tablets

The number of characterization parameters can be performed to check the standard level of prepared formulation. These include hardness, friability, disintegration, dissolution etc. some of these are given below [17-20].

Hardness: Monsanto hardness testers are also used to measure the hardness of tablets. In the hardness tester, a tablet is placed, and the force required to crush it is measured. Because the tablet's hardness is increased, it takes longer for it to disintegrate. ODTs have a lower hardness than normal tablets. The force is measured in kilograms, and uncoated tablets with a hardness of roughly 3-5 kg/cm2 are regarded satisfactory.

Friability: The friability of ODTs is higher than that of traditional tablets due to efforts to reduce disintegration time, for example, is a highly delicate dosage form. The mechanical strength of a tablet is measured by its friability. The Roche friabilators friability is determined using the procedure below. The friability is filled with pre-weighed pills. A plastic chamber revolves at 25 revolutions per minute, dropping the tablets 6 inches apart with each revolution. For at least 4 minutes, the tablets are replaced in the friabilator. The tablets are dusted and reweighed at the end of the test. Friability is measured by the reduction in tablet weight, which is given as a percentage:

$$\% \text{ Friability} = (\text{loss in weight} / \text{Initial weight}) \times 100$$

Disintegration Test: The test was carried out on six tablets using distilled water as the disintegration medium at 37°C 20°C, and the time in seconds it took for the tablet to totally disintegrate with no solid mass left in the instrument was recorded.

Wetting Time: The wetting time of the dosage form is influenced by the contact angle. The wetting time of a fast-dissolving oral tablet is another crucial characteristic to explore in order to obtain insight into capillarity and, as a result, the disintegration qualities of the tablets. A shorter wetting time means the tablet will disintegrate faster. The wetting time was calculated using the method provided. In a little Petri dish (I.D = 6.5 cm) containing 6 ml of room temperature water, a piece of tissue paper folded twice was placed. On the tissue paper, a pill was inserted and allowed to absorb all of the liquid. The time it took to completely moisten the tablet was recorded in the second.

Tablet Thickness: To evaluate thickness, a tablet was put between two arms of the Vernier calipers. Five tablets were set aside, and their thickness was limited.

Water Absorption Ratio (%): The weight of the pill is used to calculate the water absorption ratio before an observation in a Petri plate (Wb). In the Petri plate, the wetted tablet is occupied and reweighed (Wa). The following equation can be used to calculate the water absorption ratio.

$$R = 100 (Wa - Wb) / Wb$$

Where Wa is the tablet's weight after water absorption and Wb is the tablet's weight before water absorption

Dissolution Test: The strategy used to design dissolve methods for ODT is similar to that used to design dissolve methods for conventional tablets and is nearly identical when ODT does not include taste masking. As stated in the USP monograph, medicines may have dissolving conditions. Other media, such as 0.1 N HCl, pH 4.5, and pH 6.8 buffers, should be used in the same way as their tablet equivalents for ODT evaluation. The USP 2 paddle apparatus, with a paddle speed of 50 rpm, has shown to be the most ideal and common choice for the Dissolution test of ODT tablets, according to experience. When employing USP monograph circumstances, ODTs usually dissolve fairly quickly. As a result, a relative profile can be obtained by using a slower paddle speed. Large tablets, including those weighing more than one gramme and containing thick particles, may cause an amount in the dissolve vessel, which can be avoided by increasing Paddle speeds. The optimum range of stirring for these two circumstances is now 25-75 rpm. Although the USP 1 (basket) apparatus has compelling applications for ODT, it is not widely employed due to the unique physical features of tablets.

RESULTS AND DISCUSSION

Fig 1: Oro dispersible Tablets

Table 1: Different formulation batches with different excipients concentration

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tween	20	20	20	20	20	20	20	20	20
MCC	46	41	46	41	46	41	46	41	44
Carmellose sodium	---	---	---	---	10	15	---	---	---
Crospovidone	---	---	10	15	---	---	---	---	---
SSG	10	15	---	---	---	---	---	---	---
Mannitol	20	20	20	20	20	20	20	20	20
Aspartame	2	2	2	2	2	2	2	2	2
Chitosan	--	--	--	--	--	--	10	15	12
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	1	1	1	1	1	1	1	1	1
Total wt. (mg)	100	100	100	100	100	100	100	100	100

