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Studies on Formulation and Evaluation of Dapagliflozin Tablets for Treatment of Diabetes Mellitus

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ABSTRACT: Background: The present study was undertaken to develop Dapagliflozin Immediate release tablets. Dapagliflozin is a sodium glucose transporter 2 inhibitor used to treat type 2 diabetes mellitus. **Aim:** The present study was aimed at formulation of immediate release Dapagliflozin with lactose, pregelatinized starch, microcrystalline cellulose DC grade binders, super disintegrants and dibasic calcium phosphate as filler. **Methods:** The formulated tablets were studied for their pre and post compressional properties. Tablets were subjected for drug content, disintegration and *In vitro* dissolution studies in USP II dissolution apparatus. The drug release data is subjected to various plots and the drug release profiles were analyzed using kinetics models. **Results:** The pre-formulation studies revealed that Dapagliflozin drug procured was pure. Analytical method developed and validated was linear, accurate and sensitive. The rheological characterization of powder beds of all Dapagliflozin formulations were freely flowable, obeyed the ideal limits and was suitable with compression abilities. *In vitro* studies showed Dapagliflozin immediate release in 120 min with uniform release profiles. D1 optimized formulation released 93.18 % with r^2 0.99998, slope (n) 0.8743. Dapagliflozin release from all the developed formulations followed the pattern as D9 (99.58 %) >D6 (98.41 %) >D3 (96.61 %). **Conclusion:** The drug release occurred via rapid disintegration due to super disintegrants followed by tablet erosion and drug solubilization. The release data of all formulations showed high regression coefficients. Optimized Formulation (D1) and Marketed DPG Tablet showed comparatively similar DPG release profiles. The DPG IR tablets could be formulated for rapid release, which gives better oral bioavailability and patient compliance for better type II diabetes mellitus control.

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INTRODUCTION:

Diabetes is a metabolic disorder characterized by chronic hyperglycemia due to defects in the metabolism of carbohydrate, fat and protein. Persistent hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs. Insulin is secreted by the beta (ß) cells and glucagon is secreted by the alpha (α) cells both are located in the islets of Langerhan's. Insulin decreases the blood glucose level by glycogenesis and transports glucose into the muscles,

liver and adipose tissue [1]. In recent decades, India has witnessed a rapidly exploding epidemic of diabetes. Indeed, India today has the second largest number of people with diabetes in the world. The homeostasis of glucose in the body is maintained by a number of hormones. However two hormones namely, insulin and glucagon play a dominant role in the regulation of glucose homeostasis. Glucagon is secreted by the α cell of pancreas when the concentration of glucose is low. Glucagon acts by a) Antagonizing the effect of insulin by enhancing glycogenolysis and gluconeogenesis in the liver. b) In addition to glucagon, cortisol and catecholamines also increase the plasma glucose levels [2].

A number of non-insulin based oral therapies have emerged for treatment of type II diabetes mellitus. Insulin Secretagogues; Biguanides; Insulin Sensitizers; Alpha Glucosidase Inhibitors; Incretin mimetics (DPP 4 Inhibitors); Amylin antagonists; SGLT2 inhibitors. Sodium Glucose Transporter 2 (SGLT2) Inhibitors inhibit SGLT2 located on the proximal convoluted tubule of the kidney thus causing glycosuria.

Reabsorption of glucose in proximal convoluted tubule (PCT) is achieved by passive transporter, facilitative glucose transporter (GLUT) and active co-transporter, sodium glucose co-transporter (SGLT). SGLT2 inhibitors inhibit the SGLT2 present in PCT which prevents reabsorption of glucose and enhances the excretion of glucose in urine. The available molecules in this category are Canagliflozin, Dapagliflozin, Empagliflozin, Ipragliflozin, Luseogliflozin and Tofogliflozin [3].

