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Review Article

Formulation & Evaluation of Sustained Drug Delivery System Containing Metformin

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ABSTRACT
Metformin hydrochloride is a Biguanides derivative, which is widely used as an oral anti-hyperglycemic agent in the management of non-insulin dependant diabetes mellitus (NIDDM), in an initial dosage of 500mg & 850mg. Metformin is highly water soluble drug with bioavailability of 40 to 60% with high renal clearance hence the dose of 850 mg is insufficient to achieve therapeutic plasma concentration for long duration of time, so dosage regimen of twice or thrice a day is required. The present manuscript describes formulation of Meformin HCl sustained release tablet using few polymers. From *in vitro* drug release profile, formulation MVII showed better release profile i.e. 96.97% drug release at the end of 24 hours. This formulation was optimized and subjected for accelerated stability studies. The data obtained from the stability studies indicated that there is no much change in the release profile of the tablets after storing at 45ºC for 6 weeks.

Keywords: Metformin HCl, sustained release, drug release, stability studies.

INTRODUCTION

Diabetes cannot be cured, but proper treatment can improve a patient's condition considerably. Treatment is designed to control glucose levels in the blood. This is the immediate goal, which is stabilizing the blood sugar and eliminates the symptoms of high blood sugar. In such case, a dosage form has to be administered several times during the day. So the sustained release formulation will be beneficial than the immediate release dosage form as therapeutic level is maintained for a extend period of time, eliminating maxima in drug concentration commonly associated with multiple doses. Biguanides one of the most commonly used hypoglycemic drugs which increases the uptake of glucose by muscle and also reduced the absorption of glucose by the intestine and the release of glucose from the liver. They include Phenformin and Metformin. Metformin is the safest drug than phenformin. In the present work the Metformin hydrochloride was chosen as the model drug. Metformin Hydrochloride being a highly water-soluble drug (> 300 mg/ml at 25 c). It is widely used as an anti hyperglycemic agent in the management of non-insulin dependant diabetes mellitus (NIDDM). Metformin Hydrochloride having only 40 to 60% bioavailability high renal clearances, hence the initial dosage of 500 mg and 850 mg are insufficient to achieve therapeutic plasma concentration for a long duration of time, so dosage regimen of twice or thrice a day is required marketed preparation available earlier with 850 mg dose of Metformin hydrochloride having label of retard tablet (Glucophage RTM retard) have not been able to demonstrate any advantage in limited volunteer trials. This is probably due to the inappropriate choice of polymer and low dose, desired for sustained release action.

MATERIAL AND METHOD

Metformin (Coral drug (P) Ltd. New Delhi), Ethyl cellulose (Medicore Laboratories Pvt. Ltd. Aurangabad) Stearic acid (Venus Chemicals), Carnauba wax (Rajesh Chemicals, Mumbai), Magnesium stearate (Research Labs Fine Chemicals), Colloidal Silicon dioxide (Research Lab, Mumbai), Potassium chloride (Venus Chemicals), hydrochloric acid (Samar Chemicals, Nagpur), Potassium dihydrogen phosphate (Research Lab Fine Chem. Industries, Mumbai),

Preparation of standard curve of Metformin Hydrochloride[17]

Accurately weighed quantity of powder equivalent to 0.1 g of Metformin hydrochloride was shacked with 70 ml of water for 15 minutes, diluted to 100 ml with water and filtered. 10 ml of the filtrate was again diluted to 100 ml with distilled water. From this stock solution (100 µg/ml) 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 ml of the aliquots were transferred in to a series of 50 ml standard volumetric flask and made up to the mark with distilled water. Thus it gave a concentration range of 2 to 20 µg/ml. The absorbance of each sample was measured at 232 nm on UV- visible single beam spectrophotometer, against distilled water as a blank.

