RESEARCH ARTICLE

Design, Formulation, Optimization and *In-vitro* Evaluation of Colon-targeted Tablet Utilizing Polymer Isolated from *Artocarpus heterophyllus*

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ABSTRACT

Objective: The objective of the present study is to formulate, optimize, and evaluate the colon-targeted oral Tablet by utilizing the polymer obtained from Artocarpus heterophyllus. Ibuprofen was used as a model drug in the study.

Methods: The Polymer was extracted from the fresh fruits of Artocarpus heterophyllus and subjected to identification and characterization. The formula of the Tablet was optimized using 3 factors 3 levels Box-Behnken design (Design Expert Software). The colon-targeted Tablets were then formulated and coated with pH-dependent polymer to avoid release in the upper gastrointestinal tract.

Results: Pre-compression and post-compression characteristics of the Tablet were studied which were within the standard limits. The drug-excipient compatibility study was performed by the Fourier transform infrared spectroscopy (FT-IR) study and found no incompatibility. The optimized formulation was not released in acidic pH the release was found to be less than 5%. The drug was completely released during in-vitro evaluation. The formulation shows significant release in pH 6.8 within 6 hours.

Conclusion: The biodegradable and swelling properties of the polymer can sustain the release of the drug at lower gastrointestinal pH.

Keywords: *Artocarpus heterophyllus,* BoxBehnken design, Colon targeted, pH-dependent.

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INTRODUCTION

The oral route of drug administration is the most commonly used route of administration for systemic drug delivery through pharmaceutical products. The oral route of administration is the convenient route with patient compliance. Depending upon the physicochemical properties of the drug may dissolve in the upper gastrointestinal tract (UGIT) or lower gastrointestinal tract (LGIT). The colon-targeted drug delivery offers good bioavailability for poorly absorbed drugs. Colon has longer retention times and hence shows enhanced absorption of poorly soluble drugs.[1]

Ibuprofen is the most commonly used non-steroidal anti-inflammatory drug (NSAID) and is widely used as an analgesic, anti-inflammatory, and antipyretic.[2] Ibuprofen is used to treat inflammation and pain related to the colon. Ibuprofen shows very good absorption orally and the peak plasma concentration can be achieved within 2 hours after oral administration. Frequent Ibuprofen consumption may cause abdominal pain, nausea, vomiting, and drowsiness.[3]

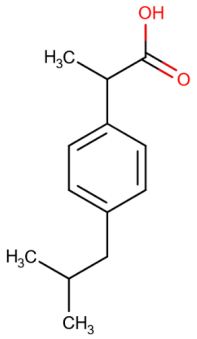

Figure 1: Chemical structure of ibuprofen

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Artocarpus heterophyllus from the family Moraceae also termed as Jackfruit. It is an evergreen tree found in the Western Ghats at an altitude of 450–1200 m. The stem is straight and cylindrical, whereas the leaves are broad. It is a great source of carbohydrates and functions as a great source of energy. While performing the hydrolysis of fruit pulp it gives glucose, galactose, galacturonic acid, and rhamnose as it also contains iron, calcium, and fats. Seeds of *A. heterophyllus* contain a reasonable amount of thiamine, pectin, and protein. The polymer obtained from *A. heterophyllus* contains carbohydrates, polysaccharides, natural gum, proteins, and uranides.[2]

MATERIALS AND METHODS

The fresh Jackfruit (Artocarpus heterophyllus) was collected from the local fruit vendor of Mandi District Himachal Pradesh and authenticated by the Department of Botany, Abhilashi University, Chail Chowk, Mandi HP, India. All the ingredients and solvents were used as AR grades.

Isolation of the Polymer

The fresh pulp of the *A. heterophyllus* was taken and oaked in about 2000 mL of distilled water for 24 hours. The soaked pulp was then ground and kept aside to release the polymer. After 2 hours the material was squeezed to separate the marc from the filtrate, and the acetone was added to the filtrate in the ratio (1:3) to separate the mucilage from the filtrate. The polymer was subjected to preliminary drying in the open air, dried in a hot air oven at 40°C, powdered, and passed through sieve no 80.[4,5]

Determination of Physicochemical Properties of Polymer

After isolation of polymer the following properties like swelling Index, viscosity, and Loss on Drying (LOD) porosity were determined as per the Indian Pharmacopoeia procedure.

Determination of Solubility

The solubility of the obtained polymer was evaluated into various solvents such as Ethanol, Acetone, Hot water, Distilled water, Methanol, and Dimethyl Sulfoxide (DMSO).[6]

Fourier Transform Infrared Spectroscopy (FT-IR)

FT-IR of Polymer extracted from *A. heterophyllus* is taken by using an FT-IR spectrophotometer.