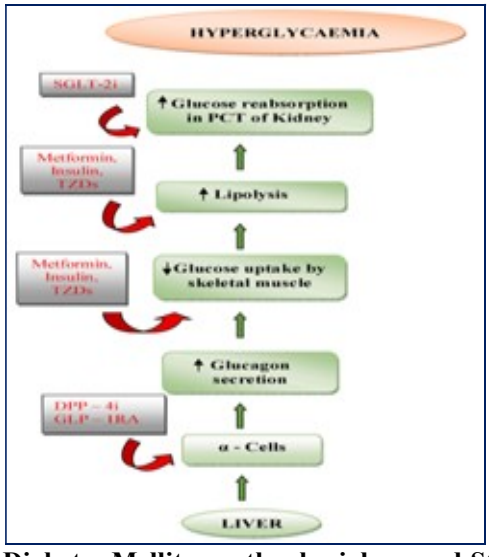

Fig 1. Diabetes Mellitus pathophysiology and SGLT2 targets.

Dapagliflozin is the first in a new class of oral selective sodium-glucose cotransporter 2 (SGLT2) inhibitors designed for treating type 2 diabetes as represented in Fig 1. Dapagliflozin is highly SGLT2 selective and contains a C-glucoside for increased *in vivo* stability, prolong half-life and produce consistent pharmacodynamic activity [4-5].

Dapagliflozin (DPG) was an inhibitor of sodium-glucose co-transporter-2 (SGCT-2) used for the treatment of Type 2 Diabetes Mellitus. IUPAC name: (2S,3R,4R,5S,6R)-2-[4-Chloro-3-(4-ethoxybenzyl) phenyl]-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol. It is a white to off-white odourless fine powder freely soluble in water. It is a Sodium-glucose cotransporter with molecular formula $C_{21}H_{25}ClO_6$, molecular weight of 408.873 Da and 74 to 78 °C melting point with 10 to 20 mg *bid* dose. DPG is an inhibitor of SGLT2. By inhibiting SGLT2, DPG reduces reabsorption of filtered glucose; thereby increases urinary glucose excretion and was used in the treatment of Type II Diabetes Mellitus. Pharmacokinetic profile of DPG shows 78 % oral bioavailability, 91 % protein binding. DPG shows the mechanism of action as Sodium-glucose cotransporter 2 (SGLT2), expressed in the proximal renal tubules, is responsible for reabsorption of filtered glucose from the tubular lumen [6-10].

Tablets may be defined as solid pharmaceutical dosage forms containing medicament or medicaments with or without suitable excipients & prepared either by compression or moulding. Immediate release dosage forms are those for which ≥ 85 % of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is the simple disintegration stage, accomplished in less than one hour. Super-disintegrants available commercially like Croscarmellose sodium, Crospovidone and Sodium Starch Glycolate play a major role in disintegration and dissolution. Super disintegrants provide quick disintegration due to the combined effect of swelling and water absorption by the formulation which forms a porous structure [11-12].

In the direct compression method of tablet production, dry ingredients are thoroughly mixed and then compressed into tablets. The method consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself [13].

Objective of the investigation is to Characterize of Dapagliflozin, for physico-chemical properties.

MATERIALS AND METHODS:

Dapagliflozin was procured from Concord Drugs Ltd., Hyd. Crospovidone, Croscarmellose sodium and Sodium starch glycolate were obtained from Sigma Aldrich, Bengaluru. Lactose DC, Pregelatinized starch DC and Micro crystalline cellulose DC from Micro Labs Ltd, Bengaluru. Magnesium stearate, Talc and Dibasic calcium phosphate from SD Fine Chem Ltd, Chennai.

Analytical method development and validation studies:

Estimation of DPG by U.V spectroscopy:

The stock solution was prepared by dissolving accurately weighed 100 mg of DPG in 10 ml of 1:1 ethanol:water / Phosphate buffer pH 7.4 and then the volume was adjusted to 100 ml with the same solvent to get 1 mg/ml solution. Further the above stock solution of drug was subsequently diluted with respective solvents to get 2, 4, 6, 8 and 10 µg of drug per ml. Later, 5 ml of 10 µg/ml solution was taken and scanned for maximum absorbance between 200 nm to 400 nm in UV Spectrophotometer against blank solution. Further calibration curve of DPG was plotted by measuring absorbance of 2 to 10 µg/ml solutions at a λ_{max} of 224 nm. Average of triplicate readings was taken and tabulated. Regression equation was derived from the slope of the curve. The analytical method developed was validated for linearity [14].

