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FORMULATION, DEVELOPMENT AND EVALUATION OF METFORMIN HYDROCHLORIDE SUSTAINED RELEASE TABLETS

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ABSTRACT

The Study was undertaken with an aim to formulation development and evaluation of Metformin sustained release tablets using different polymers as release retarding agent. Preformualtion study was done initially and results directed for the further course of formulation . Based on preformualtion studies different batches of Metformin was prepared using selected excipient . Granules were evaluated for tests loss on drying, bulk density, tapped density, compressibility index, Hausner ratio before ring punched as tablet. Tablets were tested for weight variation, thickness, hardness, friability and in vitro drug release as per official procedure. Change in dissolution parameter study made it suitable for minute physiological variables. It is concluded that formulation of sustained release tablet of Metformin containing 13 % HPMC K100 with binder PVP K30 can be taken as an ideal or optimized formulation of sustained release tablets for 10 hour release as it fulfills all the requirements for sustained release tablet and our study encourages for the further clinical trials and long term stability study on this formulation.

KEYWORDS: Metformin, Preformulation, HPMC, PVP K30, Weight variation.

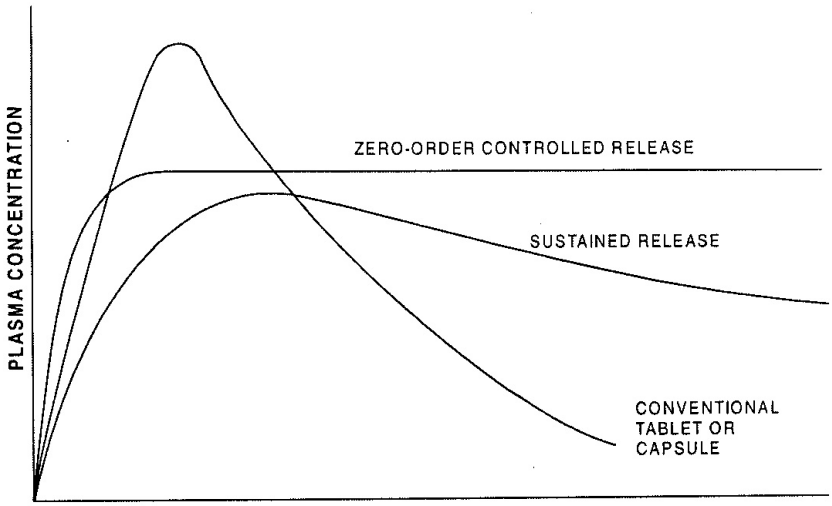
INTRODUCTION

Diabetes Diabetes a global public health problem is a chronic disease and is now growing as an epidemic in both developed and developing countries.It is a serious ailment caused by the failure of the organ pancreas in our body to produce the hormone insulin that is essential to carry out carbohydrate metabolism. If insulin is unavailable, then the body is able to

metabolize the carbohydrates; as a result, the blood of people suffering from diabetes is high sugar.

Sustained Release Dosage Forms Sustained release, sustained action, prolonged action, extended action are the terms used to identify drug delivery system that are designed to achieve a prolong therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.[1]

Plasma drug concentration profiles for conventional tablet or capsule formulation, a sustained release formulation and a zero order controlled release formulation.



FACTORS AFFECTING RELEASE OF DRUG FROM MATRIX[2]

The following factors affect the release of drug from matrix systems.

Viscosity of polymer, Mixture of polymer,Ratio of polymer to drug, Particle size of drug, Tablet thickness, Compression pressure ,Microenvironment, pH of matrix

Tablet surface area, Entrapped air in tablet, Drug solubility.

MATERIAL AND METHODS USED

Sl. NO	MATERIAL NAME
1.	Metformin (Abhilash chemicals)
2.	Hydroxy propyl methyl cellulose (Dow chemicals)

3.	Hydroxy propyl cellulose (Dow chemicals)
4.	Ethyl cellulose (Sigachi chloro chemicals)
5	Starch (International fine chemicals)
6.	Micro crystalline cellulose (Degussa)
7.	Polyvinyl pyrolidone (International fine chemicals)
8	Aerosil (Sigachi chloro chemicals)
9.	Magnesium stearate (Anushi drug & chemicals)

Sl. NO	INSTRUMENTS	MANUFACTURER
1	Electronic Balance & Top loading Balance,	Shimadzu Corporation, AW 220 and BX 6205
2	Tray Dryer	*Erweka Pvt. Ltd*
3	Dissolution Apparatus (USP)	Electrolab Pvt. Ltd.
4	Tablet Harness tester.	Monsanto hardness tester.
5	Friability test apparatus	roche friabilater
6	Ultra Violet Visible spectro photometer	Shimdzu Corporation. UV-1700
7	FTIR Spectrophotometer	Shimdzu Co UV-1700
8	Tap Density Apparatus	Erweka Pvt. Ltd
9	Granulate Flow Tester	Erweka Pvt. Ltd
10	Vernier Caliper	Digimatic
11	pH Meter,	systronic 335

12	LOD apparatus	Sartorius
13	Tablet punching machine	CADMACH 16 station

Method

Triturate 1-2 mg of the substance to be examined with 300-400 mg , specified quantity , of finely powered and dried potassium bromide .These quantities are usually sufficient to give a disc of 10-15mm diameter and spectrum of suitable intensity.

BULK CHARACTERIZATION:

Sample	Bulk density (g/cm^3)	Trapped density(g/ cm^3)	Compressibility index	Hausner ratio
DRUG	0.418	0.513	14.28	1.24
HPMC K 100	0.463	0.581	20.91	1.26
HPMC K4M	0.413	0.493	16.32	1.19
MCC	0.41	0.46	10.20	1.21

Value show mean of three determination

Preliminary evaluation of drug

S.NO	Test	Result	Specificetion
1	Description	White crystalline powder hygroscopic and free from visible extraneous matter	White crystalline powder hygroscopic and free from visible extraneous matter
2	Solubility	Freely soluble in water slightly soluble in ethanol(95%); practically insoluble in acetone , chloroform , dichloromethane and in	Freely soluble in water , slightly soluble in ethanol (95%);practically insoluble in acetone , chloroform , dichloromethane and in ether

		ether	
3.	Identification	complies	Shall comply
4.	Sulphated ash	0.069%	Not more than 0.1%
5.	Heavy metals	Less than 20ppm	Not more than 20ppm
6.	Loss on drying	0.34%	Not more than 0.5%ww
7.	Assay on dried basis	99.1%	Not less than 98.5% and not more than 101.0%

Drug Excipient Compatibility study

A drug or active principle is most often delivered to patient along with other chemical substance within a pharmaceutical formulation, which should comply with strict specification, often prescribed by law .In order to be approved a formulation should warrant well defined level of stability.

Method

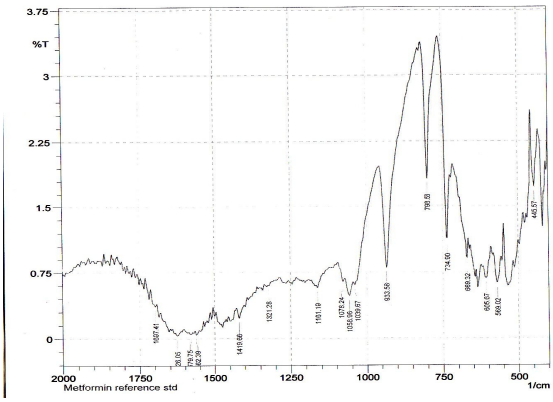
The drug and individual excipient mixture of all excipient and drug were taken in the ratio of 1:1 in a flint vial and stored at 25 degree centigrade , 60%RH,30 degree centigrade , 65%RH and 40 degree ,75% RH for 4 weeks . The sample were observed for any physical change every week .The two method employed are open vial and closed vial. In closed vial method after placing the material the vial is not closed and placed for the study. The observation of drug excipient compatibility study as shows:

Preformulation study

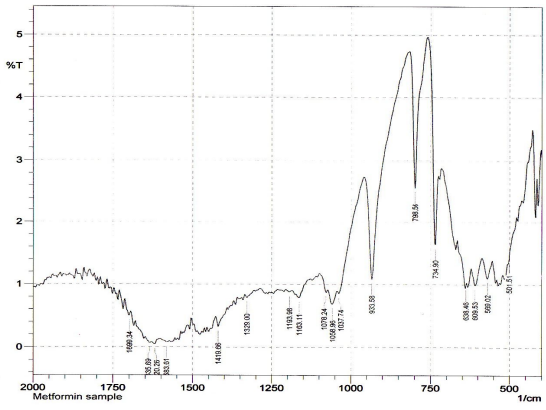
Drug	*Observation*			*Open vial*	*Closed vial*
1:1 Excipient	Initial	30oC /65% RH offer 30 days	40oC /75% RH offer 30days	Result	Result
Metformin	White to off white	White to off white	White to off white	Compatible	Compatible
Metformin+M	White to off	White to off	White to off	Compatible	Compatible