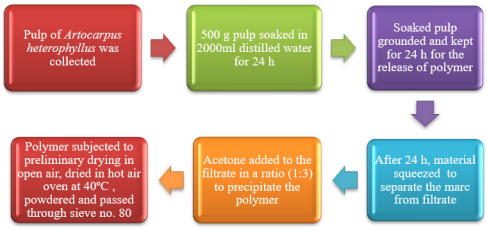

Figure 2: Schematic representation of extraction of polymer from *A. heterophyllus*

Preformulation Studies

Swelling Index

1 g of polymer was transferred to a 50 mL measuring cylinder. Add 25 mL of water and shake it every 10 min for 1-hour. After 1 hour, allow it to stand for 3 hours. Note down the final volume occupied.[6] The swelling Index was calculated using the formula:

$$Swelling\ Index = \frac{Final\ volume - Initial\ volune}{Initial\ volume}$$

Moisture Absorption

1 g of polymer was kept in a desiccator containing 100 mL of calcium chloride. It is allowed to stand for 3 days in the desiccator. After 3 days, the polymer was taken out of the desiccator, weighed, and recorded. Moisture uptake percentage was reported by calculating the difference between initial weight and final weight concerning that initial weight.[7]

pH of Polymer

The pH of 1% w/v dispersion of polymer was reported by using a digital pH meter.[8]

Loss of Drying (LOD)

LOD was calculated by using the formula:[9]

$$LOD = \frac{Wieght\ of\ moisture\ in\ sample}{Weight\ of\ sample\ before\ drying} \times 100$$

Bulk Density and Tapped Density

A known quantity of polymer was taken in the measuring cylinder. The initial volume occupied by the polymer was recorded as the bulk volume. Initially measuring cylinder was subjected to 100 taps and it was continued until the volume became constant. The final volume obtained is termed as tapped volume. Bulk density and tapped density are calculated by dividing the weight of Polymer powder by bulk volume and tapped volume.[10,11]

Angle of Repose

A funnel was fixed above the graph paper and placed on a flat surface. The powder was poured into the funnel until the conical pile's apex touched the funnel's tip. The radius of the base of the pile and height was calculated.[5]

The angle of repose was calculated using the following formula:

$$\theta = tan^{-1}\left(\frac{h}{r}\right)$$

Hausner's Ratio

Hausner's ratio is calculated by using the formula:[12,13]

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

Carr's Index

Carr's Index is calculated by using the formula:

$$Carr's\ Index = \frac{Tapped\ density - Bulk\ density}{Tapped\ denisty} \times 100$$

Table 1: Variables and their levels in Box-Behnken design for tablet formulation

	Levels		
	-1 (Low)	*0 (Medium)*	*+1 (High)*
Independent variables			
A= Ibuprofen (mg)	50	75	100
B= Artocarpus Polymer (mg)	50	75	100
C= PVP K30 (%)	5	7.5	10
Dependent variables			
Constraints			
Y_1= Disintegration time (seconds)	In range		
Y_2= Dissolution %	In range		

Preparation of Standard Calibration Curve

Preparation of HCl Buffer pH 1.2

250 mL of 0.2 M potassium chloride solution is taken and transferred to a 1000 mL volumetric flask. After taking potassium chloride, 425 mL of 0.2 M HCL was added into the volumetric flask, and volume makeup is done up to 1000 mL.

Preparation of 0.2 M Potassium Chloride

14.91 g of potassium chloride is dissolved in the water and further diluted with a sufficient quantity of water and volume makeup was done up to 1000 mL.

Preparation of 0.2 M HCl

16.66 mL of concentrated HCL is taken in a volumetric flask and further diluted with water and volume makes up to 1000 mL.

Preparation of Phosphate Buffer pH 6.8

28.20 g of disodium hydrogen phosphate and 11.45 g of potassium dihydrogen phosphate was dissolved in sufficient water and then volume makeup is done up to 1000 mL.

Preparation of Dilutions

After the preparation of buffers, the dilutions were made that are of different concentrations of 2, 4, 6,8,10, and 12 ppm. After preparing dilutions with different pH buffers their readings were noted down after examining their absorbance in the UV spectrophotometer at 255 nm and the plot is being prepared accordingly.

Table 2: Experimental layout for 3 factors 3 levels Box-Behnken design for Tablet formulation

Run	*A*	*B*	*C*
F1	50	75	10
F2	50	100	7.50
F3	50	50	7.50
F4	75	75	7.50
F5	100	75	10
F6	50	75	5
F7	75	100	5
F8	75	50	5
F9	100	100	7.50
F10	75	50	10
F11	100	50	7.50
F12	100	75	5
F13	75	100	10

* A =Ibuprofen, *B*= Artocarpus Polymer, *C*= PVP K30

Preparation of Tablets

Optimization of the Tablet Formulation

In the present work, two 13 runs, 3 factors, 3-level Box-Behnken design was used to create second-order polynomial models and analyze quadratic response surfaces for optimizing the control release Tablets using Design-Expert software (Trial version 11.0.5.0, Stat-Ease Inc., MN). The design was used for assessing the main, interaction, and quadratic effects of independent variables on dependent variables using the following quadratic model:

$$Y=\beta_0+\beta_1A+\beta_2B+\beta_3C+\beta_4AB+\beta_5AC+\beta_6BC+\beta7A^2+\beta8B^2+\beta9C^2$$

Where, *Y* is the dependent variable; β_{0-9} are the regression coefficients of independent variables and their mutual interactions; A, B, and C are the independent variables. The factors evaluated in the present work are concentrations of Ibuprofen (mg), Artocarpus polymer (mg), and PVP K30 (%) at low, medium, and high values. The dependent variables/ responses were disintegration time (seconds) and Dissolution%. The design matrix used for the experiment has been presented in Tables 1 and 2.[14,15]

Response Surface Analysis of Formulation Characteristics

Response surface analysis of formulation characteristics was performed using a counterplot (2-D) and response surface plot (3-D) generated from Design-Expert software.