***Linearity studies*:**

The analytical method developed for DPG was validated for linearity. To establish linearity of the proposed method five different concentrations of DPG (0-10 µg/ml) drug solutions were prepared from respective stock solutions and analyzed for their absorbance at 224 nm for DPG. The obtained data was subjected individually to linear regression analysis by using the method of least squares [14].

***Validation studies of DPG*:**

Later the analytical method was validated for accuracy and precision by drug content determination for developed DPG (10 mg) formulations. Respective drug quantity recovered with accuracy and precision was reported [15].

Pre-formulation studies:

***Melting point*:**

It was determined by taking a small amount of drug in a capillary tube closed at one end and was placed in theil's melting point apparatus and the temperature at which the drug melts was noted. Average of triplicate readings was noted [16].

***Solubility* study:**

Solubility of the drug was determined in distilled water, acetone, ethanol, methanol and different pH buffers according to the method proposed by Diez, *et al*., An excess amount of the drug was taken and dissolved in a measured volume of solvent or buffers in a volumetric flask to get a saturated solution. The solution was shaken on a rotary shaker for 24 h to attain equilibrium. Then the measured quantity of the filtered drug solution was withdrawn and successively diluted and concentration was measured in a UV spectrophotometer at 224 nm. Average of triplicate readings was taken [17].

***Fourier Transform Infrared (FTIR) Spectroscopy studies*:**

To investigate any possible interaction between the drug and the utilized polymers the FTIR spectra of pure drugs (DPG) alone and their tablet formulations with various polymers were recorded by using FTIR spectrophotometer. The range selected was from 400cm^{-1} to 4000 cm^{-1} using potassium bromide discs [18].

DPG IR tablet preparation and evaluation:

The DPG IR tablet formulations D1 to D9 of 150 mg each were formulated with 10 mg DPG dose by direct compression. All formulation ingredients were accurately weighed, milled and passed through sieve # 80/ 100 individually and blended in a cube mixer. The powder beds were further studied for the following rheological parameters [19-20].

Pre-compression evaluation of granules:

***Bulk density*:**

Determined by placing a fixed weight of powder blends in a measuring cylinder on a bulk density testing unit and the total volume was noted. Bulk density was calculated by using the formula. Bulk density was obtained as Total weight of powder or granules / Total volume of powder or granules [21].

***Tapped density*:**

Determined in a bulk density testing apparatus by placing the powder blend in the measuring cylinder and

the total volume of powder blend was noted before and after 100 tappings. Tapped density was calculated by using the formula; Tapped density = weight of powder/ Total volume of powder after 100 tappings.
Average of three densities were taken and tabulated [21].

***Carr's Compressibility index*:**
Determined by placing the powder in a measuring cylinder and the initial volume (V_0) was noted before tapping. After 100 tapping again the final volume (V) was noticed. *Compressibility index = (1- V/ V_0) x 100.* Where V_0 is volume of powder before tapping, V is volume of powder after 100 tappings. Average of three was taken [21].

***Angle of repose (q°)*:**
Angle of repose of power blends was determined using cut funnel method by measuring height and radius of the heap of the powder bed. A glass made cut stem funnel was fixed to a stand and the bottom of the funnel was fixed at a height of 3 cm from the horizontal plane. Powder was placed in a funnel and allowed to flow freely to form a heap. Height and radius of the heap were measured by vernier calipers and noted. $ø = \tan^{-1} h/r$. Where h is the height of heap of powder/granule bed and r was radius of heap [21].

DPG IR tablets by Direct compression method:
DPG IR *tablets* were formulated from powder blends containing DPG, super disintegrants and other excipients of various formulations D1 to D9 by direct compression on a tablet punching machine using 6 mm flat punches at a compressional force of 4 to 6 kg/cm^2 [22].

Post compressional parameters evaluation:
***Tablet weight uniformity*:**
This was done according to Indian Pharmacopoeia (2007 edn), by taking twenty randomly selected tablets, weighed together and individually. The mean and standard deviations were determined. Tablets comply with the test if not more than two of the individual weights deviate from the average weight by more than the percentage and none deviate more than twice the percentage as below [22].

***Diameter and tablet thickness*:**
Tablet diameter and thickness was evaluated by using vernier Caliper from randomly selected tablets. Results were tabulated as mean ± SD (n=3) [22].

