Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

Study of Tablet in Tablet Approach for the Designing and Evaluation of Antidiabetic Combined Immediate and Modified Release Tablets

Amul N Mishra[1], Chandni Yadav[1]

[1]Faculty of Pharmacy, Bhupal Nobles' University, Udaipur, Rajasthan, India

Corresponding author: Ms. Chandni Yadav, Research Scholar, Bhupal Nobles' University, Udaipur, Rajasthan, India

(Received: 16 January 2025 Revised: 20 February 2025 Accepted: 31 March 2025)

KEYWORDS

Tablet in tablet technology, Antidiabetic drugs, Dry coating techniques, Compression coating, Gliclazide, Metformin

ABSTRACT:

Oral administration is the most common method, when it comes to medication. Although there are certain medications that are meant to be dissolved in the mouth when they are taken orally, the overwhelming majority of medications that are taken orally are still swallowed. When compared to other methods of drug administration, the oral route of drug administration is the most common and has been used with great effectiveness for the delivery of drugs following traditional methods. Tablets are the most extensively used dosage form among all of the possible dosage forms. This is due to the fact that they are easy to administer, have a reduced manufacturing cost, and are elegant. Coating processes largely determine the visual qualities of a product, including its colour, texture, mouth feel, and ability to disguise flavour. There are several limitations or problems associated with this coating technique; nevertheless, one of the greatest options is the tablet in tablet, which works to overcome these limitations. For the purpose of conducting anti-diabetic research, the current work is to conduct a full assessment of the formulation, characterization, and obstacles involved in the production of tablets in tablet dosage form. The formulation is to create a tablet-in-tablet of gliclazide, metformin by developing a modified release core tablet of gliclazide SR and its outer shell, which will act as an immediate release tablet of metformin.

Introduction:

Tablets are the most frequently used oral dosage form amongst the patient because of their simplicity, accuracy in the administration of dose, stability, and economy [1]. Coating of the tablet is one of the most important techniques to mask the bitter taste, unpleasant odor and also for a better quality of tablets like color and texture. The compression coating technique was firstly introduced by Noyes in an 1896 patent. In the development of a new drug delivery system, the compression coating is one of the best alternatives, a novel coating technology. It has been used for a different purpose in the pharmaceutical such as the development of modified release, pulsatile release, colon-specific release, and programmable release [2]. According to the various available literature, the press coating technology is used for the development of tablet like as compress coating tablets, e.g., development of glipizide tablet which is designed to achieve zero-order release. Tablets are classified into various types; in one class of tablet, preparations are modified release dosage form that has added significance in drug therapeutics because it offers a variety of advantages. Nowadays, to develop modified released products, the Tablet in Tablet technology is the best alternative for bilayer tablet formulation for the incompatible drug. It involves the compression of granular materials around a preformed tablet core using specially designed tableting equipment. The Tablet in Tablet is also known as compression coating or solvent-free–coating technique [3].

The internal core and outer layer are the two parts of the Tablet in Tablet dosage form. The internal core is a small tablet and prepared by using a somewhat small size of tooling than tooling used for the preparation of the outer coat. After internal tablet core was produced, it is placed (centrally positioned) to another die which is moderately occupied with coating powder and which is

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

larger than core tablet then the remaining amount of coating powder is placed on the top of core tablet and compressed resulting in the formation of tablet within tablet [4].

