ejpmr, 2025, 12(7), 205-215

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

SJIF Impact Factor 7.065

Research Article

ISSN (O): 2394-3211

ISSN (P): 3051-2573

MICROWAVE ASSISTED PVA-GRAFTED-LOCUST BEAN GUM AND ITS APPLICATION IN SUSTAINED RELEASE DRUG DELIVERY SYSTEM

Dr. Darakhshan Afreen Shaikh*[a], Momin Subura[a] and Dr. Ganesh G. Tapadiya[a]

[a,a]Shreeyash Institute of Pharmaceutical Education and Research. Aurangabad, Maharashtra-India.

***Corresponding Author: Dr. Darakhshan Afreen Shaikh**

Shreeyash Institute of Pharmaceutical Education and Research. Aurangabad, Maharashtra-India.

Article Received on 07/05/2025 **Article Revised on 28/05/2025** **Article Accepted on 17/06/2025**

ABSTRACT

Polymers are macromolecules with high relative molecular mass. Natural gums are biodegradable and renewable sources with negligible adverse effects on human being. Natural polymers, because of their similar macromolecular structure to tissues, offer the convenience of recognition from the biological system. This further leads to the avoidance of issues related to toxicity and stimulation of a chronic inflammatory reaction, as well as lack of recognition by cells, which are frequently provoked by many synthetic polymers. The aim of this study is to graft locust bean gum with poly-vinyl alcohol [PVA] as monomer using ceric ammonium nitrate as initiator by microwave radiation technique and compare their physico-chemical properties. The obtained copolymer was evaluated for (% G) grafting efficiency (% GE) and percentage conversion (%C). Further 2^3 randomized full factorial design with 03 factors were evaluated at 02 levels, high level (+1) and low level (-1). DSC results shows that shift and changes occur in the graph of grafted gum as compared to the native gum. XRD results of native gum and grafted gum shows that, increase in crystallinity as well as increase peak intensity is comparatively more in grafted gum, than native gum. The apparent growth of fungi in mineral salts agar medium (contains no carbon) proves that the carbon present in the grafted gum had been utilized by the fungi for its growth. Thus it can be concluded that poly vinyl alcohol grafted locust bean gum is biodegradable in nature and can be used in sustained release dosage form.

KEYWORDS: Locust bean gum, PVA, microwave radiation technique, sustained release dosage form, ceric ammonium nitrate, Copolymer.

INTRODUCTION

Chemical modification of natural polymers or macromolecules defines new shape in research in the recent years, by utilizing advanced methods or techniques.[1] Natural polymers are biocompatible, nontoxic, renewable, economic and easily available.[2] Stannett defined graft copolymers as "Graft copolymers consist of a polymer backbone with lateral covalently linked side chains. Grafting is a method where monomers are covalently bonded onto the polymeric chain.[3] Copolymerization with natural polymers offers tremendous applications. Locust bean gum is extracted from the seed endosperm of the carob tree plant botanically known as C. siliqua. It belongs to the subfamily Caesalpinioideae of the Leguminosae family.[4] The most common application of locust bean gum is the formulation of oral delivery systems based on tablets, hydrogels and multiparticulate systems. PVOH polymers have found applications in different industries including textile, paper, adhesives, food, biomedical and pharmaceutical in particular.[5] Grafting with CE ions onto polymeric chain with microwave radiation technique makes the final product pure, nonirritant and contamination free.[6] There are number of techniques of polymer grafting like Grafting through living Polymerization, Photochemical Grafting, Radiation-Induced Grafting etc.[7-10]

In the present study we report the polymer grafting of poly vinyl alcohol onto the natural polymer of locust bean gum using ceric ammonium nitrate as initiator by microwave radiation technique, once grafting was done it was used as the graft polymer in the formulation of sustained release tablet for class two model drugs. The grafted polymers were characterized by FTIR, SEM, XRD, DSC, TGA, elemental analysis and melting point.

MATERIALS AND METHOD

Locust bean gum (LBG) was kindly provided by Triveni chemicals (Gujarat, India) as a gift sample. Poly vinyl alcohol (PVA) and ceric ammonium nitrate (CAN) were purchased from Fisher scientific. Satranidazole was gifted by Alkem laboratories (Mumbai, India) and PVP K 30 was purchased from Encore Pharma (Aurangabad, India). Lupin lab. ltd. provided the Aerosil and Lactose was gently provided by DFE Pharma, (Germany).

Preparation of Poly vinyl alcohol grafted locust bean gum

Polymer grafting was done using polymer of locust bean gum where, it was grafted by poly vinyl alcohol used as monomer and ceric ammonium nitrate used as initiator by microwave radiation technique. Once the copolymer was obtained, it was intented in application of sustained release formulation.

Grafting Procedure

01 gram of locust bean gum was dissolved in 100 ml of distilled water in an Erlenmeyer flask, desired amount of PVA (2.5 g) was dissolved in 30 ml water and was added to the solution of locust bean gum, to this solution specified amount of ceric ammonium nitrate was added by dissolving it in 30 ml water The solution was kept for stirring on a magnetic stirrer at constant temperature for 1 hour. The solution was then transferred to reaction vessel (beaker) and placed in a microwave oven. The reaction vessel was irradiated at different watts for desired amount of time ranging from 2 minutes to 4 minutes following 1 minute heating and 1 minute cooling cycle. Once the microwave irradiation for intended amount of time was complete the gel like mass left in the reaction vessel, it was cooled and poured into excess of acetone. The precipitate was then collected and added to 50 ml of aqueous ethanol to remove unreacted polymer. The grafted polymer was finally washed with water and dried at 400^0 C in a hot air oven. After drying the copolymer was pulverized and sieved via a 100 # sieve. Different grafting parameters such as percent grafting (% G), grafting efficiency (% GE) and percentage conversion (%C) were calculated using following formulae:

1) Percent Grafting (%G)

%G = (W1-W0) / W0 × 100

2) Percent Grafting Efficiency (%GE)

%GE = (W1-W0) / W2 × 100

3) Percent Conversion (%C)

% C = W1 / W2 × 100

Where,

W0 = weight of locust bean gum, W1 = weight of grafted gum, W2 = weight of polyvinyl alcohol

Table 1: Synthesis detail of poly vinyl alcohol -g-LBG.