Statistical Assessment of Formulation Characteristics

Design-Expert software (version 11.0.5.0) was used for statistical assessment of the results of the experimental design. Statistical validation involved assessing statistical parameters of *F*-value, correlation coefficient (R^2), adjusted R-squared (R^2_{Adj}), predicted R-squared (R^2_{Pred}), predicted residual error sum of squares (PRESS), and adequate precision (AP) generated by ANOVA provision to ascertain model sufficiency and adequacy. An *F*-value with $p < 0.05$ implied the significance of the model. A difference of less than 0.2 between R^2_{Adj} and R^2_{Pred} would prove that both value was in reasonable

agreement with each other. The measure of fit was provided by PRESS statistics with a PRESS statistic of smaller value being preferred. adequate precision was used to measure the signal-to-noise ratio with an AP value greater than 4 indicating adequate model discrimination.

Diagnostic Analysis of Formulation Characteristics

Design-Expert software developed diagnostic plots like externally studentized residuals *vs.* predicted plots, predicted *vs.* actual plots, normal probability plots, and externally studentized residuals *vs.* run number plots. These plots were analyzed to check if the points fell on the diagonal in the normal probability plot and if they lay within the described limits or not.[16]

Optimization and Validation

Statistical validation of polynomial equations was done by assessing ANOVA specifications. Optimal values of the variables were then estimated using the numerical and graphical optimization tool by providing a set criterion of desirability to the software.[17]

Coating of Optimized Tablet Formulation

The optimized Tablet formulation is coated with the 5% Eudragit S100 w/v solution. The coating is using the spray coating method. Eudragit S100 is being used for coating as it will be able to retain the Tablet formulation into the stomach until it crosses the acidic media of the stomach and will help to retain the release of the drug into the stomach. Four optimized batches were prepared and all were coated using the Eudragit S100 solution.[18]

In-vitro Drug Release Study

The release of Tablet dosage form was studied using the six-basket dissolution apparatus taking 900 mL of HCl buffer pH 1.2 for the first two hours and after that phosphate buffer pH 6.8 for the next 6 hours. The temperature was maintained at 37 ± 0.5ºC in the dissolution media. The rotation speed of the paddle was maintained at 50 rpm and an aliquot equal to 5 mL was withdrawn every 30 minutes for 8 hours, respectively that is for the first 2 hours from the HCl buffer 1.2 pH and then for 6 hours from the phosphate buffer 6.8 pH and then dissolution media volume was introduced with a fresh and equal volume of buffer to maintain the sink conditions. The samples were filtered and scanned and the drug release from the Tablet formulation was determined spectrophotometrically at a wavelength of 275 nm.[19]

RESULTS AND DISCUSSION

The Percentage Yield of the Sample

The percentage yield of the extracted sample from the *A. heterophyllus* was found to be 0.6% as 3.01 g of the sample was extracted from 500 g of fruit pulp.

Physicochemical Properties

Solubility studies showed that isolated polymer was insoluble in ethanol, methanol, acetone, and DMSO, and swellable in water and hot water.[20] The pH of the polymer was found to be 6.7 ± 0.57, and the flow properties of the polymer were examined in terms of angle of repose (29.56 ± 0.05º), tapped density (0.86 ± 0.05 g/mL), bulk density (0.62 ± 0.01 g/mL), Hausner's ratio (1.36 ± 0.01) and carr's Index (27.25 ± 0.02%) and with an accepTable limit of loss on drying (6.8 ± 0.1%). These properties are tabulated in Table 3.

Granules of formulation were evaluated for various parameters such as Tapped density, bulk density, Angle of repose, Hausner's ratio, and Carr's Index for checking out its flow property and pre-compression parameters, and the results were shown in Table 4.

Fourier Transform Infrared Spectroscopy (FT-IR)

In the FT-IR spectra absorption peaks were found at 1103 to 1153 (C-O stretching), 1683 (C=O of aldehyde), 1747 (C=O of COOH), 2927 (C-H stretching), 3275 to 3334 (-OH absorption), which show that the product isolated from *A. heterophyllus* is a carbohydrate.

Preparation of Calibration Curves

The dilutions were made that are of different concentrations in buffers 2, 4, 6,8,10, and 12 ppm. After preparing dilutions

Table 3: Physicochemical property of isolated *A. heterophyllus* polymer

S. no.	*Parameters*	*Results*
1	pH	6.7 ± 0.57
2	Loss on drying (%)	6.8 ± 0.1
3	The angle of repose (º)	29.56 ± 0.05
4	Bulk density (g/mL)	0.62 ± 0.01
5	Tapped density (g/mL)	0.86 ± 0.05
6	Carr's Index (%)	27.25 ± 0.02
7	Hausner's Index	1.36 ± 0.01

Values are in mean ± SD (n=3) (SD= standard deviation)