Simplex Lattice Design For The Preparation of Sustained Release Metformin Hydrochloride Tablets[23,24]

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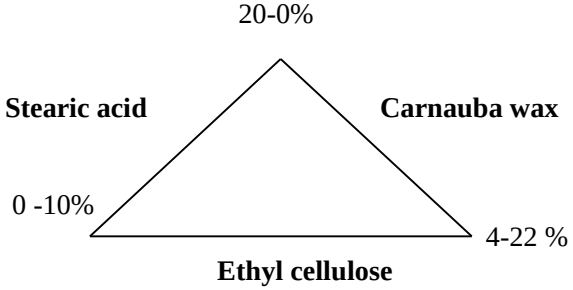
The techniques for optimization are well documented in pharmaceutical literature recently many researchers have demonstrated the applicability of optimization technique for developing formulae of solid dosage forms. This study illustrates the use of three-component simplex lattice for the determination of optimum amount of stearic acid, carnauba wax and ethyl cellulose.

Simplex lattice design provide the advantage of changing the quantity of different ingredients in the formulation in a systematic manner, yet keeping their total amount constant therefore, this design was chosen in this study.

The three components are represented as equilateral triangles in two dimensional space. Seven batches were prepared one each at vertex one halfway between vertices and one at center point. Each vertex represents a formulation containing the maximum amount of that component, with other two components at minimum level. The formulation represented halfway between two vertices contained the average of the minimum and maximum amount of the two ingredients represented by two vertices. Formulation contains middle of each vertices of equilateral triangle.The seventh point contained one third of each component and it lies in the center of the equilateral triangle.

Concentration of drug carrier for simplex lattice drug design.

1. Stearic acid -0-20% - wax material
2. Carnauba wax-0-22%- wax material
3. Ethyl cellulose-4-10%- as a retardant agent
4. Magnesium stearate-0.5%- lubricant
5. Colloidal silicon dioxide-1%- glidant



Concentration of drug carrier for simplex lattice drug design.

Formulation of Metformin SR tablets.

Category I

Each vertex represent a formulation containing maximum amount of that component, with other two components are at minimum level.

Category II

The formulation represented halfway between two vertices contained the average of the minimum and maximum amount of the two ingredients represented by two vertices.

Category III

Sixth may be prepared by middle of each vertices of equilateral triangle.

The seventh formulation contained one-third of each component and it lies in the center of the equilateral triangle.

Preparations of Matrix Tablet by Direct Compression

Accurately weighed quantity of stearic acid and carnauba wax was melted in a crucible at 60^0 to 80^0C on a hot plate. Weighed quantity of Metformin Hydrochloride was dispersed in the molten wax. The mixture was gradually cooled to room temperature and the hard mass formed was pulverized in a pulverizer. Predetermined quantity of ethyl cellulose, diluent and lubricant was then mixed with drug:wax dispersion.

The above mixture was then directly compressed under a single punch tableting machine fitted with a standard flat punch. Compression pressure was adjusted during tableting of each formula to get the tablet hardness in the range of 5 to 7 kg/cm^2.

Evaluation of Matrix Tablets[25, 26]

Prepared batches of Metformin Hydrochloride were evaluated for following test.

1. Hardness

Although hardness is not official but the tablet should have sufficient hardness to withstand handling during packaging and transportation. Hardness of tablet was measured with Monsanto tablet hardness tester. It measures the pressure required to fracture diametrically placed tablet by applying the force with two plungers and coiled spring. Hardness of 6 tablets form each batch was determined and mean hardness was taken into account, which was expressed in kg/cm^2.

2. Friability

The crushing strength test may not be the best measure of potential tablet behavior during handling and packaging. The resistance to surface abrasion may be more relevant parameter as exemplified by those tests that measure the weight loss on subjecting the tablets to a standardized agitation procedure. The most popular version is Roche friabilator. The percentage friability of the prepared tablet was determined by subjecting pre-weighed tablets of each batch to 100 revolutions, in a Roche type friabilator, where the tablet were subjected to the combined effects of abrasion and stroke in a plastic chamber over a 4 minute period. The final weight of tablet was noted. The weight loss was expressed as % and was taken a friability value. Friability was calculated by using following formula.

