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RESEARCH ARTICLE
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PREPARATION AND EVALUATION OF METOPROLOL SUCCINATE TABLETUSING JACKFRUIT MUCILAGE

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Abstract
The aim of the current research work was to isolate and evaluate Jackfruit mucilage to develop metoprolol succinate tablets using varying concentration of jackfruit mucilage. Tablets containing 50mg drug were prepared by wet granulation method. Compatibility study was carried out by using FTIR and confirmed that no chemical interaction took place during entrapment process. Pre-compression parameters like Bulk density, Tapped density, Carr's index, Hausner's ratio, and angle of repose were evaluated and post-compression parameters like Friability, Hardness, Thickness, Diameter, Weight variation, Disintegration, and Drug content estimation and Dissolution were evaluated and the results were within the acceptable official limits. In-vitro drug release was carried out by using USP dissolution rate apparatus type- II using two different dissolution media (0.1 N HCl and phosphate buffer of pH 6.8). In-vitro drug release shows, as the concentration of jackfruit mucilage increases, drug release decreases. The drug release follows first order kinetics and mechanisms was found to be supercase II. The stability studies were carried out for two months. In conclusion result suggested that formulation containing jackfruit mucilage delayed the drug release could therapeutically better than conventional dosage form leading to improved efficacy and better patient compliance.

Keywords: Sustained release tablet, Metoprolol succinate, Jackfruit mucilage,Wet granulation.

INTRODUCTION

Over the past 30 years, as the expense and complication involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of sustained release or controlled release drug delivery systems. The attractiveness of these dosage forms is due to awareness to toxicity and ineffectiveness of drug when administered or applied by conventional dosage form of tablets, capsules, injectables, ointments etc.

Usually, conventional dosage forms produce wide ranging fluctuation in drug concentration in the blood stream and tissue with consequent undesirable toxicity and poor efficiency. This factor as well as factors such as repetitive dosing and unpredictable absorption led to the concept of controlled drug delivery system. (1, 2, 3)

The goal in designing sustained or controlled delivery system is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing thedose required or providing uniform drug delivery. So, the controlled release dosage form is a dosage form that release one or more drugs continuously in a predetermined pattern for a fixed period of time, either systemically or to a specified target organ. (4, 5, 6) Controlled release dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effects, increased efficacy and constant delivery. (7, 8)

MATERIALS AND METHODS

ISOLATION OF MUCILAGE FROM JACKFRUIT:

In the month of June, the local market was where the fresh fruits were purchased. To get rid ofdirt and other debris, the fruits were carefully cleaned with water. The fruit's seeds were takenout before eating. Fruit pulps were cut into slices and dried in an oven at 35°C until totally dry. gathered, crushed, sieved through #80, and stored in a desiccator until use.

i) Determination of Jackfruit mucilage viscosity: Using a Brooke field viscometer at variousrpms, the viscosity of 3% aqueous jackfruit mucilage was measured. (9, 10)

FORMULATION DESIGN

Every tablet was produced using the wet granulation process. For each batch of 20 tablets, calculations were done.

i) **Preparation of starch paste:** Using a water bath over boiling water, the necessary amount of starch powder was added until the mixture had the consistency of paste. The resulting combination was then utilised to create a binder solution for granule preparation.

ii) **Preparation of damp mass:** Each time, the starch paste was added after precisely weighed amounts of metoprolol succinate, dicalcium phosphate, microcrystalline cellulose, bentonite, jackfruit mucilage and magnesium stearate, had been combined in a mortar to form a damp cohesive mass. The moist mass was sieved through a 1.7mmsieve and baked for 30 minutes at 37°C.

iii) **Punching of Tablets:** To get granules of the same size, the dried granular material was run through a 1.0 mm sieve. The various batches of granules were then combined with calculated equal amounts of talc, and using a pilot press machine (Lab Press Multi punch machine, India), using 12 mm diameter, flat faced punches at a pressure of roughly 5kgs/cm, the mixture was then compressed into tablets. (11, 12, 13)

