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Research Article

Design and Evaluation of Bull's Eye (In-Lay) Tablet of Glipizide and Metformin Hydrochloride by Steam Granulation Technique

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Abstract

The main objective of the investigation was to design and development of the fixed dose combination of Glipizide and Metformin Hydrochloride in-lay tablets prepared by steam granulation technique. The prepared granules were evaluated for angle of repose, bulk density, carr's index and Hausner's ratio, results revealed that preparation of granules were found to be good flow properties and the tablets were evaluated for hardness, friability, thickness, %drug content and in vitro release studies. In-lay tablet comprises of glipizide immediate release layer formulated with neem gum as disintegrating agent and metformin hydrochloride for sustained release formulated with different grads of HPMC (HPMC K4M, HPMC K15M, HPMC K100M) in which SR layer surrounded by glipizide immediate release granules. The drug-excipient compatibility studies were conducted by FT-IR studies. The mechanism of drug release from glipizide IR layer follows first order kinetics and zero order kinetic observed for metformin hydrochloride SR layer and the stability studies were performed as per ICH guide lines for formulated F9 and results obtained found to be stable.

Keywords: Metformin hydrochloride; Glipizide; HPMC (HPMC K4M; HPMC K15M; HPMC K100M)

Introduction

Granulation is one of the most important unit operation in the production of pharmaceutical oral dosage forms, it improve the flow and compression characteristics. Granulation has been defined as process whereby small particles are gathered into larger permanent massess in which the original particles can still be identified. It is an example of particle design intended to produce improved perfor-mance through the combination of formulation composition and manufacturing process and modified particle morphology is achieved through the use of a liquid acting on the powder blend to form interparticulate bonds which then result is granules of varying sizes. As practised in the pharma industry granulation is often the first processing step where multiple formulation components are combined. performance during tablet compression is dependent on all process unit operations and as granulation is frequently the most complex and difficult process to control.

The wet granulation process has been implemented over the last 25 years by the development of improved equipment, innovative research and novel polymeric binders.

"Steam granulation" is the modification of wet granulation method. Here steam is used as a binder instead of water. Steam granules are more spherical its have several benefits includes large surface area hence increased dissolution rate of the drug from the granules its processing time is shorter, no health hazards to operators, no restriction by ICH on traces of organic solvents left in the granules and more number of tablets are produced per batch, compared to the use of organic solvents, water vapour is environmentally friendly. It can be used for preparation of taste masked granules without modifying availability of the drug. This method is un suitable for thermo labile drug. The concept of inlay tablet technology is utilized for stabilization of two incompatible drugs to delivering of two drugs having synthetic effect/to defines a drug for biphasic drug release profiles for the purpose of extinction of patients.

Advantages:

a. Higher rate of diffusion.

b. Higher dissolution rate of granules because of large surface area generated.

c. Uniformly distributed in the powder particle.

d. No health hazards to operator.

Methods

Drug-excipient compatibility studies

Drug-excipient compatibility studies were performed for Metformin Hydrochloride, Glipizide, physical mixture of Metformin Hydro-chloride and Glipizide with various polymers and gums .by FTIR studies by employing KBr pellet method and spectra were recorded in the wave length range between 4000 cm^{-1} to 400 cm^{-1}.

Preparation of metformin hydrochloride and glipizide inlay tablets by steam granulation technique

Preparation of Immediate release Glipizide granules

The composition of glipizide granules as shown in Table 1 Glipizide granules were prepared by using steam granulation technique the composition was given in Table 1 in which Micro crystalline cellulose (MCC) was used as diluent; PVP (10%) and neem gum were used as dry binder and super disintegrant respectively. The components for 20 tablets were weighed accurately and passed through sieve no.20. Required amounts of glipizide, micro crystalline Cellulose, PVP and neem gum was transferred into the perforated plate which is arranged on steam granulation apparatus. The steam was passed into the mixture through the perforated plate to obtain the granules, Simultaneously air from cylindrical tank was passed to dry the granules. The dried granules were passed through sieve no.16. and obtained The granules were lubricated with magnesium Stearate and talc for compression.

