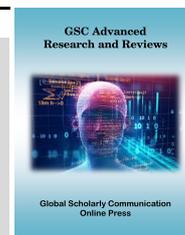


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(RESEARCH ARTICLE)



Formulation and evaluation of gastro retentive extended release formulation of metformin hydrochloride.

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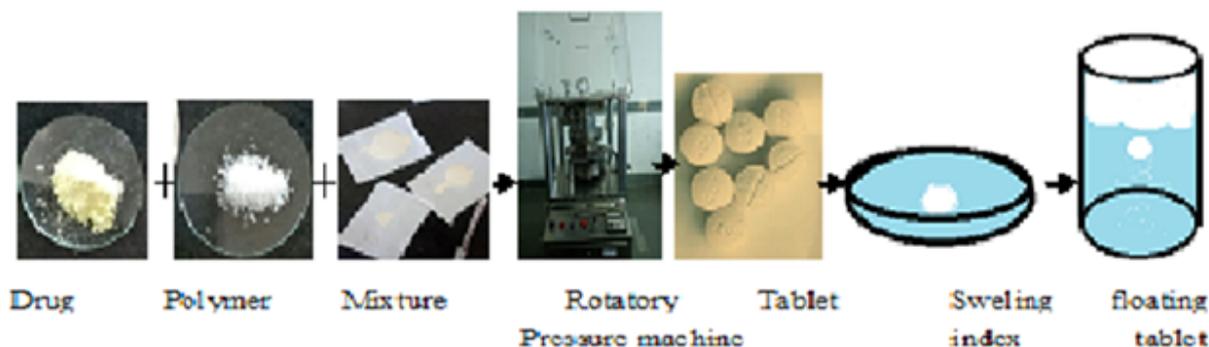
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Abstract

The present research think about was to deliver definition and assessment of gastro retentive extended release formulation of metformin hydrochloride. The programming interface metformin hydrochloride and polymer and all excipients were weighed precisely, blended well and by utilizing rotatory pressure machine.(F.P. hardware,accura little press multistation tooling machine) and by utilizing 9 mm punch of case shape which has length of 2cm and inside breadth of 9 mm. Utilizing this punch tablets were arranged and continues for promote study. Metformin hydrochloride is hostile to hyperglycaemic specialist, which utilize for the most part for patients experiencing diabetes-2. Because of low penetrability medicate requires more opportunity to apply pharmacological impact, which may likewise enhances bioavailability of medication metformin hydrochloride is debased in colon, having least retention at upper gastro intestinal tract. To expand the discharge rate of medication by utilizing reasonable polymer. To diminish the day by day dosage by expanding its action. To shield the medication from acidic condition in stomach and in this manner enables it to corrupt in colon. to assess the definition in-vitro for tablet qualities like hardness, friability, thickness, consistency of substance of medication, sedate discharge profile.

Keywords: Metformin HCl; Polymer; Rotatory pressure machine: Tablet

Graphical Abstract



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1. Introduction

Oral course of organization has gotten more consideration in the pharmaceutical field in view of greater adaptability in the outlining of measurement frame than alternate courses of medication delivery¹. The arrival of medication from the conveyance systems might be by dispersion, disintegration or by mix of the two systems in a coveted and controlled way. One primary essential for the oral execution of the medication conveyance systems is that medication ought to have great retention all through the gastrointestinal tract (GIT) ². This approach of oral medication conveyance of medications has a few physiological challenges, for example, powerlessness to limit and find the controlled medication conveyance systems inside the coveted district of the gastrointestinal tract because of variable gastric purging and motility³. Gastroretentive medication conveyance systems (GRDDS) is a kind of novel medication conveyance systems which can stay in the stomach for delayed timeframe and there by increments gastric living arrangement time of medications, and furthermore enhances the bioavailability of medications. ^{4,5} Some medications are consumed at particular site as it were. They require discharge at particular site or a discharge with the end goal that greatest measure of medication spans to the particular site. Gastro-retentive conveyance is one of the site particular conveyance for the conveyance of medications either at stomach or at digestive tract. It is acquired by holding measurements frame into stomach and medication is being discharged at controlled way to particular site either in stomach, duodenum and digestive tract.