Table 1: Formulation Chart

S. No.	Ingredients (mg)	MT1	MT2	MT3	MT4	MT5	MT6
1	Metoprolol succinate	50	50	50	50	50	50
2	Dicalcium phosphate	45	25	25	25	25	20
3	MCC	55	50	45	40	35	30
4	Bentonite	-	26	26	26	26	26
5	Talc	5	2	2	2	2	2
6	Mag. stearate	5	2	2	2	2	2
7	Starch paste	q.s	q.s	q.s	q.s	q.s	q.s
8	Jackfruit mucilage	-	5	10	15	20	25
9	Total weight	160	160	160	160	160	160

PRE-COMPRESSION EVALUATION [14, 15, 16]

i) Bulk Density (Bd):

$$Bd = M/V$$

Where,

M = weight of samples in grams,

V= bulk volume of powder in cm^3

ii) Tapped density (Td):

$$Td = M/ Vp$$

Where,

M = weight of samples in grams and

Vp = final tapped volume of powder in cm^3

iii) Carr's Index

CI =100 (Td- Bd) / Td

iv) Hausner's ratio (HR):

$$HR= V_O / V_f$$

Where,

V_O: unsettled apparent volume,

V_f: final tapped volume

v) Angle of Repose:

$$\Theta = \tan^{-1} h/r$$

Where, h and r are the height and radius of the powder cone respectively.

POST COMPRESSION EVALUATION (17, 18, 19, 20)

Appearance: Color and odour were assessed as organoleptic qualities. Ten pills were randomly chosen from each batch, and their colours and odours were compared.

Hardness: The fpizer hardness tester was used to measure hardness. Five pills per batch were utilised.

Dimensions: Using a Digital Vernier Caliper, the tablet's diameter and thickness were measured. Five of the formulation's pills were chosen at random, and each one was measuredseparately.

Friability: Twenty tablets were weighed and put in the Roche friabilator, which was circulated for 4 minutes at a speed of 25 rpm. The tablets were dusted off, then weighed oncemore. The formula was used to calculate the percentage of friability:

$$F = \{1-(W_t /W)\} \times 100$$

Where, F = Friability in percentage W = Initial weight of tablets W_t= Weight of tablets after friabiation.

Drug Content Estimation: Metoprolol succinate sustained release tablets weighing 150 mg are weighed, dissolved in a little amount of methanol in a 100 ml volumetric flask, sonicated for 5 minutes, and then the volume was increased to 100 ml with 0.1N HCl and then filtered through membrane filter; Following further dilutions, absorbance is measured at 278 nm against a blank solution of 0.1 N HCl, and the drug content is estimated using a standard curve". Each test is carried out three times.

% Drug content = actual drug content in tablet/theoretical amount of drug in tablet x 100

Weight Variation Test: From the entire batch, 20 pills were randomly chosen, weighed separately, and their average weight was calculated. Calculated was each tablet's weight's %departure from the average weight. If no more than two of the individual weights vary fromthe average weight by more than 5%, the test conditions are met.

Weight variation = Average weight -tablet weight / tablet weight x 100

Disintegration test: Using disintegration test equipment in accordance with the USP, the disintegration time was measured. Each tube in the basket contained one tablet. The mesh number 10 stainless steel screen-bottomed basket was submerged in water that was 37±2°C. The amount of time needed for the tablet in each tube to completely dissolve was calculated.

In-vitro Dissolution Studies: Using a paddle, the USP XXIII dissolving type II device was used to dissolve the tablets. The dissolution medium was maintained at a temperature of 37 ±0.5 °C and contained 900 ml of pH 1.2 buffer (N 0.1HCl) for the first two hours and phosphate buffer pH 6.8 from three to twelve hours. The paddle's rotational speed was set to 50 rpm. At predefined intervals of 1 hour to 10 hours, 5ml of the sample was removed, and the same volume of fresh medium was substituted. The withdrawn samples were diluted to 0 ml with pH 6.8 filtered and then examined at 278 nm using a pH 6.8 blank on a UV spectrophotometer. Calculated was the cumulative drug release percentage.