% Friability= [1-w_o/w]

Here

W_o = initial weight of tablets.

W = final weight of tablets.

3. Content uniformity test

It was determined as per method given in Indian Pharmacopoeia (1996) 20 tablets were taken and powdered in a mortar. Accurately weighed quantity of the powder equivalent to 0.1 g of Metformin Hydrochloride, was shaken with 70 ml of the distilled water and the solution was filtered. 10 ml of the filtrate was further diluted to 100 ml with water. Again 10 ml of the above solution was diluted to 100 ml with water and the absorbance of resulting solution was measured at 232 nm. Quantity of Metformin Hydrochloride present was calculated from the standard curve.

4. Weight variation Test (weight uniformity)

The uniformity of the weight was tested as per the Indian

pharmacopoeial standard. 20 tablets were weighed individually and average weight was calculated. The limit of ±5% (for tablet weight more than 250mg) was applied to average tablet weight to set the lower and upper limit of weight variation. The 20 tablets from each batch were analyzed for the weight variation.

5. Thickness

The samples were selected randomly from every batch. The tablet thickness was measured by Vernier calliper.

Drug Release Studies[17, 27]

The dissolution testing of dosage form is considered as one of the most important quality control tools while assessing the efficacy of a product. In vitro studies of drug release rate are useful in predicting the drug release pattern in-vivo. However due to complexities involved in the mechanism of drug release in vivo, it become difficult to co-relate in-vivo release when tested in vitro. Since in, in-vitro only one mechanism of drug release (Diffusion or Erosion) is prominent. Where as in in-vivo, in addition to this mechanism, biodegradation of carrier also takes place simultaneously. However the in-vitro release rated is used for predicting in-vivo release rate of the drug. Like any other solid dosage forms the rate of drug release depends on rate of dissolution.

There are not only drug products but also devices and therefore "no single in-vitro test will completely reflect the availability of drug" [62]. The usual test of disintegration time found in pharmacopoeias, do not apply to oral modified release dosage forms, since the release rate per unit time is the critical factor[63] and modified release dosage systems may actually be complicated due to one or more combination of following factor.

Drug release studies dissolution studies of Metformin SR matrix tab were carried out by using IP apparatus with paddle stirrer at 50 rpm and $37^0 \pm 0.5^0$ C in 900 ml dissolution fluid contained in beaker change in pH method was adopted for dissolution studies.

Preparation of standard buffer solution

Simulated gastric fluid: Hydrochloric acid buffer, pH 1.2

250 ml of 0.2 M potassium chloride solution was placed in a 1000 ml volumetric flask. The specific 85 ml of 0.2M hydrochloric acid were added and then the volume was made with the distilled water.

Simulated intestinal fluid: Phosphate buffer, pH 6.8

250 ml of 0.2 M potassium dihydrogen phosphate solution was placed in 1000 ml volumetric flask. Then 22.4 ml of 0.2 M NaOH solution was added and the volume was made with the distilled water.

In vitro Dissolution Studies

Drug release studies of Metformin Hydrochloride SR matrix tablet was studied in simulated gastric fluid U.S.P. pH 1.2 for 0-2 hr and in simulated intestinal fluid U.S.P pH 6.8 for 3-24 hr using IP paddle type dissolution test apparatus at 50 rpm and 37^0 C in 900 ml dissolution fluid. 10 mL of aliquot was withdrawn by single mark pipette at regular interval and volume withdrawn was replaced by equal quantities of fresh fluid. The drug content was determined spectrophotometrically by using standard curve of Metformin hydrochloride after suitable dilution. Cumulative drug release and the percent drug release was calculated from the drug release data.