Table 2: Weight Variation of different formulation batch

Formulations	Total wt. (gm)	1	2	3	4	5
F1	0.51	0.10	0.11	0.10	0.10	0.10
F2	0.52	0.10	0.11	0.10	0.10	0.10
F3	0.53	0.11	0.11	0.11	0.11	0.10
F4	0.52	0.11	0.11	0.10	0.10	0.11
F5	0.58	0.11	0.11	0.14	0.11	0.11
F6	0.50	0.11	0.11	0.10	0.10	0.10
F7	0.52	0.10	0.11	0.11	0.11	0.09
F8	0.51	0.09	0.11	0.09	0.10	0.08
F9	0.48	0.11	0.11	0.10	0.10	0.09

Table 3: Wetting time of the formulations

Formulations	Wetting Time (minutes)
F1	2.11
F2	4.0
F3	1.52
F4	10.48
F5	1.80
F6	1.20
F7	1.44
F8	0.51
F9	0.40

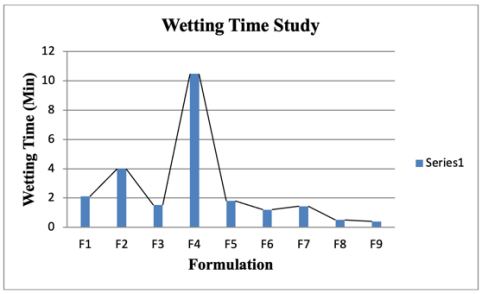

Fig 2: Wetting time of the formulations

Table 4: Disintegration time of preparation batches

Formulations (F)	Disintegration Time (min)
F1	1.50
F2	2.27
F3	2.27
F4	4.30
F5	0.58
F6	1.26
F7	2.52
F8	1.65
F9	1.50

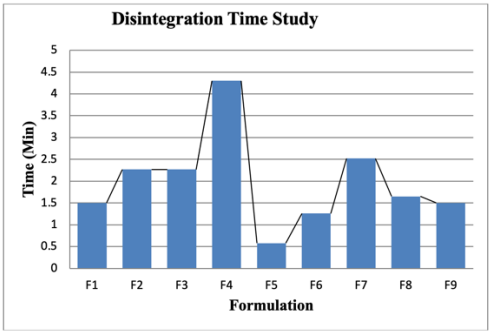

Fig 3: Disintegration time of tablets

Table 5: Thickness of the preparation batches

Formulations (F)	Thickness (mm)
F1	2.4
F2	2.4
F3	2.3
F4	2.3
F5	2.4
F6	2.3
F7	2.4
F8	2.4
F9	2.2

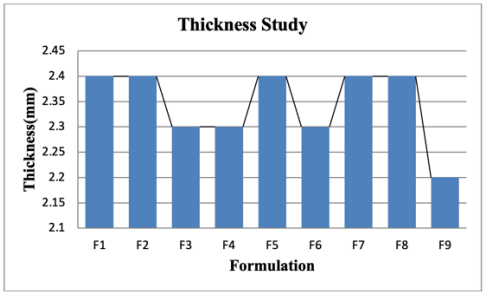

Fig 4: Thickness of prepared tablets

Table 6: Hardness of the different batches

Formulations (F)	Hardness (kg/cm^2)
F1	3.0
F2	3.0
F3	3.0
F4	1.5
F5	1.5
F6	1.5
F7	2.4
F8	2.2
F9	2.1

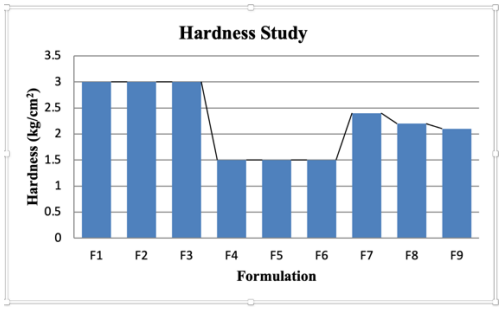

Fig 5: Hardness of the tablets

Table 7: Cumulative % Drug release of formulation F8

Time	Absorbance (λ max)	Concentration (µg/ml)	In 2ml (µg)	In 2ml (mg)	In 900ml (µg)	In 900ml dilution factor (mg)	Cumulative frequency (mg)	% Drug release
0	0	0	0	0	0	0	0	0
10	0.102	2.02	4.0	0.004	1818	18.18	18.18	90.9
20	0.109	2.16	4.2	0.0042	1944	19.44	19.444	97.2
30	0.110	2.18	4.3	0.0043	1962	19.62	19.624	98.12
40	0.115	2.28	4.4	0.044	2052	20.52	20.524	102.6
50	0.120	2.38	4.7	0.47	2142	21.42	21.464	107.32