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Immediate release layer									
Glipizide	5	5	5	5	5	5	5	5	5
PVP K 30	25	25	25	25	25	25	25	25	25
Neem gum	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
MCC	202.5	202.5	202.5	202.5	202.5	202.5	202.5	202.5	202.5
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total Weight	250	250	250	250	250	250	250	250	250
Sustained release layer									
Metformin HCl	500	500	500	500	500	500	500	500	500
HPMC K 4M	100	150	200	-	-	-	-	-	-
HPMCK 15M	-	-	-	100	150	200	-	-	-
HPMCK 100M	-	-	-	-	-	-	100	150	200
MCC	100	50	-	100	50	-	100	50	-
Magnesium Stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Talc	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Total weight	715	715	715	715	715	715	715	715	715

Table 1: The composition of combination of Glipizide and Metformin Hydrochloride inlay tablet with various polymers.

Preparation of sustained Metformin Hydrochloride granules

The composition of Metformin hydrochloride granules as shown in Table 1 were prepared by steam granulation method in which different grdes of HPMC polymers (HPMC K 4M, HPMC K15M, HPMC K100M) were used as release retardants Polymers. Microcrystal-line cellulose (MCC) was used as diluent and a mixture of talc-magnesium Stearate was used as glidant and lubricant. The components for 20 tablets were weighed accurately and passed through sieve no.20. Required amounts of Metformin hydrochloride, polymer/gums and MCC were transferred into the perforated plate which is arranged on steam granulation apparatus. The steam was passed into the mixture through the perforated plate to obtain the granules. Simultaneously air from cylindrical tank was passed to dry the granules. The dried granules were passed through sieve no.16 and the obtained granules were lubricated with magne-

sium Stearate and talc.

Preparation of In-Lay Tablets

It consists of two steps, in the first step lubricated Metformin hydrochloride granules were first compressed into tablet by using in 16 station rotary compression machine with 12 mm round flat punches. then the obtained Metformin hydrochloride sustained release tablet was placed manually at the center of 16 mm die cavity over the immediate release glipizide granules, then compressed into in-lay tablet by 16 station rotary compression machine (Cadmach, Ahmadabad).

Micromeritic Properties of Granules

The pure drug and formulation powder blend prepared before compression is evaluated for Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio.

Angle of repose: The flow characteristics of different granules were studied by measuring the angle of repose employing fixed funnel method. The angle of repose was calculated by using the following formula.

$$\grave{e} = Tan - 1\frac{h}{r}$$

Where,

h = height of pile, cm

r = radius of the base of the pile, cm θ = angle of repose.

Bulk Density: Apparent bulk density (gm/ml) is determined by pouring granules in to a graduated cylinder and measured the volume, from weight and volume intial bulk density was calculated. Tapped bulk density was measured by placing a graduated cylinder on a mechanical tapper apparatus operated for 100 taps. The intial bulk and tapped bulk density calculated by the following equations.

Bulk density = Mass of granules/Bulk Volume of granules

Tapped density = Mass of granules /Tapped volume of granules

Carr's Index and Hausner's ratio

Carr's index and Hausner ratio were determined from the tapped and bulk densities of a known weight of samples using a bulk density apparatus. The following formulas were used for calculating Carr's index and Hausner's ratio:

$$Carr's\ index = \frac{Tapped\ density - bulk\ density}{Tapped\ density}$$

$$Hausner'\ ratio = \frac{Tapped\ density}{Bulk\ density}$$

Evaluation of Tablets

Thickness

The thickness of the tablets was determined by using vernier calipers. Five tablets from each batch were used, and average values were calculated.

Hardness

Hardness of the tablet was determined by using the Monsanto harness tester. The lower plunger was placed in constant with the tablet and zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet factured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force.

Friability

The Roche friability test apparatus was used to determine the friability of the tablets. 20 pre-weighed tablets were placed in the apparatus, operated for 100 revaluations. Then the tablets were re-weighed, percentage friability was calculated according to the following formula.

$$Friability\ (\%) = \frac{Initial\ weight\ of\ tablets - Final\ weight\ of\ tablets}{Initial\ weight\ of\ tablets} \times 100$$

Weight variation test: The formulated tablets were tested for weight uniformity, 20 tablets were weighed collectively and individu-ally. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it is within permissible limits. The following formula was used to calculate % weight variation.

$$on = \frac{AverageWeight - IndividualWeight}{AverageWeight} \times 100$$

Drug content

Twenty tablets of each formulation were collected, weighed and powdered. Powder equivalent to 100 mg of drug was weighed dissolved in 5 ml of methanol and diluted with 6.8 phosphate buffer. It was allowed to sonication for 15 min. The solution was filtered and the absorbance was measured after suitable dilutions by using Shimazdu UV spectrophotometer at 275 nm.