Stability Studies of SR Metformin Hydrochloride Matrix Tablets[28]

Stability of a medicinal product may be defined as the capability of a particular formulation in a specific container to remain within its physical, chemical, microbial, therapeutic and toxicological specifications, i.e. stability of drug is its ability to resist deterioration. 90% of labeled potency is generally recognized as the minimum acceptable potency level. Deterioration of drugs may take several forms arising from changes in physical, chemical and microbiological properties. The changes may affect the therapeutic value of preparation or increase its toxicity.

Accelerated Stability Testing

Accelerated stability testing is defined as the validated method by which the product stability may be predicted by storage of the product under conditions that accelerate the change in defined and predictable manner. Acceleration of chemical decomposition is achieved by raising the temperature of preparations. The result of accelerated stability tests carried out at three or more elevated temperatures enable prediction to be made of the effects of the products at normal temperature. Maximum and minimum time at which potency must be at least 90% of labeled claim at the temperature in order to predict a shelf life of two year at room temperature.

Stability Studies of Prepared SR Metformin Matrix Tablets

The optimized formulation was stored at room temperature and 45ºC for 6 weeks. At the end of testing period, the formulation was observed for changes in physical appearance and analyzed for drug release

RESULT AND DISCUSSION

Qualitative analysis of raw materials

All the carriers used for formulation of matrix tablet were found satisfactory as per their standard. The purity of carriers was checked from their respective melting points and thus used further for the work

Preparation of standard curve of Metformin hydrochloride

Metformin hydrochloride, received as gift sample, was analyzed for various physical parameters and was found to compile with the in house certificate of analysis of coral pharmaceutical Pvt Ltd.

Metformin Hydrochloride was found to be obeying Beer Lambert's Law in the concentration range 2 –20 µg/ml at 232 nm against distilled water as a blank. Metformin HCl received as a gift sample was analyzed and compared with the certificate of analysis of the supplier and it was found that the purity was as per report.

Evaluation of SR Metformin matrix Tablets

All the batches were compressed into tablet using uniform compression pressure and same tooling setting of the compression machine. such tablets were evaluated. All methods were carried out as per the method described in the pharmacopoeia. The results of evaluation are discussed here. The hardness values of the formulations

Table 1: Composition of tablet

S. No.	Ingredient (%)	(M1) %	(M1) mg
1.	Metformin hydrochloride(HCl)		500mg
2.	Stearic acid	20%	140mg
3.	Carnauba wax	-	-
4.	Ethyl cellulose	4%	28mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1%	6.5
	Total weight		681mg

Table 2: Composition of tablet

S. No.	Ingredient (%)	(M II) %	(M II) mg
1.	Metformin HCl		500mg
2.	Stearic acid	-	-
3.	Carnauba wax	22%	164
4.	Ethyl cellulose	4%	28mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1.0%	6.5
	Total weight		702mg

Table 3: Composition of tablet

S. No.	Ingredient (%)	(M III) %	(M III) mg
1.	Metformin HCl		500mg
2.	Stearic acid	10%	70mg
3.	Carnauba wax	11%	77mg
4.	Ethyl cellulose	4%	28mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1%	6.5mg
	Total weight		685mg

Table 4: Composition of tablet

S. No.	Ingredient (%)	(M IV) %	(M IV) mg
1.	Metformin HCl		500mg
2.	Stearic acid	-	-
3.	Carnauba wax	11%	77mg
4.	Ethyl cellulose	7%	49mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1%	6.5mg
	Total weight		636mg

Table 5: Composition of tablet

S. No.	Ingredient (%)	(M V) %	(M V) mg
1.	Metformin HCl		500mg
2.	Stearic acid	10%	70mg
3.	Carnauba wax	-	-
4.	Ethyl cellulose	7%	49mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1%	6.5mg
	Total weight		629mg

ranged from 5.88 to 6.36 kg/cm^2 which indicates good strength of the tablet. Hardness was determined using Monsanto hardness tester. The hardness values of the formulations ranged from 5.88 to 6.36 kg/cm^{2}which indicates good strength of the tablet.