***Hardness test*:**
Hardness was performed by random selection of five tablets from each formulation and crushing strength of each tablet was measured using Pfizer tablet hardness tester. The mean hardness was determined and expressed in Kg/cm^2 [22].

***Friability*:**
Friability was carried out in Roche friabilator. Ten tablets were selected randomly and initial weight (w_o) was noted down after dedusting and placed in a tumbling chamber of rotating drum. They were subjected to 100 falls of 6 inches height (25 rpm for 4 min). After completion of 100 rotations, tablets were removed, dedusted and weighed (w) accurately. The percent loss in weight was calculated by formula % Friability = $(1 - w/w_o) \times 100$ [22].

***Disintegration test*:**
Disintegration of tablets was determined according to Indian Pharmacopoeia (2007 edn), by placing one tablet in each of the six tubes of the basket and the assembly was suspended into a beaker containing 0.1 N HCl maintained at 37 ± 0.5 °C and operated for 2 h [22].

***Drug content*:**
It was determined from randomly sampled tablets which were crushed into powder in a mortar and weight equivalent to 10 mg of drug was taken into a volumetric flask containing ethanol: water (1:1) and kept aside with constant shaking for 24 h on a rotary flask shaker to extract total drug present in the tablet. Then absorbance was measured after suitable dilution at 224 nm against blank [23].

***In vitro dissolution studies of DPG IR (D1-D9) tablets*:**
The tablet dissolution apparatus USP II (paddle) was used for DPG IR tablet formulations D1 – D9 *in vitro* dissolution studies. Dissolution studies were carried out for 120 min under sink conditions in pH 7.4 at 37±0.5^{0}C and paddle speed at 50 rpm. Samples were taken at predetermined time intervals. DPG release was detected by UV absorbance using a UV spectrophotometer at 224 nm [19-20].

In vitro Release Kinetics:
The analysis of drug release mechanisms from a pharmaceutical dosage form is a complicated process and is practically evident in the case of matrix systems. The mechanism of drug release was studied by using the Higuchi equation and the Peppa's Korsemeyer equation [24-27].

Zero Order Release Kinetics:
It defines a linear relationship between the fractions of drug released versus time. $Q=k_0t$. Where, Q is the

fraction of drug released at time t and k_o is the zero order release rate constant. A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics [24].

First Order Release Kinetics:

Wagner assumed the exposed surface area of a tablet decreased exponentially with time during the dissolution process described adequately by the first-order kinetics. The equation that describes first order kinetics is given as Log C= Log C_o-kt/2.303. Where C is the amount of drug dissolved at time t, C_o is the amount of drug dissolved at t=0, k is the first order rate constant. A graph of log cumulative of log % drug remaining vs time yield straight line [25].

Higuchi equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) and the square root of time. $Q=K_2t^{1/2}$. Where K_2 is release rate constant. A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependent [26].

Korsemeyer Peppa's:

In order to define a model, which would represent a better fit for the formulation, dissolution data was further analyzed by the Peppas-Korsmeyer equation (Power Law). $Mt/ M_\infty = K.t^n$. Where, Mt is the amount of drug released at time t, M_α is the amount released at time α, M_t/M_α is the fraction of drug released at time t, K is the kinetic constant and n is the diffusion exponent. A plot between log drug release up to 60 % against log of time will be linear if release obeys Peppa's equation and slope of plot represents "n" value [27].

RESULTS:

DPG was characterized for its physico-chemical properties. The U.V. absorption maximum was found to be 224 nm which is the same as literature value 225 nm. The analytical method was validated for linearity, accuracy and precision as represented in Table 1.

The UV method was found to be robust, simple, linear, accurate and precise at 2 to 10 µg/ml concentration as represented in Fig 2. Melting point of DPG was 76.33 °C,1 which corroborates with literature. Solubility of DPG in different solvents was studied. It was found to be 1.55 mg/ml in distilled water, 11.83 mg/ml in ethanol and 1.87 mg/ml in pH 7.4 buffer. Drug excipient compatibility studies of DPG formulations indicated minimum drug- excipient interactions which are evident by replication of DPG peaks in pure drug and physical mixture FTIR spectral studies. This shows that the drug was compatible with the formulation excipients and forms stable tablet formulations.