1.1. Floating drug delivery systems (FDDS): [6]

Floating drug delivery systems (FDDS): When the medication conveyance systems is skimming on the gastric substance, the medication is discharged gradually at the coveted rate from the systems . This outcomes in expanded gastro maintenance time and a superior control of vacillations in the plasma sedate concentration. Based on the lightness instrument, gliding systems are arranged.

2. Material and methods

2.1. Material

The API Metformin HCl and polymer and all excipients HPMC K4 and K100M , Xanthan gum , Sodium bicarbonate , Avicel PH 102, Magnesium stearate , Talc were weighed precisely, blended well and by utilizing Rotatory pressure machine.

2.2. Methods

The API Metformin HCl and polymer and all excipients were weighed precisely, blended well and by utilizing Rotatory pressure machine (F.P. Hardware, Accura small scale squeeze multistation tooling machine) and by utilizing 9 mm punch of case shape which has length of 2 cm and interior width of 9 mm. Utilizing this punch tablets were arranged and continues for additionally ponder.

3. Evaluation

3.1. Tablet Thickness

Thickness and width were estimated utilizing aligned Vernier Caliper. Five tablets of every detailing were picked arbitrarily and thickness and breadth was estimated independently.

3.2. Tablet disintegration time

Place 1 tablet in every one of the six containers of the bin and, if the tablet has a solvent outside sugar covering, inundate the bin in water at room temperature for 5 minutes. At that point work the mechanical assembly utilizing reenacted gastric liquid kept up at 37 ± 2 °C as the submersion liquid. Following 1 hour of task in recreated gastric liquid, lift the crate from the liquid, and watch the tablets: the tablets demonstrate no confirmation of crumbling, breaking, or softening. Work the contraption, utilizing reenacted intestinal liquid kept up at 37 ± 2 °C as the submersion liquid, for the time determined in the monograph. Lift the bin from the liquid, and watch the tablets: the greater part of the tablets crumble totally.

3.3. Weight Variation Test

Twenty tablets were chosen haphazardly from each clump and measured independently to check for weight variety. A little variety was permitted in the heaviness of a tablet as per U.S. Pharmacopeia.

3.4. Uniformity of drug content

Standard Solution: Dissolve 50mg of Metformin HCl in water and weaken to 100 ml with water. Weaken 2ml to 100 ml with water Test Solution: Select arbitrarily 20 tablets and squash to fine powder. Break down equal to 50 mg of Metformin HCl in water and weaken to 100 ml with water. Weaken 2ml to 100 ml with water and channel.

Methodology: Measure the UV absorbance at around 231.5 nm, utilizing water as clear. Ascertain the substance of Metformin HCl by following recipe.

3.5. *In-vitro* swelling study

The swelling of polymers utilized were dictated by water take-up. It was watched that the swelling records were expanded with increments in polymer focus. Typically swelling is basic to guarantee coating. For gliding the tablet, there ought to be proper harmony amongst swelling and water take-up.

Tablets were weighed independently and put independently in receptacle of disintegration medium containing hydrochloric corrosive cradle (pH 1.2) arrangements 900 ml at $37 \pm 0.5^\circ\text{C}$. At standard interims 1, 2, 3, 4, 5, 6, 7 and 8 hours, the tablets were pulled back from the bin and blotched with tissue paper to expelled abundance surface water and the swollen tablets were reweighed on logical balance. Swelling file (SI) of tablets was figured utilizing the accompanying equation.

3.6. Floating Properties

The drifting slack time can be characterized as the time took to rise on the surface of the disintegration medium, and the time the tablet continually glide on the surface of the medium is referred to as Total coating time as assessed in a disintegration vessel loaded with 900ml of 0.1 N HCl (pH 1.2).