Compression coating is essentially a dry process and thus may be suitable for coating tablets containing heat and moisture liable drug(s) such as aspirin and penicillin. This coating process has also been used to separate two incompatible active pharmaceutical ingredients; one contained in the tablet core and the other in the coating. Repeat action and sustained action tablets are produced by this coating method [5]. Although traditionally a less popular process, compression coating has gained increased interest in recent years as a means of creating specialized modified release products. It involves the compaction of granular materials around a preformed tablet core using specially designed tableting equipment. Compression-coated formulations can be used to protect hygroscopic, light-sensitive, oxygen or acid labile drugs, or to separate incompatible drugs from each other. They can also be used to achieve controlled release, and a number of studies have evaluated compression-coated time-controlled drug delivery systems [6]. The main goals of anti-diabetes therapy are to reduce symptoms of hyperglycaemia and to reduce the risk of long-term complications of diabetes. The proposed study deals with characterization and evaluation of tablet in tablet formulation in which a single drug is incorporated in both the tablet i.e the outer shell as well as the internal core tablet. The further study is proposed on the release of the mechanism for the repeated dosing of the anti-diabetic drug. Here sustained release formulation avoids the side effects associated with the immediate release formulation & also provides effects for longer period of time. The result of the project would provide a process that would provide stable formulation of tablet in tablet of anti-diabetic drugs [7].

Material And Methods:

Materials

Gliclazide and Metformin Hydrochloride was obtained as a gift sample from Intas Pharm. Pvt. Ltd., Ahmedabad. The following ingredients: HPMC K4M, Sodium Starch Glycollate, lactose, MCC (Avicel® PH 102), and Di basic calcium Phosphate dihydrate were bought from S D fine chemicals, Mumbai, India. Every other substance, including reagents, was of analytical grade.

Preparation of calibration curve: Accurately weighed required quantity of drug 50 mg (gliclazide and metformin HCl) separately were dissolved in 50 ml of dissolution medium containing Phosphate buffer pH 1.2 in 50 ml volumetric flask with the help of sonication in bath sonicator for 20 min to obtain 1000 µg/ml solution. From resulting solution take 10 ml and was diluted up to 100 ml with Phosphate buffer pH 1.2 solvent separately with sonication for 20 min to get 100 µg / ml solution. From above prepared resulting solution of 100 µg / ml, withdrawn 0.5 ml, 1.0 ml, 1.5 ml upto 4.0 ml aliquots and diluted up to 10 ml with respective solvent (Phosphate buffer pH 1.2) in 10 ml volumetric flasks to get concentration of 5 µg / ml, 10 µg / ml, 15 µg / ml, upto 40 µg / ml respectively. The absorbance of each solution was measured separately at 225 nm for gliclazide and 232 nm for metformin HCl separately were Phosphate buffer pH 1.2. The absorbance was measured and standard curve was plotted between absorbance vs. concentration.

Preformulation study:

Organoleptic properties*:* The organoleptic properties of drug (gliclazide and metformin HCl) separately were determined such as color, odor and taste will be noted visually.

Microscopic examination: The microscopic examination of the drug samples (gliclazide and metformin HCl) separately were identified the nature / texture of the powder. The required amount of powder will spread on a glass slide and examine under phase contrast microscope and drug powder was crystalline in nature.

Particle size: The average particle size (d_{avg}) of drug powders (gliclazide and metformin HCl) separately were determined by means of optical microscope fitted with ocular micrometer and stage micrometer.

Flow properties: The flow properties of drug powders (gliclazide and metformin HCl) separately were were characterized in terms of carr's index, hausner's ratio and angle of repose. The Carr's index ((I_C)) and Hausner's ratio (H_R) of drug powders were calculating according to following equation:

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

Carr's Index (I_C) = $\rho_{Tapped} - \rho_{Bulk} / \rho_{Tapped}$

Hausner's ratio (H_R) = $\rho_{Tapped} / \rho_{Bulk}$

The angle of repose (θ) was measured by fixed height method. This was calculated by following equation:

Angle of repose (θ) = $\tan^{-1}$ 2 H / D

Where H is the surface area of the free-standing height of the powder pile and D is diameter of pile that formed after powder flow from the glass funnel.

Solubility determination: Saturation solubility of drug API (gliclazide and metformin HCl) separately were determined by incremental method analysis method in various solvents. The exact quantity of drug 50 mg was placed on the conical flask and the various solvents i.e. distilled water, 0.1 N HCl, Phosphate buffer pH 6.8 and pH 7.4 phosphate buffers separately filled in burette. The solvent was slowly added into drug containing conical flask until the drug was solubilized and stirred constantly overnight at 37±0.5ºC. The samples were filtered by using whatmann filter paper (0.45µm pore size). The solubility assessment of drug was determined by calculation of concentration µg/ml unit.