Table 6: Composition of tablet

Sr. No	Ingredient	Batch VIth %	Batch VIth mg
1.	Metformin hydrochloride	-	500mg
2.	Stearic acid	10 %	70mg
3.	Carnauba wax	11%	77mg
4.	Ethyl cellulose	75%	45.5mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1.0%	6.5mg
	Total weight		703.5mg

Table 7: Category IV,

Sr. No	Ingredient	Batch VIth %	Batch VIth Mg
1.	Metformin hydrochloride	-	500mg
2.	Stearic acid	5.3 %	46.62mg
3.	Carnauba wax	6.33%	51.31mg
4.	Ethyl cellulose	6%	29.4mg
5.	Magnesium stearate	0.5%	3.5mg
6.	Colloidal silicon dioxide	1.0%	6.5mg
	Total weight		637.33mg

Table 8: Determination of melting points.

Sr. No.	CARRIER	MP as per IP	Actual Melting Point
1	Carnauba wax	$80^0 – 86^0$ C	$82^0 – 84^0$ C
2	Stearic acid	54^0C	$52^0 – 53^0$ C
3	Magnesium stearate	130^0 C	$126^0 – 128^0$ C

Table 9: Standard curve of Metformin Hydrochloride

Sr. No.	Concentration µg/mL	Absorbance at 232nm
1	2	0.151
2	4	0.294
3	6	0.441
4	8	0.585
5	10	0.714
6	12	0.862
7	14	0.996
8	16	1.145
9	18	1.285
10	20	1.400

Friability was determined by using Roche friabilator and the weight loss was calculated and represented in terms of the percent friability. Friability values were less than 1% indicates good strength of the tablet. Friability values of all above formulations were less than 0.5% that indicates good strength of the tablets. The assay values of all the formulations were within the range of 95 to 101% as can be seen from the above table and it realizes to the pharmacopoeial standards.

As per the general pharmacopoeial requirements a tablet weighing more than 250mg should have weight variation not more than ± 5%. Formulation was found to have weight variation not more than ± 5%. Thickness of the different tablets was determined by using Vernier calliper.

Table 10: Evaluation parameter of SR Metformin Hydrochloride matrix tablet.

Test parameter	Batch lable						
	M1	M2	M3	M4	M5	M6	M7
Hardness (kg/cm^2)	6.08 (±0.4)	6.14 (±0.41)	6.00 (±0.42)	5.88 (±0.45)	6.34 (±0.41)	6.25 (±0.40)	6.36 (±0.4)
% Friability	0.211	0.289	0.343	0.380	0.481	0.319	0.350
Content Uniformity	101%	98.1%	97.74%	98.76%	99.49%	99.24%	97.11%
Weight uniformity ±5.00	681mg ±4.32	702mg ±4.58	685mg ±4.02	636mg ±4.24	629mg ±4.07	703.5mg ±4.62	637.33mg ±4.03
Thickness (mm)	6.08	6.14	6.00	5.88	6.34	6.24	6.36

Table 11: Drug release from formulation M I and M II

Batch	Cumulative percent drug release (%)							
	1hr	2 hr	4 hr	6 hr	8 hr	10 hr	12 hr	24 hr
MI	6.912	13.341	17.553	21.411	24.530	28.810	33.313	70.630
MII	8.890	15.322	18.961	22.423	28.321	33.560	39.144	80.862

Table 12: Drug release from formulation M III, MIV and MV

Batch	Average percent drug release							
	1hr	2 hr	4 hr	6 hr	8 hr	10 hr	12 hr	24 hr
MIII	11.121	17.622	23.912	28.226	34.850	41.189	47.771	89.361
MIV	9.215	16.414	20.411	24.080	30.421	35.763	42.271	82.610
MV	10.040	16.860	19.122	25.755	32.510	39.836	46.211	85.762