Batch Code	Amount of LBG (gm)	Ceric ammonium nitrate (gm)	Microwave irradiation time (minutes)	Microwave irradiation power (Watts)	Amount of PVA (gm)	% GE
G1	5	2.5	2	350	2.5	89.3
G2	5	5	2	350	2.5	92
G3	5	2.5	4	350	2.5	75.13
G4	5	5	4	350	2.5	98.6
G5	5	2.5	2	700	2.5	68.37
G6	5	5	2	700	2.5	58.3
G7	5	2.5	4	700	2.5	63
G8	5	5	4	700	2.5	60

Full Factorial Design

A 2^3 randomized full factorial design was employed in the present study. In this design 03 factors were evaluated each at 02 levels, high level (+1) and low level (-1) and experimental trials were performed for all 08 possible combinations. The amount of ceric ammonium nitrate, microwave irradiation time and microwave irradiation power were chosen as independent variables in the design. While percent grafting efficiency (%GE), and percent drug release (%DR) were selected as response. Statistical treatment was carried out to the factorial design batches using design expert stat ease software.

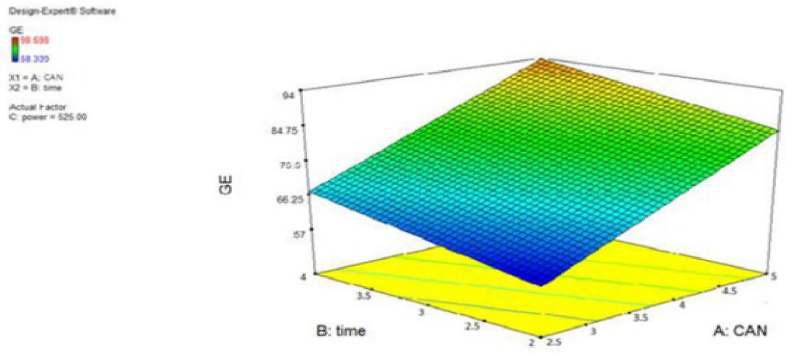

Figure 1: 3D plot.

Characterization of grafted and native gum
The structure of locust bean gum and locust bean-g-PVA was determined by Fourier Transform (FT) IR spectrum using KBr pellets. Scanning electron micrographs (SEM) of pure and the grafted copolymer were obtained on JEOL, JSM-840 SEM.

The thermograms of the locust bean and locust bean-g-PVA were obtained by using differential scanning calorimetry (DSC) under nitrogen atmosphere at a heating rate ranges from 30 to 500^0C of 10^0C per minute. X-ray diffraction (XRD) was carried out on X-ray powder Diffractometer.

Rheological parameters: Rheogram of native locust bean gum and grafted gum was obtained using Brookfield viscometer 2 %w/v solution of native gum and grafted gum. The samples were dissolved in water.

Elemental analysis: of native locust bean gum and the grafted locust bean gum was done to determine the carbon, hydrogen and nitrogen content, using K-fisher calibration method.

TGA study: of locust bean gum and grafted gum were done in the temperature ranges of 100-7000^0C, under nitrogen atmosphere.

Biodegradability studies of Grafted gum: Sample solution of grafted gum was inoculated with Aspergillus Niger on a medium and incubated at surrounding temperature for 21 days. In a petri-plate agar medium was added containing no additional carbon source, before placing the samples agar surface were cultivated with Aspergillus Niger. The solution were examined for colony Growth.

Acute oral toxicity studies: of grafted gum was performed as per the "organization of economics co-operations and development (OECD) guideline for the test of chemicals 425, adopted 17 Dec 2001". Six nulliparous and non-pregnant eight weeks old female mice were taken for the study, one of which was taken as control.

***Histopathological Study*:** One animal from each controlled and test randomly selected were euthanized with diethyl ether. After scarification their kidney, lungs, liver and stomach were separated for the Histopathological study. After separation each organ was cleaned and washed with 0.9 % w/v NaCl solution and then fixed in 10 % formalin solution. Each organ was then dehydrated with 50 % alcohol and then finally with absolute alcohol. It was embedded in melted paraffin and cooled. A thin section of each organ was obtained by cutting the embedded block with a microtome. The section were then mounted on glass slides and stained with hematoxylin and a counter stain eosin. A cover slip was fixed on each section to obtain a permanent slide. Finally the slides were examined through a light microscope fitted with a camera (Magnus, MITS, and India) and the fields were captured by the camera to obtain photomicrograph. The photomicrographs of the test organs were compared with that of controlled organs. Melting point of API, locust bean gum and grafted gum were done, using optimelt automated melting point system. The samples were placed in the capillaries by keeping the temperature of 50-3000^0C.

Melting point determination Melting point of API, locust bean gum and grafted gum were done, using optimelt automated melting point system. The samples were placed in the capillaries by keeping the temperature of 50-3000^0C.

RESULTS

Locust bean –g – PVA: Initially the synthesis was tried without the application of microwave irradiation following the normal heating at 60^oC. Two different groups of batches were made, out of which the grafted polymer was precipitated on the same day when the irradiation was done and the second was obtained on the other day, after keeping it overnight. But the results showed no significant yield of grafted gum indicating the fact that the only combination of the initiator and supply of energy in the form of normal heat was not sufficient for grafting in non-nitrogen environment. While synthesizing the grafted gum using microwave without initiator, the grafting efficiency was too low to be considered that the process is significant.

(a) Dry powder of grafted polymer **(b) Gel like mass of grafted polymer**

Figure 2: (a and b) Synthesis of PVA –g – locust bean gum.

FTIR analysis: The Infrared spectra of Locust bean gum (LBG) and grafted LBG are shown in **Figure 3 and 4** LBG showed a characteristic peak at 3309 cm-1 for –OH stretching group and it was due to hydrogen bonding involving the hydroxyl groups on the gum molecules. The C-O stretching vibrations were observed at 1639 cm−1, and additional characteristic bands of LBG appearing at1018 and 1639.49 cm−1 were attributed to C-O bond and C-O stretch respectively. Marked changes were observed in spectra of PVA-g-LBG compared to LBG. The peaks at 1081.41for C-O stretch and peaks at 1541.12 for N-H bend confers the presence of alcoholic group and nitro group.