Partition coefficient: The partition coefficient of drug samples (gliclazide and metformin HCl) separately were observed in mixed solvent of 100 ml containing n-octanol: phosphate buffer pH 1.2. 100 mg of drug was added into 50 ml each of an n-octanol and buffer phase in a separating funnel. The mixture was shaken for 24 h until equilibrium reached. Both medium were divided and collected individually, filtered. The quantity of API dissolved in aqueous medium was diluted and determined by UV spectrophotometric method. The partition coefficient of API was calculated from the proportion between the concentrations of drug in organic and buffer solution quantity using following equation.

Log $P_{(oct / pH\ 1.2)}$ = Log ($C_{noct} - C_{pH1.2}$) equilibrium

Melting point: The melting point of drug samples (gliclazide and metformin HCl) separately were obtained by pinch of drug material sample filled in capillary tube by manually. Capillary tube sealed from one end with a bunsen flame burner individually. The filled capillary tube was kept in melting point apparatus and identified the temperature at which the drug was starting to melt.

Drug excipient compatibility study: The functional group determination of drug samples (gliclazide and metformin HCl) separately were identified by IR spectroscopy. Infra-red spectroscopy was carried out by using Shimadzu IR Spectra photometer as method given below. The characteristic peaks were reported as wave number. The FTIR spectra of dried drug samples (gliclazide) independently were obtain by FTIR spectrophotometer by means of the potassium bromide disc method. The drug sample was pulverized and thoroughly mixed with a dried powder of IR grade potassium bromide material with weight ratio of 3:1 (i.e 9 mg of KBr in 1 mg of drug). The mixture of materials was pressed using a hydrostatic press at a pressure of 10 tons for 5 min at room temperature with required humidity. The disc of sample was placed in the sample holder for measuring the spectrum and the spectra were recorded as the wave number ranges 4000-400/cm at a resolution of 4/cm. The compatibility i.e. drug-excipients interaction studies are helpful for dosage form design. For compatibility studies drug / excipients ratio are selected and investigated based on the reasonable drug / excipient ratio in the final product. Drug and other Excipients were weighed as 1:1 ratio and passed through sieve # 40, mixed well. The blend was filled in amber color glass vials and stopped with grey rubber stoppers followed by aluminium seal.

Formulation of sustained release tablets: The tablets prepared by direct compression method. Drug (gliclazide 20mg), guargum (35 mg), xanthan gum (20 mg), carrageenan (7.5), and HPMC (7.5), The tablets were prepared by direct compression method. All ingredients sieved through #30 sieves. Magnesium stearate (5 mg) and MCC (5 mg) used were sieved through #60 sieves before the use. All the materials were accurately weighed and blended using hand blender and directly compressed on a manual single punch tablet compression machine into 90 mg tablets using flat-faced, round punches 4 mm in diameter [8].

Formulation of layered tablet by using tab-tab technology: The prepared sustained release tablets of gliclazide (GDT4) was further compression layered as tab in tab technology with other drug (metformin) containing blend of different weight ratios as shown in Table 2. The antidiabetic formulation of metformin coating blend (700 mg) in different ratio was prepared by direct compression technique. A mixture of

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

magnesium stearate and talc (1:2) was used for lubricating on coated blend. First, the die cavity (12 mm) was filled with 30% of coating polymer blend containing metformin HCl. Now the core tablet carefully placed in the center of the die cavity over the coating material and then the core tablet covered with the remaining 70% of the coating material blend in upper portion of the die. The placed coating material was compressed around the core tablet (GDT4; 100 mg) with a maximum compression force using 12mm round and concave punches. Finally, the whole content was compressed using 12 mm concave punches [9-10].