Table 13: Drug release for MVI

Batch	Average percent drug release							
	1hr	2 hr	4 hr	6 hr	8 hr	10 hr	12 hr	24 hr
MVI	8.02	14.320	18.424	23.548	27.100	31.331	36.650	76.541

Table 14: Drug release profile for Formulation MVII

Batch	Average percent drug release							
	1hr	2 hr	4 hr	6 hr	8 hr	10 hr	12 hr	24 hr
MVII	12.10	19.800	27.531	34.312	40.265	46.630	53.124	96.970

Table 15: Release studies of SR Metformin matrix tablets kept at room temperature for 6 weeks

	1hr	2hr	4hr	6hr	8hr	10hr	12hr	24hr
MVII	12.369	20.126	27.910	34.642	40.842	46.130	53.620	96.712

Table 16: Release studies of SR Metformin matrix tablets kept at 50^{0}C temperature for 6 weeks

	1hr	2hr	4hr	6hr	8hr	10hr	12hr	24hr
MVII	13.140	20.310	28.462	35.142	41.639	46.240	51.190	97.210

In vitro drug dissolution studies

Drug release studies of Metformin SR tablet containing category I

Here formulation M I is containing the maximum amount stearic acid with the minimum amount of carnauba wax and ethyl cellulose, while formulation M II contains the maximum amount of Carnauba wax and the minimum concentration of stearic acid and ethyl cellulose. The release profile from matrix containing maximum concentration of hydrophobic substances stearic acid and minimum concentration of retardant agent ethyl cellulose (M I) were release-retarding effect as shown in above figure. The factor important in influencing the rate of release from hydrophobic matrix is the drug: stearic acid: Ethyl cellulose ratio. This ratio cause an increase in drug dispersed in hydrophilic material and thus a decrease in effective erosion of matrix tablet and subsequent reduction in drug release rate.

Formulation M1 showed maximum drug release retardation with only 70.63% drug release at the end of 24 hours.

The release profile from matrix containing maximum amount of carnauba wax and minimum concentration of ethyl cellulose are shown in fig. Important factor affecting the drug: carnauba wax: ethyl cellulose ratios.

This ratio (M2) showed drug release retardation with 80.86% drug release at the end of 24 hour.

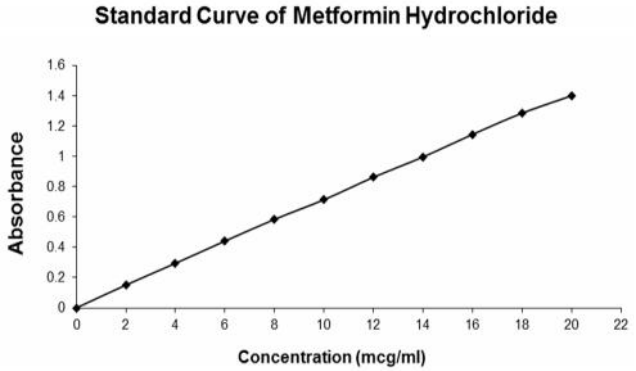


Fig. 1: Calibration curve for Metformin HCl.