Table 4: Pre-Compression evaluation of Tablet formulation granules with polymer

S. no.	*Parameters*	*Results*
1	The angle of repose (º)	21.08 ± 0.08
2	Tapped density (g/mL)	0.64 ± 0.03
3	Bulk density (g/mL)	0.43 ± 0.03
4	Hausner's Ratio	1.47 ± 0.05
5	Carr's Index	32.20 ± 0.01

Values are in mean ± SD. (n=3) (SD = standard deviation)

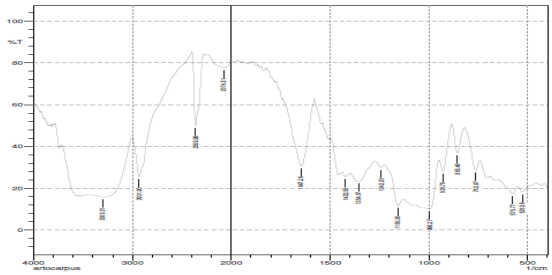

Figure 3: FT-IR spectrum of polymer isolated from *A. heterophyllus.*

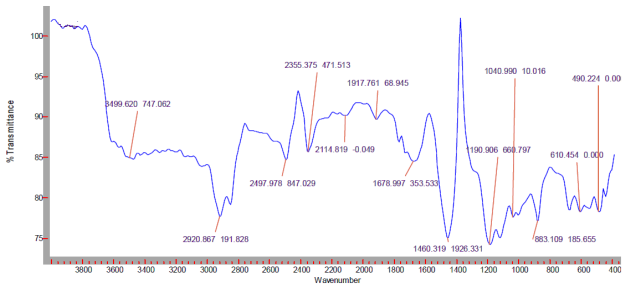

Figure 4: FT-IR spectrum of ibuprofen

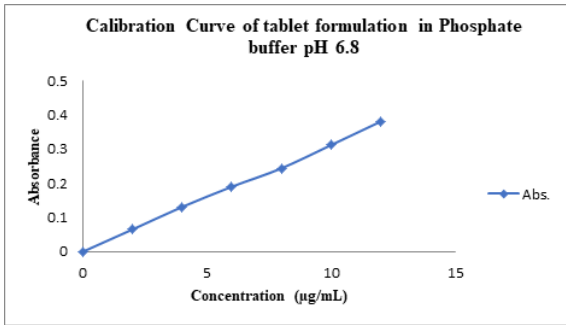

Figure 5: Calibration curve of Tablet formulation phosphate buffer pH 6.8

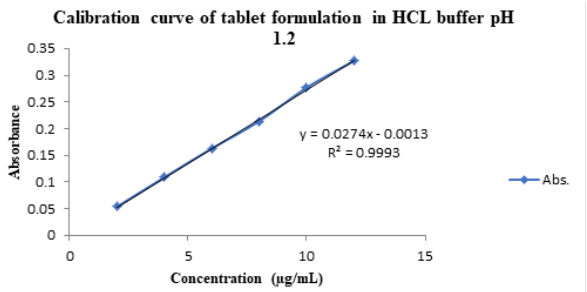

Figure 6: Calibration Curve of Tablet formulation in HCL buffer pH 1.2

with different pH buffers, the readings were noted down after examining their absorbance in the UV spectrophotometer at 255 nm and 243 nm in pH buffers 6.8 and 1.3, respectively the plot is being prepared accordingly (Figure 5 and. 6).

Response Surface Analysis of Disintegration Time

The factors affecting disintegration time were concentrations of ibuprofen (*A*), artocarpus polymer (*B*), and PVP K30 (*C*) (p=0.0236, Table 5) as depicted from the given equation:

Disintegration Time= 7.00-0.3750*A+1.88*B+1.00*C-0.5000*AB +1.75*AC+0.2500*BC+1.25*A^2+1.25*B^2+3.50*C^2 (r^2= 0.9783)

The observed Disintegration time in Tablet formulation varied from 7 minutes to 15 minutes. The predicted values of disintegration time obtained by the model using the above equation were compared with the observed values and a low % error proved that the designed model has good predictability (Table 6). The R^2 value was 0.0.9783, which ascertained good data fitting. The concentration of ibuprofen *(A)*, artocarpus polymer *(B)*, and PVP K30 *(C)* affect the disintegration time as shown in the equation above the ibuprofen *(A)* has a negative impact on the disintegration time, whereas the Polymer *(B)* and the PVP K30 *(C)* has a positive impact on the disintegration time. (Figure 7)depict the consequence of varying concentrations of ibuprofen *(A)*, Polymer *(B)*, and PVP K30*(C)* when one factor is kept constant. The polymer is insoluble and prevents the entry of aqueous media into the formulation. Hence disintegration time increases with an increase in the concentration of the polymer. Due to a positive interaction between ibuprofen and polymer, the disintegration varies with an increase in concentration whereas PVP K30 being a very strong binder prolongs the disintegration time with an increase in concentration. These findings are in agreement with previous reports.