In-vitro drug release studies

In-vitro drug release studies for immediate release layer of Glipizide

The in-vitro drug release studies for immediate release layer of Glipizide were studied by USP Type II dissolution testing apparatus. The release study of Glipizide was carried out in 900 ml of pH 7.4 phosphate buffer maintained at the temperature 37 ± 0.5°C at 50 rpm. 5 ml samples were withdrawn at specific period of time and replaced with same amount of fresh dissolution medium. Then the samples were filtered and analyzed by using U.V spectrophotometer at 276 nm.

In-vitro drug release studies for immediate release layer of Glipizide and Metformin Hydrochloride Inlay tablet: The in-vitro drug release studies for immediate release layer of Glipizide and Metformin hydrochloride inlay tablet was studied by USP Type II dissolution testing apparatus. The release study of Glipizide and Metformin hydrochloride inlay tablet was carried out in 900 ml of 0.1N hydro-chloric acid for 0-2 hrs and then 3 to 14 hours were carried out in pH 6.8 phosphate buffer maintained the temperature of dissolution medium at 37 ± 0.5°C at 100 rpm. 5 ml samples were withdrawn at specific period of time and replaced with same amount of fresh dissolution medium. Then the samples were filtered and analyzed by using U.V spectrophotometer at 276 nm for glipizide and 233 nm for Metformin hydrochloride.

Results and Discussion

Preformulation studies

Drug Excipients compatibility studies

Drug-Excipient Compatibility studies for drug polymer and mixture of drug and polymers were conducted by FT I.R spectral studies results given in the below. In which I.R spectra of glipizide, Metformin hydrochloride and the physical mixtures of drug and excipients was showed in figures 1,2,3 and 4, results revealed that no chemical interactions were obtained from FT-IR spectra's.

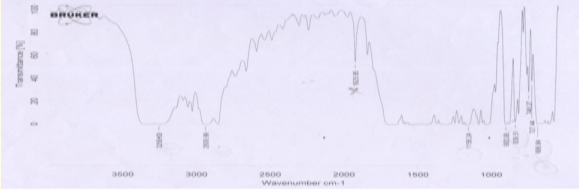

Figure 1: IR studies of Glipizide.

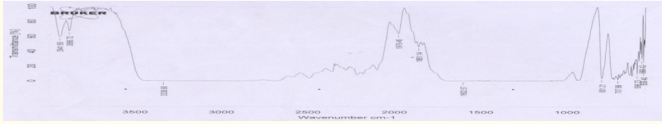

Figure 2: IR spectra of Metformin Hydrochloride.

Figure 3: IR studies of Physical mixture of Glipizide and excipients.

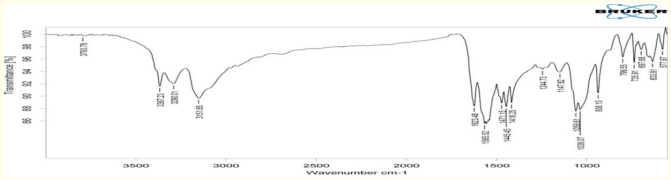

Figure 4: IR studies of Physical mixture of Metformin Hydrochloride with Guar gum.