Table 8: Cumulative % Drug release of formulation F9

Time	Absorbance (λ max)	Concentration (µg/ml)	In 2ml (µg)	In 2ml (mg)	In 900ml (µg)	In 900ml dilution factor (mg)	Cumulative frequency (mg)	% Drug release
0	0	0	0	0	0	0	0	0
10	0.110	2.18	4.3	0.0043	1962	19.62	19.62	98.1
20	0.111	2.20	4.4	0.0044	1980	19.80	19.804	99.0
30	0.114	2.26	4.5	0.0045	2034	20.34	20.344	101.7
40	0.120	2.38	4.6	0.0046	2142	21.42	21.424	107.1
50	0.122	2.42	4.8	0.0048	2178	21.8	21.784	108.9

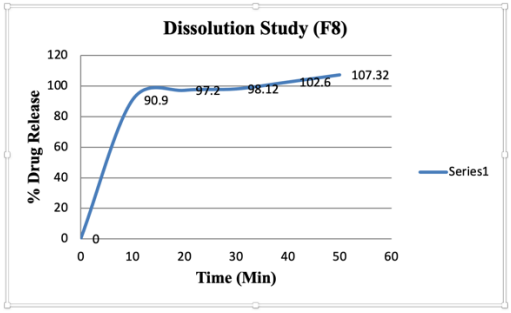

Fig 6: Cumulative % drug release of formulation F8.

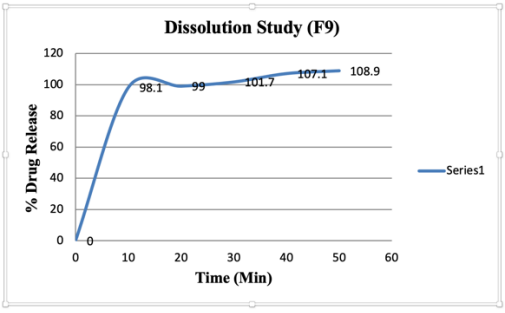

Fig 7: Cumulative % drug release of formulation F9

Preparations Batches of the Teneligliptin Oro dispersible Tablets

The various batches i.e., 9 batches of orodispersible tablets were prepared by incorporating the different excipients or polymers in each batch in different concentration as shown in table 1 as depicted tablet in fig 1.

Weight Variation

It is a significant characterization parameter especially in the case of tablets. About 20 tablets were ingested and weighed for this purpose. Now the weight of individual tablet was measured. By comparing these, the variation in weight was calculated (as shown in table 2).

Wetting time

The contact angle influences the wetting time of the dosage form. Another significant characteristic to check is the oral dissolving tablet's wetting time, which provides insight into capillarity and, as a result, the tablets' disintegration qualities. A shorter wetting time means the tablet will disintegrate faster. The method given was used to determine the wetting time. A piece of tissue paper folded twice was introduced into a tiny Petri dish (I.D = 6.5 cm) containing 6 ml of room temperature water. On the tissue paper, a pill was inserted and allowed to absorb all of the liquid. The time it took to completely moisten the tablet was then recorded in the second section (table 3).

DISINTEGRATION TIME

The test was performed on six tablets at 37°C 2°C with distilled water as the disintegration medium, and the duration in seconds it took for the tablet to completely disintegrate with no delectable mass remaining in the instrument was recorded. (Table 4)

Tablet Thickness

To evaluate thickness, a tablet was put between two arms of the Vernier Caliper. Five pills were set aside, each with a maximum thickness. (Table 5)

Hardness

Hardness testers produced by Monsanto are used to determine the hardness of tablets. In the hardness tester, a tablet is placed, and the force required to crush it is measured. Because the tablet's hardness is increased, it takes longer for it to disintegrate. ODTs have a lower hardness than normal tablets. The force is measured in kilograms, and uncoated tablets with a hardness of roughly 3-5 kg/cm2 are regarded satisfactory (Table 6).

Water absorption ratio (%)

The weight of the pill is used to calculate the water absorption ratio before an observation in a Petri plate (Wb). The wetted tablet is placed in the Petri plate and reweighed (Wa). The water retention rate could be calculated using the equation below.

$$R = 100 (Wa - Wb) / Wb$$

Where Wa is the tablet's weight after water absorption and Wb is the tablet's weight before water absorption.

Uniformity of Dispersion

Swirl the two pills lightly in 100ml water for 2 minutes.22 meshes are used to filter the dispersion. If there is no residue on the screen, the tablets will pass the test. It was found that the formulation batch 8 and 9 qualifies for the test easily.