Response Surface Analysis of Percentage Drug Release

The initial model without transformation did not fit into the model as it had a high % error. Hence, based on the suggestion of the software, log transformation was applied and further analysis and validation were done based on the percentage of drug release. The factors affecting Percentage drug release were concentrations of ibuprofen *(A)*, Artocarpus Polymer *(B)*, and PVP K30 *(C)* (p=0.0391) as depicted from the given equation:

Percentage Drug Release= 87.54 - 0.5000*A – 3.38*B – 2.38*C(r^2= 0.7384)

The observed percentage of drug release of Tablet formulation varied from 82 to 95%. The predicted Percentage drug release values obtained by the model using the above equation

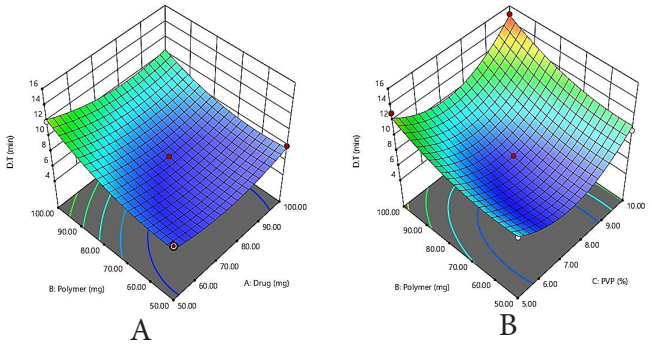

Figure 7: Response surface graph showing the effect of varying concentrations of polymer, drug, and PVP

Table 5: Statistical analysis of disintegration time *(Y_1)* and dissolution *% (Y_2)*

Parameters	Y_1		Y_2	
	β_i	*p-value*	β_i	*p-value*
A	-0.3750	0.2591	-0.5000	0.3822
B	1.88	0.0061*	-3.38	0.0063*
C	1.00	0.0342*	-2.38	0.0167*
AB	-0.5000	0.2817	-	-
AC	-1.75	0.0195*	-	-
BC	0.2500	0.5594	-	-
A^2	1.25	0.0897	-	-
B^2	1.25	0.0897	-	-
C^2	3.50	0.0062*	-	-

βi = Coefficients; *significant (p <0.05)

were compared with observed values. A low %error of <5% ascertained that the model has good predictability. The concentration of ibuprofen *(A)*, polymer *(B)*, and PVP K30 *(C)* have a negative effect on the percentage of drug release due to the insolubility in the drug release as the increase in the concentration of the polymer leading to a decrease in the drug release whereas a decrease in the concentration leads to increase the drug release (Figure 9).

Statistical Assessment of Formulation Characteristics for Tablet Formulation

The model generated for percentage drug release was found to be significant as suggested by the *f*-value of 15.05 (*p-value* < 0.0236). The adjusted R^2 value was 0.9133.

The model generated for percentage drug release was found to be significant as suggested by the *f*-value of 8.47 (*p-value* < 0.0055). The difference between predicted R^2 and adjusted R^2 was greater than 0.2, which was expected. The predicted R^2 value was 0.4356 and the adjusted R^2 value was 0.6512. Adequate precision was found to be 8.8869, which was greater than 4 thus, suggesting an adequate signal and the model could be used for navigating the design space. PRESS value of 105.67 indicated that the model is fit (Table 6).

Optimization and Validation of Formulated Tablet Formulation

Design-Expert software explored the desirability function to obtain an optimized formulation, which was obtained using a set paradigm of disintegration time and percentage drug release. Therefore, an additional batch of Tablet formulation was prepared for validation. Composition and optimized formulation (Tables 7 and 8) with desirability function 1 and confirmation that the experimental value lies within the limit.

Table 6: Model statistics of disintegration time (Y1) and percentage drug release (Y2)

Parameters	Y_1	Y_2
R^2	0.9783	0.7384
Adjusted R^2	0.9133	0.6512
Predicted R^2	-	0.4356
PRESS	-	105.67
Adequate Precision	11.7561	8.8869

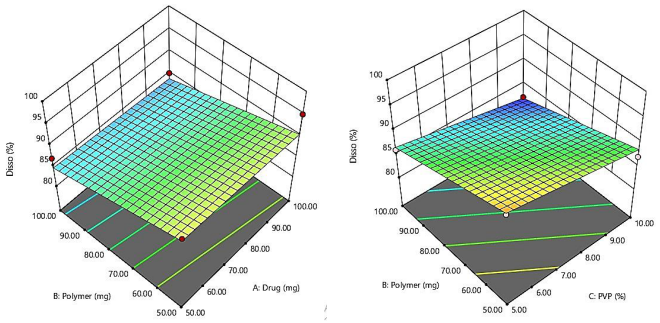

Figure 9: Response surface graph showing the consequence of (a) concentration of ibuprofen and polymer and (b) concentration of polymer and PVP K30 on percentage drug release

Table 7: Composition of optimized formulation

Factor	*Name*	*Level*	*Low level*	*High level*	*Std. dev.*
A	Ibuprofen	70.65	50.00	100.00	0.0000
B	Artocarpus polymer	63.03	50.00	100.00	0.0000
C	PVP K30	9.87	5.00	10.00	0.0000

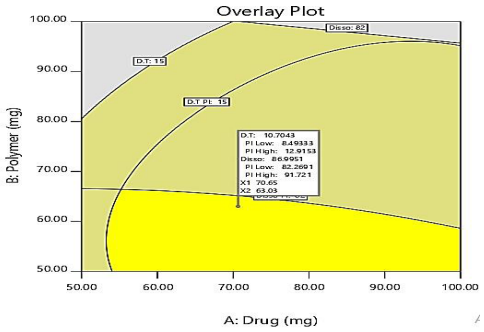

Figure 10: Overlay plot of the Tablet formulation.