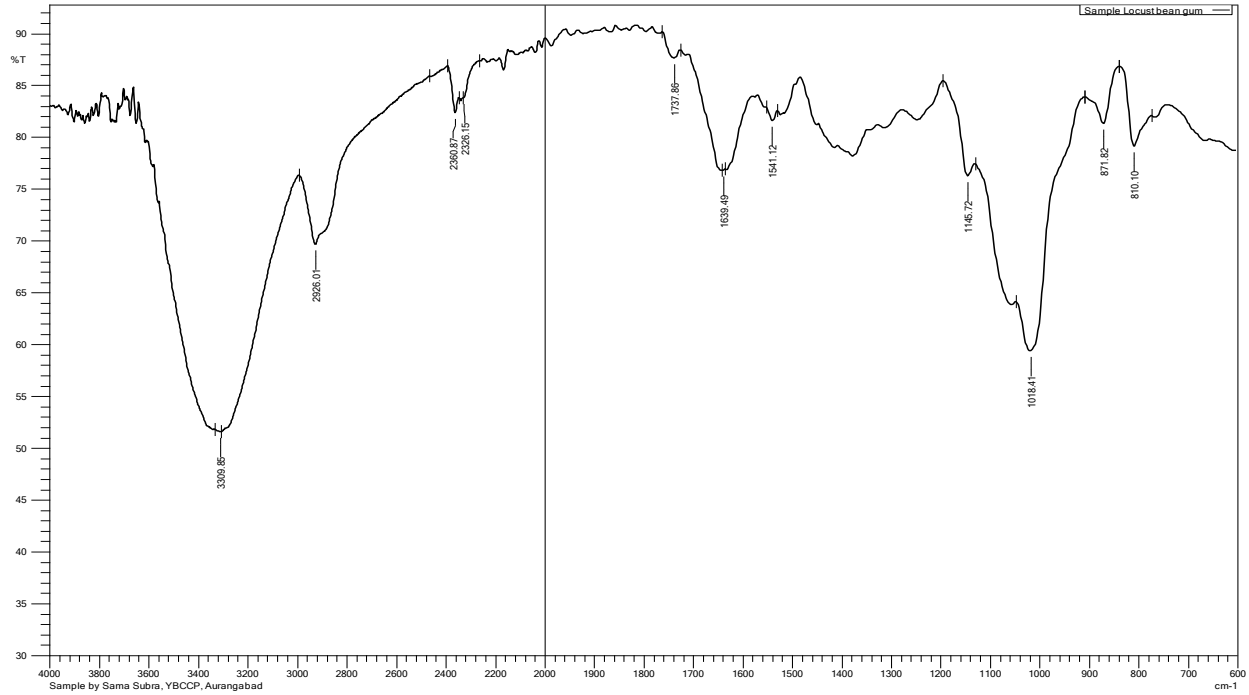

Figure 3: IR Spectra of Locust Bean Gum.

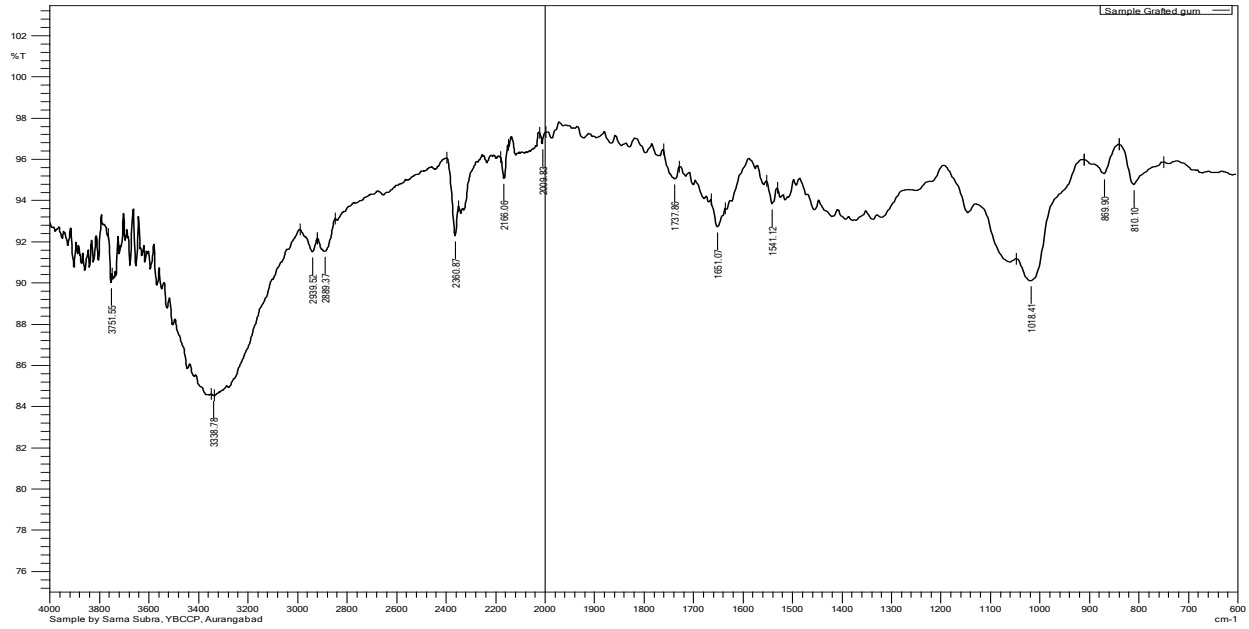

Figure 4: IR Spectra of Grafted gum.

***Scanning electron microscopy*:** Figure 4 shows the scanning electron micro figures of locust bean gum and its grafted form. As the PVA particles are polyhedral in nature, and Locust bean gum being fibrous, the surface morphology, texture and topofigurey of the locust bean gum gets changed due to the process of grafting.