CC	white	white	white		
Metformin+ E.cellulose	White to off white	White to off white	White to off white	Compatible	Compatible
Metformin + HPC	White to off white	White to off white	White to off white	Compatible	Compatible
Metformin + HPMC K100M	White to off white	White to off white	White to off white	Compatible	Compatible
Metformin + HPMC K4M	White to off white	White to off white	White to off white	Compatible	Compatible
Metformin with all excipient in 1 : 1	White to off white	White to off white	White to off white	Compatible	Compatible

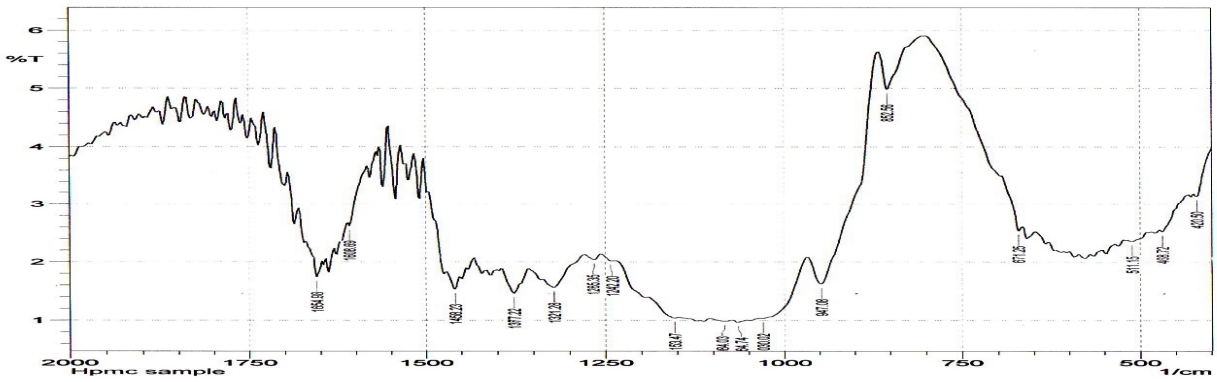
METFORMIN STANDARD



METFORMIN SAMPLE



HPMC STANDARD



Assay (By HPLC)

A) Mobile Phase: 0.087% sodium pentane sulfonate =0.12% sodium chloride PH =3.5 by H3PO4

B) Flow: 1 ml/min

C) Wave length: 218nm

D) Column : Grace mart C18,250 x 4.6nm(column No.75)

Standard: weight metformin HCl 100 mg in 100ml, make up with water.

Test: weight 100mg equivalent of metformin into 100ml flask & make up with water.

Calculation: Ready mixing of active with excipient on day of Analysis.

$$\frac{\text{Test Area}}{\text{Std Area}} \times \frac{\text{Std wt}}{100} \times \frac{100}{\text{Test wt}} \times 1\text{gm}$$

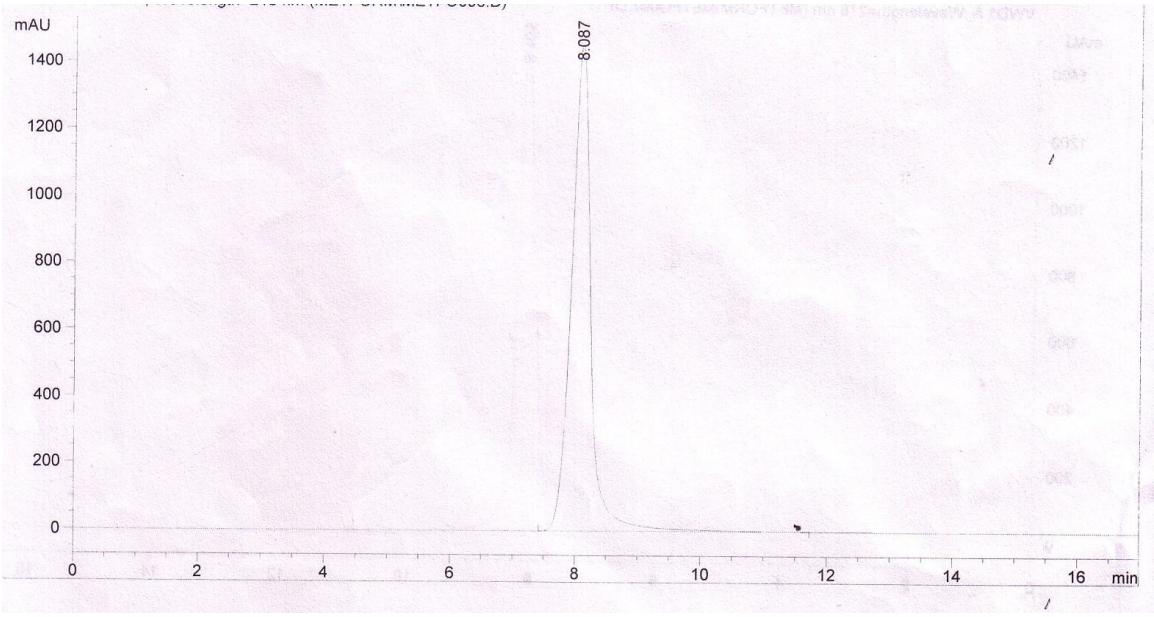
Ready Mixing of Active with excipient on the day of analysis

Sr. No	Raw materials	Assay Value	Limit
1	Metformin +HPMC K 100	859.86mg	854.7+1%
2	Metformin + HPMC K 4M	8.44.54mg	848.56+1%
3	Metformin + MCC	949.86mg	952.38+1%
4	Metformin+PVPK30	958.1mg	952.38+1%
5	Metformin+ HPC	973.46mg	962.26+1%
6	Metformin +Starch	962.46mg	956.46+1%
7	Metformin +Aerosil	975.63mg	985.22+1%
8	Metformin +Mg.Stearate	994.2mg	985.22+1%

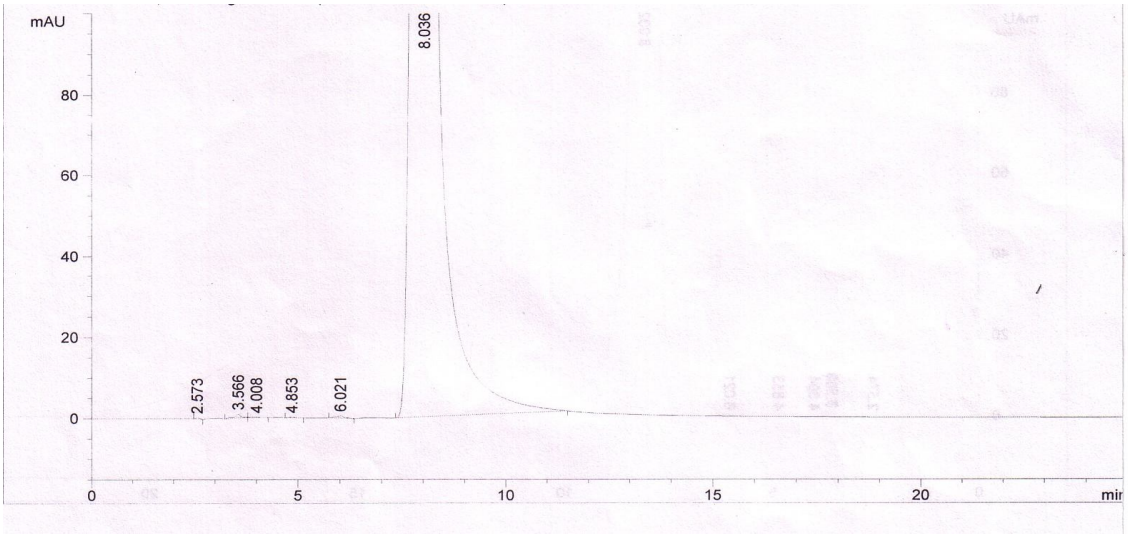
For The premix blend, active with excipient kept in storage condition 30^0C/65%RH, 40^0C/75%RH analysis done after 4 weeks.