Table 1: Composition of metformin HCl tab in tablet coating on core gliclazide (GDT4) 100 mg prepared by direct compression coating

Composition	**Ingredients**	**Amount (mg / tablet)**								
		GMT T1	**GMT T2**	**GMT T3**	**GMT T4**	**GMT T5**	**GMT T6**	**GMT T7**	**GMT T8**	**GMT T9**
Core Tablet	Gliclazide SR tablet (GDT4)	100	100	100	100	100	100	100	100	100
Coating material	Metformin HCl	500	500	500	500	500	500	500	500	500
	Microcrystalline cellulose (Avicel pH 102)	50	50	50	50	50	50	50	50	50
	Di basic calcium Phosphate dihydrate (DBP)	30	40	50	60	70	45	40	35	30
	Lactose anhydrous	100	90	80	70	60	70	80	90	100
	Potato Starch	-	-	-	-	-	30	25	20	15
	Sodium starch glycollate	15	15	15	15	15	-	-	-	-
	Purified Talc	5	5	5	5	5	5	5	5	5

Evaluateion as follows: Along with the evaluation criteria of tablets that are specified in the Pharmacopoeias, which are covered here, there are also certain specific tests that need to be evaluated.

Weight variation: For the purpose of determining whether or not there was a variance in weight, twenty tablets were chosen at random from the batch and each one was weighed separately.

Thickness: A screw sight was used to determine the thickness of the core tablets, and the findings are presented as the mean values of 10 such determinations.

Hardness: In order to promote early disintegration in the mouth, the limit of hardness is often maintained in a lower range throughout the manufacturing process. Conventional hardness testers, such as the Monsanto tablet hardness tester, may be used in order to determine the magnitude of the tablet's hardness. The unit of measurement is either kilograms or pounds [11].

Friability: It is a problem for a formulator to produce a percentage of friability for a tablet that falls within the boundaries from 0.1 to 0.9 degrees Celsius. This is because all ways of manufacturing TT are responsible

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

for raising the percentage of friability values. The "Electro lab friabilator" was used to determine the degree of friability of each batch. The following equation was used to determine the percentage of weight loss that occurred when ten tablets that had been pre-weighed were spun at a speed of 25 revolutions per minute for a period of four minutes, which is equivalent to a total of one hundred revolutions.

$$\text{Friability test} = \frac{\text{Weight of tablets before test} - \text{weight after test}}{\text{weight of tablets after test}} / 100$$

Disintegration test: To test for disintegration time, one tablet was inserted in each tube, and the basket rack was positioned in a 1-liter beaker of the medium at 37±2 °C. The typical motor driven device was utilized to move the basket assembly housing the tablets up and down across a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs were placed on top of the tablets.

Determination of drug content: In order to determine the amount of drug present, ten tablets were ground to a very fine consistency, and then a quantity of powder that was comparable to one hundred milligrams of T & T tablets (GMTT) was precisely weighed. The weighed sample was transferred to volumetric flasks with a capacity of 100 ml, each of which contained approximately 50 ml of phosphate buffer with a pH of 1.2. In order to dissolve the drug, the flasks were shaken, and then they were sonicated for ten minutes. The volume was diluted with phosphate buffer with a pH of 1.2 until it reached 100 milliliters, and then it was properly mixed. The drug samples were diluted using the same solvent until they reached a concentration of 10 micrograms per milliliter. A membrane filter with a pore size of 0.45 µm was used to filter the solutions, and then the plumbagin concentration was determined at a wavelength of 232 nm using the UV technique described above [12].