S. No	Wave number in cm^{-1}		Functional group
	Range	Observed	
Glipizide	2700-3300	2939.67	N-H stretching
	1149-1180	1156.85	S = O stretching
	728-725	727.37	C-H stretching
	650-900	839.51	C-H deformation
Glipizide + PVP + SSG + MCC	2700-3300	2942.84	N-H stretching
	1149-1180	1156.37	S = O stretching
	728-725	726.77	C-H stretching
	650-900	839.14	C-H deformation
Metformin HCl	3400-3200	3338.48	N-H stretching
	1626-1567	1602.54	C = N Stretching
	820-790	801.62	C-H deformation
	736-705	707.36	N-H wagging
Metformin Hydrochloride+ Gaur gum	3400-3200	3290.57	N-H stretching
	1626-1567	1623.64	C = N Stretching
	820-790	799.21	C-H deformation
	736-705	735.16	N-H wagging

Studies on Immediate release Glipizide granules

The granules of immediate release glipizide formulation was evaluated for the micromeritic properties like bulk density, tapped density, Carr's index, Hausner's ratio and Angle of repose, from the results it was observed that the bulk density was found to be 0.699 ± 0.52 g/ml and tapped density was found to be 0.763 ± 0.45 g/ml. The other micromeritic properties such as Carr's index, Hausner's ratio and Angle of repose was found to be 8.69 ± 0.61, 1.09 ± 0.32 and 25.420 ± 0.13 respectively indicating prepared granules were found.

Studies on In-vitro drug release data of Glipizide immediate release layer

The results of percentage of glipizide released from the immediate release formulations were observed as 95.06 ± 0.20 at the end of 25 mins. The drug release data was plotted against time as given in the Figure 5.The drug release mechanism was analyzed by in-vitro drug release data was fitted into various release equations and kinetic models (First order, Zero order, Higuchi and Peppas), The drug release from the formulation exhibits first order kinetics as shown in Figure 6.

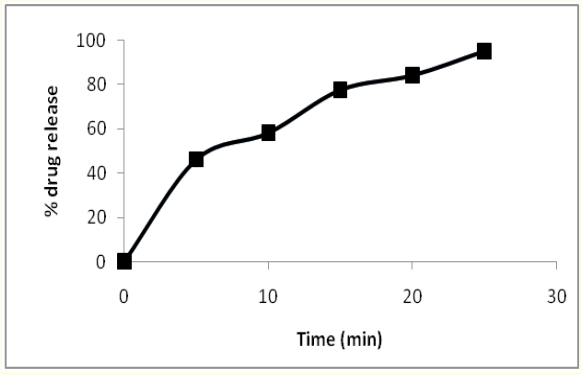

Figure 5: In-vitro drug release profile of Glipizide immediate release layer.

Studies on Inlay tablets containing Glipizide and Metformin HCl with HPMC K 4 M

The result of evaluation parameters for the formulations F1, F2 & F3 were depicted in the Table 2 and 3.The results and micromer-itic properties of granules showed in Table 2, indicates good flow properties. Thickness of the tablets was found in between 3.4 ± 0.11 mm to 3.8 ± 0.15 mm. The weight variation was observed in between 3.08 ± 0.22 to 3.12 ± 0.15. There was no significant weight varia-tion observed between average weight and individual weight of the tablets. The hardness of the in-lay tablet was found in between 7.3 ± 0.20 kg/Cm^2 to 7.8 ± 0.25 kg/Cm^2. The percent friability of prepared tablets are lies within the acceptable limit, i.e.0.62 ± 0.12 to 0.78 ± 0.11. Drug content of all the formulations was within the range of 98.12 ± 0.44% to 99.78 ± 0.35%, ensuring uniformity of the drug present in the formulations.

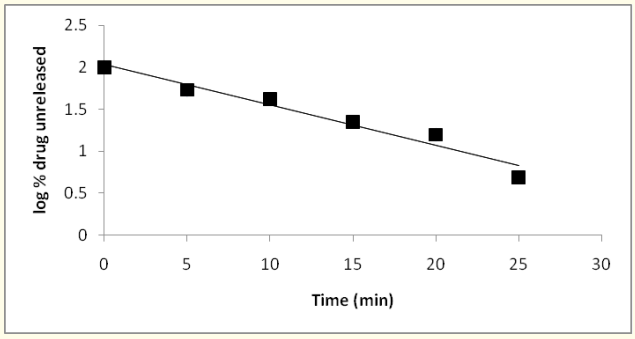

Figure 6: First order plot of Glipizide immediate release layer.