SL NO	Raw materials	Assay value		
		30^0C/65%RH	40^0C/75%RH	Limit
1	Metformin +HPMC K 100	85.03	852.23	854 +1%
2	Metformin + HPMC K 4M	846.32	894.32	848.56+1%
3	Metformin + MCC	949.86	946.23	952.38+1%
4	Metformin+PVPK30	961.01	984.24	952.38+1%
5	Metformin+ HPC	956.33	950.46	962.26+1%
6	Metformin +Starch	963.24	984.21	956.26+1%
7	Metformin +Aerosil	982.8	978.46	985.22+1%
8	Metformin +Mg.Stearate	989.8	982.29	985.22+1%

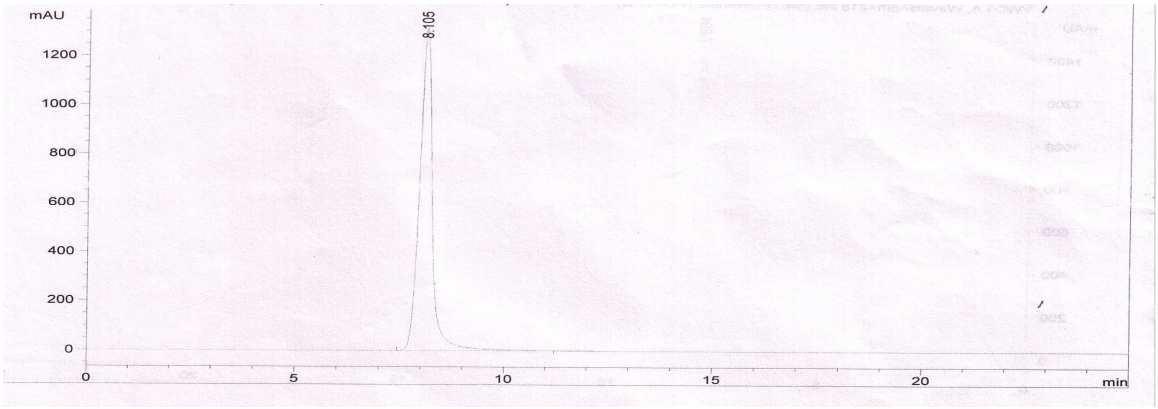
METFORMIN STANDARD



METFORMIN + HPMC (Initial)



METFORMIN + HPMC (ACC)



Fine Particle Characterization

Value shown in table are mean of three Determmination

TABLE NO. 11 Powder Flow Characterization

Sample	Bulk Density g/cm^3	Tap Density g/cm^3	Compressibility index	Hausner ratio
Drug	0.78±0.18	0.96±0.13	18.73±0.11	1.230±0.18
HPMC k100	0.46±0.33	0.58±0.34	20.91±0.15	1.264±0.10
HPMC k4M	0.39±0.29	0.53±0.33	26.16±0.33	1.362±0.20

PREPARATION OF STANDARD CURVE [14]

An Accurate weight 100mg of Metformin was dissolved in 100ml of water then pipettes 10ml to 100ml and make up to volume with water to get a stock solution of 100msg/ml. From this stock solution , 4ml, 6ml, 8ml, 10ml, 12ml, 14, 16 was pipettes out in different 100ml volumetric flask and volume was made up to 100ml, in order to get concentrated ranging from 4-16mcg.The absence of the resulting solution was then measured 232 nm using u.v spectrophotometer against respective parent solvents as a balance .The standard curve was obtained by plotting observation vs. concentration in mcg/ml and data was subjected to weighted linear regression analysis in Microsoft Excel.

STANDARD CURVE OF METFORMIN IN WATER AT 232nm

Sr. NO	Concentration(ug/ml)	Absorbance
1	00	00
2	4	.0.317
3	6	0.457
4	8	0.634
5	10	0.793
6	12	0.951
7	14	1.11
8	16	1.26

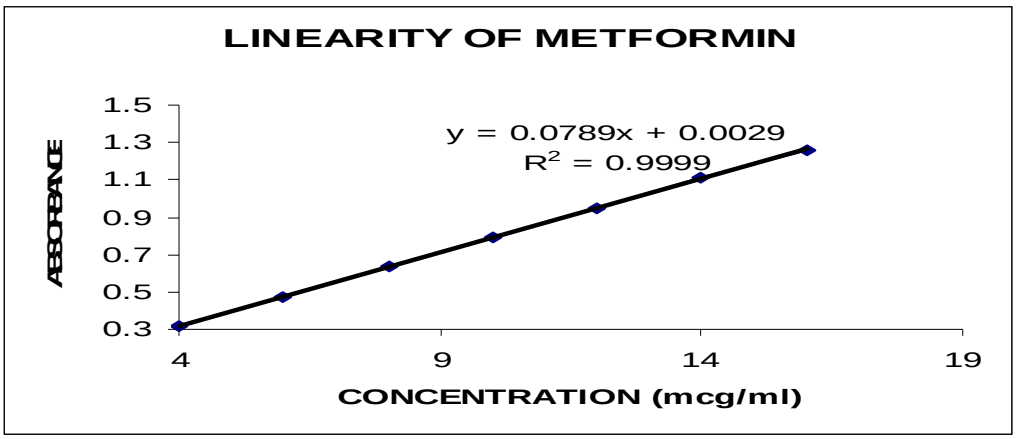


FIG NO -13 Standard curve of metformin in water at 232nm

CONSIDERATION OF FORMULATION AND DEVELOPEMENT

- Use of different concentration of polymer
- use of material in different concentration
- Different method of granulation
- Amount of Polymer: Depending on drug content randomly batches are selected , change in amount of polymer to grip the dose release specified amount were used under guidance of standard reference

FORMULATION AND DEVELOPMENT OF METFORMIN SUSTAINED RELEASE TABLET[16,17]

Formulation of batch I -XI

Ingredients	I	II	III	IV	V	VI	VII	VIII	IX	X	XI
Metformin	**500 mg**	**500 mg**	**500 mg**	**500mg**	**500mg**	**500mg**	**500mg**	**500mg**	**500mg**	**500mg**	**500mg**
HPMC K100	**20 mg**	**32mg**	**52 mg**	**85 mg**	**97 mg**	**13 mg**	**32 mg**	**52 mg**	**85 mg**	**85 mg**	**85mg**
HPMC K4M	**----**	**-----**	**----**	**-----**	**------**	**7mg**	**20 mg**	**33mg**	**-----**	**------**	**------**
Avicel	**90 mg**	**78mg**	**58mg**	**25mg**	**13 mg**	**90mg**	**58 mg**	**25 mg**	**25mg**	**25mg**	**25mg**
PVP K30	**25mg**	**25mg**	**25mg**	**25mg**	**25mg**	**25mg**	**25mg**	**25mg**	**25mg**	**-----**	**----**
Starch	**----**	**----**	**----**	**----**	**-----**	**----**	**------**	**----**	**-----**	**25mg**	**-----**
HPC	**---**	**----**	**-----**	**-----**	**-----**	**-----**	**-----**	**-----**	**----**	**-----**	**25mg**
IPA	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**Q.S**	**-----**	**Q.S**
Water	**----**	**-----**	**----**	**----**	**---**	**----**	**-----**	**-----**	**-----**	**Q.S**	**-----**
Mg Stearate	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**
Aerosil	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**	**7.5mg**
Total	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**	**650mg**

- Amount of Avicle:It helped in direct and wet granulation method as diluent , availability in different grade of granular and powder form based on utility high compressibility and excellent flow property was making it best on available option of starch derivatives .
- Avicle Why? Availability in different grade of granular and powder form based on utility, high compressibility and excellent flow property was making it best on available option of starch derivatives.
- Selection of PVP:It was used as an adhesive binder to get proper compactness and due to its slightly disintegrating property.
- Use of manufacturing additives: it was based on initial drug ,polymer flow property evaluation and by reference of book of excipient.

IN PROCESS EVALUATION STUDIES [18,19,20,21]

EVALUATION OF GRANULES

Batch No	Bulk density g/cm^3	Tapped density g/cm^3	Loss on Drying (%)	Compressibility Index	Hauser Ratio	Angle of Repose(in degrees)
1.	0.422	0.492	2.2	14.28	1.16	37.85
2.	0.418	0.500	2.0	16.32	1.21	36.11
3.	0.413	0.493	2.2	16.32	1.19	34.11
4.	0.423	0.483	1.8	12.5	1.14	34.83
5	0.418	0.513	2.2	14.28	1.24	33.71
6.	0.417	0.499	1.8	16.32	1.19	36.56
7.	0.423	0.483	2.21	12.5	1.14	34.22
8	0.417	0.499	2.1	16.32	1.19	36.21
9	0.428	0.492	2.0	13.00	1.14	32.11
10.	0.4316	0.485	2.0	12.50	1.12	34.26
11	0.4483	0.4820	1.8	6.99	1.07	27.24

EVALUATION OF TABLETS

Batch No	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability	Drug Content(%)
1.	622 ±2.68	5.30±0.04	5	0.61%	96.03
2.	633 ±3.42	5.32±0.02	6	0.69%	99.36
3.	644±2.71	5.30±0.02	4	0.64%	96.93
4.	641±2.41	5.32±0.02	5	0.67%	99.81
5.	638±3.32	5.34±0.04	7	0.55%	96.21
6.	647±3.21	5.38±0.02	6	0.49%	99.91
7.	634±2.21	5.32±0.02	6	0.43%	99.36
8.	643±2.21	5.40±0.02	7	0.41%	96.75
9.	648±2.21	5.38±0.04	6	0.49%	99.85
10	646±3.31	5.36±0.02	7	0.45%	99.28
11.	634±2.21	5.34±0.04	6	0.49%	99.36

