doi.org/10.36721/PJPS.2023.36.5.SP.1677-1685.1

Formulation design and evaluation of epalrestat mouth dissolving tablets comprising superdisintegrant from natural sources manufactured by direct compression method and stability studies of optimized formulation

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Abstract: Among the oral route, mouth dissolving tablets (MDTs) offer a benefit for drugs with slow dissolution and having low oral bioavailability. Epalrestat is one of the best effective diabetic neuropathy medication used for treating nerve pain. The problem associated with this drug is high first pass metabolism and low solubility in acidic media as well in basic media leads to short half-life, delayed dissolution and side effects. Therefore, the goal of the current work is to developed an epalrestat MDTs tablet that will provide quick drug dissolution and a quick onset of action for the treatment of nerve pain. MDTs of epalrestat were formulated by direct compression using natural superdisintegrants obtained from the various sources such as fenugreek, gum karaya and banana powder. All of the pre- and post-compression parameter results were shown to be in accordance with established specifications. In comparison to other formulations of MDTs, formulation F3 with 15 mg (7.5%) of banana powder displayed a higher rate of dissolution. It was determined that epalrestat MDTs containing natural superdisintegrant were successfully formulated with acceptable physical and chemical properties, quick oral cavity disintegration, a quick onset of action, and improved patient compliance.

Keywords: Mouth dissolving tablets, epalrestat, natural superdisintegrants, direct compression, stability studies.

INTRODUCTION

Oral administration route is the most preferable for various dosages forms like conventional tablets, capsules and liquid dosages form but sometimes bioavailability of a drug hampered severely due to their first-pass metabolism (Alqahtani *et al*., 2021). For some category of patients like pediatric and geriatric face problem to swallow solid dosage forms like capsules and tablets, resulting in many incidences of non-compliance and making the therapy ineffective. Therefore, scientists developed MDTs to increase bioavailability and patients' acceptability and decrease side effect of the drugs (Cornilă *et al*., 2022; Preis, 2015). MDTs is a solid, unit and tempered proof dosage forms containing active ingredients which disintegrate or dissolve within a minute, when it will be wetted with saliva, therefore no need of water during administration. That's why these dosage forms more popular among pediatric and elderly patients (Gupta *et al*., 2015). MDTs are also referred to as melt in mouth tablets, oro-dispersible tablets, fast-dissolving, porous tablets, etc. Even without access to water, MDTs are tablets that dissolve quickly in saliva within seconds. As per the European Pharmacopoeia, MDTs tablets are the tablets that dissolve on the tongue before being swallowed, and they should dissolve in less than three minutes (Chandrasekhar *et al*., 2009) MDTs were developed as an alternative to traditional tablets, particularly for young children and elderly patients who have trouble swallowing solid dosage forms. So to develop MDTs remain interesting to generate new orally disintegrating formulations for both academia and industry persons by applying new industrial approaches (Shirsand *et al*., 2009; Ali *et al*., 2016; Gupta, 2022). MDTs have advantages over conventional tablets, as absorption of drug started from oral cavity. The quick disintegration ability of tablet is achieved by incorporating super-disintegrants during formulation (Thakur and Verma, 2012; Sharma *et al*., 2015; Naji *et al*., 2023).

Epalrestat (fig. 1) is one of the most frequently used oral antidiabetic drugs that inhibits aldose reductase, an enzyme in the sorbitol (polyol) pathway (Ramirez and Borja, 2008). It is a carboxylic acid derivative. It is used to treat late-onset diabetic complications like retinopathy, nephropathy, and diabetic neuropathy (Ohmura *et al*., 2009). Epalrestat prevents the buildup of sorbitol in erythrocytes, sciatic nerves, and ocular tissues, which not only aids in treating the severity of the illness but also stops the disease's progression. It increases the activity of Na+/K+ ATPase and speeds up nerve conduction velocity (Sharma and Sharma, 2008; Sun *et al*., 2017; Bailly, 2022). This drug falls under BCS class II. The problem associated with this drug is high first-pass metabolism and low solubility in acidic media as well as basic media

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(Huang *et al*., 2017; Putra *et al*., 2017; Nirogi *et al*., 2013). Many dosage forms, such as tablets, capsules, syrups, and suspensions, are available for the current medication. The bioavailability of these dosage forms is poor because of the low solubility of epalrestat. The success of enteric-coated formulations is also lacking because of their lower solubility in basic media than in acidic media. Many researchers developed NDDS, like nanoparticles, to deliver this drug via nasal routes and SNEDDs via oral route, but their use is still not clear due to a lack of clinical trial data, the stability of the dosage form, and the fact that they are not economical because they need medication for a prolonged duration of time (Mora-Huertas *et al*., 2010; Alvi *et al*., 2021; Naik *et al*., 2021).