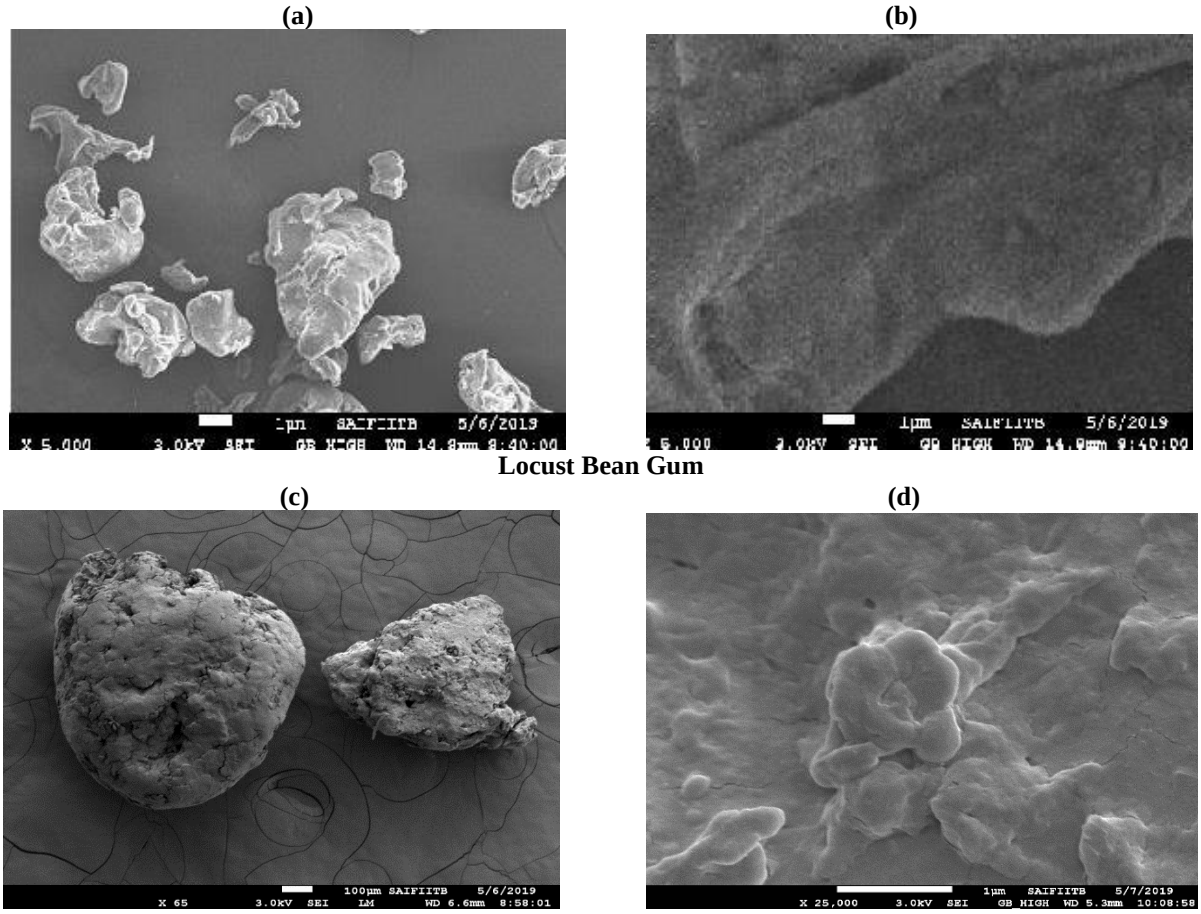

Figure 5. (a-d) SEM analysis of locust bean gum and grafted gum.

Differential scanning Calorimetry: DSC results shows that shift and changes occur in the graph of grafted gum as compared to the native gum.

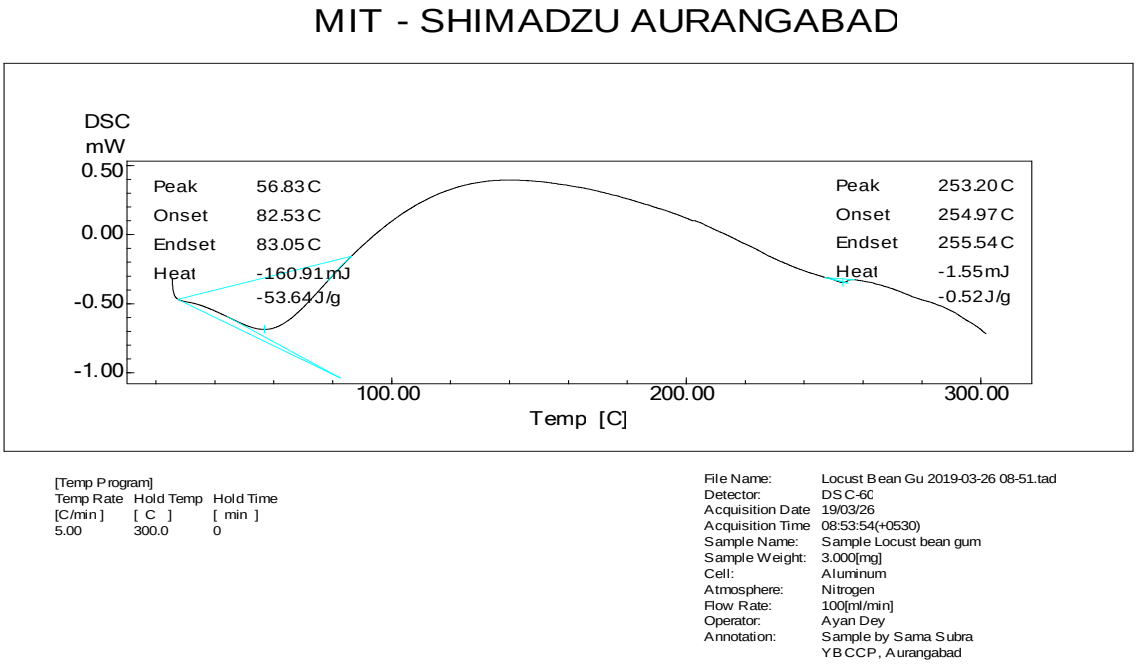

Figure 6: DSC Locust Bean Gum.