For thickness and hardness

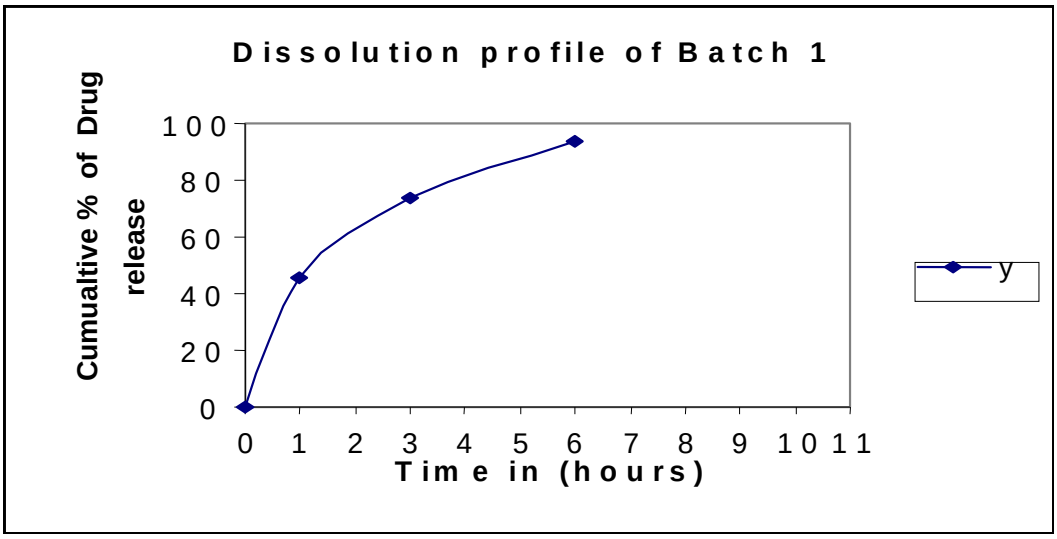
Each value represent the mean ± standard deviation (n=10)

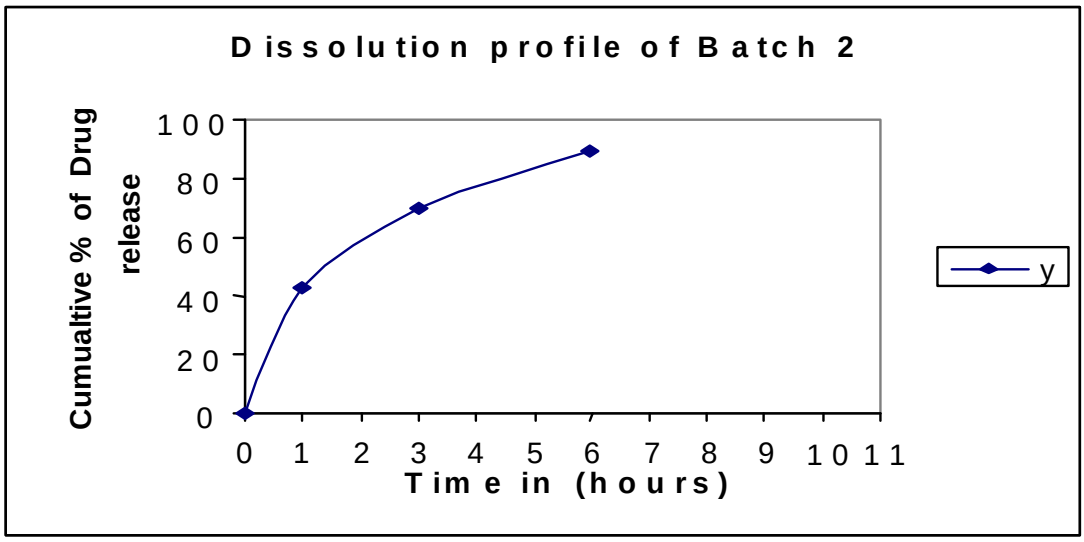
For weight variation and friability

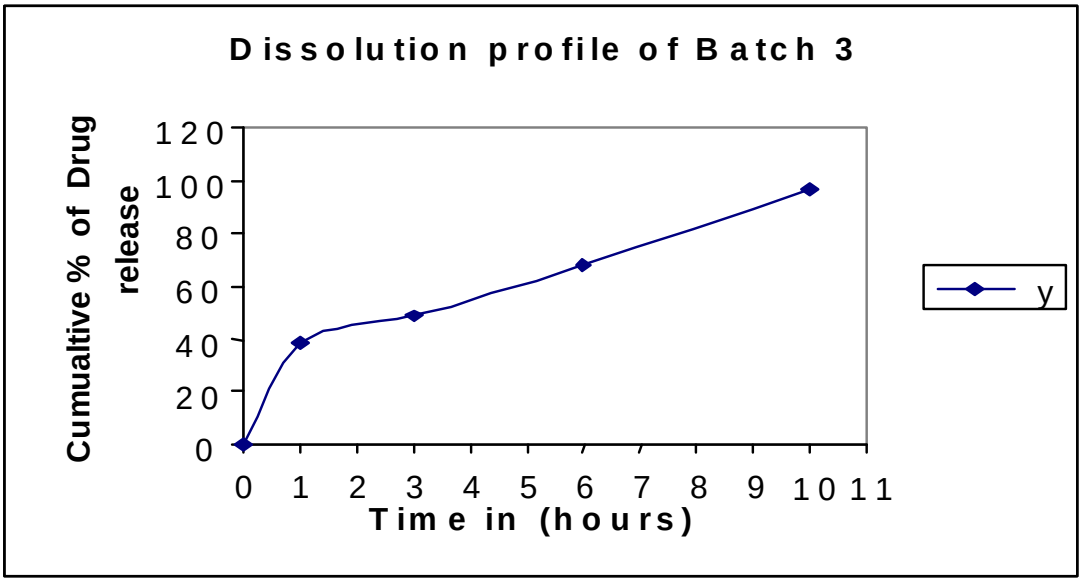
Each value represent the mean standard deviation (n=20)

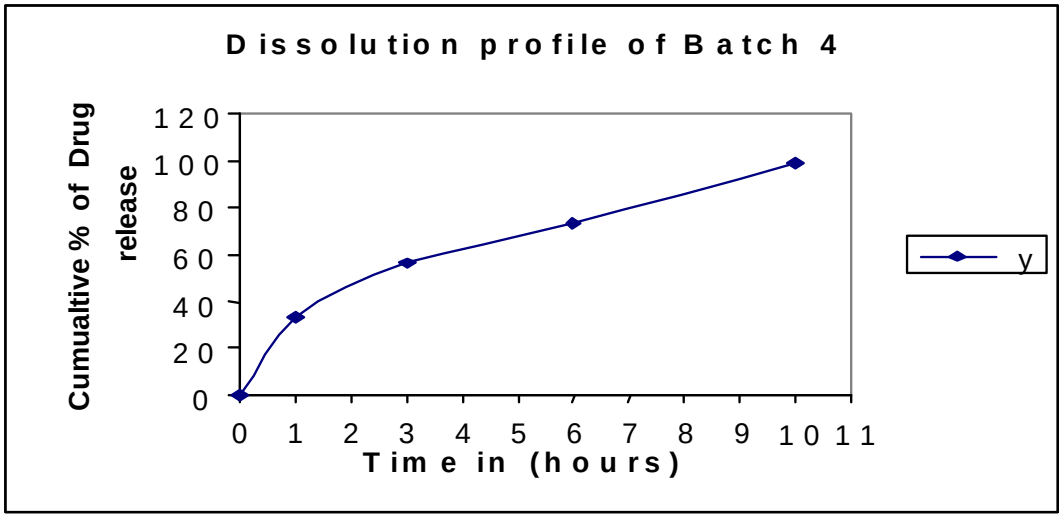
***IN VITRO* DRUG RELEASE** [22,23,24,25]

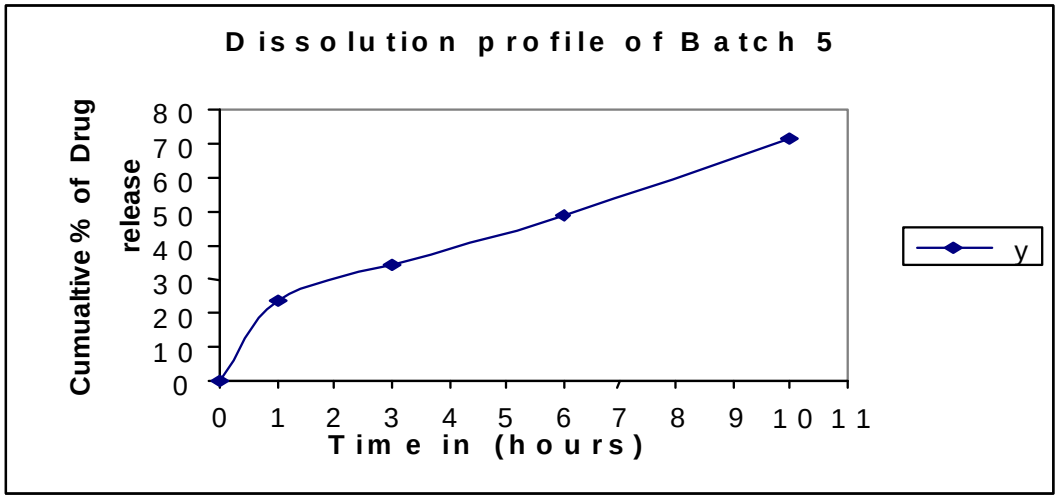
The *in vitro* dissolution studies were performed using USP – 22 type I dissolution apparatus at 100 rpm. The dissolution medium consist of water 1000ml, maintained at 37^0C . An aliquot (5ml) was withdrawn at specific time interval and drug content was determined by UV-Visible Spectrophotometer at 233nm..