***In vitro* drug release studies from DPG IR formulations D1 to D9 tablets.**

Sl. No.	Conc. (µg/ml)	Absorbance (nm) ± SD	Regression data
1	0	0	* m = 0.06664
2	2	0.135±0.0036	* c = -0.00071
3	4	0.264±0.0012	* r^2 =0.999966
4	6	0.399±0.0021	Linearity range 2-10 µg/ml
5	8	0.523±0.0025	
6	10	0.662±0.0006	
Where: *m = slope; c = intercept; r = regression.			

Each data presented as Mean ± Standard deviation (n-3).

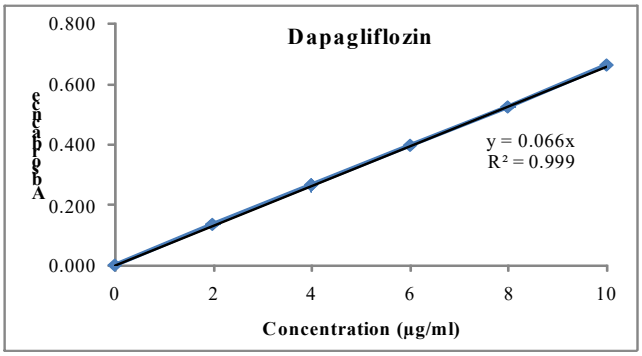

Fig 2. Calibration curve of Dapagliflozin in Ethanol: Water (1:1) by U.V. method.

The DPG IR formulation blends D1 to D9 studied for micromeritic properties. The powder blends were dried in the oven at 40 °C and at 35 % RH. The lubricants/ glidants were incorporated and blended thoroughly. Before compression powder beds were studied for various rheological characteristics, bulk density, compressibility index, angle of repose etc. Bulk density of all D1 to D9 formulations is less than 1. However it was also observed that the order of bulk density of various DPG formulations was D6> D4> D7> D8> D5> D9> D3> D2> D1. Compressibility index was found to be in a range of 12.90 to 18.10. Indicating DPG powder beds are free flowing, since compressibility index was < 20 % and it can be compressed into a compact mass of tablet.

Angle of repose (°q) indicates powder flowability from hopper to die cavity. A repose angle of 20 to 30 °q indicated excellent flowability of DPG powder blends. The DPG powder blends D1 to D9 after adding talc and magnesium stearate showed good flow indicates

improved flow of powder bed. The directly compressed DPG tablets D1 to D9 exhibited post Compressional properties like weight uniformity, friability, thickness within the pharmacopoeia's limits. All DPG tablets D1 to D9 friability studies indicated formulations showed good mechanical strength against chipping. DPG IR formulations due to the presence of super disintegrants tablets showed a disintegration range of 62.22 to 96.49 s. DPG tablets D1 to D9 showed drug content uniformity in the range of 96.91 to 99.75 as represented in Table 2.

Table 2. Accuracy and precision studies of Dapagliflozin analytical method.

F. Code	Qty added (mg/50 ml)	Qty recovered (mg/50ml)	Accuracy (%)	Precision
D1	10	9.76	98.82	0.019
D2	10	9.94	99.68	0.032
D3	10	9.83	99.14	0.017
D4	10	9.94	99.68	0.032
D5	10	9.77	98.87	0.032
D6	10	9.78	98.92	0.037
D7	10	9.60	98.01	0.019
D8	10	9.70	98.49	0.049
D9	10	9.74	98.71	0.065

D1 IR tablet formulation containing 10 mg DPG with 5% crospovidone super disintegrant and 30% Lactose DC binder released DPG 50.81 % at 60 min and 93.18 % at 120 min. Whereas D2 IR tablet formulation containing 10 mg DPG with 5 % crospovidone super disintegrant and 20 % Lactose DC binder released DPG 59.77% at 60 min and 95.27 % at 120 min. Later D3 IR tablet formulation containing 10 mg DPG with 5 % crospovidone super disintegrant and 10 % Lactose DC binder released DPG 70.78 % at 60 min and 99.61 % at 120 min. Studies indicated drug release was dependent on amount of binder i.e. D3 (10 %) > D2 (20 %) > D1 (30 %) but more than 90 % of DPG released from D1, D2, and D3 at 120 min.