Formulations	Angle of epose (0)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio
F1	25.820.12	0.674 ± 0.15	0.712 ± 0.21	5.33 ± 0.17	1.05 ± 0.22
F2	24.020.22	0.575 ± 0.32	0.612 ± 0.27	6.02 ± 0.33	1.09 ± 0.12
F3	23.020.53	0.424 ± 0.15	0.502 ± 0.31	4.23 ± 0.27	1.03 ± 0.11

Table 2: Micromeritic properties of sustained release granules for Inlay tablets of Metformin hydrochloride formulated with HPMC K4M.

Formulations	Thickness (mm)	Hardness (Kg/cm^2)	%Weight variation (mg)	% Friability	Drug content (%)
F1	3.4 ± 0.11	7.3 ± 0.20	3.21 ± 0.19	0.62 ± 0.12	98.68 ± 0.29
F2	3.5 ± 0.23	7.8 ± 0.52	3.56 ± 0.52	0.42 ± 0.56	97.08 ± 0.35
F3	3.4 ± 0.11	7.3 ± 0.20	3.21 ± 0.19	0.62 ± 0.12	98.68 ± 0.29

Table 3: Evaluation of Inlay tablets containing Glipizide and Metformin hydrochloride with HPMC K 4 M.

The results of *in-vitro* drug release kinetic data of were reported in Table 4. The percentage of Metformin Hydrochloride released from the formulations F1, F2 and F3 were observed as 98.51 ± 0.46%, 98.69 ± 0.43% and 99.71 ± 0.32% at the end of 9th, 10th and 11th hr respectively. The percent drug release data were plotted against time as given in Figure 7. The drug release mechanisms were analyzed and

reported in table no 4, In-vitro drug release data were fitted into various release equations and kinetic models (First order, zero order, Higuchi and Peppas) and drug release mechanism plots as given in figure.no.8.The drug release from the formulations followed zero order kinetics and exhibit the Peppas transport mechanism. The values of release exponents 'n' for formulations F1, F2 and F3 was 0.513, 0.507 and 0.536 indicating the release governed by non-Fickian anomalous transport.

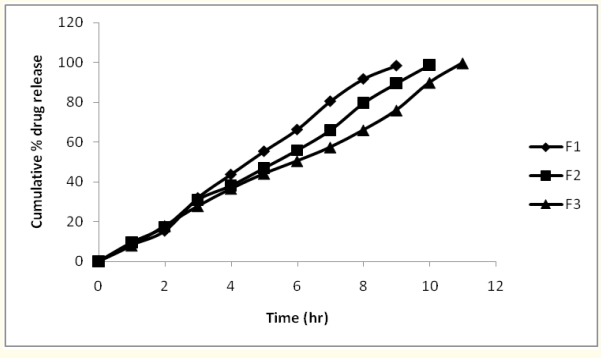

Figure 7: In-vitro drug release profile for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 4M.

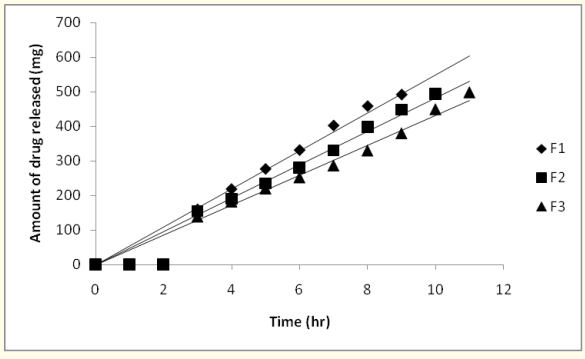

Figure 8: *In-vitro* drug release profile for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 4M.

Studies on Inlay tablets containing Glipizide and Metformin HCl with HPMC K 15 M

The results of evaluation parameters for the formulations F4, F5 & F6 were depicted in the table no.5 and 6. The thickness of the tablets was found in between 3.4 ± 0.16 mm to 3.6 ± 0.25 mm and the weight variation was found to be between 3.24 ± 0.19 to 3.79 ± 0.12 where there was no significant weight variation observed between average weight and individual weight of the tablets.

Formulation	Correlation coefficient (R^2)				Exponential coefficient (n)	Release rate constant (K) (mg/hr)
	Zero Order	First Order	Higuchi matrix	Korsmeyer Peppas		
F1	0.9361	0.9089	0.9811	0.9859	0.513	60.36
F2	0.9533	0.9011	0.9645	0.9839	0.507	51.68
F3	0.9633	0.8534	0.9884	0.9263	0.536	45.39

Table 4: In-vitro drug release kinetics for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 4 M.