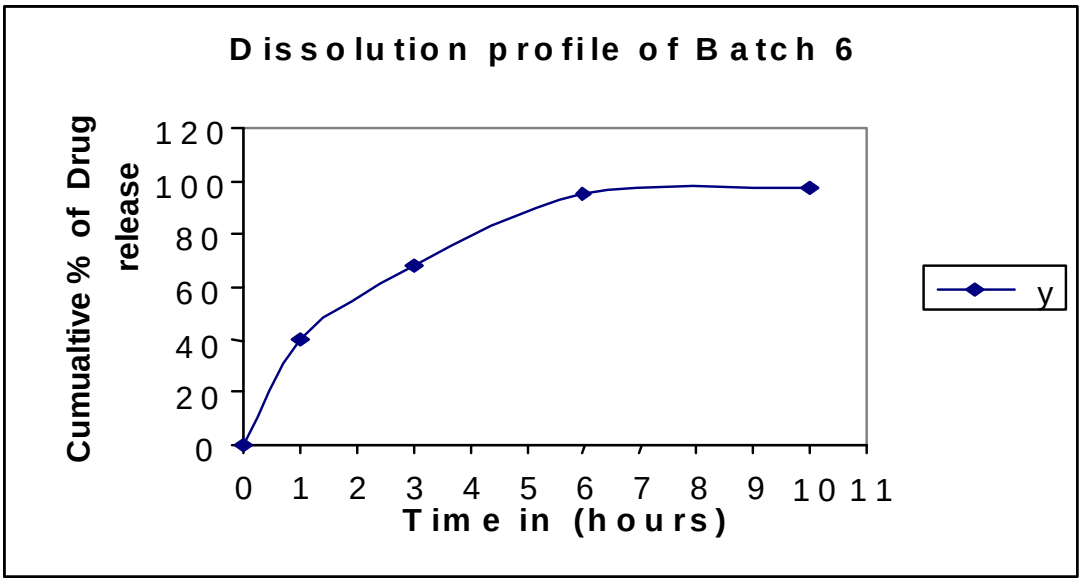

Dissolution profile of Batch 1
Cumualtive % of Drug release
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

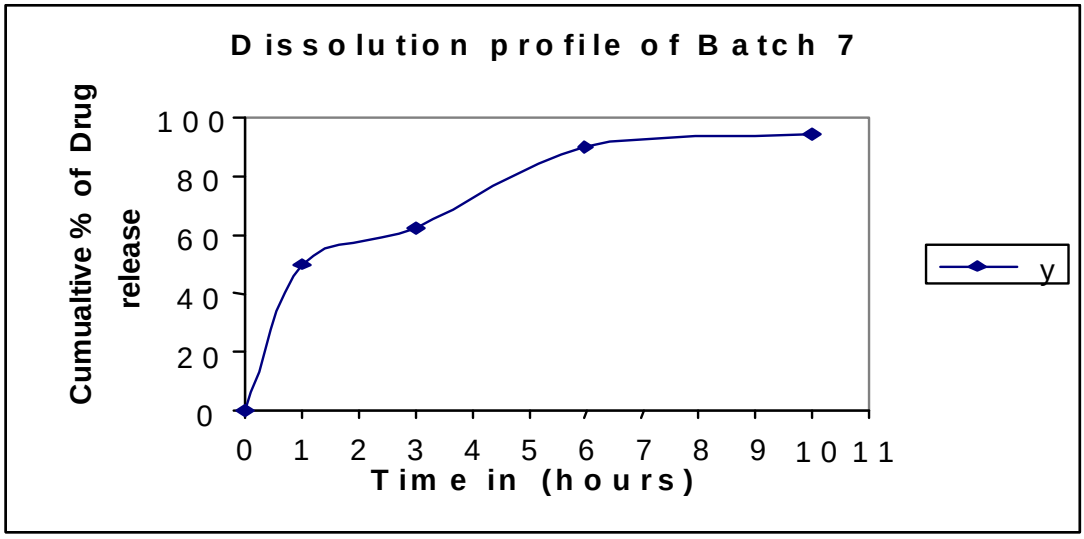

Dissolution profile of Batch 2
Cumualtive % of Drug release
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

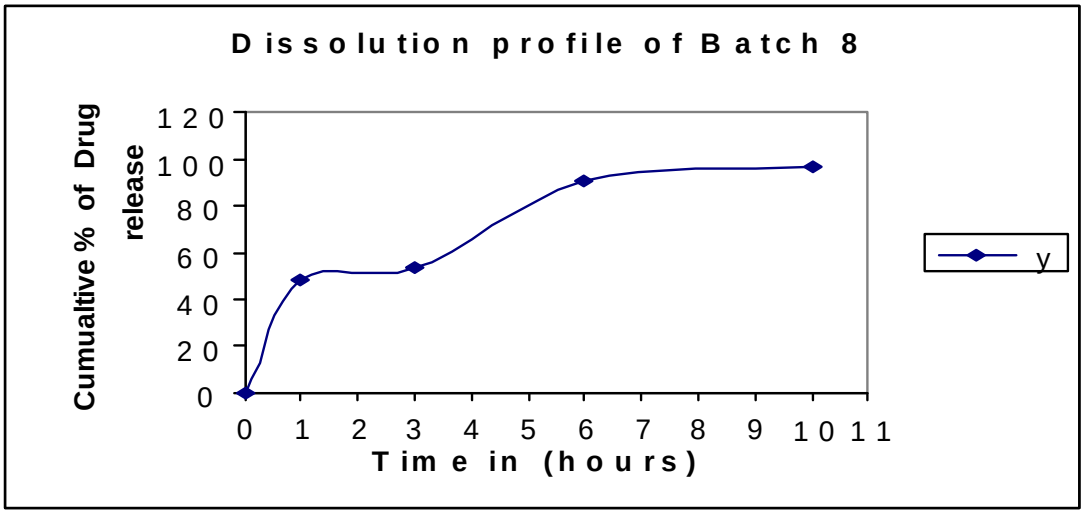

Dissolution profile of Batch 3
Cumualtive % of Drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

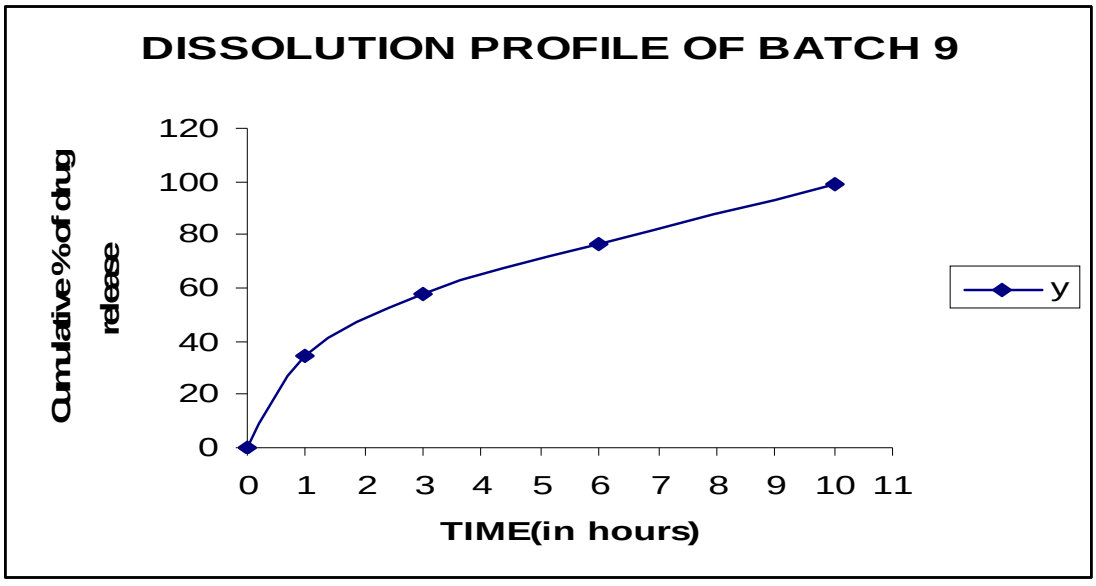

Dissolution profile of Batch 4
Cumualtive % of Drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