Superdisintegrants, both natural and artificial, are used to prepare MDTs. With the aid of a superdisintegrant, tablets can be broken down into the mouth with saliva within a matter of seconds without needing to swallow thoroughly. The biocompatibility, low cost of production, and increased patient acceptability of natural superdisintegrants are additional benefits. Incorporation of natural polymers in MDTs as a superdisintegrant can be helpful to minimize side effects associated with the excipients because they are easily digested and terminated in the human body. MDTs dissolve quickly in water, are well absorbed, and do so in a matter of seconds. As a result, MDT functions much like a tablet that quickly dissolves and is absorbed (Patni *et al*., 2013; Kumar and Saharan, 2017; Bhatti and Kaushik, 2020; Shobana *et al*., 2020; Sharma, 2021). For this study, mouth-dissolving epalrestat tablets were made using the direct compression method so that the drug could be delivered safely and effectively, with better patient satisfaction or acceptance, a quick start of action, and ease of administration.

MATERIALS AND METHODS

Materials

The drug epalrestat was procured from Sigma Aldrich, USA (St. Louis, MI, USA). Natural superdisintegrants like banana powder, gum-karaya and seed of fenugreek were procured from Jazan local market, Jazan, KSA. Avicel 101 was also obtained from Sigma Aldrich, USA (St. Louis, MI, USA). Methanol and distilled water were supplied by Dawaa Al Gharbyah, KSA. Magnesium stearate, talc and saccharine were obtained from BS Goodrich in Cleveland, OH, USA. Further an extra agents used in the formulations were of highest analytical quality grade.

Methods

Construction of standard plot

In order to make the standard plot, 20 mg of accurately weighed epalrestat was put into a 10ml volumetric flask. The flask was then filled with methanol to the right level. Then, 100ml of distilled water was added to 1 ml of this solution. After that, 5 ml of the solution was taken and diluted with distilled water up to a maximum of 10ml. This results in a stock solution of epalrestat with a 10µg/ml concentration. Serial dilutions were made from the stock solution with distilled water to get solutions with concentrations of 1, 2, 3, 4, 5, 6, 7, 8, and 10 mg/ml. Then, a UV-spectrophotometer (UV mini-1700, Labomed, USA with 1 cm quartz cells) was used to measure the absorbance at a wavelength (max) of 389 nm (Biswas *et al*., 2014).

Drug excipient interaction studies

Interaction studies of drugs with excipients were conducted using Fourier transmission infrared (FTIR) spectroscopy (Thermo Nicolet 380 FTIR) (Liltorp *et al*., 2011; Matos *et al*., 2017). The FTIR makes it possible to identify functional groups in various chemicals and to determine whether a drug and its excipients are incompatible or not. FTIR spectroscopy was used to characterize the pure drug and the optimized MDT formulation (a blend of the drug and different excipients used in the preparation of the MDT formulation) to determine whether they are compatible or not. The samples' IR spectra were obtained using the KBr disk technique, with a scanning range of 500–4000 cm^{-1} (Moisei *et al*., 2014).

Preparation of epalrestat MDTs tablets by using the direct compression method

MDTs were formulated by the direct compression method using natural superdisintegrants like banana powder, gum karaya, and fenugreek. Using a single tablet punching machine (Single punch eccentric tablet press EP-1, ERWEKA, D-63150 Heusenstamm/Germany, No. 125823 1072), the powder mixture containing the drug and excipient blend was compressed to formulate the tablets with a 9-mm diameter (Alam *et al*., 2014). The weight of the total tablet was kept at 200 mg. Table 1 lists the components of each formulation.

Pre-compression evaluation parameters

Flow properties of powder blend

Powder mixture undergoes evaluation for different factors like bulk density, angle of repose, tap density, carr's index, Hausner's ratio to find out the powder mixture having good flow (Kadria *et al.*, 2014; Eraga *et al*., 2015).