3.7. Dissolution investigation

This investigation was directed by crate compose disintegration mechanical assembly (Electrolab disintegration analyzer USP) at $37^\circ \pm 0.5^\circ\text{C}$ temperature utilizing 900 ml of 6.8 pH phosphate support as a medium at 100 rpm. Pull back a reasonable volume of the medium with appropriate time interims, and channel, weaken reasonably with support and measure the absorbance of the subsequent arrangement at λ_{max} 231.5 nm. Figured the percent tranquilize arrival of Metformin hydrochloride.

4. Results and discussion

4.1. FTIR Study 24

From the FTIR outputs of Drug and polymers, the pinnacles get was of gatherings display in tranquilize and in polymers henceforth it was reasoned that no covering between tops were watched, subsequently it was presumed that no connection amongst medication and polymer was Metformin HCl and the polymers was bona fide. What's more, in Compatibility investigation of medication with polymers no covering of crests amongst medication and polymers were watched, thus continue for next examinations.

4.2. Precompression parameters [11, 12]

The readied powder mix for all definitions were assessed. It was watched that the group F1 to F9 for the parameter like mass thickness, tapped thickness, hausners, carrs file, point of rest All these outcomes demonstrated that, the powder mix indicated great stream properties into the kick the bucket depression and compressibility properties and thus, complies with as far as possible.

4.3. Post compression parameters of enhancement groups [13, 14]

Post compression parameters of enhancement groups was finished. It was inferred that the centralization of HPMC K 100M polymer and of Sodium bicarbonate assumed a vital part in light of the fact that as their focus changed the post pressure parameter likewise changed.

4.4. Dissolution study [15]

The outcomes acquire from disintegration contemplates, it was inferred that the group F8 demonstrated a decent % discharge upto 12 hours contrasted and another bunches, as beforehand talked about HPMC K100M polymers assume a key part in plan, it appeared by the disintegration comes about and consequently because of good % discharge F8 cluster was chosen as upgraded clump.

4.5. Contour Plot

The shape plot is a two-dimensional portrayal of the reaction over the select elements. The full scope of two factors at any given moment can be shown. Fig. illustrates the impact of Sodium bicarbonate and HPMC K100M polymer on % discharge and on crumbling time.

4.6. 3D Plot

The 3D reaction surface plots of the factorial model were attracted to demonstrate the impact of the factors on the % Release and on Disintegration time. It is exhibited that the % Release and Disintegration time relies upon both the polymer and sodium bicarbonates focus.

4.7. Release Kinetic Models: [20, 21]

The equation of Hixoncrowell model describes that the release from systems where there is a change in surface area and diameter of particles or tablets. It was observed in studies and hence from R2 value and from Constant value obtain from graph of Hixoncrowells model Optimized batch obeys Hixoncrowell model.

Using level 3 and by 32 factorial design further batches were prepared using HPMC K100M which were as follows;

Table 1 Preparation of Optimization batches

Batch	Metformin HCL (mg)	HPMC K100M (mg)	Sodium Bicarbonate (mg)	Avicel 102 (mg)	PH	Magnesium stearate (mg)	Talc (mg)
F1	500	50	100	110		10	5
F2	500	50	125	110		10	5
F3	500	50	150	110		10	5
F4	500	100	100	110		10	5
F5	500	100	125	110		10	5
F6	500	100	150	110		10	5
F7	500	150	100	110		10	5
F8	500	150	125	110		10	5
F9	500	150	150	110		10	5

Table 2Precompression parameters of optimization batches

Batch	Bulk density (g/mL)	Tapped density (g/mL)	Hausner Ratio	Angle of Repose(°)	Carrs Index (%)
F1	0.587	0.839	1.42	27.11	30.03
F2	0.591	0.821	1.38	26.30	28.01
F3	0.612	0.836	1.36	26.70	26.78
F4	0.556	0.729	1.31	35	23.69
F5	0.535	0.664	1.23	37.52	19.35
F6	0.547	0.694	1.27	36.26	21.26
F7	0.512	0.593	1.16	38.86	13.69
F8	0.503	0.608	1.21	40.06	17.35
F9	0.509	0.605	1.19	39.46	15.96