D4 IR tablet formulation containing 10 mg DPG with 5 % Croscarmellose sodium super disintegrant and 30 % Pregelatinized starch DC binder released DPG 58.39 % at 60 min and 96.58 % at 120 min. D5 IR tablet formulation containing 10 mg DPG with 5 % Croscarmellose sodium super disintegrant and Pregelatinized starch DC binder released DPG 79.03 % at 60 min and 97.63 % at 120 min. Later D6 IR tablet formulation containing 10 mg DPG with 5 % Croscarmellose sodium super disintegrant and 10 % Pregelatinized starch DC binder released DPG 83.59 % at 60 min and 98.41 % at 120 min. Studies indicated that drug release was dependent on amount of binder employed i.e. D6 (10 %) > D5 (20 %) > D4 (30 %) but more than 95 % of DPG released from D4, D5 and D6 at the end of 120 min.

D7 IR tablet formulation containing 10 mg DPG with 5 % Sodium starch glycolate super disintegrant and 30 % MCC DC binder released DPG 60.45 % at 60 min and 95.40 % at 120 min. D8 IR tablet formulation containing 10 mg DPG with 5 % Sodium starch glycolate super disintegrant and MCC DC binder released DPG 63.13 % at 60 min and 95.83 % at 120 min. Later D9 IR tablet formulation containing 10 mg DPG with 5 % Sodium starch glycolate super disintegrant and 10 % MCC DC binder released DPG 68.25 % at 60 min and 99.58 % at 120 min. Studies indicated that drug release was dependent on amount of binder employed i.e. D9 (10 %) > D8 (20 %) > D7 (30 %) but > 95 % of DPG released from D7, D8, and D9 at the end of 120 min. The effect of Binder was attributed as MCC DC > Pregelatinized starch DC > Lactose DC for DPG release from D1 to D9 formulations as represented in Table 3.

Kinetic analysis of release data of DPG from D1 to D9 tablets showed that the majority of formulations exhibited Peppa's kinetics for DPG release. D1 DPG IR tablet formulation was found to be optimized with highest correlation coefficient 0.99998, with slope (n) value 0.8743 and released 50.81 % at 60 min and 93.18 % DPG at 120 min as represented in Fig 3.

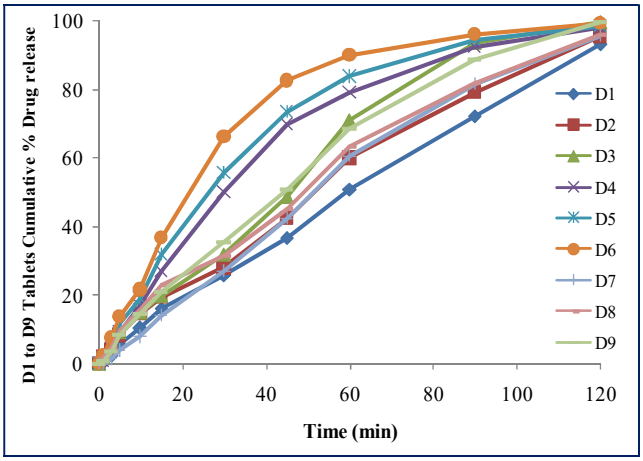

Fig 3. Dapagliflozin from tablets *In vitro* drug release studies (D1 to D9).

In vitro drug release comparative studies of DPG were conducted to compare release profile of DPG from Optimized Formulation (D1) and Marketed DPG Tablet in dissolution apparatus paddle type (USP II) for 120 min pH 7.4. Dissolution samples collected at different time intervals under sink conditions and absorbance quantified in UV spectrophotometer at 224 nm. Both Optimized D1 and DPG marketed tablets showed

Table 3. Kinetic analysis of drug release data of Dapagliflozin tablets formulations.

F. Code	Zero order (r^2)	First order (r^2)	Higuchi (r^2)	Peppas (r^2)	Best fit	Slope (n)
D1	0.99855	0.98825	0.98847	0.99998	Peppa's	0.8743
D2	0.99354	0.98649	0.99083	0.99990	Peppa's	0.6735
D3	0.98403	0.95608	0.98753	0.96972	Higuchi	0.5056
D4	0.99085	0.99784	0.98639	0.99011	First	0.7166
D5	0.98690	0.99848	0.98437	0.98668	First	0.6607
D6	0.97792	0.99717	0.98416	0.99615	First	0.6049
D7	0.99302	0.98328	0.95295	0.99745	Peppa's	0.6627
D8	0.98939	0.98710	0.97739	0.99945	Peppa's	0.6041
D9	0.98536	0.98228	0.97513	0.99369	Peppa's	0.5512

comparatively similar DPG release profiles as represented in Fig 3.