Dissolution test

When ODT does not contain taste masking, the process used to create dissolve methods for ODT is nearly identical to that used to design dissolve methods for regular tablets. Medicines may have dissolving conditions, according to the USP monograph. Other media, such as 0.1 N HCl, pH 6.8 buffers, should be utilized for ODT evaluation in the same way as their tablet counterparts. The USP 2 paddle apparatus, with a paddle speed of 50 rpm, has shown to be the most ideal and common choice for the Dissolution test of ODT tablets, according to experience. When employing USP monograph circumstances, ODTs usually dissolve fairly quickly. As a result, a relative profile can be obtained by using a slower paddle speed. Large tablets, including those weighing more than one gramme and containing thick particles, Increase Paddle speeds to avoid an amount in the dissolving vessel. The optimum range of stirring for these two circumstances is now 25-75 rpm. Despite the fact that the USP 1 (basket) apparatus has compelling ODT applications, it is not frequently used because to the physical characteristics of tablets.

Based on different parameters, it was found that the formulations F8 and F9 are the best suitable. Due to this, the dissolution test of both these formulations was performed and results were obtained (Table 7 and 8).

Based on different parameters, it was found that the formulations F8 and F9 are the best suitable. Due to this, the dissolution test of both these formulations was performed and results were obtained. The results show that the Cumulative drug release % from F8 is about 71% while the F9 shows the release of 85% of the drug in 1 hour as shown in the table below. This depicts that the formulation F9 is the best possible optimized formulation from the batch of all nine formulations

COMPATIBILITY DRUGS –EXCIPIENTS

The compatibility between drug and excipients was predicted through the infrared spectrum (IR) of the pure drug as well as the drug- Polymer mixture. The infrared spectrum of both pure drug as well as the mixture of drug and Polymer was compared (as shown in fig 3.7 and 3.8). It was discovered that the medication and the polymer had no interaction.

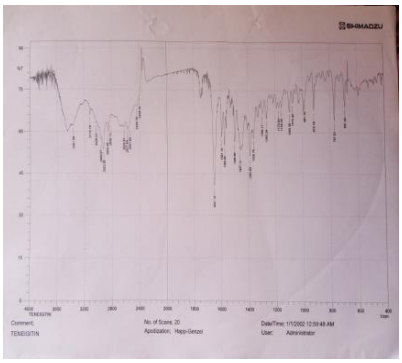

Fig 8: Infrared Spectrum of Pure Teneligliptin drug

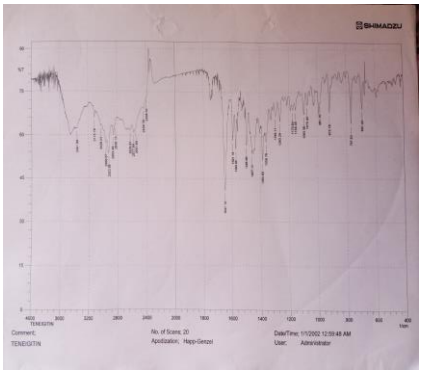

Fig 9: Infrared Spectrum physical mixtures of polymers/pure drug

CONCLUSION

Orodispersible tablets (ODTs) are novel drug delivery systems that have the potential to significantly affect traditional dosage forms in terms of patient compliance, convenience, bioavailability, and time to action. More research is needed in this potential sector in order to generate novel, more expense technologies and better commodities, despite the fact that extensive study has been done into producing ODT formulations and technologies. Because of the availability of new technologies, as well as good market acceptance and patient compliance, the potential of dosage forms is bright. With the continuing development of new pharmaceutical excipients, additional unique technologies for ODTs are forecast to increase in the immediate future. ODTs can be used by pharmaceutical companies for product line expansion or the first products. More unique ODT technologies are anticipated to emerge in the near future as novel pharmaceutical excipients are developed.

Future Prospects

These formulations may be ideal for oral administration of medications with low bioavailability when taken as tablets, such as protein and peptide-based treatment. In the stomach, these compounds normally disintegrate quickly. Peptide-based or primarily protein-based medications should be developed in the future. The tablet may no longer be the preferred method of

administering such medications. Injections are not commonly desired by patients, unless they are aided by twist auto-injectors. Inhalation is one of the most effective ways to administer these medications, however current biopharmaceutical research has primarily produced chemical units with modest molecular weights. For high molecular weight separation of proteins delivery, the development of improved powder material processing methods using ODTs, that could produce these drugs in the oral cavity, is particularly promising.

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