In-vitro drug release study: The drug release study procedures for TT are almost equivalent to those used for conventional tablets, according to the in-vitro drug release dissolution test methodologies. Drugs frequently have dissolution conditions that are similar to those described in the USP monograph. It is recommended that buffers with a pH of 1.2 and 0.1N HCl be used for the assessment of TT in the same manner as their conventional tablet equivalents. When compared to the USP1 (basket) apparatus, the USP 2 paddle apparatus is the most suited and common alternative for dissolving TT tablets. This is because the USP2 paddle apparatus takes into account the special physical qualities of tablets. In paddle equipment the paddle speed of 50 rpm is usually utilized. Considering that the dissolution of TTs occurs at a highly rapid rate when USP monograph conditions are applied, slower paddle speeds may be utilized in order to get a statistically significant profile. Large tablets, which weigh at least one gram, have the potential to generate a mound within the dissolution vessel. This mound can be avoided by employing higher paddle speeds. Through the use of a UV-Visible Spectrophotometer set to 232 nm, the quantity of drug that was released was evaluated [13].

Results and discussion:

The absorbance of the resulting solution were measured at λmax 225 nm for drug gliclazide and at λmax 232 nm for drug metformin HCL against a blank solution prepared similarly without drug using systronics double beam spectrophotometer. Calibration curve was prepared by plotting concentration versus absorbance. Preformulation studies are the first step for the rational development of dosage forms of model drug substances. Gliclazide is pale cream-colored, odorless, slightly bitter and crystalline powder in nature and metformin HCl is white colored, fishy smell, bitter and crystalline powder in nature. The bulk and tapped density of drug gliclazide 0.881 gm / cm^3 and 0.921gm / cm^3, respectively and 0.992 gm / cm^3 and 0.948gm / cm^3, respectively for drug metformin HCL. The particle size of unmilled gliclazide was to be 29.7 µm and 72.1 µm for drug metformin HCL. Both drug powders exhibited good flow characteristics as the drug gliclazide has carr's index 26.01±0.61, hausner's ratio 1.13±0.012 and angle of repose 24.2°±0.16, whereas for drug metformin HCL carr's index 23.01±0.11, hausner's ratio 1.12±0.007 and angle of repose 23.1°±0.11 respectively. The solubility of drug gliclazide was determined in various solvents (Water, 0.1 N HCl,

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

Phosphate buffer pH 4.5, pH 6.8, pH 7.4) at room temperature (25±2 ºC). The results are shown in Table 5.11 and the solubility in water 241.5±9.21 (µg / ml), 0.1 N HCl 1089.0±27.91 (µg / ml), phosphate buffer pH 6.8 331.8±8.32 (µg / ml) and phosphate buffer pH 7.4 302.2±7.87 (µg / ml). The result indicated that the drug have maximum solubility water, and also soluble in pH 1.2 phosphate buffer. The solubility of drug metformin HCL was determined in various solvents (Water, 0.1 N HCl, Phosphate buffer pH 4.5, pH 6.8, pH 7.4) at room temperature (25±2 ºC). The results are shown in Table 5.12 and the solubility in water 1.39±0.14 (µg / ml), 0.1 N HCl 1.21±0.82 (µg / ml), phosphate buffer pH 1.08±0.79 (µg / ml) and phosphate buffer pH 7.4 was 1.12±0.96 (µg / ml). The result indicated that the drug has maximum solubility water, and also soluble in pH 1.2 phosphate buffer. The partition coefficient of drug gliclazide and metformin HCl were found to be (1.09 and 0383) separately. The melting point of drug gliclazide and metformin HCl were found to be 169°C ± 0.12°C and 232°C ± 0.11°C separately.

Table 2: Evaluation parameters of various tablets

Formulation code	Weight variation (mg)	Thickness (cm)		Hardness (kg/cm^2)	Friability (%)	Disintegration Time (h)	Percent Drug content (%)
		Diameter	Thickness				
GMTT1	822.9±6.00	0.211±0.003	0.192±0.002	5.27	0.44	1.04	98.2±0.89
GMTT2	827.6±6.22	0.213±0.002	0.191±0.002	5.29	0.45	1.11	98.8±1.01
GMTT3	823.6±6.80	0.210±0.001	0.193±0.001	5.28	0.43	1.18	98.1±1.22
GMTT4	827.6±5.75	0.212±0.001	0.192±0.001	5.29	0.49	1.11	98.7±0.92
GMTT5	823.5±6.26	0.213±0.001	0.191±0.001	5.32	0.47	1.12	98±0.58
GMTT6	819.2±6.17	0.211±0.002	0.192±0.002	5.27	0.42	1.08	98.7±0.09
GMTT7	821.1±6.01	0.212±0.003	0.193±0.002	5.38	0.46	1.16	98.4±0.11
GMTT8	824.3±6.02	0.210±0.002	0.192±0.003	5.34	0.43	1.15	98.6±0.13
GMTT9	826.2±6.21	0.212±0.002	0.193±0.002	5.29	0.47	1.11	98.3±0.12