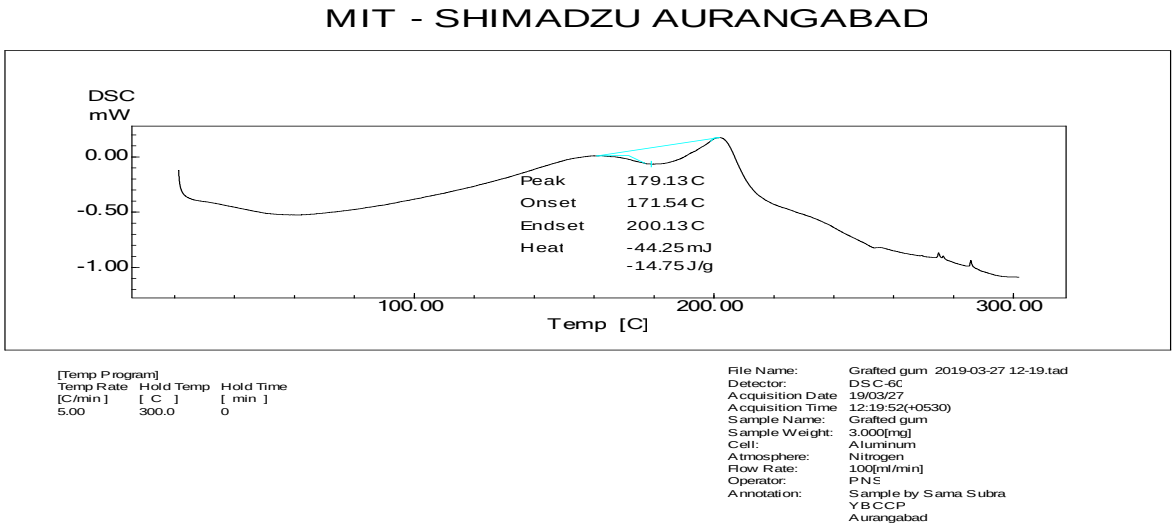

Figure 7: DSC Grafted Gum.

Powder XRD: The outcome of XRD analysis of native locust bean gum and poly vinyl alcohol -g-locust bean gum is shown below:

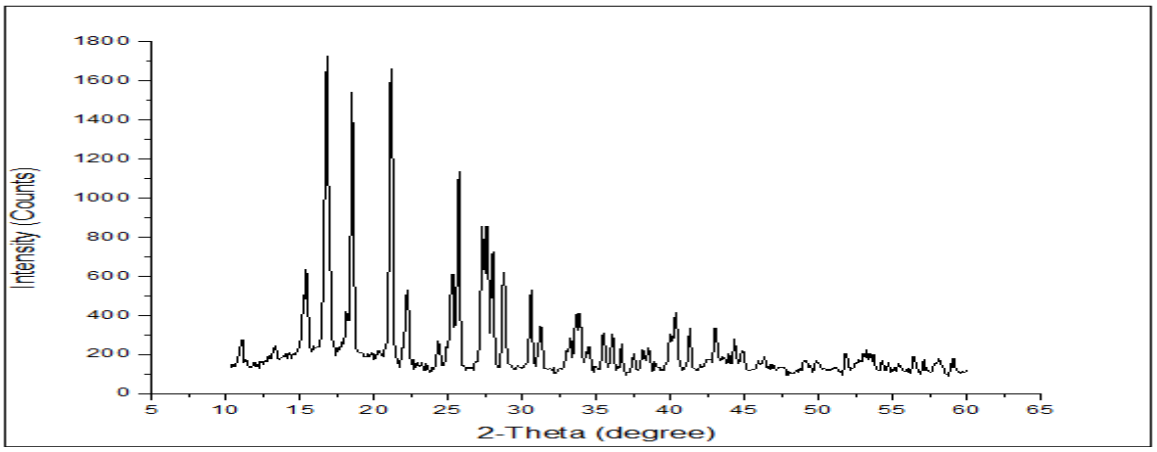

Figure 8: Powder XRD of Locust Bean Gum.

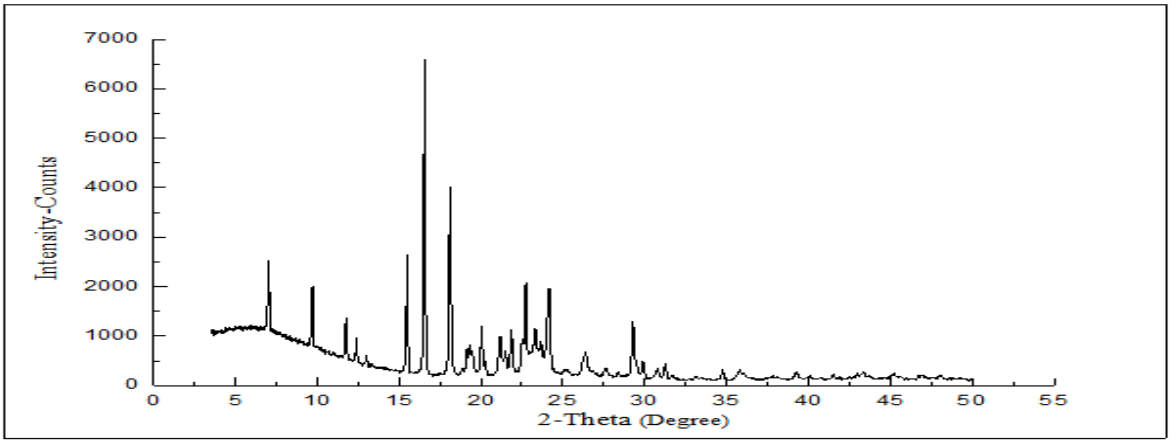

Figure 9: Powder XRD of Grafted Gum.

Viscosity measurements: The rheological characteristic of native gum and grafted gum were studied using Brookfield Rheometer. It was found to be as shear rate increases the viscosity decreases. In grafted gum the reduction of viscosity was due to breakage of galactose branch points of native gum under drastic irradiation by microwave.

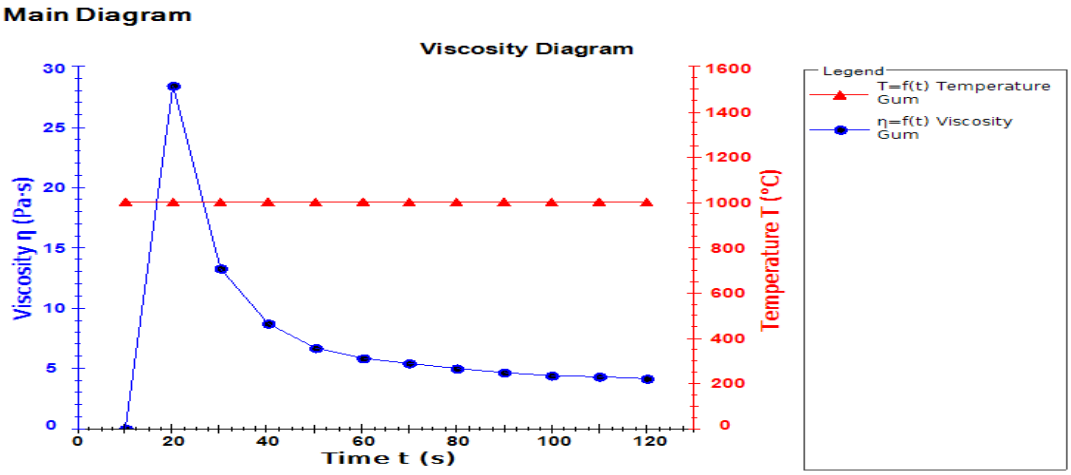

Figure 10: LBG.