Angle of repose

By using the fixed funnel method, it was possible to calculate the powder blend's repose angle. For this, the precisely weighed powder mixture was poured into a fixed funnel. The funnel's height was kept so that the top of the powder pile was just barely touched by the funnel's tip. The powder was permitted to pass from side to side through the funnel and onto the surface without encountering any resistance. The height and diameter of

the powder cone were measured. Then the angle of repose was calculated by using the following equation, given below:

$$\tan\theta = \frac{h}{r}$$

Where the letters r and h, respectively, stand for the powder cone's radius and height

Bulk density and tapped density

In a 25-ml measuring cylinder, 5 g of powder from each formulation was added. First, a light shake was applied to dislodge any possible agglomerates. After recording the early volume, the measuring cylinder was endorsed to drop at 2-second intervals from a 2.5 cm height onto a tough surface while supporting its own weight. As soon as a steady volume was noticed, the tapping was resumed. The following formulas were employed to determine the loose bulk density (LBD) and tapped bulk density (TBD):

LBD = Powder weight / Powder packing volume
TBD = Powder weight / tapped powder packing volume

Compressibility index (%)

The % compressibility index also known as Carr's index of the granules of the powder blend was calculated by using the following formulas:
Carr's compressibility index (Carr's index) = [(TBD - LBD) × 100] / TBD

Hausner's ratio

The flowability of a powder or granular substance is correlated with a number called the Hausner's ratio, determined by using the following formula given below:
Hausner's ratio = Tapped density / Bulk density

Post-compression evaluation parameters of MDTs

Thickness of tablets

To measure the thickness of the tablet, it was positioned between the two arms of a Vernier caliper (Mitutoyo, Japan). There were five measurements made (Kalia *et al.*, 2009).

Weight uniformity

To ensure that the prepared tablets of MDTs have a uniform weight, a weight variation test is conducted. For the weight variation test, it is generally performed with 20 tablets, and each tablet individually weighs by an electronic digital scale (Adam PW124), and then together all the tablets weigh and determine the average weight by applying the percentage limit of allowance as per USP guidelines. Each tablet was checked individually to pass or fail (Jain and Naruka, 2009).

Hardness test

This test is performed to ensure that the tablet is hard enough not to break during handling, but it should break into small pieces as soon as it reaches the stomach to facilitate absorption. The tablet should be placed diagonally in the Monsanto tester (Monsanto hardness tester, VMT - 1), and then the screw is tightened just to touch the tablet edge. The scale should read zero, or record the reading as an initial reading. Tighten the screw until the tablet breaks down. Then the final reading on the scale was recorded, and the actual hardness was calculated by subtracting the initial value. The measure of hardness is represented in the unit of kg per cm^2 (Kalia *et al.*, 2009).

Friability test

This test is done to check for loss of medicament during transportation, packaging, and other means of handling. A Roche friability tester (Copley friability tester FR-200) was used to estimate the weight loss of six tablets after 100 rotations at a speed of twenty-five rotations per minute, allowing the tablets to fall from 6 inches in height. All six tablets were weighed together and transferred to the tester. Again, all six tablets were weighed together. The percent loss of weight was calculated. The friability test of the tablet showed a weight loss of not more than 1%, which is considered acceptable (Chacko *et al*., 2010).

% loss of weight =

Initial 6 tablets weight–final 6 tablets weight after rotation X 100 / Initial 6 tablets weight

Uniformity of drug content

In a mortar, six pre-weighed tablets were crushed into a powder. A 10-ml volumetric flask was filled with a powder equivalent to 10mg of epalrestat before being diluted with methanol. Then one ml was taken and diluted to 100ml with distilled water. The absorbance was measured at a wavelength (max) of 389 nm. The concentration of epalrestat was estimated with the help of a standard plot (Biswas *et al*., 2014).

Tablet wetting time

Fold the tissue paper so that it covers a petridish's six-inch diameter. The tablet should be kept on the tissue paper close to the center of the petridish, and then six ml of measured water should be added. Both the tissue paper and the tablet have started to absorb water. The time noted as wetting time is when the tablet is completely wet (Prakash *et al*., 2011).