Formulations	Angle of repose(0)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Drug content (%)
F4	25.65 ± 0.22	0.652 ± 0.13	0.712 ± 0.16	8.42 ± 0.15	1.09 ± 0.13	98.68 ± 0.46
F5	24.75 ± 0.34	0.681 ± 0.54	0.610 ± 0.23	6.22 ± 0.56	1.07 ± 0.23	99.73 ± 0.45
F6	24.65 ± 0.23	0.612 ± 0.32	0.612 ± 0.26	8.02 ± 0.23	1.02 ± 0.12	97.68 ± 0.29

Table 5: Micromeretic properties of sustained release layer for Inlay tablets of Metformin hydrochloride formulated with HPMC K 15 M.

The hard-ness of the in-lay tablet was found in between 7.5 ± 0.26 kg/Cm2 to 7.8 ± 0.18 kg/Cm2 and The percent friability of prepared tablets are found within the acceptable limit.i.e.0.67 ± 0.13 to 0.73 ± 0.19. Drug content of all the formulations was within the range of 97.68 ± 0.029 to 98.68 ± 0.46%, ensuring uniformity of the drug content in the formulations.

Formulations	Thickness (mm)	Hardness (Kg/cm^2)	%Weight variation (mg)	% Friability
F4	3.5 ± 0.14	7.4 ± 0.13	3.23 ± 0.17	0.63 ± 0.12
F5	3.4 ± 0.52	7.5 ± 0.26	3.24 ± 0.16	0.67 ± 0.13
F6	3.6 ± 0.13	7.8 ± 0.18	3.78 ± 0.12	0.73 ± 0.19

Table 6: Evaluation of Inlay tablets containing Glipizide and Metformin hydrochloride with HPMC K 15 M.

The results of in-vitro drug release kinetic studies of were reported in Table 7. The percentage of Metformin hydrochloride released for the formulations F4, F5 and F6 were observed as 97.89 ± 0.42%, 98.83 ± 0.40% and 99.72 ± 0.38% at the end of 8th, 9th and 10th hr respectively. The percent drug release data were plotted against time and the drug release mechanisms were analyzed by In-vitro drug release data were fitted into various release equations and kinetic models (First order, zero order, Higuchi and Peppas), and drug re-lease mechanism plots as given in Figure 9 and 10. The drug release from the formulations followed zero order kinetics and exhibits the Peppas transport mechanism. The values of release exponents 'n' for formulations F4, F5 and F6 was 0.517, 0.515 and 0.612 indicating the release governed by non-Fickian anomalous transport.

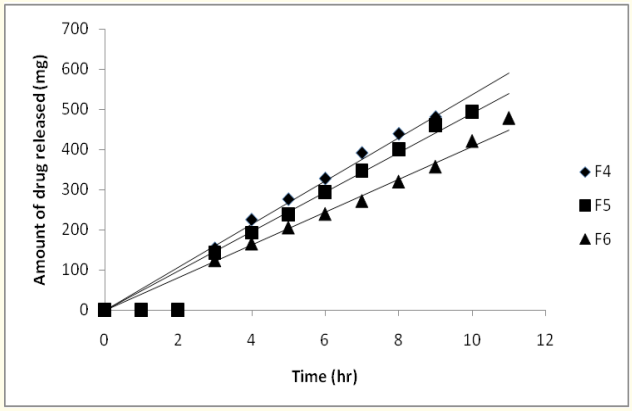

Figure 10: Zero order plots for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 15 M.

Formulation	Correlation coefficient (R^2)				Exponential coefficient (n)	Release rate Constant (K) (mg/hr)
	Zero Order	First Order	Higuchi Matrix	Korsmeyer Peppas		
F4	0.9289	0.8879	0.9881	0.9903	0.517	58.62
F5	0.9633	0.9234	0.9784	0.9163	0.515	48.56
F6	0.9413	0.9034	0.9045	0.9834	0.612	46.78

Table7: *In-vitro* drug release kinetics for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 15 M.