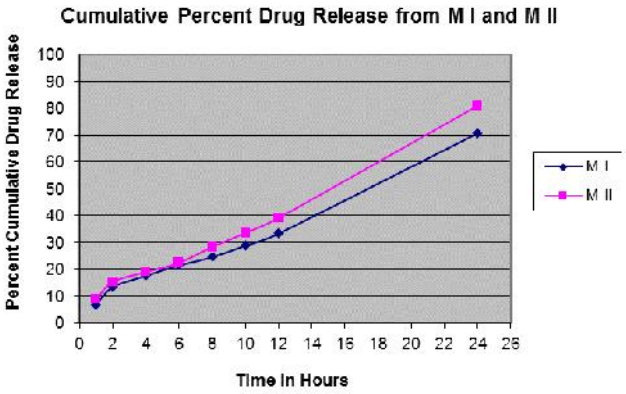


Fig 2: Release of Metformin hydrochloride SR matrix tablet from batch MI and MII

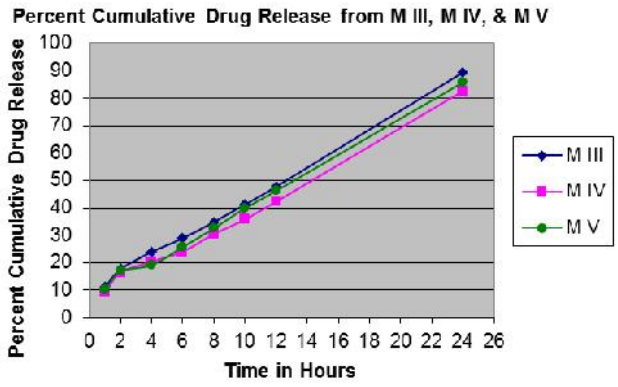


Fig.3: Release of Metformin hydrochloride SR matrix tablet from batch MIII, MIV and MV

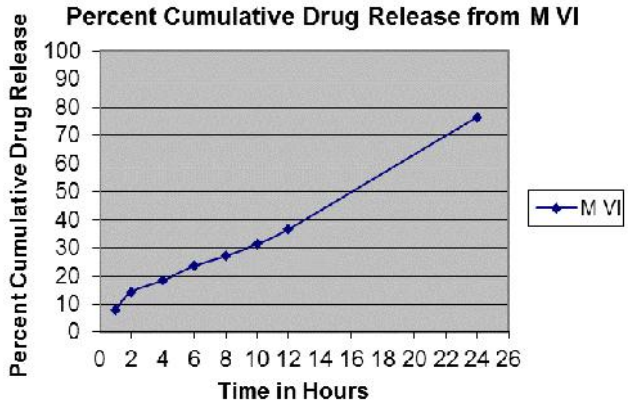


Fig. 4: Release rate studies from Metformin SR matrix tablet formulation MVI

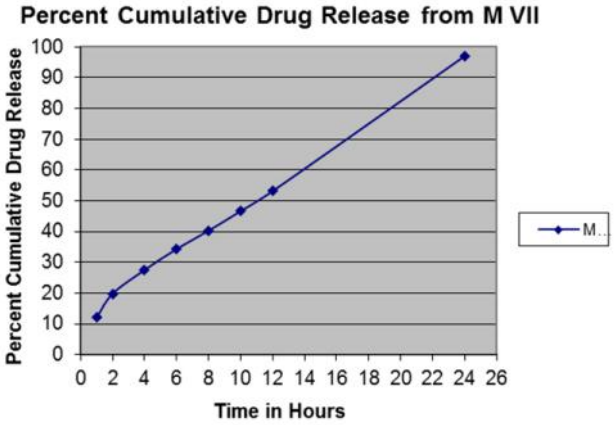


Fig. 5: Release rate studies from Metformin SR tablet formulation MVII

Drug release studies of Metformin SR tablet containing category II

The formulation represented halfway between two vertices contained the average of the minimum and maximum amount of the two ingredients represented by two vertices. The release profile from matrix tablet containing the average of the minimum and maximum amount of hydrophobic material are given in table.

Formulation M III predicted much higher release of drug i.e. 89.36% at the end of 24 hour as compared to that of 82.61% of formulation MIV, and in MV drug release was 85.76% after 24 hour. Incase of formulation MIII the release was found to be quiet higher, which can be attributed to the less concentration of the retarding material ethyl cellulose.

Drug release studies of Metformin SR tablet containing category III

Formulation contains middle concentration of each component from each vertices of an equilateral triangle.The release profile from matrix tablet are shown in fig. above. The factor influencing the rate of release from middle concentration of hydrophobic matrix tablet is the drug : carnauba wax : stearic acid : ethyl cellulose.

This formulation MVI showed maximum drug release retardation with only 76.54% drug release at the end of 24 hour.

