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FORMULATION AND DEVELOPMENT OF SUSTAINED RELEASE TABLET OF BCS CLASS III DRUG BY USING NATURAL POLYMER

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ABSTRACT

The development of sustained release tablets for BCS Class III drugs, which are characterized by high solubility and low permeability, presents a unique challenge in pharmaceutical formulation. This study aims to formulate and develop a sustained release tablet utilizing natural polymers, focusing on enhancing the drug's bioavailability and therapeutic efficacy. Natural polymers offer several advantages, including biocompatibility, biodegradability, and minimal side effects, making them ideal candidates for sustained release formulations. The research involves the selection and characterization of Bhara Gum and Gum Karaya, formulation development, and comprehensive evaluation of the tablet's physical and chemical properties. Key parameters such as drug release profile, dissolution rate, and stability are assessed to ensure consistent and prolonged drug release. The goal is to achieve a formulation that provides sustained therapeutic action, reduces dosing frequency, and enhances patient compliance. This study contributes to the growing field of natural polymer applications in drug delivery systems, offering potential for improved treatment outcomes for BCS Class III drugs.

Keywords: Metformin, Sustained release, Bhara gum, Gum Karaya, Matrix Tablet.

INTRODUCTION

Sustained release dosage forms seek to create a longer therapeutic impact by releasing the medicine over an extended period of time. This therefore makes it possible to lower the overall dosage of the medication given as wellas the frequency of negative side effects (1). Which in turn improves patient compliance. On the other hand, matrix systems refer to those in whichthe medicine is evenly dissolved or distributed within a substance that delays its release.These systems can be designed as bi- or tri-layered matrix systems, (2). Standard matrix systems, or in a matrix system, the active and inactive components are combined and uniformly distributed throughout the dosage form (3).

Natural gums Because they are inexpensive, environmentally friendly, safe, non-toxic, biocompatible, biodegradable, and plentiful in nature, Natural excipients are preferredover synthetic ones, as gums are often pathological by products resulting from plant damage or poor growing conditions. These are the aberrant by products of plant metabolism, thus. "Gummosis" is the term for the process. It's likely that gum originatedfrom the

natural plant exudates that seeped out of tree bark. Palants create transparent, amorphous substances called gums. Gums can dissolve in water completely or partially.Most organic solvents and alcohol do not dissolve them. When combined with water, they either swell or absorb water, forming viscous sticky solutions. Typically, an aqueous gum solution is laevorotary; they are Guar gum, gum ghatti, tragacanth, gum acacia, and gum are significant gums in the pharmaceutical industry. Neem chewing gum Moringa leaf. In general, gums are employed mostly in the printing, textile, paper, paint, confectionery, food, and pharmaceutical sectors as thickening agents or adhesives. They serve as stabilisers, thickening agents, emulsifiers, suspending agents,and tablet binding agents.

There are three main types of gums: modified gums, synthetic gums, and natural gums.

Natural gums: These come from extracts of some legume seeds, seaweed hydrocolloids, or tree exudates in their natural condition. Examples include neem gum, tragacanth, moringa gum, and Arabica gum.

Modified gums: They are natural gums that have undergone chemical modification or are made from substances that are found naturally, such starch or cellulose. For example, carboxymethylcellulose.

Synthetic Gums: These are entirely artificial chemical compounds. For example, polyethylene oxide and polyvinyl pyrrolidone (5).

MATERIALS AND METHODS

Metformin hydrochloride

Metformin HCI is a biguanide-type drug used along with a diet and exercise program to control high blood sugar in patients with type 2 diabetes. Controlling high blood sugar helps prevent heart disease, strokes, kidney disease, blindness, circulation problems, and sexual function problems. To reduce frequency of administration and to improve patient compliance, a sustain release formulation is required.

Materials: Metformin Hydrochloride Bhara gum, Gum Karaya Magnesium stearate, Talc, Starch, ethyl cellulose, Microcrystalline Cellulose,

Table 1 Formulation study and development of trial batches

Ingredient	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**	**F4 (mg)**	**F5 (mg)**	**F6 (mg)**
Metformin HCL.	500	500	500	500	500	500
Bhara Gum	90	135	180	-	-	-
Gum Karaya	-	-	-	90	135	180
Carrageenan	184	139	94	184	139	94
Talc	18	18	18	18	18	18
Ethyl Cellulose	36	36	36	36	36	36
Magnesium Stearate	18	18	18	18	18	18
Chitosan	36	36	36	36	36	36
Starch	18	18	18	18	18	18
	900	900	900	900	900	900