Water absorption Ratio

Two tissue papers were divided into two parts, placed one over the other in four layers, and put in a petri dish with six ml of water. One tablet was then placed on the paper. The time required by the tablets to absorb water until it was completely wet was determined. The following formula, shown below, is used to evaluate the water absorption ratio of the tablet (R) (Aslani and Beigi, 2016):

$$R = \frac{Wa - Wb}{Wb} \times 100$$

In the above formula, Wa and Wb represent the weight of the tablet after water absorption and the weight of the tablet before water absorption, respectively.

In vitro disintegration time of MDTs

Disintegration test is used to ensure that the tablet should break into very small pieces up to granular level to liberate drug to surrounding medium under specified time and given condition. Disintegration of prepared MDTs were performed according to USP "Disintegration Test" for tablet dosage forms using a Copley disintegration tester (DTG 200i). Then put the tablets to each cylindrical tube of the basket assembly move up and down to the beaker containing 900 ml of phosphate buffer pH 6.8 as a disintegration medium maintained at 37±2ºC temperature as the immersion liquid. The time required for complete disintegration of tablets was noted down, considered as disintegration time. If one or two tablets fail to disintegrate within the mentioned time limit and condition, then test is repeated on 12 more tablets. Now out of 18 not less than 16 must be disintegrate to pass the disintegration test (Kumar and Babu, 2014).

In vitro dissolution studies of MDTs

The in-vitro drug release profile of the developed MDTs was performed as per USP guidelines. The USP paddle method (Copley tablet dissolution tester, DIS 6000, No. 17719) was used at a speed of 50 rpm. The media used for the study contains 900 ml of phosphate buffer with a pH of 6.8 and is maintained at 37±0.5ºC throughout the study. Epalrestat from MDTs (in the dissolution samples) was determined by a UV spectrophotometer. A 5 ml sample from the medium was taken at predetermined intervals and analyzed spectrophotometrically at 389 nm. After removing each sample, the volume was maintained by adding the same volume of dissolution medium that was kept at the same temperature to maintain the sink condition. Then, using the standard plot, the drug concentration was determined (Wagh et al., 2010).

Stability study

The primary goal of stability studies is to determine how various environmental variables, such as light, humidity, and temperature, as well as various suggested storage conditions, affect how consistently high-quality a drug substance is over time. In order to conduct short-term stability (accelerated) studies, tablets were stored in an amber-colored rubber stopper bottle for three months at a 40 ± 2 °C temperature and 75 ± 5% relative humidity (Temperature Humidity Test Chamber, TH-100, LIB). Then, after every month, the tablets underwent a visual examination to check for any physical alterations as well as their friability, hardness, in-vitro disintegration time, and in-vitro dissolution time (Devi *et al*., 2010; Gandhi *et al*., 2011; Venugopalarao *et al*., 2013; Vivek *et al*., 2017).

STATISTICAL ANALYSIS

All tests were repeated three times, mean values ± standard deviations (SD) were reported. Statistical analysis was carried out using the one-way ANOVA test by GraphPad prism software (version 8, San Diego, USA), with a p-value of <0.05 considered statistically significant. Microsoft Excel (Office 16) was used for the analysis.

RESULTS

Drug excipient interaction studies

To do this, FTIR analysis was done on a pure drug, a placebo formulation, and an optimized mouth-dissolving tablet. No significant differences in the pattern of the absorption peak were found after analyzing the IR spectra. The absorption profile for the pure drug was the only one visible in the IR spectra of the optimized formulation and placebo (fig. 2).

Construction of standard plot of epalrestat

Using a UV-Vis spectrophotometer, the absorbance of the diluted epalrestat solutions were measured at 389 nm and the concentrations were extrapolated from the calibration curve. The developed calibration curve for epalrestat is shown in fig. 3. The linearity was discovered to be in the range of 1–10 µg/ml. The standard curve's correlation coefficient (R^2) was found to be 0.9988, indicating high linearity.

Pre-compression evaluation parameters of MDTs

The direct compression method, which is the most time- and cost-effective, was used to formulate the MDTs of epalrestat using natural superdisintegrants in various concentration ratios (2.5%, 5%, and 7.5%). Alternative methods are only used if this approach is unsuccessful. For the direct compression of tablets, preparation required a free-flowing powder blend of the formulation. Numerous pre-compression evaluation parameters, including bulk density, tapped density, Hausner ratio, Carr's index, and angle of repose, were assessed in order to check the free-flowing characteristics of the powder mixture. table 2 provides the values of each of these parameters.