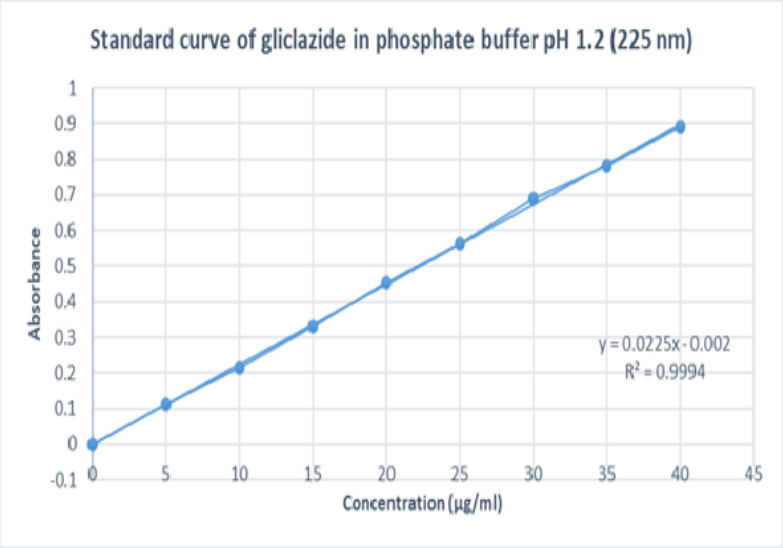

Figure 1: Standard curve of gliclazide in phosphate buffer pH 1.2 (225 nm)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

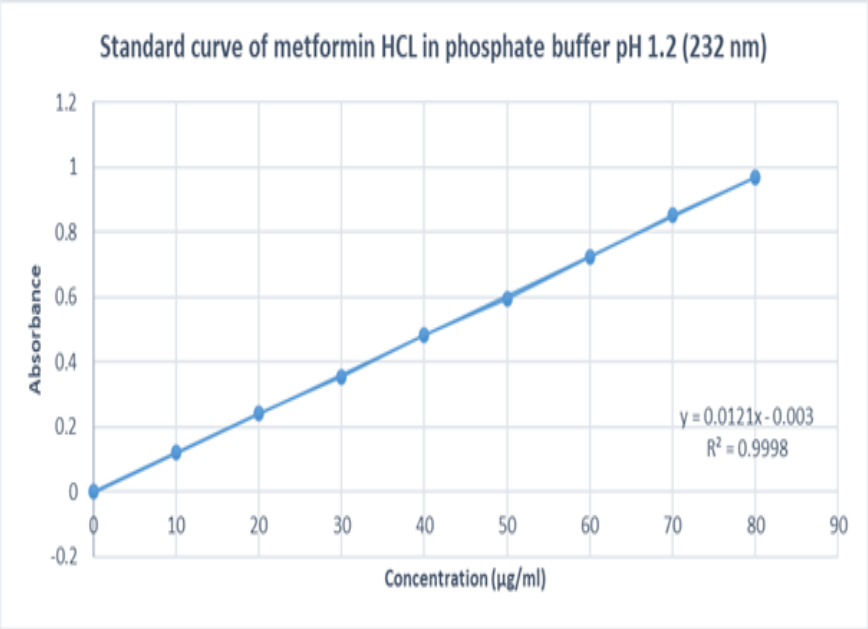

Figure 2: Standard curve of metformin HCL in phosphate buffer pH 1.2 (232 nm)