Method of preparation of sustained release tablet of Metformin HCL:

The sustained release tablet of Metformin Hydrochloride was formulated by using wet Granulation method (6,7). The active ingredient was passed through the sieve#40 followed by the other ingredients were passed the same sieve. Metformin Hydrochloride, Carrageenan, (8,9). Chitosan, Bhara gum, Gum karaya, Ethyl cellulose, and Micro crystalline cellulose were taken in a poly bag according to the formulation table and mixed for 5minutes to ensure uniform mixing of the ingredients with the drug (10,11). Weigh Starch accurately (22) and it is mixed with water to form a paste is used as binder solution and kept separately (12, 13). The binder solution was added slowly to the dry mixed ingredients with constant mixing till to get solid mass to form uniform and optimum granules (14, 15). Then the wet granules were dried in trays and pass the air for drying Samples were removed randomly at different time intervals from the total bulk of the granules and then checked out for moisture content (16, 17). The dried materials were passed through the sicvc#20. After sieving dry granules were lubricated using Magnesium stearate and Talc (18, 19). After lubrication granules were sent to compression. Metformin Hydrochloride tablets was compressed using 12mm round punch (20, 21).

Evaluation of Metformin Hydrochloride Tablets

Appearance: The thickness of tablet and dimensional variable was evaluated. The tablet thickness was controlled within average value. The colour, odour, texture are other important characteristics were observed

Hardness: Tablet Tester Tablet requires certain amount of mechanical strength or hardness, which was measured by Monsanto Hardness Tester. Ten tablets were randomly picked from batch formulation batch and evaluated for hardness during manufacturing and expressed in Kg/cm². For each batch five tablets were used

Thickness: The thickness of tablet and diameter were measured by digital Vernier calliper apparatus.

Friability: The 10 reweighed tablets were placed in the Roche friabilator, which were then perated for 100 revolutions (25 rpm). The tablets were then dusted and reweighed. The tablets dukes less than 1.0% of their weights are generally considered acceptable

Friability = [1- (Wt. /W)]* 100 Where,

F friability in percentage

W = initial weight of tablet,

Wt. = weight of tablet after friability

Weight Variation test: To study weight variation test according to IP the test was run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weight to the average.

Table 2 Weight Variation test

Average weight of tablet (mg)	Maximum percent difference allowed
80 or less	10%
80-250	7.5%
250 or more	5%

Uniformity in Drug Content: From each batch of prepared tablets, five tablets were collected randomly and powdered. A quantity of powder equivalent to 250 mg was transferred to 100 ml volumetric flask. 10 ml of 0.1 N HCL was added and then the solution was subjected to sonication for 10 min. The solution was made up to 100 ml with 0.1 N HCL. The solution was filtered and suitable dilutions were prepared with 0.1 N HCL and then the drug content was estimated by recording absorbance at 239 nm by using UV- spectrophotometer.

Dissolution study: The in vitro release of dissolution studies from the formulated tablets was carried out in Tablet dissolution tester USP- Electro lab USP-TOT-081, using 900 ml of dissolution medium maintained at 37.0 +0.5°C at a stirring rate of 50 rpm. One tablet from each formulation were rested individually in 0.1 N HCL for the first 2 hr. and in phosphate buffer (pH 6.8) for the following 10 hr. Samples measuring 5 ml were withdrawn at different time intervals such as 15 min 30 min, 1 hr.2 hr. During sampling samples were filtered through 10 um filter. The fresh dissolution medium (37 C) was replaced every time with the same quantity of the sample Collected Samples were suitably diluted with purified water and analyzed at 233 nm using 0.1 N HCL as blank. Dissolution is continued till 12 hr. by withdrawn sample at 3 to 12 hours by following the same procedure by using pH 6.8phosphate buffer as the cumulative percentage drug release was calculated.

RESULT AND DISCUSSION

Pre-formulation Study

Organoleptic Properties of natural gum: The organoleptic characteristics of Bhara gum and Gum karaya like state, colour, odour and taste were studied as shown in following table.