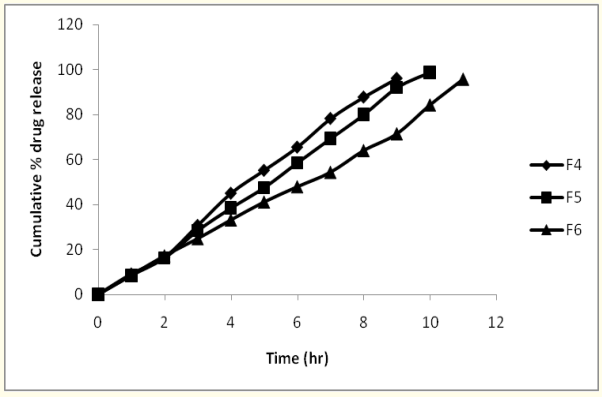

Figure 9: *In-vitro* drug release profile for Inlay tablets of Glipizide and Metformin hydrochloride HPMC K 15M.

Studies on Inlay tablets containing Glipizide and Metformin HCl with HPMC K 100M

The results of evaluation parameters for the formulations F7, F8 & F9 were depicted in the Table 8 and 9 The results and micromer-itic properties of granules showed in table 8, indicating good flow properties. the thickness of the tablets was found in between 3.4 ± 0.28 mm to 3.6 ± 0.16 mm, The weight variation was found to be between 2.92 ± 0.12 to 3.84 ± 0.20 There was no significant weight variation observed between average weight and individual weight of the tablets. The hardness of the in-lay tablet was found in between 7.6 ± 0.12 kg/Cm2 to 8.0 ± 0.18 kg/Cm2. The percent friability of prepared tablets are observed within acceptable limit The friability was found to in between 0.59 ± 0.24 to 0.76 ± 0.27.

Formulations	Angle of repose (0)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Drug content (%)
F7	26.72 ± 0.12	0.695 ± 0.19	0.764 ± 0.23	9.03 ± 0.17	1.09 ± 0.12	99.87 ± 0.36
F8	28.02 ± 0.22	0.605 ± 0.09	0.664 ± 0.33	8.23 ± 0.27	1.08 ± 0.02	99.94 ± 0.49
F9	25.02 ± 0.12	0.795 ± 0.17	0.664 ± 0.33	8.03 ± 0.16	1.09 ± 0.12	99.66 ± 0.66

Table 8: Micromeretic properties of sustained release granules for Inlay tablets of Metformin hydrochloride formulated with HPMC K 100 M.

Drug content of all the formulations were found within the range of 98.94 ± 0.49% to 99.66 ± 0.66%, ensuring uniformity of the drug content in the formulations.

Formulations	Thickness (mm)	Hardness (Kg/cm^2)	%Weight variation (mg)	% Friability
F7	3.6 ± 0.15	7.2 ± 0.25	3.25 ± 0.18	0.62 ± 0.11
F8	3.4 ± 0.28	7.6 ± 0.12	2.72 ± 0.12	0.59 ± 0.24
F9	3.6 ± 0.16	8.0 ± 0.18	3.84 ± 0.20	0.76 ± 0.27

Table 9: Evaluation of Inlay tablets containing Glipizide and Metformin hydrochloride with HPMC K 100 M.

lets were evaluated; results reveal that all the prepared Inlay tablets were observed as satisfactory.

Based on the results *In- vitro* release data for Inlay tablets of Glipizide formulated with neem gum showed optimum release profile for immediate release, where as Metformin Hydrochloride formulated with HPMC K4 M (F1,F2,F3), sustained release for prolonged period of time, among all the formulations F9 retard the release for 12 hours. The formulations formulated HPMC K100 M prolonged the release due to the formation of viscous gel layer its sourroundigs, among all the formulations F9 sustained the release for 12 hrs Therefore Inlay tablets of Glipizide and Metformin Hydrochloride with HPMC K100 M optimized as better formulation among all the formulations.

Formulation	Correlation coefficient (R^2)				Exponential coefficient (n)	Release rate Constant (K) (mg/hr)
	Zero Order	First Order	Higuchi Matrix	Korsmeyer Peppas		
F7	0.9595	0.8780	0.9761	0.9850	0.542	49.35
F8	0.9465	0.8220	0.8767	0.9052	0.531	45.98
F9	0.9435	0.8680	0.9221	0.9435	0.618	41.78

Table 10: *In-vitro* drug release kinetics for Inlay tablets of Metformin hydrochloride with HPMC K 100 M.