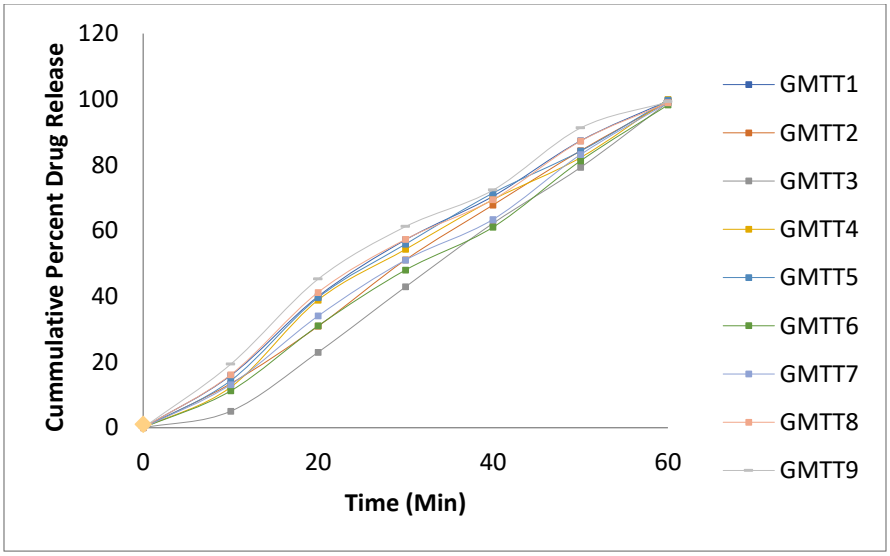

Figure 3: Zero-order kinetic plot of the prepared various antidiabetic tablet (GMTT1-GMTT9)

The antidiabetic tablet by tab-tab technology dosage form helps in absorption of the drugs from the upper gastrointestinal tract. The other characterization includes weight variation, thickness, hardness, friability, mechanical strength, measurement of tablet porosity, wetting time and water absorption ratio, moisture uptake studies, in-vitro dispersion time, disintegration test, determination of drug content, *in-vitro* drug release dissolution test, *in-vitro* drug release kinetic study and stability study. The flow properties of powder blend were evaluated in terms of carr's index, hausner's ratio and angle of repose. All the blend powders exhibited good flow properties. The physical properties (i.e., weight, thickness, hardness, friability, water uptake

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

capacity, swelling ratio, disintegration time and drug content) of antidiabetic tab in tablet were studied. The tablet was varied from 0.210 to 0.213 cm in diameter and 0.191 to 0.192 cm in thickness, average weight was varied from 812.9 to 817.6 mg, hardness was varied from 5.22 to 5.32 kg / cm^2, friability was varied from 0.42 to 0.49 %, disintegration time was varied from 1.04 to 1.18 hr and drug content was varies from 98.0 to 98.8 % for for GMTT1 to GMTT2. The release of drug from the antidiabetic tablets was influenced significantly by the variation of excipents of tablet in dissolution media. This was evidenced by the whole amount of drug released from tablets through direct compression tablets. The preliminary and screening studies were performed using different polymers and the polymers citric acid, sodium bicarbonate, HPMC, promised excellent properties for controlled release and muco-adhesion. Using selected polymers, the final batches were prepared by direct compression method and were evaluated for buoyancy lag time and total buoyant time, swelling index, drug content, ex-vivo mucoadhesive strength, in-vitro dissolution study. The formulation GMTT3 was found to be the best formulations in terms of sustained drug release. Drug release kinetics was performed by using various kinetic models such as Zero order, First order, Korsmeyer-Peppas and Higuchi's equation. The regression coefficient (r^2) value of various models was found to be non-fickinon drug release diffusion mechanism and followed supercase II transport mechanism respectively.