The overlay plot for the tablet formulation design suggested the values for ibuprofen (X1) to be 70.65 mg, artocarpus Polymer (X2) to be 63.03 mg, and PVP (X3) to be 9.87 (Figure 10). The predicted value of the disintegration time according to the plot was 10.7 min. and for the percentage of drug release, the predicted value was 87% (Figure 11 and 12).

The predicted values for desirability were 1, disintegration time was 10.7 minutes and percentage of drug release was 86.99%. The experimental values had to be close to these values.

Post-compression evaluation results are shown in Table 9. The post-compression characteristics of the prepared formulations were found to be within the range compared with the official monograph for uncoated Tablets.

Drug Release of the Prepared Formulations

In-vitro drug release studies are performed after preparing four different optimized formulations and the drug release for the

Table 8: Composition of the optimized tablet formulation

S. no	*Ingredients*	*Quantity (mg)*
1	Drug	70.65
2	Polymer	63.03
3	PVP (%w/v)	9.87 (%w/v)
4	Magnesium stearate	45
5	Talc	21

Table 9: Post-Compression evaluation of tablet formulation

S.No.	*Parameters*	*Results*
1	Hardness (kg/cm^2)	5.90 ± 1.00
2	Thickness	10.25 ± 0.05
3	Friability (%)	0.65 ± 0.32
4	Tablet Thickness	3.97 ± 0.11
5	Weight Variation (mg)	220 ± 1.05
6	Content Uniformity (%)	99.8 ± 0.63
7	Disintegration Time (min)	9.59 ± 1.01

Values are in mean ± SD. (n=3) (SD = standard deviation)