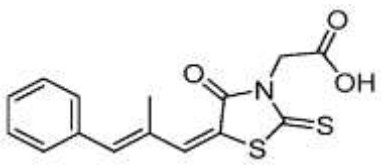

Fig. 1: Structure of epalrestat

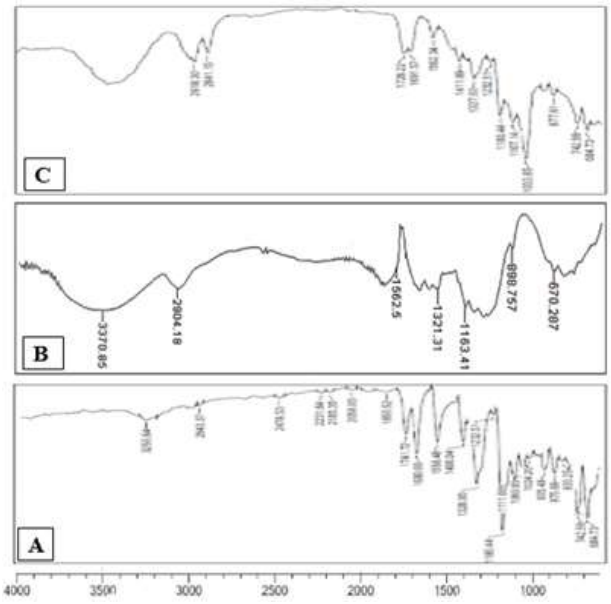

Fig. 2: FT-IR of epalrestat pure drug (A), placebo formulation (B), optimized formulation of epalrestat (C)

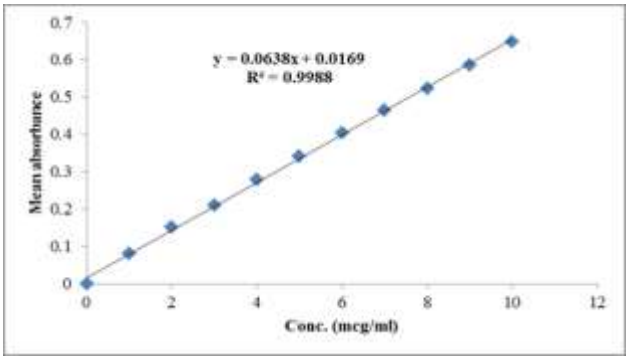

Fig. 3: Calibration curve of epalrestat

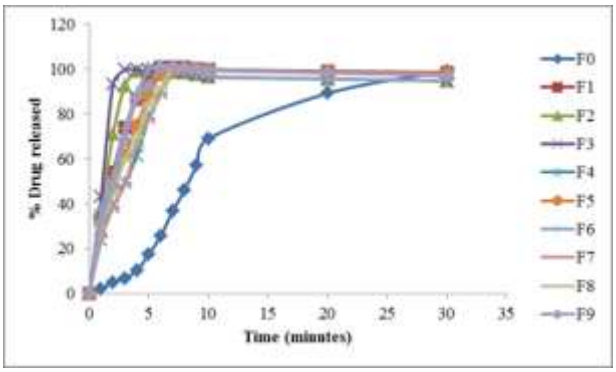

Fig. 4: Dissolution profile of prepared formulations of epalrestat MDTs

Post-compression evaluation parameters of MDTs

MDTs of epalrestat were prepared and visually inspected for shape and color. After compressing the formulations, a surface with a concave shape and a white color was seen. A total of 10 formulations of MDTs were prepared, of which the formulation F0 did not contain natural superdisintegrants and was used for comparison purposes. Table 3 lists the post-compression parameters, including thickness, weight variation, hardness, friability, uniformity of drug content, wetting time, water absorption ratio, and in-vitro disintegration time.

In vitro dissolution studies (% drug release)

The USP paddle method was used at a speed of 50 rpm. The media used for the study contains 900 ml of phosphate buffer with a pH of 6.8 and is maintained at 37 ± 0.5 ºC throughout the study. Fig. 4 depicts the ways in which drugs are released from tablets.