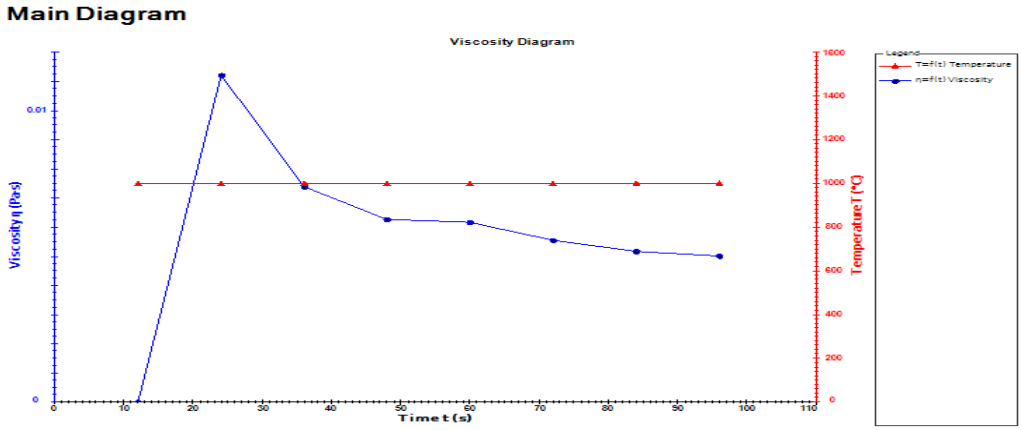

Figure 11: Grafted gum.

Elemental analysis: The results of elemental analysis for grafted gum and locust bean gum are given in **table 2.** The presence of Nitrogen in case of grafted gum to a greater extent conforms that the monomer chain have indeed been grafted on the backbone of the locust bean gum. The **Figure 12** give the peaks of the C-H-N analysis**.**

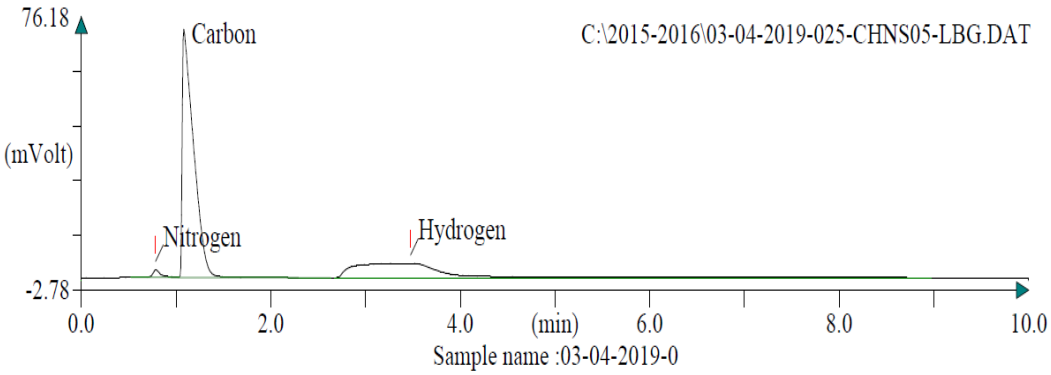

Figure 12: LBG.

Table 2: Elemental composition.

Material	Elemental composition (%)			
	C	H	N	S
Locust bean gum	39.961	6.763	1.533	-
Grafted gum	44.158	7.140	13.410	-

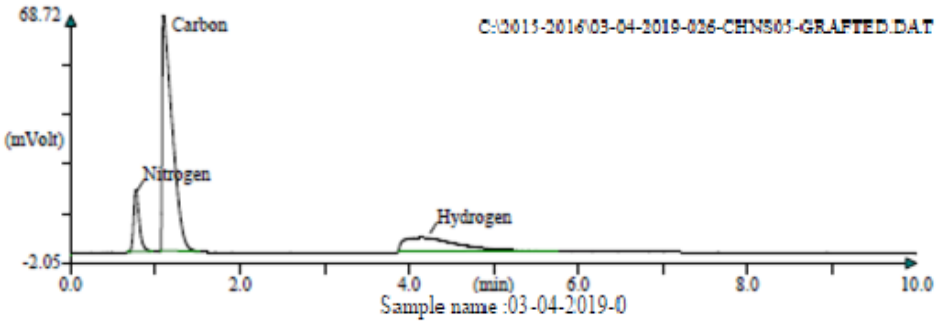

Figure 13: Grafted gum.

Biodegradability studies of grafted gum: Figures below show the fungal growth of Poly vinyl alcohol grafted locust bean gum. The apparent growth of fungi in mineral salts agar medium (contains no carbon) proven that the carbon present in the grafted gum had been utilized by the fungi for its growth. Thus it can be concluded that poly vinyl alcohol grafted locust bean gum is biodegradable in nature.