The results of in-vitro drug release kinetic studies are reported in Table 10. The percentage of Metformin hydrochloride released for the formulations F7, F8 and F9 were observed as 98.62 ± 0.29%, 96.52 ± 0.32% and 98.96 ± 0.43% at the end of 10th, 11th and 12th hr respectively. The percent drug release data were plotted against time as given in the Figure 11. The drug release mechanisms were analyzed by In-vitro drug release data were fitted into various release equations and kinetic models (First order, zero order, Higuchi and Peppas), and the drug release mechanism plots as given in the Figure 11 and 12. The drug release from the formulations followed zero order kinetics and Peppas transport mechanism. The values of release exponents 'n' for formulations F7, F8 and F9 was 0.542, 0.531 and 0.618 indicating the release governed by non-Fickian anomalous transport.

The combination of Glipizide and Metformin Hydrochloride inlay tablets were prepared by steam granulation technique, in which Metformin Hydrochloride as core tablet designed for sustained release, formulated with different grades of release retardant polymer HPMC surrounded by Glipizide granules for immediate release.

The granule properties for Glipizide and Metformin Hydrochloride were exhibited the good flow properties and Inlay tab-

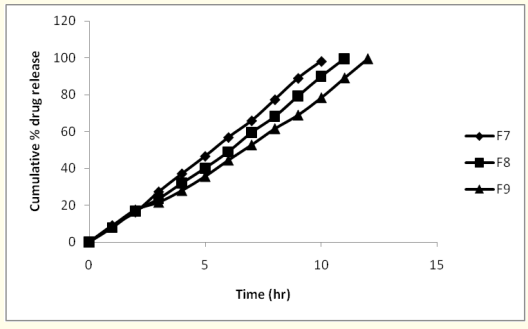

Figure 11: In-vitro drug release profile for Inlay tablets of Glipizide and Metformin hydrochloride with HPMC K 100M.

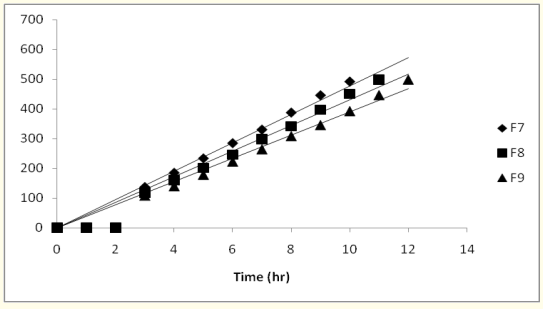

Figure 12: Zero order plots for Inlay tablets of Glipizide and Metformin hydrochloride with Guar Gum.

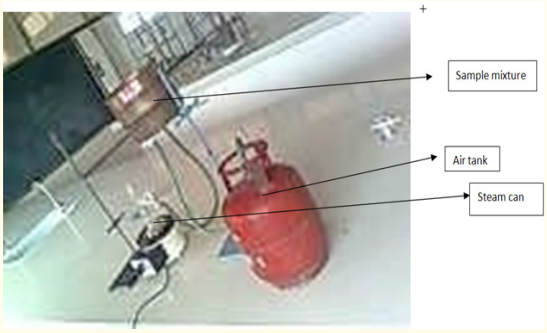

Figure 13: Equipment for steam granulation.

Conclusion

In order to achieve the development of a combination of conventional and sustained release dosage forms, the inlay technology with multiple layers having a rapid and sustained phase has been investigated. This formulation can be used for the treatment for type-2 Diabetes Mellitus. For the study, Metformin hydrochloride and Glipizide were used as model drugs, they were used for the for the treatment of type-2 Diabetes Mellitus, which were formulated by using steam granulation method, which was modified equipment in the laboratory scale.

The combination of Glipizide and Metformin Hydrochloride inlay tablets were prepared by steam granulation technique, in which Metformin Hydrochloride as core tablet for sustained the drug release formulated with different grdes of release retardant polymer HPMC, it was surrounded by Glipizide granules for immediate release.

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