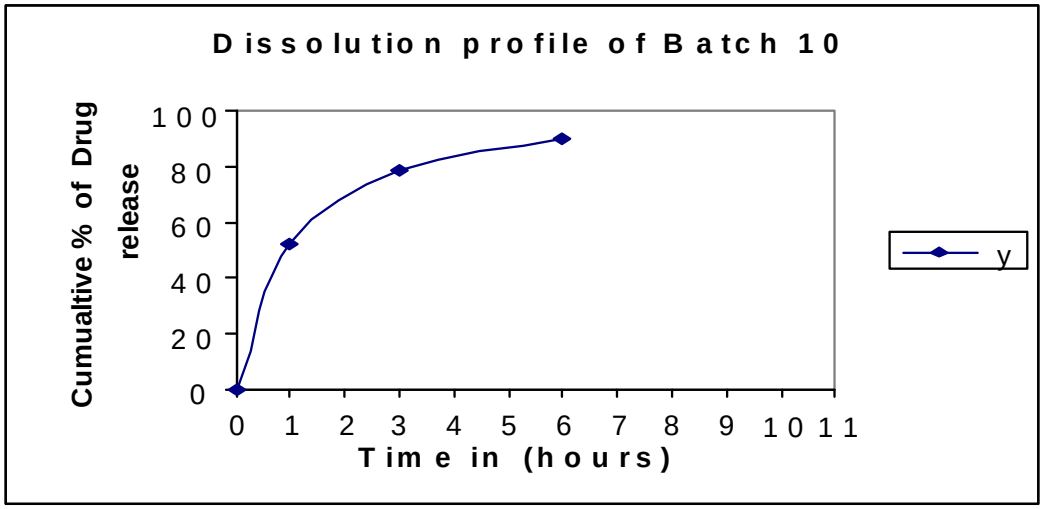

Dissolution profile of Batch 5
Cumualtive % of Drug release
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

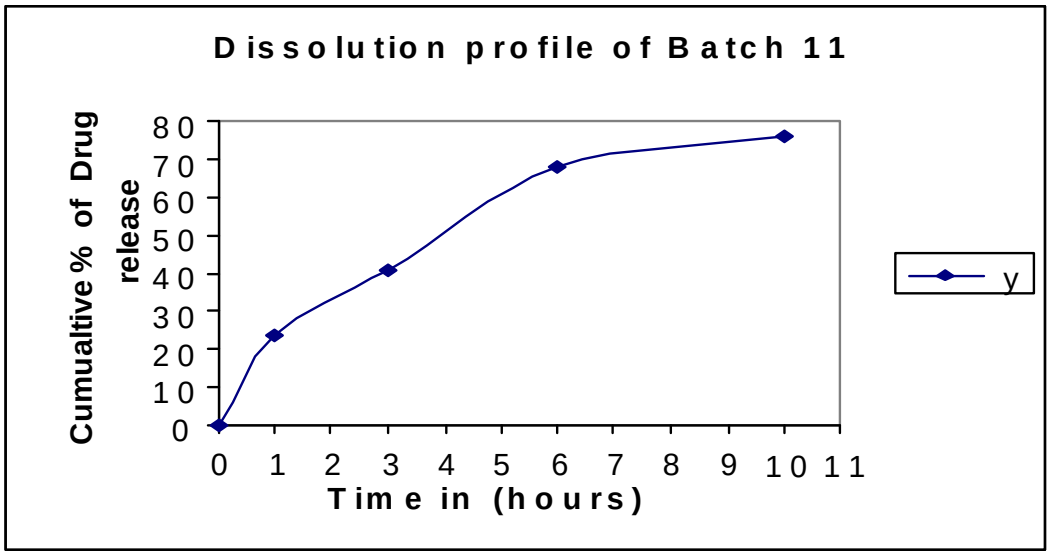

Dissolution profile of Batch 6
Cumualtive % of Drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

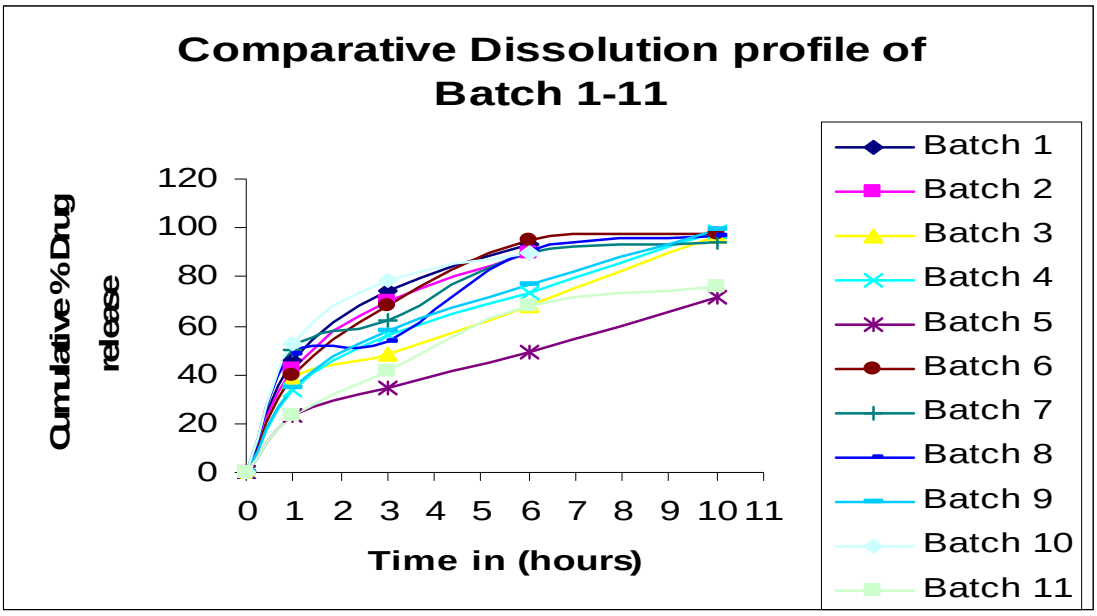

Dissolution profile of Batch 7
Cumualtive % of Drug release
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y


Dissolution profile of Batch 8
Cumualtive % of Drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y


DISSOLUTION PROFILE OF BATCH 9
Cumulative%of drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
TIME(in hours)
y


Dissolution profile of Batch 10
Cumualtive % of Drug release
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y

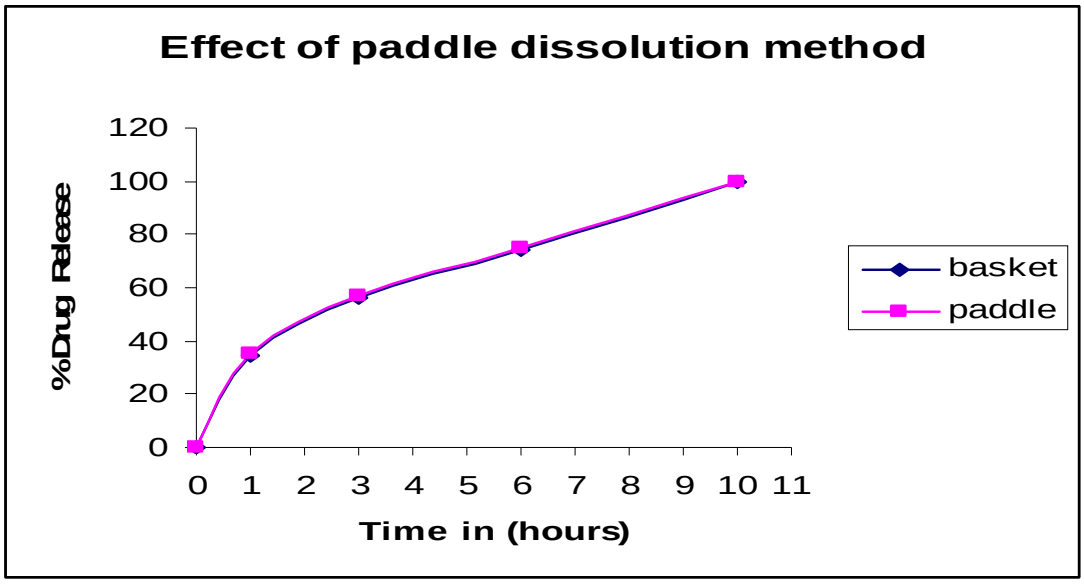

Dissolution profile of Batch 11
Cumualtive % of Drug release
80
70
60
50
40
30
20
10
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
y


Comparative Dissolution profile of Batch 1-11
Cumulative %Drug release
120
100
80
60
40
20
0
0 1 2 3 4 5 6 7 8 9 10 11
Time in (hours)
Batch 1
Batch 2
Batch 3
Batch 4
Batch 5
Batch 6
Batch 7
Batch 8
Batch 9
Batch 10
Batch 11

Effect of different dissolution parameter on release profile of Metformin hydrochloride SR tablet of Batch IX

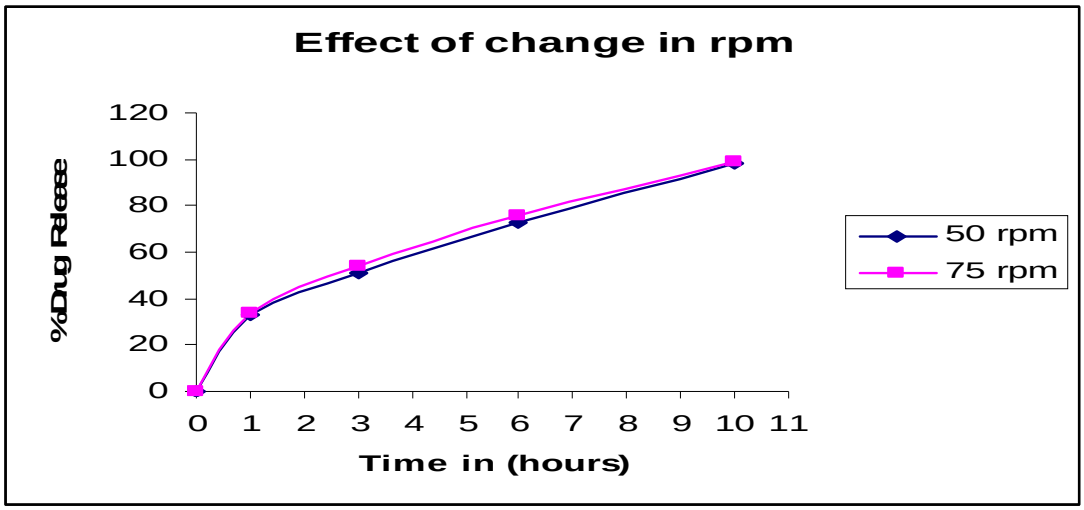
Table no 20 Change in apparatus assembly