Stability study

The Stability studies on optimized mouth dissolving tablets (F3) were carried out over a three-month period in accordance with ICH regulations (Ali *et al*., 2013). Accelerated stability tests were performed on optimized tablets at 40 °C and 75% RH. Variation in weight, hardness, friability, drug content, and time of disintegration were all taken into consideration when evaluating formulations. The data were shown in table 4.

DISCUSSION

FTIR spectroscopy makes it possible to identify functional groups in various chemicals and to determine whether a drug and its excipients are incompatible. The purpose of the interaction studies was to find out if there were any possible interactions between the drug and the other ingredients used in the preparation, such as the superdisintegrants. According to the findings shown in fig. 2, there was no interaction between the drug and its excipients. Therefore, it can be concluded from the study that the drug's major peaks are still intact and there is no drug-excipient interaction. Drugs and excipients are therefore compatible with each other.

Table 1 demonstrates that F0, the control formulation, does not contain a superdisintegrant. Formulations F1, F2, and F3 contain banana powder; formulations F4, F5, and F6 contain gum karaya; and formulations F7, F8, and F9 contain fenugreek as a natural superdisintegrant. According to Table 2, it was discovered that the powdered mixture of the control formulation F0 for direct compression had a high angle of repose, percentage compressibility, and excellent flowability. According to the findings, bulk density, tapped density, Carr's index, and Hausner's ratio of all formulations that contain superdisintegrants decrease as the concentration of Avicel 101 rises, but the angle of repose rises. Pre-compression blends' bulk densities were found to be between 0.498 and 0.560 g/ml, tapped densities between 0.548 and 0.661 g/ml, Carr's index values between 10.04 and 15.46%, Hausner's ratio between 1.10 and 1.18, and angle of repose between 19.64 and 23.11 degrees.

Table 1: Formulation components of the epalrestat MDTs tablets

Name of Ingredients	Formulations									
	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9
Epalrestat (mg)	50	50	50	50	50	50	50	50	50	50
Banana powder (mg)	-	5	10	15	-	-	-	-	-	-
Gum Karaya (mg)	-	-	-	-	5	10	15	-	-	-
Fenugreek (mg)	-		-	-	-	-	-	5	10	15
Avicel 101 (mg)	139	134	129	124	134	129	124	134	129	124
Saccharine (mg)	4	4	4	4	4	4	4	4	4	4
Talk (mg)	3	3	3	3	3	3	3	3	3	3
Magnesium stearate (mg)	2	2	2	2	2	2	2	2	2	2
Orange flavor (mg)	2	2	2	2	2	2	2	2	2	2
Total weight of tablet (mg)	200	200	200	200	200	200	200	200	200	200

Table 2: Pre-compression evaluation parameters of MDTs powder blends

Formulation code	Bulk density (g/ml)	Tapped density (g/ml)	% Compressibility	Hausner's ratio	Angle of repose (Degree)
F0	0.560 ± 0.13	0.661 ± 0.08	15.15 ± 0.04	1.17 ± 0.08	23.11 ± 0.13
F1	0.516 ± 0.11	0.582 ± 0.31	11.34 ± 0.03	1.12 ± 0.13	19.64 ± 0.11
F2	0.511 ± 0.16	0.574 ± 0.48	12.32 ± 0.04	1.12 ± 0.11	19.75 ± 0.04
F3	0.498 ± 0.09	0.548 ± 0.70	10.04 ± 0.02	1.10 ± 0.09	19.95 ± 0.10
F4	0.531 ± 0.32	0.587 ± 0.42	11.17 ± 0.07	1.11 ± 0.15	19.76 ± 0.02
F5	0.521 ± 0.14	0.560 ± 0.02	12.12 ± 0.01	1.13 ± 0.01	21.01 ± 0.11
F6	0.516 ± 0.21	0.578 ± 0.55	12.01 ± 0.08	1.12 ± 0.07	20.03 ± 0.03
F7	0.544 ± 0.20	0.597 ± 0.62	11.17 ± 0.11	1.11 ± 0.14	19.67 ± 0.01
F8	0.541 ± 0.13	0.640 ± 0.11	15.46 ± 0.11	1.18 ± 0.12	21.01 ± 0.11
F9	0.537 ± 0.19	0.599 ± 0.39	12.81 ± 0.09	1.12 ± 0.10	19.82 ± 0.07