Table 3 Organoleptic characteristics of Bhara gum and Gum karaya

Parameter	Bhara gum	Gum karaya
State	Translucent	Translucent
Colour	Yellowish	White or pale
Odour	Myrtales	odourless
Taste	Tasteless	Tasteless

Physicochemical evaluation of Bhara gum and Gum karaya

Table 4 Evaluation of gum

Parameter	Bhara gum	Gum karaya
Bulk density (g/ml)	0.59	0.30
Tapped density (g/ml)	0.86	0.98
Angle of repose (0)	23	38.73
Compressibility index (%)	17.66	10.55
Swelling index	7.4	1.02
Loss on drying (% w/w)	3.96	4.5
Total ash (% w/w)	5.8	2.2
pH	4.8	4 - 8

Preformulation study of Metformin Hydrochloride

Organoleptic properties of Metformin Hydrochloride

The organoleptic characteristics of drug like colour, odour and taste were studied as shown in following table.

Table 5 Organoleptic Characteristics of Drug

Parameter	Observation
Colour	White-off-white
Odour	Characteristic
Taste	Bitter

FTIR Studies:

Infra-red spectroscopy is one of the most powerful analytical techniques to identify functional groups of drugs. IR spectroscopy was conducted using a FTIR and the spectrum was recorded wavelength region 4000-400cm. The procedure consisted of disappearing a sample alone. The sample was placed in light path in sample holder and the spectrum was recorded. The FTIR spectrum of drug shown in figure. The peaks observed in figure are listed in table and can be considered as characteristics peaks of each sample. These peaks were compared with the individual peaks. (12). The IR spectra of drug and polymers (Bhara gum & Gum karaya) were recorded in combination with each other's.

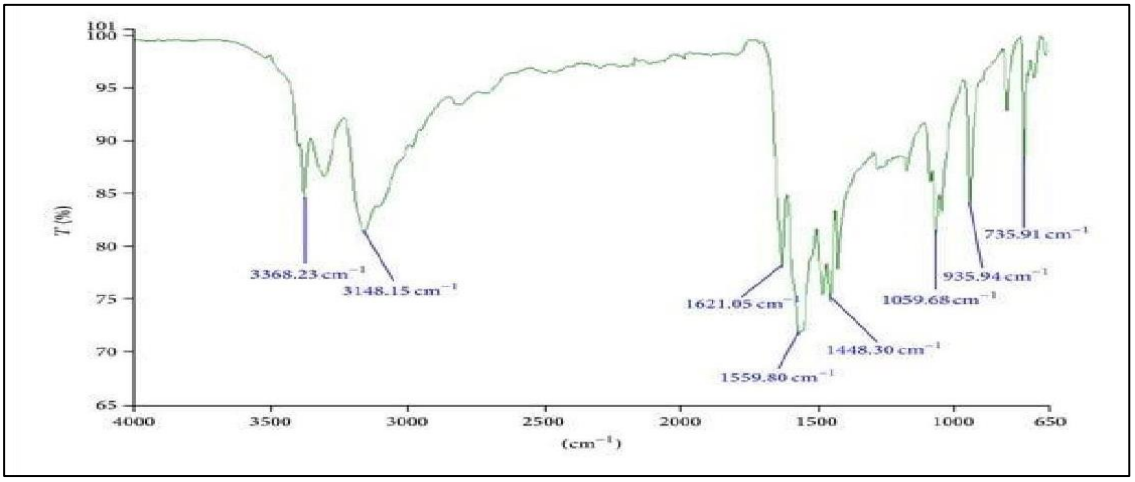

Figure 2 IR Spectrum of Metformin Hydrochloride

Table 6 characteristic peaks of Metformin HCL

Functional group	Observed frequency (cm^1)	Stretching/ Deformation
-NH Amine (3550-3250	3368.23	Stretching
()-H (3500-3200)	3148.15	Stretching
-NH deformation (1650-1581)	1621.05	Deformation
-CN Stretching (1170-1040)	1059.68	Stretching
-CN Stretching (1170-1040)	935.94	Stretching
= C-H (1000-650)	735.91	Bending

Table 7 Absorbance of Metformin Hydrochloride in Distilled Water

Concentration in PPM	**Absorbance**			
	I	II	III	Mean
02	0.214	0.289	0.312	0.271
04	0.518	0.518	0.532	0.522
06	0.740	0.808	0.789	0.779
08	1.004	1.020	1.048	1.024
10	1.229	1.292	1.408	1.309
12	1.554	1.541	1.602	1.565
Co-efficient of Correlation(r2)			0.998	
Equation of Line (y=mx+c)			Y=0.0737× + 0.0628	