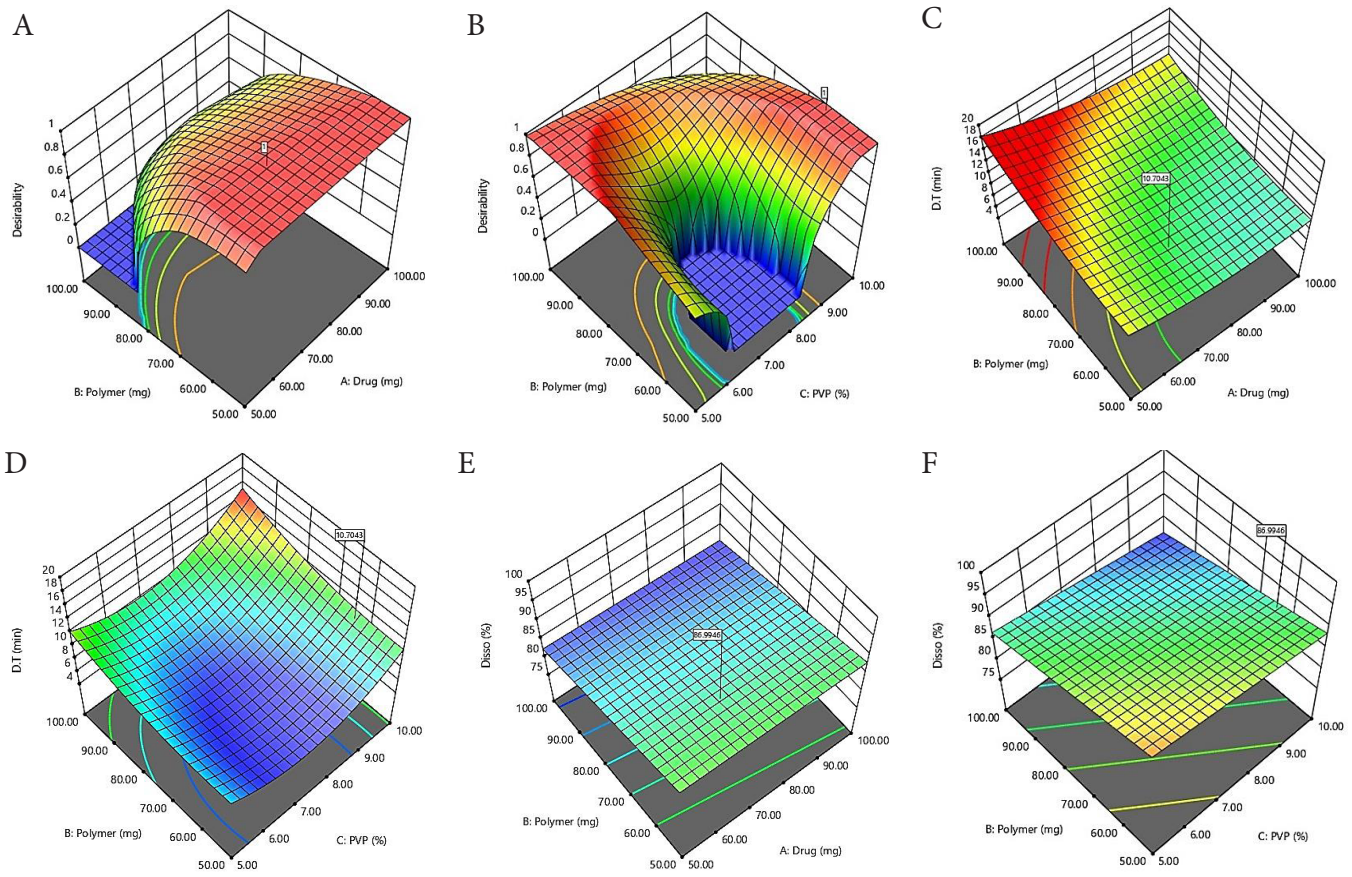

Figure 11: Response surface graph showing (a) desirability of the drug and polymer of optimized formulation (b) desirability of polymer and PVP K30 (c) predicted value drug and polymer for disintegration time (d) predicted value of polymer and PVP K30 for disintegration time (e) predicted value of drug and polymer for dissolution (f) predicted value of polymer and PVP K30 for dissolution

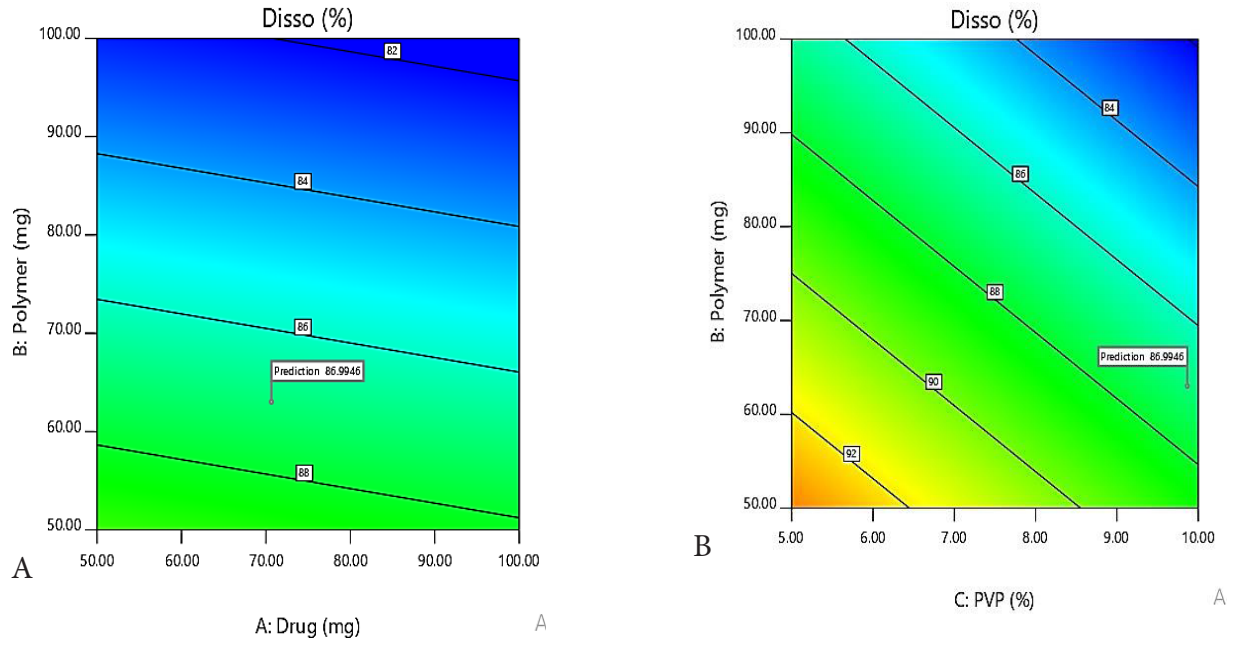

Figure 12: (a) Predicted value of drug and polymer for dissolution (b) predicted value of polymer and PVP K30 for dissolution

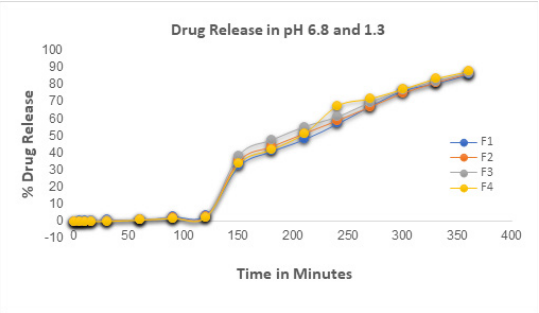

Figure 13: Drug release of optimized formulations

F1, F2, F3, and F4 were found to be 86, 86.5, 86.8, and 87% in pH 6.8 buffer for 8 hours which meets its criteria as shown in the overlay plot.