From the above results it was evident that DPG IR tablets could be formulated for rapid release of DPG which gives better oral bio availability and patient compliance. The developed tablet with DPG IR 10 mg could offer better type II diabetes mellitus control in patients. Further formulation testing is required for its anti-diabetic efficiency in suitable animal models followed by *in vivo* pharmacokinetic investigations to understand plasma drug concentration time profiles for better disease control with proper dosage regimen.

DISCUSSION:

The U.V. absorption maximum for DPG was found to be 224 nm which is the same as literature value 224 nm. The DPG UV analytical method was found to be robust, simple, linear, accurate and precise at 2 to 10 µg/ml. DPG melting point was 76.33 □C, which corroborates with literature. Solubility of DPG in different solvents was ethanol > pH 7.4 buffer > distilled water. DPG drug excipient FTIR studies indicated minimum drug-excipient interactions with good compatibility. Bulk density of D1 to D9 DPG formulations was <1 indicates better compatibility. Compressibility index < 15 % represents good compression. Angle of repose (□□) of 20 to 30 indicated excellent flow of DPG powder blends. Hardness of 4.2 to 5.5 kg/cm^2 indicated good strength of tablets. DPG tablets exhibited weight uniformity, friability, thickness within standard limits. D1 to D9 friability was <2 % indicated mechanical strength.

D1 to D9 tablets with 5 % super disintegrants disintegrated within 100 sec facilitate immediate drug release. D1 to D9 tablets exhibited drug content uniformity of 96.91 to 99.75 %.

***In vitro* drug release studies from DPG IR formulations D1 to D9 tablets:**

D1 to D3 tablets drug release was depended on amount of binder i.e. D3 (Lactose DC 10 %) released 96.61 % of DPG. D4-D6 tablets drug release was varied by amount of binder i.e. D6 (PG starch DC 10 %) released 98.41 % of DPG. D7-D9 tablets drug release was varied by amount of MCC DC binder i.e. D9 (10 %) released 99.58 % of DPG. The effect of Binder was MCC DC > PG starch DC > Lactose DC on DPG release from D1 to D9. Release Kinetics of D1 to D9 tablets showed that the majority of formulations exhibited Peppa's kinetics for DPG release. D1 was found to be an optimized tablet with high r^2 0.99998, slope (n) 0.8743 and released 93.18 % DPG. *In vitro* drug release comparative studies of DPG Optimized Formulation (D1) and Marketed DPG Tablet showed comparatively similar DPG release profiles. The DPG IR tablets could be formulated for rapid release, which gives better oral bioavailability and patient compliance. This could offer better type II diabetes mellitus control in patients.

CONCLUSION:

The U.V maximum for DPG was 224 nm, which is the same as literature value. The UV analytical method of DPG was sensitive and accurate at 2 to 10 µg/ml. DPG melting point was 76.33 □C, which corroborates with literature. Solubility of DPG in solvents was ethanol > pH 7.4 buffer > distilled water. DPG FTIR studies indicated good drug- excipient compatibility. All D1 to D9 DPG formulations exhibited good micromeritic flow properties suitable for better compaction and compression of powder blends. Hardness of the tablets of 4.2 to 5.5 kg/cm^2 indicated good strength of tablets. D1 to D9 tablets disintegrated within 100 sec ensure

quick DPG release. D1 to D9 tablets exhibited drug content uniformity of 96.91 to 99.75 %. DPG release from D1 to D9 tablets was depended on amount and type of binder i.e. MCC DC > PG starch DC > Lactose DC. D1 to D9 tablets DPG release Kinetics majorly obeyed Peppa's kinetics. D1 was found to be an optimized tablet with high correlation coefficient and slope (n) 0.8743, which showed 93.18 % DPG release. The developed DPG IR 10 mg formulation would give better diabetes control. Further formulation testing is required for its anti-diabetic efficiency in suitable models followed by *in vivo* studies.

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