Table 3 Postcompression parameters of optimization batches

Batch	Hardness (Kg/cm ²)	Disintegration time (min.)	Uniformity of drug content (%)	Friability (%)
F1	4.4	159	98.09	0.21
F2	4.4	154	98.12	0.23
F3	4.2	157	98.10	0.19
F4	4,6	179	98.34	0.20
F5	5.0	178	98.62	0.17
F6	4.8	181	98.49	0.18
F7	5.2	184	98.91	0.15
F8	4.8	181	98.95	0.19
F9	5.2	184	98.86	0.17

Table 4 Percentage release of dissolution studies of optimization batches

Time(Hr)	% Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	12.75	11.96	12.41	11.86	11.77	12.03	11.29	11.76	12.01
2	22.06	22.76	22.43	13.29	13.47	17	12.41	12.03	12.86
4	58.40	58.79	59.76	41	38.61	27.90	28.12	28.57	27.53
6	79.23	81.13	80.42	63.86	62.05	64.44	46.07	45.23	46.36
8	96.13	97.52	96.79	82.45	81.79	80.97	61	63.19	62.10
10	-	-	-	98	96.05	97.21	79.87	81	80.37
s12	-	-	-	-	-	-	98.10	98.20	97.95

Table 5 R2 Value for Model Fitting Analysis of In-Vitro Release Data for Optimized

Method	R2 value	Constant
Zero order	0.963	10.32
First order	0.962	89.34
Hixoncrowell model	0.995	3.72
Higuchi model	0.988	28.43