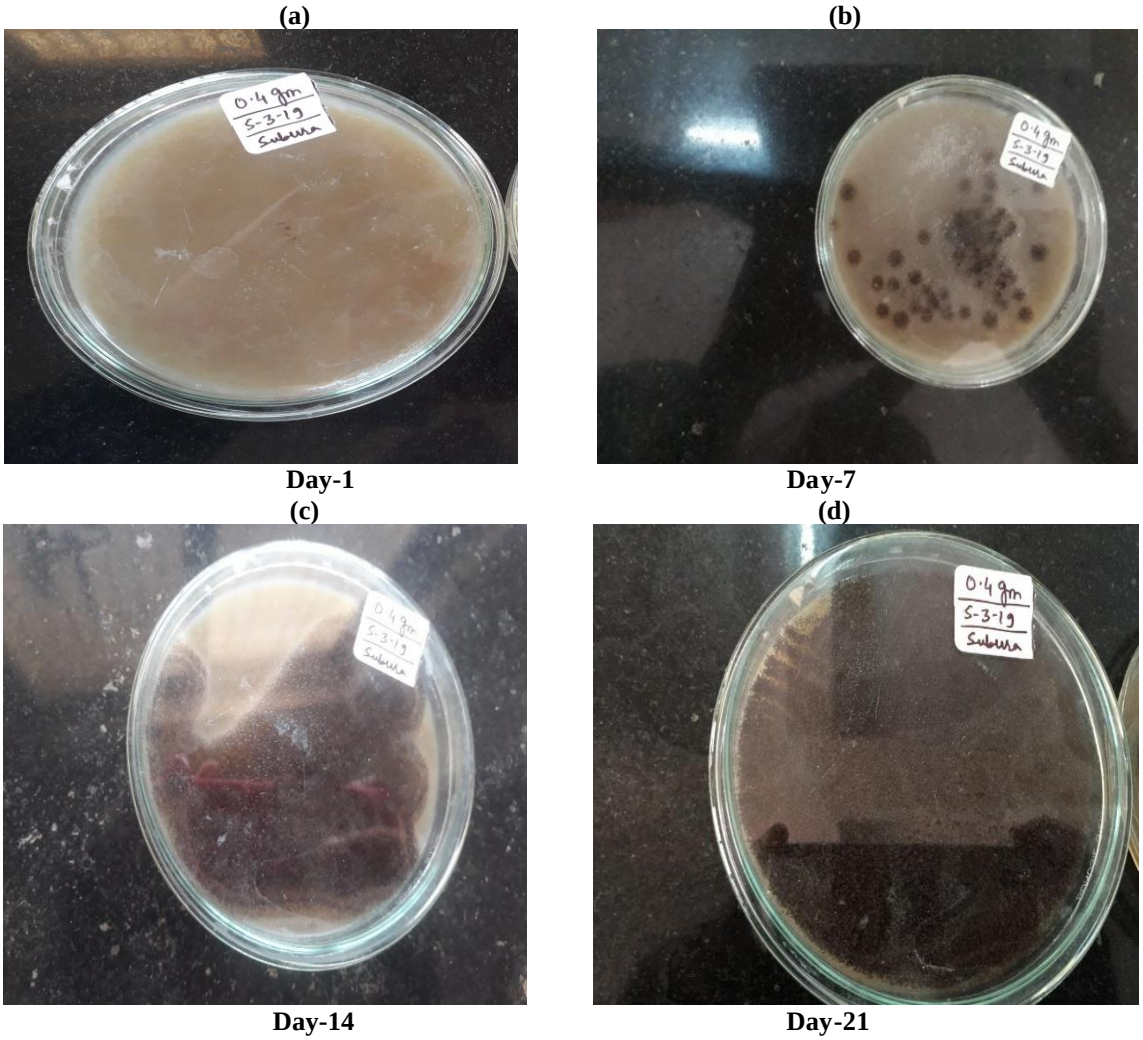

Figure 14. (a-d) Biodegradability studies.

Histopathological study: The micro figures of control, test animals and locust bean given animals of kidneys shows no sign of any type of morphological change. Micro figures of test animals, control and locust bean given animals liver depict normal hepatocytes, large polygonal cells with central nuclei and kuppfer cells. Thus, the histopathological examination establishes that the grafted Locust bean gum is physiologically compatible.

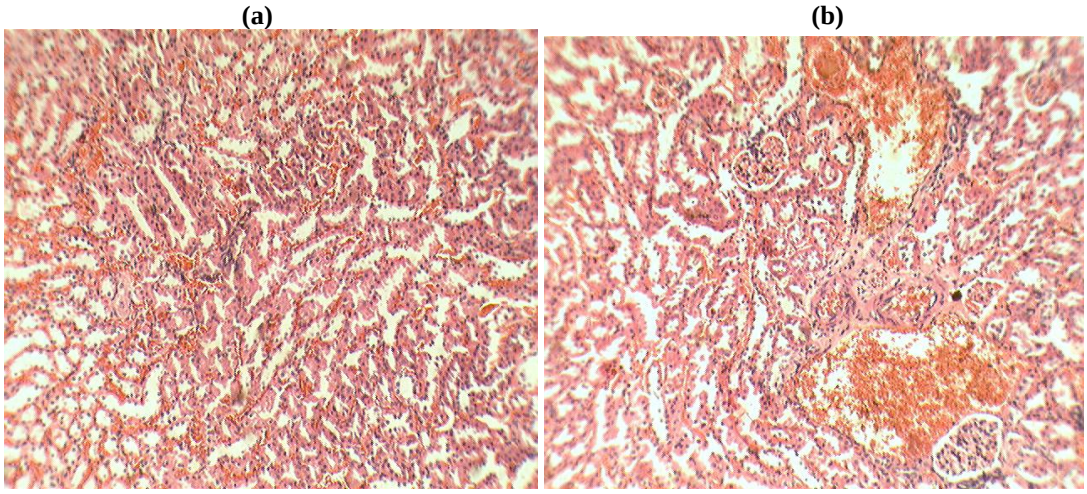

Figure 15: (a and b) Control and grafted gum kidney.

Acute oral toxicity study: The results are shown in table below. There was no mortality found within the observation period of 3 days after dosing. As per the "organization of Economic Co-operation and Development (OECD) guideline for the test of chemicals" 425, adopted "17 December 2001" Annexure-4, the LD50 value is greater than 2000mg/kg dose of dose then the test product will be fallen under the "category 5" and toxicity rating will be "zero". So, PVA -g-LBG is under the "category 5" as well as mortality rate of animals after a single dose of 2000 mg/kg body weight.

Table 3. Mortality rate of animals after a single dose of 2000 mg/kg body weight.

Observation time period	MORTALITY		
	Animal 1	Animal 2	Animal 3
30 min	0	0	0
2 hours	0	0	0
4hours	0	0	0
1st day	0	0	0
3rd day	0	0	0

Melting point of API, locust bean gum and grafted gum were done, using optimelt Automated melting point system. The samples were placed in the capillaries by keeping the temperature of 50-300^0 C.