CONCLUSION

An attempt was to develop the colon-targeted Tablet of Ibuprofen by using the polymer isolated from *A. heterophyllus.* The drug release from the Tablet in upper GIT is restricted by coating the core Tablet with a pH-dependent polymer. The organoleptic and precompression properties i.e., angle of repose, bulk density, tapped density, carr's Index, and sewllability were determined and found and found satisfactory. The Box -Behnken design was implemented by taking 3 factors that are drug, polymer, and PVP, and 2 responses included disintegration time and percentage of drug release. Four formulations of optimized Tablet formulation were prepared and *in-vitro* dissolution studies. The optimized formulation is coated with 5% w/v Eudragit S100 solution by using Isopropyl alcohol as a solvent. were carried. Percentage drug release in HCL buffer pH 1.2 was found to be zero due to the coating of Eudragit S100 for the starting two hours. In four formulations F1, F2, F3, and F4 the percentage of drug release was found to be 86, 86.5, 86.8 and 87% which were within limits as per the data obtained in the optimized formulation by using the design of experiment software and target of achieving colon targeted drug delivery were also obtained and thus concluded that due to the insoluble behavior and swelling property of the polymer it can sustain the drug release into the colon.

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Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest in this work.

REFERENCES

1. Krishnaiah YSR, Indira Muzib Y, Srinivasa Rao G, Bhaskar P, Satyanarayana V. Design and in vitro evaluation of oral colon targeted drug delivery systems for tinidazole. J Drug Target 2002;10:579-84.
2. Bushra R, Aslam N. An overview of clinical pharmacology of ibuprofen. Oman Med J 2010;25:155-61.
3. Rivai H, Kardela W, Kartanti A. Development and validation of analysis method for Tablet ibuprofen by thin layer chromatography-densitometry. J Chem Pharm Res. 2016;8:324-9.
4. Prakash O, Kumar R, Mishra A, Gupta R.Artocarpus heterophyllus (Jackfruit)_ An overview. Phcog Rev 2009;3:353-8.
5. Pathare B, Tambe V, Waichal D, Chanshetti R, Pujari R. Formulation and evaluation of sustained release mucoadhesive microspheres of lornoxicam by using novel isolated polymer of fruit artocarpus heterophyllus. Int J Pharm Chem Anal 2020;5:43-51.
6. Ren Y, Jiang L, Yang S, Gao S, Yu H, Hu J, et al. Design and preparation of a novel colon-targeted Tablet of hydrocortisone. Brazilian J Pharm Sci 2017;53:1-11.
7. Ponrasu T, Gu JS, Wu JJ, Cheng YS. Evaluation of jelly Figure polysaccharide as a shell composite ingredient of colon-specific drug delivery. J Drug Deliv Sci Technol 2021;61:101679.
8. Bahir SS, Wayal SR, Barke SA, Shelke TT, Gunjegaonkar SM, Hadke SP, et al. Preliminary phytochemical investigation of semecarpus anacardium linn. Int J Pharm Pharm Sci 2013;5:102-7.
9. Zhu K, Zhang Y, Nie S, Xu F, He S, Gong D, et al. Physicochemical properties and in vitro antioxidant activities of polysaccharide from Artocarpus heterophyllus Lam. pulp.Carbohydr Polym 2017;155:354-61.
10. Basu SK, Adhiyaman R. Preparation and Characterization of Nitrendipine- loaded Eudragit RL 100 microspheres prepared by an emulsion-solvent evaporation method. Trop J Pharm Res 2008;7:1033-41.
11. Kar NR, Dinda SC. Formulation design and characterization of colon-targeted mesalamine microspheres and their biodistribution potential study in mice. Asian J Pharm 2018;12:S1481-4.
12. Mukprasirt A, Sajjaanantakul K. Physico-chemical properties of flour and starch from jackfruit seeds (Artocarpus heterophyllus Lam.) compared with modified starches. Int J Food Sci Technol 2004;39:271-6.
13. Wiater A, Paduch R, Trojnar S, Choma A, Adamczyk P, Pi M, etal.The effect of water-soluble polysaccharide from Jackfruit (*Artocarpus heterophyllus* lam.) on human colon carcinoma cells cultured in vitro. *Plants* 2020; 9:1-16.
14. Roy H, Abdul Rahaman S. Box-Behnken design for optimization of formulation variables for fast dissolving Tablet of urapidil. Asian J Pharm 2018;12:S946-54.
15. Nath B, Nath LK. Design, development and optimization of oral colon targeted drug delivery system of azathioprine using biodegradable polymers. Pharm Dev Technol 2013;18:1131-9.
16. Sivakumar K, Koumaravelou K.Formulation Development and in vitro-in vivo studies on colon targeted oral delivery system of atorvastatin. J Pharma Sci Res 2018;10:2401-6.
17. Kotla N.G., Gulati M., Singh S.K. SA. Facts, fallacies and future of dissolution testing of polysaccharide based colon-specific drug delivery. J Control Release 2014;178:55-62
18. Desai PM, Puri V, Brancazio D, Halkude BS, Hartman JE, Wahane A V, et al. Tablet coating by injection molding technology – optimization of coating formulation attributes and coating process parameters. Eur J Pharm Biopharm. 2018;122:25-36.
19. Elkhodairy KA, Afifi SA, Zakaria AS. A promising approach to provide appropriate colon target drug delivery systems of vancomycin HCl: pharmaceutical and microbiological studies. Biomed Res Int 2014:1-14.
20. Ramteke KH, Jadhav VB, Kulkarni NS, Kharat AR, Diwate SB. Preparation, evaluation and optimization of multiparticulate system of mebendazole for colon targeted drug delivery by using natural polysaccharides. Adv Pharm Bull 2015;5:361-71.