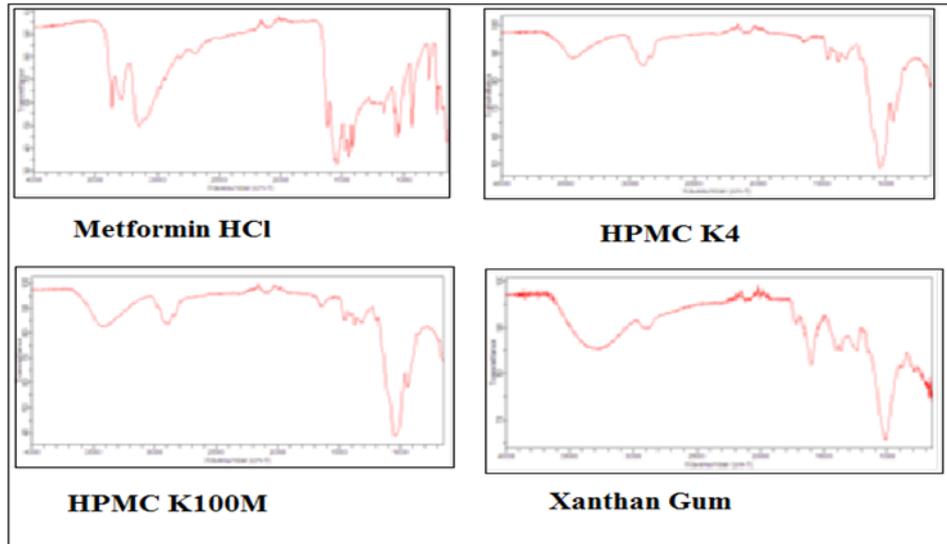


Figure 1 FTIR

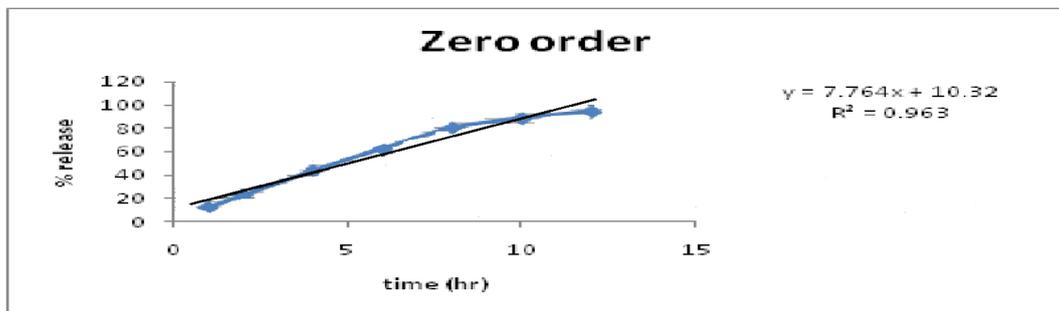


Figure 2 Release kinetic model by zero order

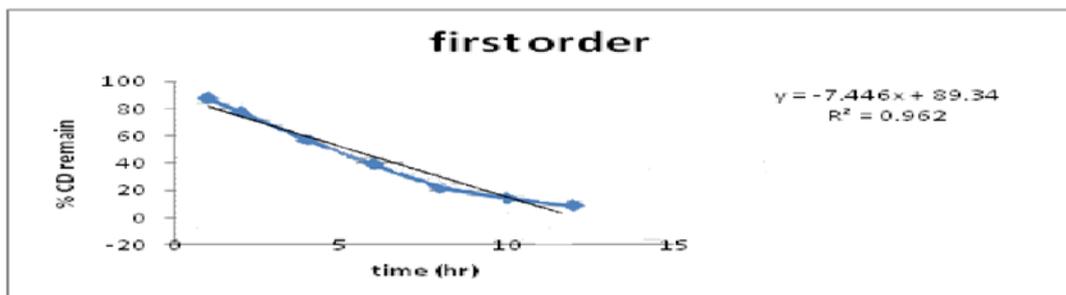


Figure 3 Release kinetic model by First order

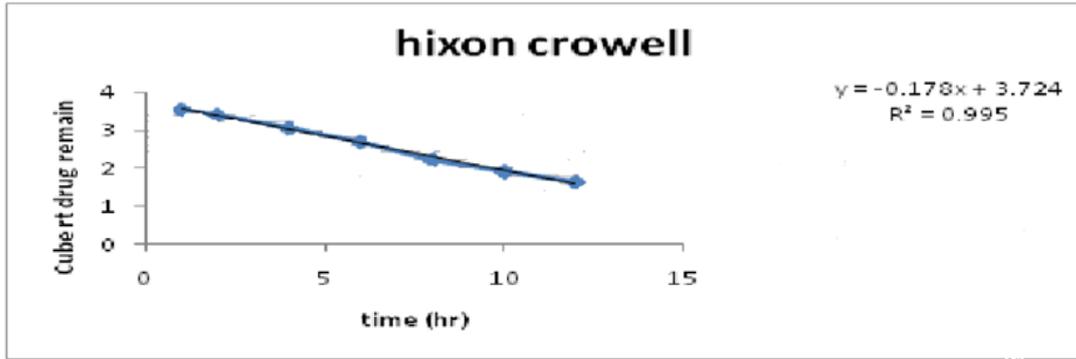


Figure 4 Release kinetic model by Hixoncrowell model

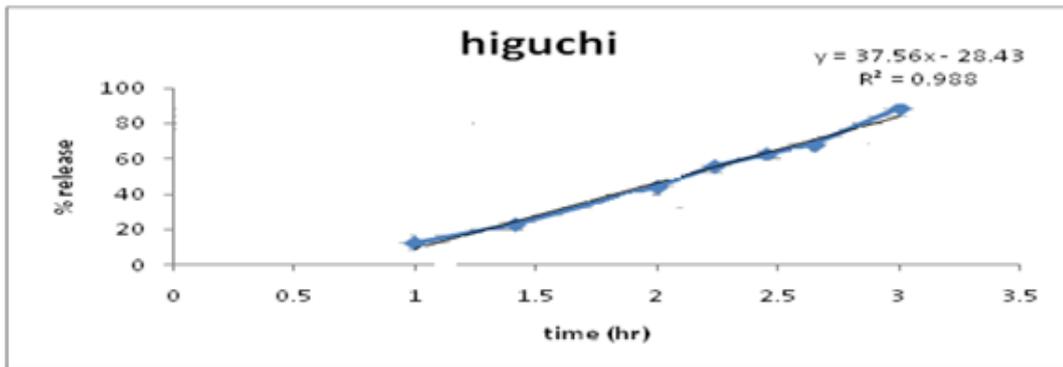


Figure 5 Release kinetic model by Higuchi model

4.8. Contour Plot

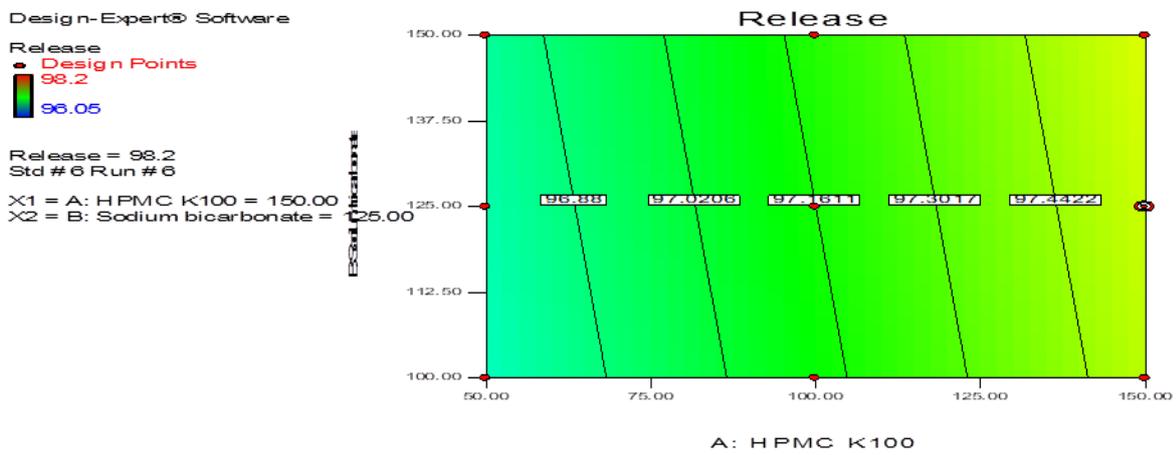


Figure 6 Counter plot of % Release