Data are shown as mean ± SD (n=3)

Table 3: Post-compression evaluation parameters of MDTs

Formulation code	Tablet thickness (mm)[a]	Weight variation (mg)[b]	Hardness (kg/cm^2)[a]	Friability (%)[c]	Drug content (%)[d]	Wetting time (sec.)[c]	Water absorption ratio[c]	*In vitro* disintegration time (sec.)[c]
F0	2.44 ± 0.09	199.9 ± 0.05	4.14 ± 0.46	0.51 ± 0.04	99.54 ± 0.12	105 ± 1.01	28.65 ± 1.8	185 ± 0.17
F1	2.42 ± 0.11	199.7 ± 1.05	3.99 ± 0.46	0.56 ± 0.05	99.99 ± 0.21	25 ± 1.22	68.65 ± 0.9	36 ± 0.17
F2	2.41 ± 0.21	198.3 ± 0.11	3.92 ± 0.21	0.57 ± 0.06	96.55 ± 0.18	22 ± 1.21	84.65 ± 1.1	26 ± 0.11
F3	2.42 ± 0.12	200.2 ± 0.02	3.89 ± 0.12	0.58 ± 0.02	99.95 ± 0.11	16 ± 1.07	98.48 ± 1.3	19 ± 0.32
F4	2.42 ± 0.14	200.5 ± 0.02	3.97 ± 0.46	0.55 ± 0.03	98.76 ± 0.10	29 ± 0.21	55.65 ± 0.8	38 ± 0.19
F5	2.43 ± 0.05	201.1 ± 0.12	3.95 ± 0.11	0.57 ± 0.04	97.69 ± 0.54	26 ± 1.31	68.65 ± 1.1	31 ± 0.19
F6	2.44 ± 0.16	198.4 ± 0.31	3.87 ± 0.43	0.63 ± 0.04	97.76 ± 0.44	22 ± 0.91	78.65 ± 1.4	26 ± 0.18
F7	2.41 ± 0.11	200.3 ± 0.02	3.95 ± 0.46	0.63 ± 0.01	99.95 ± 0.41	28 ± 0.51	61.65 ± 1.8	38 ± 0.19
F8	2.42 ± 0.13	199.5 ± 0.09	3.91 ± 0.22	0.65 ± 0.15	97.99 ± 0.07	25 ± 1.43	74.65 ± 0.7	32 ± 0.21
F9	2.43 ± 0.14	200.2 ± 0.21	3.88 ± 0.53	0.68 ± 0.17	98.11 ± 0.11	23 ± 1.33	87.65 ± 1.2	27 ± 0.12

Data are represented as mean ± SD ($n=5^a/20^b/6^c/10^d$)

Table 4: Effect of storage at 40 °C±0.5 °C and 75%±5% RH

Time (Days)	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)	disintegration time (sec.)
0	200.2 ± 0.02	3.89 ± 0.12	0.58 ± 0.02	99.95 ± 0.11	19 ± 0.32
30	200.1 ± 0.11	3.98 ± 0.33	0.58 ± 0.05	99.45 ± 0.07	18 ± 0.41
60	198.8 ± 0.04	3.99 ± 0.05	0.54 ± 0.11	97.99 ± 0.31	16 ± 0.63
90	197.5 ± 0.02	4.08 ± 0.11	0.52 ± 0.08	96.97 ± 0.18	15 ± 0.11

Data are shown as mean ± SD (n=3) followed by ANOVA test. $P < 0.05$ compare to optimized formulation.

All of the powder blends were found to have good flow properties based on the reported values. Therefore, they can be directly compressed into mouth-dissolving tablets.

Table 3 displays various tableting characteristics of the control tablet and the tablets containing various concentrations of superdisintegrants. It was found that the control tablet was harder and absorbed less water than other tablets made with different amounts of superdisintegrant. There may be stronger forces at a contact point because Avicel 101 has more free hydroxyl groups. This is because the hydrogen bonds between the hydroxyl groups are stronger. This may make the tablets harder. Amorphous regions of cellulose that are accessible during the production of Avicel 101 are hydrolyzed, resulting in Avicel 101's comparatively high crystallinity. As a result, it can only absorb a small amount of water and quickly return to equilibrium. Additionally, the concave-convex shape of the Avicel 101 particles and their relatively compressed pores cause the tortuosity of a pore in an Avicel 101 tablet to increase, which ultimately lowers the water absorption ratio. The control tabl*et al*so demonstrated the least friability, and it passed the tests for uniformity of content and weight variation. It was discovered that the control tablet's *in vitro* disintegration time was 185 ±0.17 seconds.