Time in (hour)	% Drug release (Rotary basket)	% drug release (Rotary paddle)
1	34.45	35.12
3	56.54	56.84
6	74.38	74.68
10	99.46	99.67



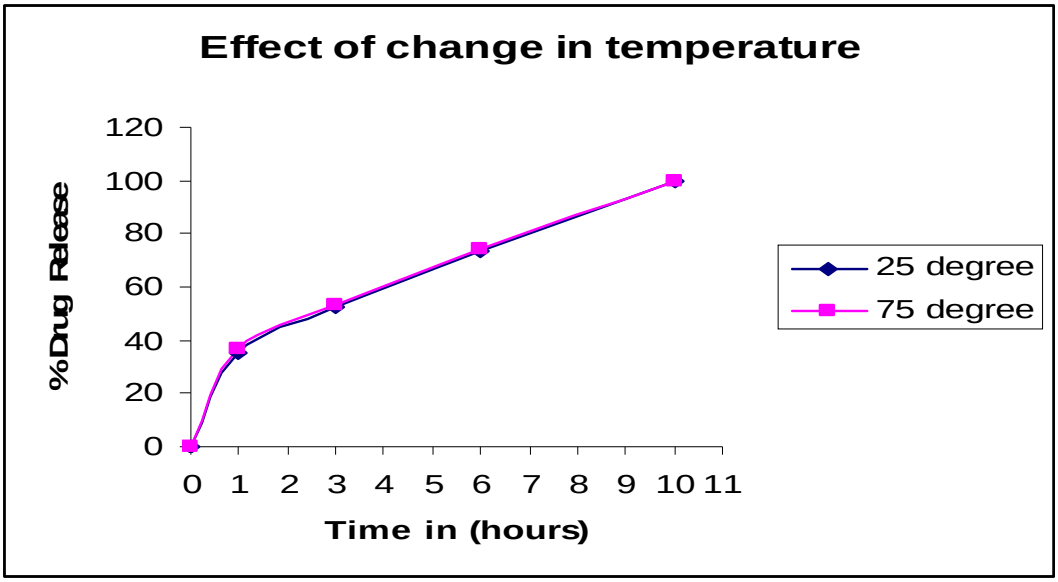
Change in agitator Speed

Time in (hour)	% Drug release(50 rpm)	% Drug release (75 rpm)
1	**32.68**	**33.61**
3	**51.24**	**53.68**
6	**72.56**	**75.94**
10	**98.54**	**98.68**



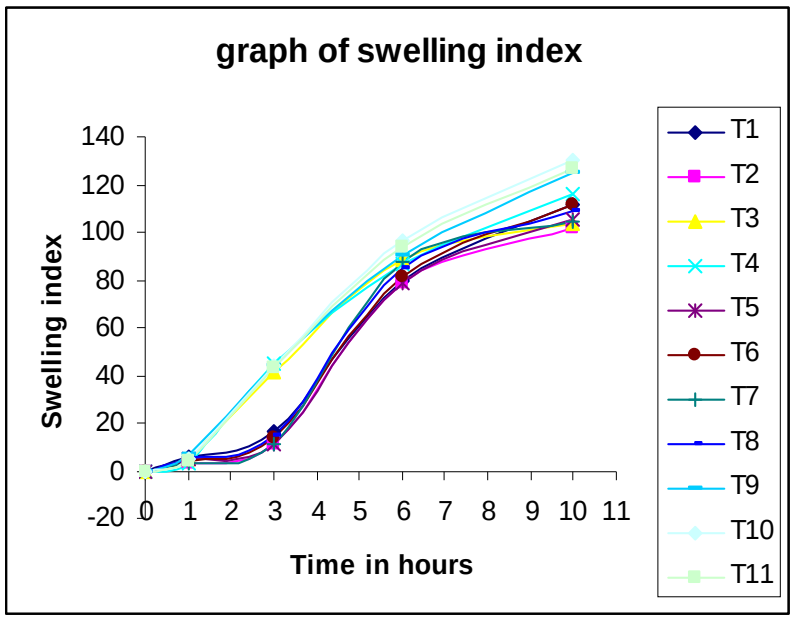
Change in temperature

Time in (hours)	% Drug release $25^0C \pm 0.5^0C$	% Drug release $75^0C \pm 0.5^0C$
1	35.24	36.68
3	52.54	53.21
6	73.21	74.18
10	99.82	100.04



Swelling study

Swelling of tablet excipients involves the Absorption of a liquid resulting in an increase in weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles of hydration of macro molecule . The liquid enter the particles through pores and bind to large molecules . Breaking the hydrogen bond and resulting in the swelling of the particle . The extent of swelling can be measured in terms of % weight gain by the tablet.



Time	T1	T2	T3	T4	T5	T6	T7	T8	T9	T10	T11
0	0	0	0	0	0	0	0	0	0	0	0
1	6.15	3.16	4.53	3.43	5.14	4.08	3.46	4.68	6.33	4.49	3.66
3	16.13	11.48	41.54	44.59	11.13	13.56	11.41	14.28	43.60	44.14	43.10
6	79.68	78.35	88.46	86.45	78.23	81.45	87.45	84.48	90.30	96.60	93.60
10	111.31	101.66	103.54	115.56	105.56	111.38	104.56	108.81	124.66	129.90	127.10

STABILITY TESTING[26]

The purpose of stability testing is to acess the effect of temperature , humidity , light and other environmental factor on the quality of drug substance or product. The results are used to establish storage condition,rest period, shelf life and to justify overages included in product for stability reason.

Optimized formulation IX th was kept for stability testing for three month at $25^0C\pm 2^0C$ 60%RH, $30^0C \pm 2^0C$,65%RH, $40^0C \pm 2^0C$,75%RH condition for period of three month. Every month tablet were tested for its dissolution study.

STABIITY STUDY OF TABLETS OF BATCH IX

The batch IX was selected as an optimum batch and the stability study was carried out at different condition of $25^0C\pm 2^0C$ 60%RH, $30^0C \pm 2^0C$,65%RH, $40^0C \pm 2^0C$,75%RH condition for period of three month

DRUG CONTENT

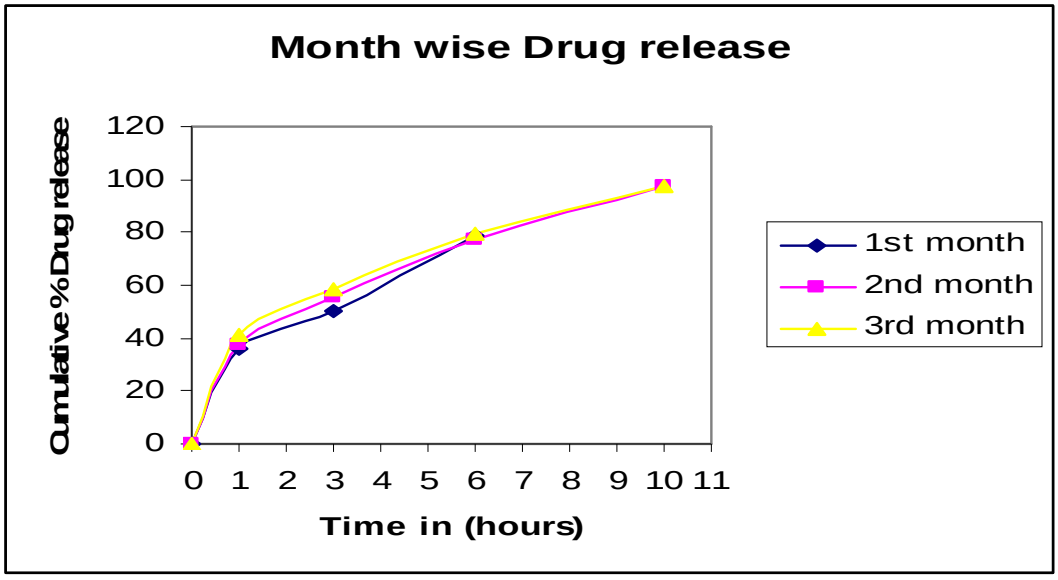
TIME	DRUG CONTENT		
	$25^0C\pm$ 2^0C,60%RH	$30\ ^0C \pm$ 2^0C,65%RH	$40^0C \pm$ 2^0C,75%RH
Initial	99.38	99.32	99.40
1st Month	99.10	99.08	99.22
2nd Month	98.86	98.78	98.74
3rd Month	98.20	98.68	98.56