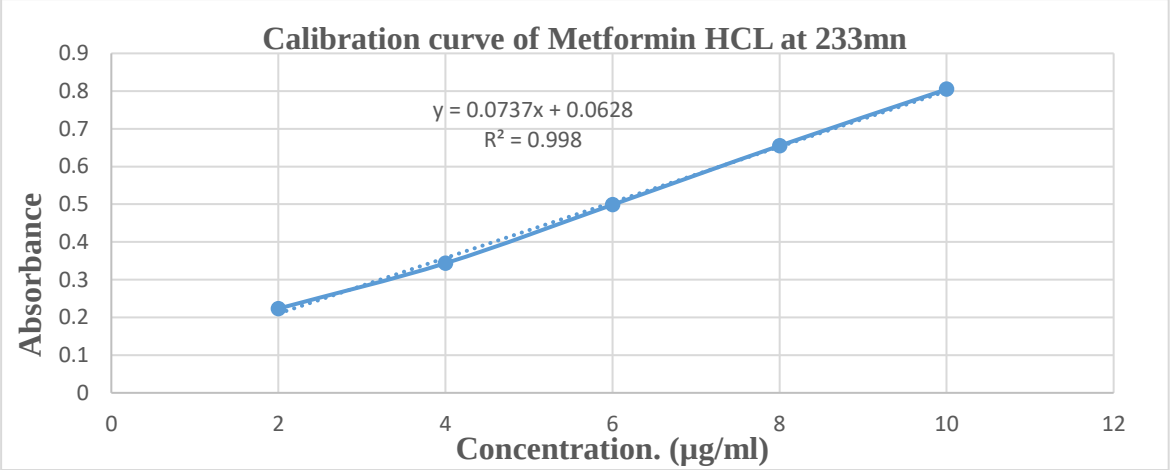

Figure 3 Calibration Curve of Metformin Hydrochloride in Distilled Water

Table 8 Post Compression Parameters of Tablet

Formulation code	**Weight variation (mg)**	**Hardness(kg / cm2)**	**Thickness (mm)**	**Friability (%)**	**Drug content (%)**
F1	895.03	7.52	9.80	0.50	97.20
F2	885.70	6.40	9.10	0.20	95.40
F3	900.30	7.30	9.35	0.70	98.33
F4	895.30	8.10	9.01	0.85	96.40
F5	901.10	8.40	9.10	0.70	95.60
F6	900.20	9.50	9.5	0.60	94.65

Uniformity of drug content: The uniformity in drug content is an important measure. It gives the percent per unit dosage form. The content uniformity was found within 98.0%-101.0% of 900 mg of Metformin Hydrochloride tablets. Hence the prepared tablets showed good content uniformity.

Table 9 Percent Cummulative Drug Release of All Batches

Percent Cummulative Drug Release						
Time(hrs)	Batch Code					
	F1	F2	F3	F4	F5	F6
0.5	7.1	3	8.3	3.1	5.1	4.5
1	11.5	6.3	15.23	8.3	7.4	9.2
2	19.6	11.9	24.76	10.8	8.7	18.6
3	28.7	20.5	35.56	21.6	28	20.8
4	32.8	25.8	44.76	28.7	37.6	33.4
5	39.7	30.5	54.76	34.3	43.8	41.8
6	44.5	35.8	62.65	46.8	51.4	50.3
7	53.6	38.5	69.67	49.2	63.4	58.6
8	62.7	47.8	76.45	55.8	75.4	64.5
9	70.8	55.4	80.5	61.3	75.4	73.8
10	80.1	64.7	86.3	66.8	89.6	81.7
11	85	84.6	90.6	87.3	93.1	88
12	90	95	98	91	97	94