Drug release studies of Metformin SR tablet containing category IV

The seventh point contained one third of each component and it lies in the center of the equilateral triangle. The release profile from matrix containing 1/3 composition of carnauba wax, stearic acid, ethyl cellulose matrix tablet are shown in fig above. The 1/3 ratio of these concentrations to drug gives best release profile 96.97% after 24 hour.

Optimization of formulation

Best-sustained release of drug showed by utilizing minimum concentration of both the ingredient maximum concentration of ethyl cellulose does not show significant effect while in low concentration showed the better drug release profile in combination of minimum quantity of waxes. As can be seen from the above results the formulation M VII has showed best release profile at the end of 24 hours with a cumulative percent drug release of 96.97%. Incase of all other formulations the release was found to be much sustained with too less drug release as compared to formulation MVII at the end of 24 hours. Also the concentrations of the wax material and the retardant material ethyl cellulose is kept minimum in formulation MVII still achieving the sustained action for the desired period of time. So we decided to optimize formulation MVII because of its best release profile.

Stability study of Metformin Hydrochloride SR tablets

From the drug release data it was observed that formulation MVII was found to be optimum. Hence, the formulations MVII was subjected for accelerated stability studies to ensure that formulation remains stable over its designated shelf life. The formulation were kept at room temperature, and at 50ºC for 6 weeks. The drug release was found to be quiet higher after storing tablets at higher temperature i.e. at 45^0C for 6 weeks. This might be attributed to the permeability changes of the retardant material ethyl cellulose. The permeability ethyl cellulose might be slightly enhanced after storing tablet at higher temperature. The percent drug released at the end of 24 hrs was found to be 97.21% in case formulation kept at 45^0C i.e. quiet higher than the formulation kept at room temperature which was 96.712%. Results indicated, the tablet was found to be stable even after subjected for accelerated temperature for 6 week.

CONCLUSION

Review of literature indicates those sustained released drug delivery systems are designed to achieve prolonged therapeutic effect by continuously releasing medicament over an extended period of time. In present study an attempt has been made to prepare sustained drug delivery tablet of Metformin hydrochloride by using matrix system. For this system, hydrophobic carrier, carnauba wax, stearic acid and retardant material ethyl cellulose used for preparing the matrix tablet as a sustained release polymer in combination. Stearic acid being a weak acid, however both stearic acid and carnauba wax shows increase in solubility as the pH of medium is raised, causing greater matrix erosion and an increase in drug release rate, so retardant agent ethyl cellulose is used for effective sustained action for a prolonged time. Direct compression technique was used for the preparation of sustained release matrix tablet of Metformin hydrochloride. The simplex lattice design for optimization was used for the formulation of matrix tablet. The seven batches of matrix tablets were prepared by direct compression technique. The prepared tablets were subjected for pharmacopoeial and non-pharmacopoeial evaluation parameters including % friability, hardness, thickness, content uniformity and weight variation. All the formulation showed hardness in between 5.88 to 6.36 kg/cm^2. Friability values of all the formulations were found to be between 0.299 to 0.478% i.e. less than 1%, which indicates good strength of the tablet. All the formulations confirmed to the general pharmacopoeial requirement of not more than +/- 5% weight variation. The assay values of all the formulation were within the range of 95 to 101% and thus confirms as per pharmacopoeial standard. From *in vitro* drug release profile, formulation MVII showed better release profile i.e. 96.97% drug release at the end of 24 hours. This formulation was optimized and subjected for accelerated stability studies. The data obtained from the stability studies indicated that there is no much change in the release profile of the tablets after storing at 45ºC for 6 weeks. In the view of above findings it can be suggested that carnauba wax- stearic acid- ethyl cellulose matrix may be employed successfully for the development of sustained release tablets of Metformin Hydrochloride. The release retardant materials are cheap, readily available safe and easy to handle for economical viewpoint, it may be beneficial to adopt such simple technology for the preparation of SR products

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