Evaluation of Physical Parameter in Accelerated Stability Condition

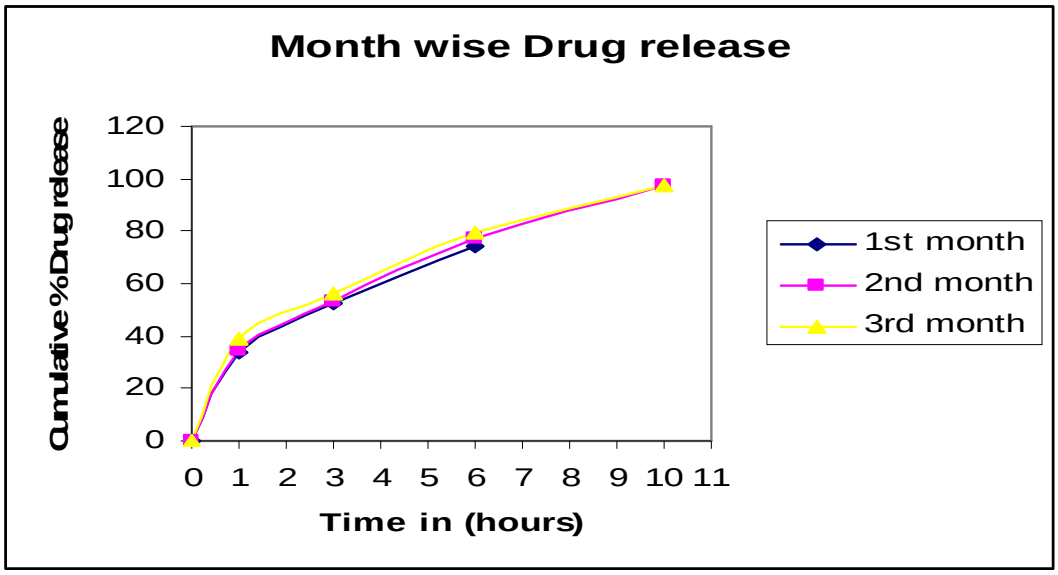
parameter	Evaluation data		
	1st Month	2nd Month	3rd Month
Weight variation	652.6 ±1.50	648.8 ± 1.42	651.6 ±1.45
Hardness	7kg/cm2	6kg/cm2	7kg/cm2
Friability	0.45%	0.43%	0.47%
Diameter	5.30 ±0.04	5.34 ±0.02	5.32 ±0.04

DISSOLUTION PROFILE OF BATCH: IX

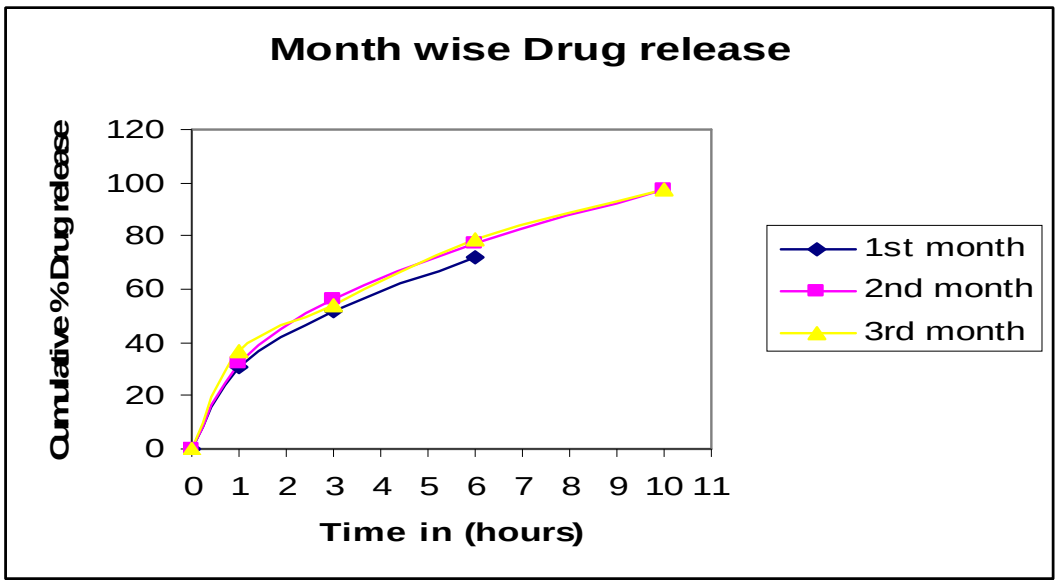
Month Wise Drug Release At 25^{0}C ± 2^{0}C 60% RH of Stability Batch



Month wise Drug Release At 30^{0}C ± 2^{0}C 65% RH of Stability Batch



Month wise Drug Release At 40^0C ± 2^0C 75% RH of Stability Batch



RESULTS AND DISCUSSSION

Identification: The procured sample of Metformin was tested for its identification by using FTIR Spectra study .Then bulk characterization of the drug is done .The manufacturer also was confirmed of quality and purity of sample.

Initial Trial

Before compression of batches all the polymer were tested with quantity of glidant and lubricant to observe the flow property .The amount was fixed after successive initial trials .

Control of Amount

The initial batches were of directly compression method which needs higher amount of excipient to reduce the friability and improve hardness indirectly which affect the release of drug from polymer .The total weight 650 mg was used successfully to meet all criteria.

Selection of batches

The selection of batches was well targeted for SR release of metformin all criteria of drug was properly studied along with polymer property the amount of drug with polymer was of great importance the initial failed batches of polymer with drug were properly performed and studied.

Tablet Parameter

In guidance of industrial scientist different parameter of tablet like flow property, dimension hardness, drug content etc. were studied with results in successful trials.

Idea after dissolution study

The amount released in fixed duration was of more importance and were performed with precision and accuracy, the change in amount of polymer was largely dependent of viscosity grade the dissolution study suggested many parameter to control of next batches.

Final batch

The batch IX immerge as a successful delivery system it was completely dependent of gel swelling and diffusion behavior of HPMC . The different viscosity grades of HPMC were used successfully.

Utility of polymer

The use of HPMC in different concentration shows different dissolution study. The drug release in specific time interval is taken as ideal concentration of polymer.

Compression / Evaluation

The sustained release tablets of Metformin were prepared by weight granulation and direct compression. The granules for the matrix tablet were prepared according to the formula given in related table and characterized with respect to angle of repose, moisture content, bulk density and total drug content. Angle of repose was less than 35^0C for all batches of granules indicating satisfactory floe behavior moisture content of less than 3 % indicates optimum drying of granules. Other parameters for granules were also found to be in acceptable range.

No significant difference was observed in the weight of individual tablets from the average weight. Tablet weights of all batches were found within recommended IP Limits .The data of uniformity of content which was performed by UV Spectroscopy , indicates that tablets of all batches had drug content within IP Limits .The hardness of tablets of all batches are in between 4-7kg/cm^2 which is acceptable limits , which shows in the literature . All the formulation showed % of friability less than 1% that indicates ability of tablet to withstand shocks which may encountered . No significant difference was observed in the thickness of individual tablet from the average value.

Dissolution discussion

The dissolution was carried out by using dissolution medium water and the release of Metformin from sustained release tablet of various formulations varied according to amount and grade of different polymer. In case of different concentration of polymer such as 5 % HPMC K100 shows release profile 93.57% in VI hour. Then 5% HPMC K100 shows release profile 89.51% in VI hour. Then 8% HPMC K100 shows release profile 96.45 in Xth hour. 13 % HPMC K100 shows release profile 98.69 in Xth hour within specification limit and 15% HPMC K100 shows release profile 71.68% of drug release in Xth hour itself.

The HPMC K100 combined with HPMC K15M taken as three trails in different concentration but the three trials are not showing the drug release in specific time interval. Then the three trials taken as different binder concentration such as PVP K30, Starch, and Hydroxypropylcellulose.

The binder solution starch with water create capping problem during compression. The binder solution HPC with IPA shows hardness is heavy so drug release is less i.e. 75.86 % in Xth hour .so the binder solution PVP K30 with IPA shows drug release in specific interval of time as per IP Limits.

Influence of changing dissolution parameter

Batch IX was subjected to different dissolution condition such as change in temperature, agitated speed and assembly to observe the effect on drug release, there was no significant change was found, but it indicates somewhat higher drug release in condition of increase in temperature and agitator speed which might be due to excessive erosion of matrix in such condition. The result of rotating paddle assembly was approximately same .Dissolution study in different temperature; agitation rate also proved that formulation could be better

suited for patients who impaired homeostasis and physiological conditions. From the above results and discussions the batch IX was subjected in stability study to seen the in vitro study in different media. It was seen that the release in different media was given near about same result. Then swelling study was done. it was clear that the matrices underwent swelling at the same time after placement in the dissolution media..

Stability

Results of stability studies of batch ix indicate that it is stable at $25^0C\pm 2^0C$ 60%RH, $30^0C \pm 2^0C$,65%RH, $40^0C \pm 2^0C$,75%RH as there was no significant difference observed for dissolution and other physical parameter of tablet after 3 month.

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