DATA ANALYSIS

The data were fitted into Higuchi matrix, Korsmeyer's, first-order, zero-order, and peppa's models in order to investigate the mechanism of release and release rate kinetics of the dosageform. The 'R'-value was used to choose the best-fit model. (21, 22)

RESULTS AND DISCUSSION

Drug - Excipients Compatibility: It is possible to identify both organic and inorganic substances using FT-IR spectroscopy. It can be used to evaluate solids, gases, and liquids as well as to quantify some components of an unidentified mixture. Metoprolol succinate's typical FTIR spectra as observed in LP was discovered to be identical to the spectrum of the drug's pure form. Figures 1, 2, and 3 display the individual FT-IR spectra of the medicine Metoprolol succinate as well as the combined spectra of the drug and mucilage. Since the FT-IR spectra revealed no new functional group peaks, showing that there was no chemical interaction between the medication and the mucilage, stable formulation could be created.

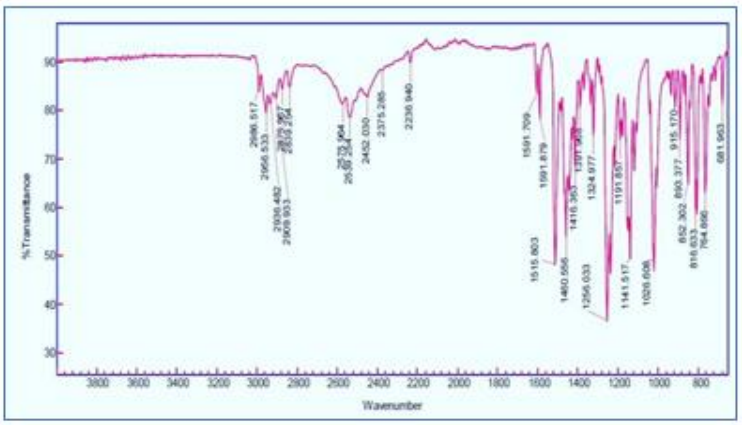

Figure 1: FT-IR spectra of Metoprolol succinate

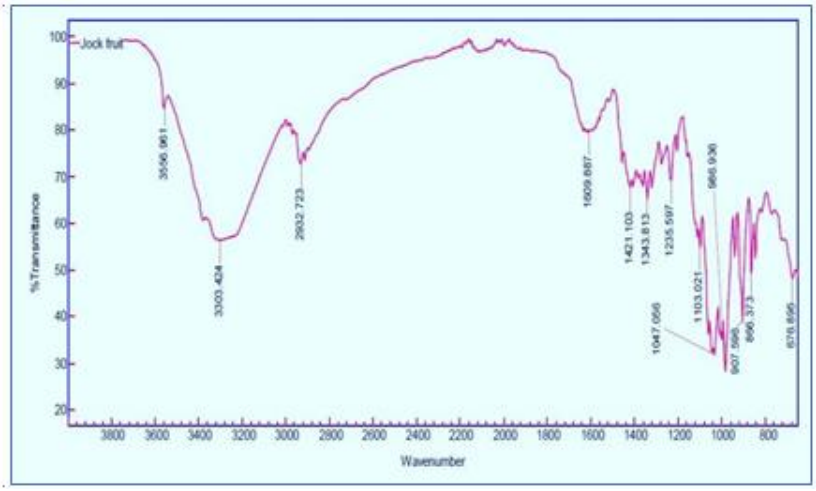

Figure 2: Jackfruit mucilage FT-IR Spectra

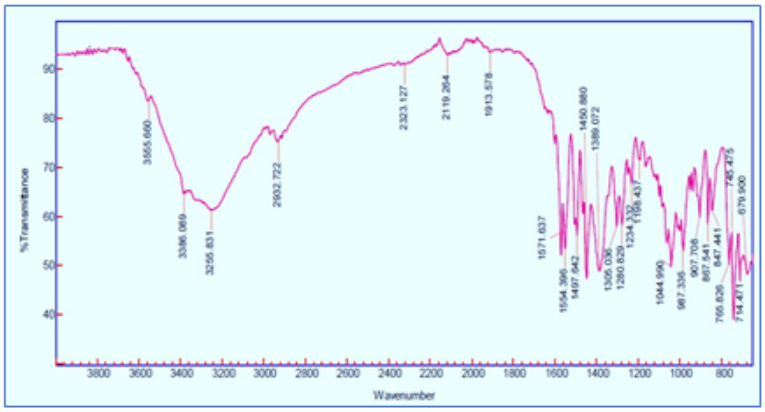

Figure 3: FT-IR Spectra of Drug + Jackfruit mucilage

E) Viscosity of Jackfruit mucilage: Mucilage's viscosity increases as the number of rotations decreases.

F)

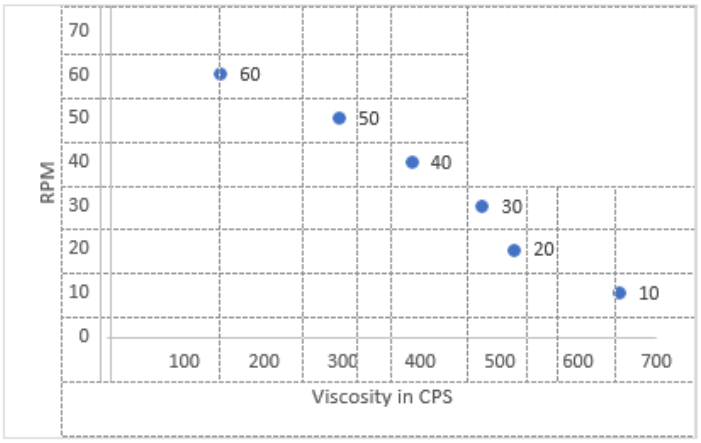

Figure 4: Viscosity of Jackfruit mucilage

PRE-COMPRESSION EVALUATION PARAMETERS