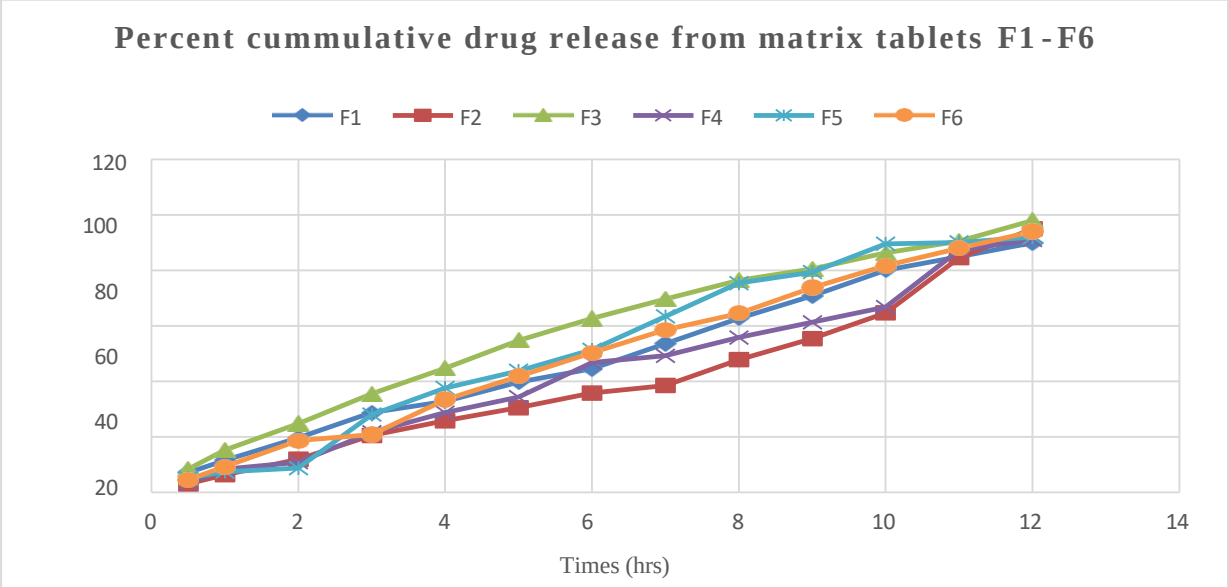

Figure 4 In-vitro drug release

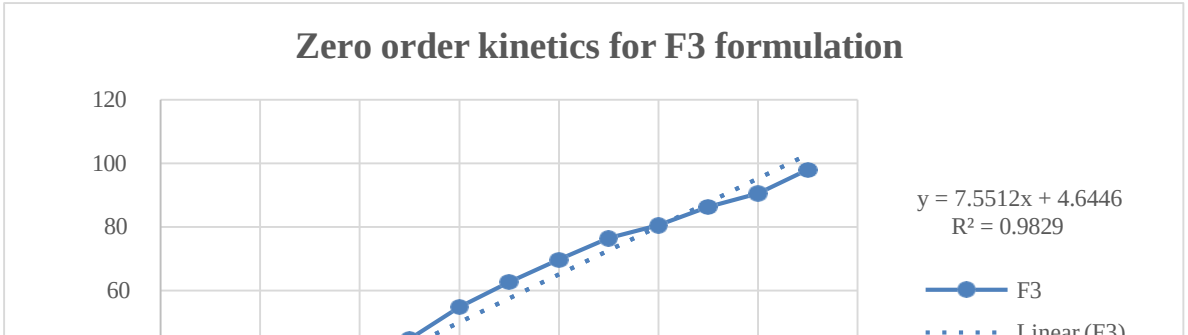

Figure 5 Zero order graph for F6 formulation

Discussion

The release profile of formulation F1, F2, F3, F4, F5, F6, comprising polymers like bhara gum gum Karaya with varying concentration. Formulations F1, F2, F3, F4, F5, and F6 exhibits release rates of 90%, 95%, 98%, 91%, 97%, 94%, at various time intervals as shown in the table. Among all of these 6 formulation F3 contains bhara gum shows maximum drug release at the end of 12hrs. Hence it was optimized and decided to develop further formulation. In the present work an attempt was made to formulate sustained release matrix tablet of Metformin hydrochloride utilizing natural gums by wet granulation technique, the identity of Metformin hydrochloride was confirmed by the physical characteristics, spectrometric analysis and FTIR spectra and thermal behavior like melting point, also the selection and isolation of natural polymers like Bhara gum and Gum karaya and then compatibility study between drug and polymer were carried out by FTIR spectrophotometer and no interactions was found. For the preparation of matrix tablet, granules were prepared and they are evaluated for properties like bulk density, tapped density, Hausner ratio, Carr's index and angle of repose. The six formulations were developed by varying the concentration of Natural Polymers (binder) Bhara gum & Gum karaya (10%, 15%, and 20%) As the concentration of polymer (Bhara gum & Gum karaya) increased in the formulation, the hardness is increased by reducing the friability and also drug release time was increased. Formulation F3 exhibits better performance for the tablet properties and drug release.

Conclusion: From the results and discussion of formulation development and evaluation of sustained release matrix tablet of Metformin hydrochloride, it was concluded that Bhara gum and Gum karaya possess potential of sustaining the drug release for 12 hours at 20% concentration in the tablet. According to study and results Bhara gum is more superior to Gum karaya.

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