Summary and Conclusion:

The optimized sustained release tablets GDT4 formulation was formulated as antidiabetic formulation by tab in tablet technology. The antidiabetic tablets (GMTT1-GMTT9) tablets were prepared by the direct compression method, using MCC, DBT, Lactose etc. as excipient blend. The post Compression evaluation of the antidiabetic tablet by tab-tab technology dosage form helps in absorption of the drugs from the upper gastrointestinal tract. The release of drug from the antidiabetic tablets was influenced significantly by the variation of excipients of tablet in dissolution media. This was evidenced by the whole amount of drug released from tablets through direct compression tablets. The preliminary and screening studies were performed using different polymers and the polymers citric acid, sodium bicarbonate, HPMC, promised excellent properties for controlled release and muco-adhesion. Using selected polymers, the final batches were prepared by direct compression method and were evaluated for buoyancy lag time and total buoyant time, swelling index, drug content, ex-vivo mucoadhesive strength, in-vitro dissolution study. The formulation GMTT3 was found to be the best formulations in terms of sustained drug release. Drug release kinetics was performed by using various kinetic models such as Zero order, First order, Korsmeyer- Peppas and Higuchi's equation. The regression coefficient (r^2) value of various models was found to be non-fickinon drug release diffusion mechanism and followed supercase II transport mechanism respectively.

References:

1. Mannan A, Rao KP. Novel chewable Tablet in Tablet dosage form of Orlistat and Venlafaxine hydrochloride: development and evaluation. Journal of Applied Pharmaceutical Science. 2015, 5(03):91–97.
2. Huang H, Wu Z, Qi A, Zhang H, Chen Q. Compression-coated tablets of glipizide using hydroxypropylcellulose for zero-order release: In vitro and in vivo evaluation. Int. J. Pharm. 2013, 446:211–218.
3. Tang Y, Teng H, Shi Y, He H, Zhang Y. Tablets of paliperidoneusing compression-coated technology for controlled ascending release. A JPharma Sci. 2018, 13:143–15416.
4. Ozekia Y, Andoa M, Watanabea Y, Danjob K. Evaluation of novel one-step dry-coated tablets as a platform for delayed-release tablets. J Control Release. 2004, 95:51–60.
5. Kanwar K. Tablet in Tablet - An Innovative and Pragmatic Approach in Tableting Technology. Asian Journal of Pharmaceutics (AJP), 2022, 16 (2), 1-9.
6. Shah R, Patel S, Patel H, Pandey S, Shah S. Formulation development of Carvedilol compression coated tablet. Pharm Dev Technol. 2011, 1–10.15.
7. Prasad MSC, Babu BN, Ajay M, Raj SB, Audinarayana N, Reddy KB. Design and characterization of modified release isoniazid and salbutamol sulfate inlay tablet. International journal of pharmacy and pharmaceutical sciences. 2011, 3(4): 153-159. 13.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(2), 15-20 | ISSN:2251-6727

8. Efentakis M, Peponaki C. Formulation study and evaluation of matrix and three-layer tablet sustained drug delivery systems based on Carbopols with isosorbite mononitrate. AAPS Pharm Sci Tech. 2008, 9(3):917-23.
9. Rajalakshmi R, Sireesha A, Lakshmi SM. Inlay Tablets – a novel approach. International journal of advanced pharmaceutics. 2011, 1(1): 1-10.
10. Makino C, Sakai H, Yabuki A, Nateglinide Controlled Release Tablet Containing Compressionable Enteric Coated Granules: chem. Pharm. Bull. 2010; 58(9): E1136-41.
11. Toyohiro S, Hiromu K, Hiroshi N, Kazuhiro S, Masahiro H, Time-release compression-coated core tablet containing nifedipine for chrono pharmacotherapy: Int J Pharm. 2004, 280, 103-111.
12. Ms. Banerjee N, Mrs. Singh S. Formulation and Evaluation of Compression Coated Tablets of Cefpodoxime Proxetil: A review. Int J pharm sci Res. 2013, vol 4: 104-12.
13. Hariharan M, Gupta V. A Novel Compression-Coated Tablet Dosage Form: Pharm Tech. 2001, 14-21.