Table 2 displays the findings for all formulations MT1 to MT6, which were assessed for variable characteristics such bulk density, angle of repose, tapped density, percent compressibility index, and Hausner's ratio.

- Carr's index: Carr's index ranged from 13.49 to 7.24, showing that all formulations werefound to fall within the acceptable range.

- Angle of repose: All formulations were determined to fit with respect to flow property, with an angle of repose of all formulations between 23° and 28° suggesting reasonableflow property.
- Hausner 's Ratio: HR was between 1.14 to 1.20.
- Tapped density: TD of all formulation was in between 0.55 to 0.632.
- Bulk density: BD of all formulation was in between 0.476 to 0.529.

Table 2: Pre-compression parameters results

F. Code	Angle of Repose (°)	Hausner'sratio	Carr's index %	Tapped density(g/cm^3)	Bulk density(g/cm^3)
1	27.65 ± 0.04	1.15	13.65± 0.26	0.633± 0.45	0.524± 0.21
2	23.59 ± 0.03	1.11	17.52± 0.11	0.623± 0.34	0.528± 0.18
3	26.76± 0.11	1.14	14.79± 0.32	0.598± 0.76	0.533± 0.11
4	24.98± 0.31	1.20	16.50± 0.12	0.627± 0.18	0.519± 0.06
5	28.36± 0.45	1.19	14.98± 0.76	0.589± 0.84	0.498± 0.03
6	23.87± 0.09	1.13	16.45± 0.56	0.645± 0.71	0.522± 0.87

POST-COMPRESSION EVALUATION PARAMETERS

Variable physiochemical characteristics like colour, odour, and shape were assessed for all formulations from MT1 to MT6. All of the formulas were discovered to be round, flat, and odourless, with a cream tint. The results are shown in Table 3.