Table 3 also displays the tableting characteristics of tablets with different superdisintegrant ratios, represented by formulation codes F1 to F9. All tablets passed the weight variation test, and it was determined that they all fell within the USP's acceptable range. A range of 2.41-2.44 mm was found to be the average tablet thickness across all batches. By measuring the absorbance at a wavelength of 389 nm, the percentage of drug content for all formulations was determined. This resulted in values ranging from 97.69% to 99.99%, which are within the USP-acceptable limit. The hardness of all tablets was recorded in the range of 3.87–3.99 kg/cm^2, while the friability was observed to be lower than 1%. Both of the above points confirmed the tablets' strong mechanical resistance. Also, a rise in water absorption ratio was found with an increase in the amount of superdisintegrants. The formulation F3 with 7.5% banana powder as a superdisintegrant had the lowest disintegration time and the maximum water absorption ratio of all the developed formulations.

Banana powder has a highly porous structure that allows it to quickly absorb water into its network while also drawing large amounts of water through a water-wicking mechanism into the tablet's porous network. Due to this, it was discovered that as banana powder concentration increased, so did the water absorption ratio, which ranged from 68.65 to 98.48 and was higher than formulations made with other superdisintegrants. Tablets made with banana powder as a superdisintegrant were discovered to have a higher water absorption ratio, which resulted in a very short in-vitro disintegration time among all the formulations. In order to comprehend a disintegrant's ability to expand when in contact with a small amount of water, the wetting time and water absorption ratio are crucial considerations. The water absorption ratio ranged from 55.65 to 98.48, whereas the wetting time was found to be between 16 and 29 seconds for all formulations containing superdisintegrants. The time of disintegration was found to be between 19 and 38 seconds.

It has been noticed that dissolution test results vary due to many factors, like the flow of fluid in the vessel, vibration, slight temperature variation, even the curvature of the dissolution bowl and the mesh size of the basket. Therefore, during dissolution studies, we critically optimized all these contributing factors.

Fig. 4 depicts the ways in which drugs are released from tablets. When comparing control tablets (F0) with those containing superdisintegrants, it was found that the control tablets showed complete drug release (roughly 100%) after 30 minutes, while the superdisintegrant-containing tablets showed 100% drug release within 3 to 8 minutes. This difference may be related to the tablets' quick ability to absorb water and their quick disintegration.

Out of all of them, formulation F3 was found to be the most effective one. The lowest disintegration and dissolution times were seen in formulation F3 with 7.5% banana powder as a superdisintegrant. This was shown by the powder properties, tableting properties, and dissolution study. As a result, the F3 formulation was chosen as the optimized formulation and was assigned to use in the stability studies.

According to the study's findings, there was no significant change (P values <0.05) shown in any of the above evaluation parameters after three months.

CONCLUSION

In the study, natural superdisintegrants like mucilages and gums were used to formulate MDTs with epalrestat that could be used to treat diabetic neuropathy. These natural ingredients are cost-effective, environmentally friendly, and compatible. The tablets m*et al*l pre- and post-compression characterization parameters. The MDTs significantly improved dissolution behavior, increasing epalrestat's bioavailability. The MDTs could also help patients with water access and swallowing difficulties. The formulation F3 containing 7.5% banana powder showed a maximum drug release of 99.98% within 3 minutes, indicating superior disintegrating qualities. This suggests that banana powder could significantly improve drug release and disintegration time, making it a promising option for patients with water accessibility and

swallowing difficulties. The use of natural superdisintegrants like banana powder could offer a safer and more sustainable alternative to synthetic disintegrants in pharmaceutical formulations.

ACKNOWLEDGEMENTS

The Deanship of Scientific Research at Jazan University provided financial support for this Wa'ed project, which is acknowledged by the authors (Reference number, W43-066).

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