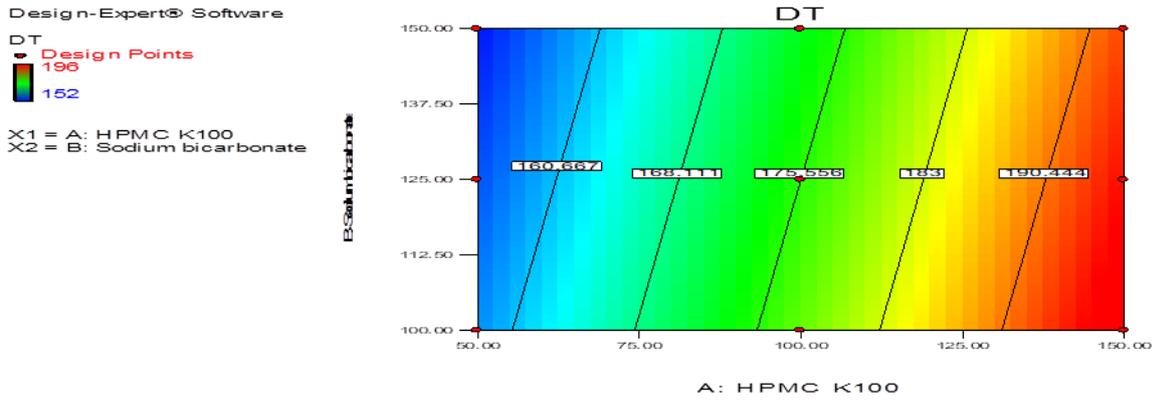


Figure 7 Counter plot of Disintegration time

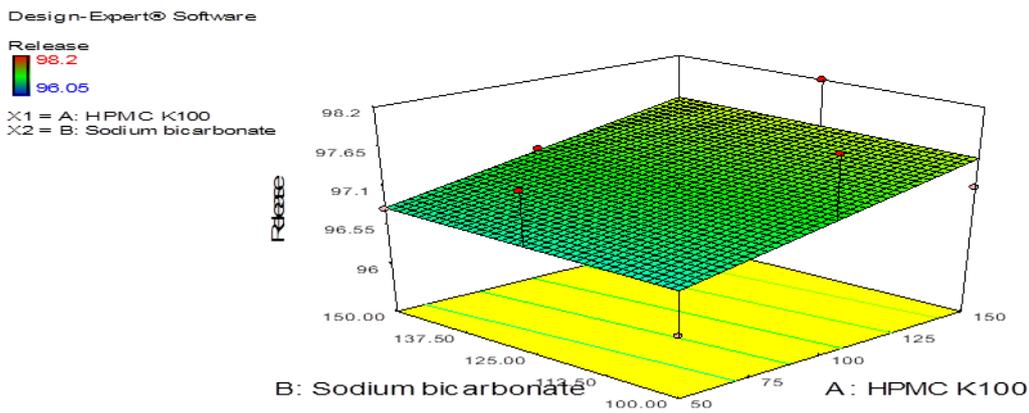


Figure 8 3D plot of % Release of optimization batches

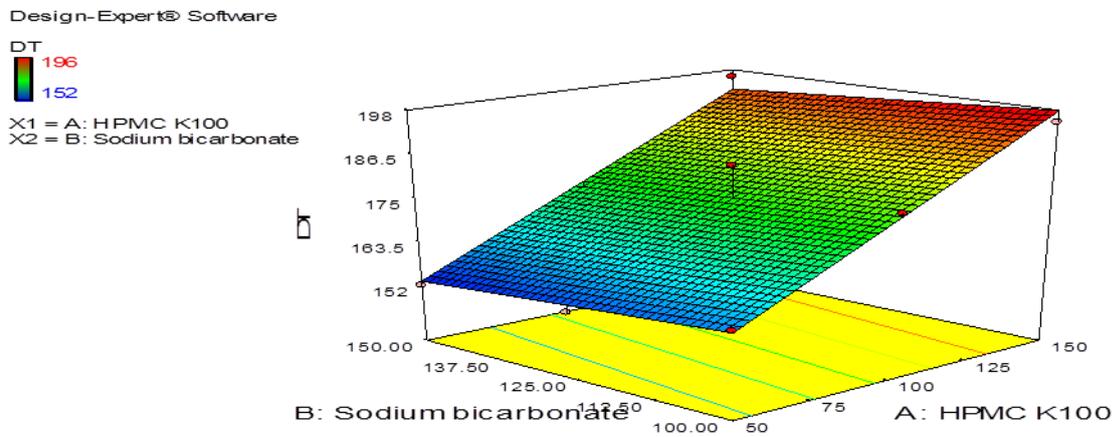


Figure 9 3D plot of % Release of optimization batches

5. Conclusion

The Gastro retentive extended release tables of Metformin Hydrochloride were prepared by direct compression method. It was observed that the HPMC K100M polymer played a key role as it controlled the release of drug. In studies, as the concentration of HPMC K100M increased the % release of drug with respect to time increased. As the concentration of sodium bicarbonate increased the floating behaviour means lag floating time and total floating time also increased. The drug release using Kinetic models was studied in which it was observed that the release of optimized batch obeys Hixoncrowells model.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and or publication of this article.

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