Table 3: Physicochemical Properties of tablets

F. Code	Colour	Odour	Shape
MT1	Cream	Odourless	Flat and round
MT2	Cream	Odourless	Flat and round
MT3	White	Odourless	Flat and round
MT4	Cream	Odourless	Flat and round
MT5	Cream	Odourless	Flat and round
MT6	White	Odourless	Flat and round

Results from the evaluation of the formulations MT1 to MT6 for variable characteristics, including weight fluctuation, hardness, thickness, friability, drug content, and disintegration, are tabulated in Table 4.

- Weight variation: The weight variance of tablets across all formulations was found tobe between 157 and 60 mg, indicating that it is within pharmacopoeia restrictions.
- Hardness: Hardness was found to be in the range of 4.03± 0.02 to 5.23± 0.03.
- Thickness: All formulations were found to have thicknesses between 3.11 and 3.44.
- Friability: Friability ranges from 0.32 to 0.42, showing that all formulations have friability lower than 1%.
- Disintegration Time: All formulations had disintegration times ranging from 26 to 50minutes.
- Drug content: All formulations' percentage drug concentration was found to be between 93.67 and 97.29, which was within the permissible range of established norms.

Table 4: Results of Post-Compression Study

F. Code	Thickness	Weight variation (mg)	Hardness (kg/cm^2)
MT1	3.11± 0.01	160.6± 0.61	4.03± 0.02
MT2	3.44± 0.02	158.9± 0.73	5.06± 0.01
MT3	3.18± 0.03	154.9± 0.49	4.56± 0.02
MT4	3.24± 0.03	160.2± 0.84	4.76± 0.05
MT5	3.29± 0.02	157.6± 0.045	5.23± 0.03
MT6	3.19± 0.01	158.7± 0.91	4.85± 0.02

Table 5: Post-Compression Parameter results

F. Code	Drug Content (%)	Friability (%)	Disintegration time
1	94.56± 0.41	0.32± 0.01	26 min
2	93.67± 0.11	0.39± 0.05	48 min
3	95.82± 0.42	0.42± 0.04	43 min
4	97.29± 0.15	0.37± 0.10	36 min
5	95.78± 0.32	0.35± 0.04	50 min
6	96.78± 0.17	0.36± 0.21	42 min

IN-VITRO DRUG RELEASE PROFILE:

The in-vitro release investigation was conducted in two distinct dissolving media, including N HCl (acidic buffer pH 1.2) for two hours and then mimicked intestinal fluid for the following ten hours (phosphate buffer 6.8 pH). After two hours, formulations MT1, MT2, MT3, MT4, MT5, and MT6 in 0.1N HCl released 95.87%, 97.64%, 95.86% 90.11% and 82.65 percent of the medication, respectively. Because there was no retardant mucilage in Formulation MTl, the majority of the drug was released at the end of 2 hours. In contrast, Formulation MT2 released 97.64% of the drug in 6 hours, Formulation MT3 released 95.86%of the drug in 10 hours, and Formulation MT4, MT5, MT6 released 95.86%, 90.11%, and 82.65% of the drug after 12 hours.

The results demonstrated that as more mucilage was added to each formulation, the amount ofdrug release from those formulations reduced. Comparing all formulations, Formulation MT6exhibits the slowest drug release. According to the drug release profile, formulation MT4 was deemed to be optimum because it releases 95.86% of the drug after 12 hours. Table 7.10 and Figure 7.8 display all formulations' in-vitro drug release data.

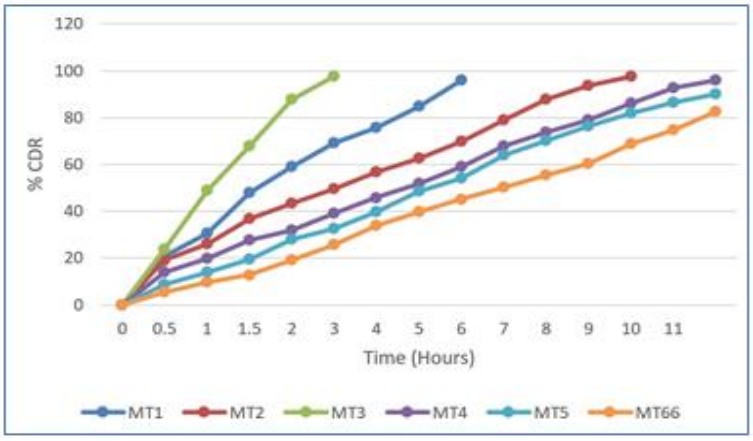

Figure 5: In-vitro Formulations MT1 to MT6RELEASE KINETICS:

Four distinct mathematical methods for data treatment were used to plot the outcomes of in- vitro drug release:

- % Cum. Drug Release Vs. Time (Zero order rate kinetics)
- Log % Cum. Drug Retained Vs. Time (First order rate kinetics)
- % Cum. Drug release was plotted against >Jr (root time). (Higuchi model)
- Log % Cum. Drug Release Vs. Log Time (Peppas exponential equation)

The Figure 6, 7, 8 and 9 display the results of the curve fitting of the developed formulation's release rate profile, which provided information on the release rate and mechanism of release.

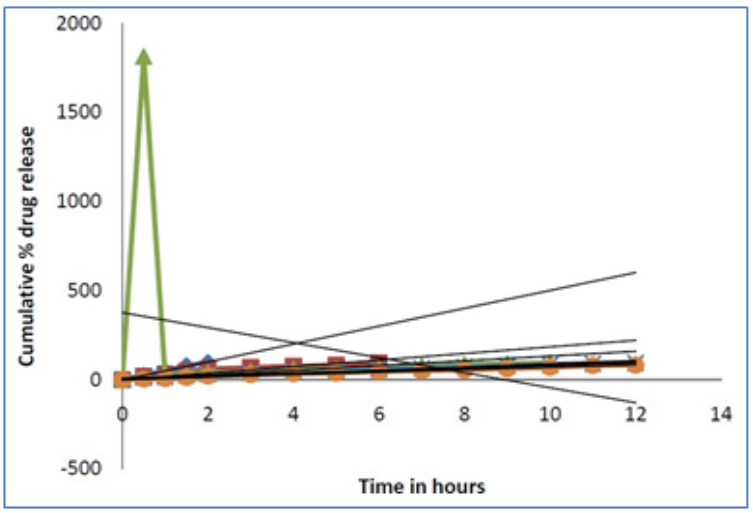

Figure 6: Zero order graph

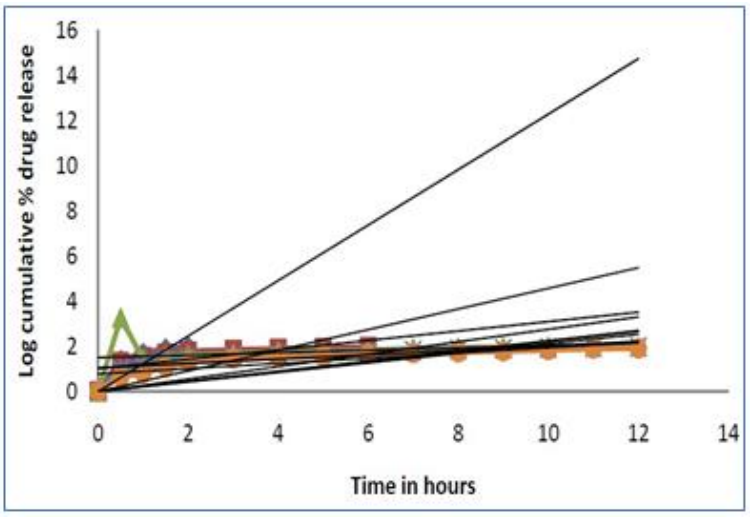

Figure 7: First order graph

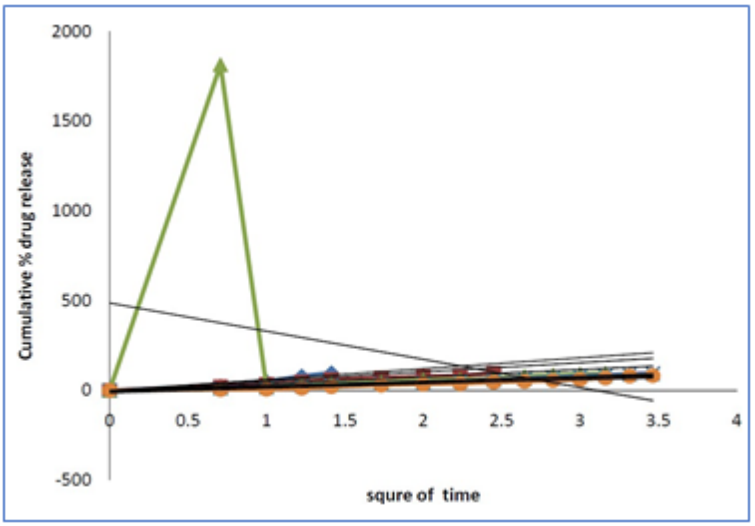

Figure 8: Higuchi graph

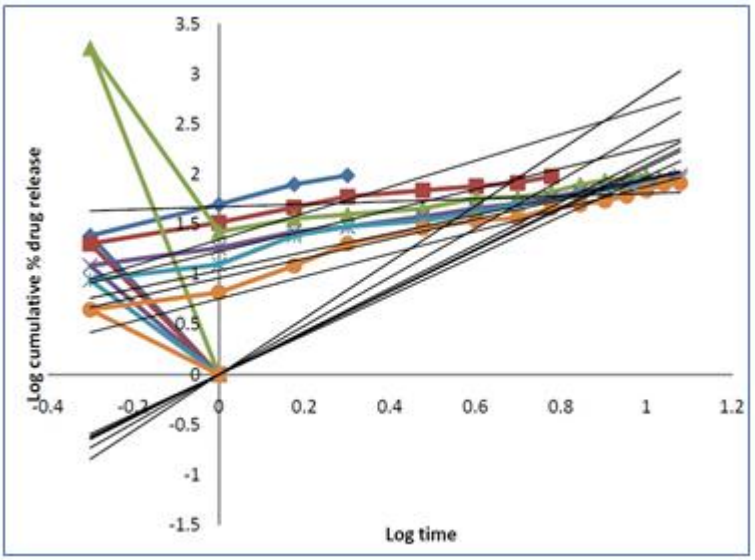

Figure 9: Peppas graph

CONCLUSION

A prospective replacement for traditional medicine delivery methods that continuously releases their active component over an extended period of time is the sustained release dosage form. The current work describes an innovative effort to extract Jack fruit-based mucilage from other plants. To create sustained release tablets of metoprolol succinate, varying concentrations of the produced mucilage were used as binders. Wet granulation was used to create tablets of metoprolol succinate for sustained release. In order to achieve sustained release of metoprolol succinate, various assessment criteria were evaluated. Previous chapters have covered specifics relating to the formulation and evaluation of sustained release tablets of metoprolol succinate as well as the isolation of jackfruit mucilage. The study's findings allowed for the following inferences: Biocompatible jackfruit mucilage was extracted and employed as a binder to create sustained release tablets. There were no new functional group peaks in the FT-IR spectra, indicating that there was no chemical interaction between the medication and the mucilage.

REFERENCES:

1. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, 4th Edition, 121, 2005, Marcel Dekker, Inc, 501-514.
2. Thomas Wait-Yip Lee and Joseph R Robinson, Controlled Release Drug Delivery system, In the Science and Practice of Pharmacy, Volume 1, 20th edition, 2001, 903.
3. Yie W. Chein, Oral Drug Delivery System, Novel drug delivery Systems, volume 50, 2nd Edition, Marcel Dekker, Inc., 139-157.
4. Donald L. Wise, Hand Book of Pharmaceutical Controlled Release Technology, 2005, Marcel Dekker, Inc, 435-440.
5. Gwen M. Jantzen and Joseph R. Robinson, Sustained and controlled Release Drug Delivery System, In Modern Pharmaceutics, Marcel Dekker, Inc., 3rd edition, 1996, 582-593.
6. Li VHK, Robinson JR, Lee VHL, Design and Fabrication of oral Controlled Drug Delivery System, In Controlled Drug Delivery, Marcel Dekkar 1987, 2nd edition, 412.
7. Agis Kydonieus, Treatise on Controlled Drug Delivery, Marcel Dekker 1st Edition, 1992, 43-93.
8. S.P. Vyas, Roop. K. Khar, Controlled Drug Delivery Concept and Advances, 1st edition, 2002, 54-71.
9. Tabandeh H, Mortazavi S.A, Guilani T.B. Preparation of sustained-release matrix tablet of asprin with ethyl cellulose, eudragit RS100 and studying the release profiles and their sensitivity to tablet hardness. Iranian J Pharm Res 2003; 2: 201-06.

10. Shantveer V, Salger, L. S. Danki, Shivanand H, Abdul S. Preparation and evaluation ofsustained release matrix tablets of Propranolol hydrochloride. Int J of Pharm and Bio Sci. 2010; 1(4):227-241.
11. Uddin M. Development of sustained release tablet of Valsartan. World J Pharm Sci 2015;3(5):1196-1205.
12. Vinith S , Sharma S, Khokra S.L, Sahu R.K.R, Jangde R, Singh J. Formulation, dev and evaluation of Pregabalin Sustained release matrix tablets. Der Pharmacia Lettre. 2011;3(5):326-31.
13. Basavaraj, Someswara Rao B, Kulkarni S.K , Pramod P and Chetan S. Design and characterization of sustained release Aceclofenac matrix tablets containing tamarind seed polysaccharide. Asian J. Pharm Tech. 2011;1(1):17-21.
14. Rakesh P.P, Mehul H.P, Bhupendra G.P, Ashok H.B. Formulation and evaluation of sustained release matrix tablet of Tizanidine Hydrochloride by direct compression technique. e-J Sci & Tech (e-JST) 2011;6(1):69-81.
15. Avinash B, Gangurde. Preliminary characterization of Abelmoschus esculentus (L) podmucilage as O/W type emulsifier. IJAPBC.2012:1(1);36-41.
16. Madhavi N, Sudhakar B, Ravikanth PV, Mohon K, Kolapalli RM. Formulation and Evaluation of Phenytoin Sodium Sustained Release Matrix Tablet. Bioequivalence and Bioavailability. J Bioequiv Availab. 2012; 4 (7):128-133.
17. Madhavi V, Parthiban P and Veera Anjaneyulu K: Formulation And Evaluation Of Lovastatin Controlled Release Tablets". International Journal Of Pharmacy And Pharmaceutical Analysis. 2017;VOl -01(03):79-84
18. Maniruzzaman M, Slipper IJ, Vithani K, Douroumis D. Sustained release solid lipid matrices processed by hot-melt extrusion (HME). Colloids Surf B 2013;110:403-10.
19. Panchagnula R, Singh R and Ashokraj Y: In vitro evaluation of modified release formulations of nifedipine from Indian market. Indian Journal of PharmaceuticalSciences 2007; 69(4). DOI-10.4103/0250-474X.36944
20. Parikh K, P. Mundada1 and Krutika Sawant: Design and Optimization of Controlled Release Felbamate Tablets by D-optimal Mixture Design: In vitro-in vivo Evaluation. Indian J Pharm Sci 2019;81(1):71-81
21. Sahu S, Dangi R, Patidar R, Rukhsaar, Rathi J, Asati V, Formulation and evaluation ofsustain released matrix tablet of atenolol, Journal of Drug Delivery and Therapeutics. 2019; 9(1):183-189
22. Sathoskar RS, S.D, Bhandarkar, Nimala N. Rege, Pharmacology and pharmacotherapeutics, 2009, Ninth edition, 884-891.