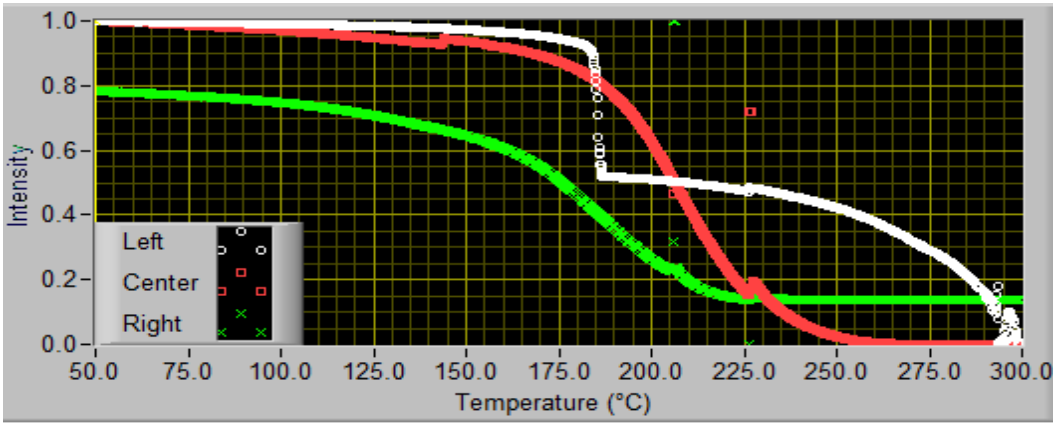

Figure 16: Melting point analysis.

Table 4: Melting point results.

Left	Satranidazole	185.4
Center	Locust bean gum	195.6
Right	Grafted gum	206

Preparation of Tablet

The optimized grafted gum (300 mg) was taken for the preparation of STZ tablet. All ingredients like drug, lactose, grafted gum and PVP K-30 except magnesium stearate and aerosil are mixed together. Damped mass was prepared with the help of ethanol and passed through sieve number 45. The granules were allowed to dry in hot air oven at 95^0 C. After complete drying aerosil and magnesium stearate were added prior to compression, the tablets were compressed at an average weight of 500 mg using a Multi station tablet press (Karnavati Rimek mini press ii.) Hardness of tablets were found to be in the range of 4–5 kg/cm2.

Table 5: Tablet formula.

Ingredients	Role	Quantity taken (500mg)
Satranidazole	API	300mg
Grafted Polymer	Copolymer	100mg
Lactose	Diluent	60mg
PVP K-30	Binder	20mg
Aerosil	Glidant	20mg
Magnesium stearate	Lubricant	2%

In- vitro drug release study

In vitro Drug release from the tablet formulation was investigated in 0.1 N HCl having pH 1.2 medium for the initial 2 h, followed by in phosphate buffer having of pH 7.5 as a dissolution medium. The volume of dissolution media was 900 ml. the paddle was rotated at a speed of 50 rpm with temperature maintained at 37^0 C. the dissolution test was first 2 hours carried out in 0.1 N HCl and then it was transferred to 7.5 pH phosphate buffer for 6 hours. The samples were analyzed by UV spectrophotometer (Shimadzu UV -1800 Japan) at λmax 318 nm. This experiment was performed in triplicate using a tablet dissolution tester (Electro Lab, TDT-08L, India) equipped with eight baskets (glass jars).

Drug Release Kinetics

For better understanding the mechanism of drug release from the formulated tablets, *in vitro* dissolution profile data was fitted to various models like **Zero order, first Order, Matrix, Korsmeyer Peppas and Hixon Crowell.**

DISCUSSION

In - vitro drug release

From the results of the primary batches, it can be easily observed that the release characteristic of A3 batch occurs fine and shows a sustain release effect till a period of 8 hours. As a result, this formulation was taken for the final batches with change in grafted polymer concentration of 80, 90.100,110,120 mg.

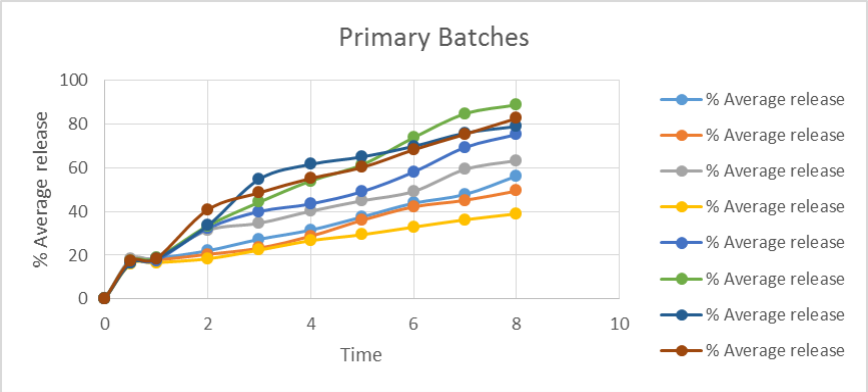

Figure 17: Drug release profile of primary batches.

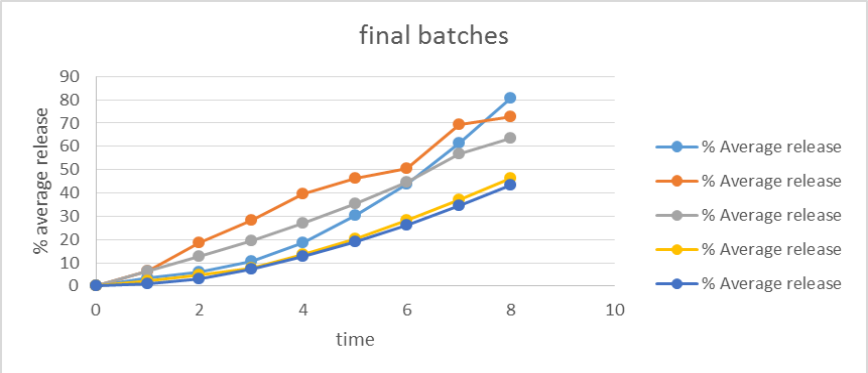

Figure 18: Drug release profile of final batches.

The in-vitro dissolution study was done for formulations F1 to F5 with different polymer concentration. It was observed that, increase in concentration of graft copolymer decreases the release of the drug.

Drug Release Kinetics

Table 6. kinetic modeling.

Formulation Code	Zero order	First order	Matrix	Korsmeyer Peppas
F1	0.9612	0.8345	0.9848	0.9496
F2	0.8538	0.9853	0.9849	0.9688
F3	0.4054	0.8751	0.9225	0.9801
F4	0.8894	0.9934	0.9858	0.9688
F5	0.6838	0.9379	0.9682	0.9670

Kinetic modeling of grafted gum **Table 6** of release data specified that the drug release from the tablet matrix was non-Fickian, Formulations followed first order release kinetics. The mechanism of drug release depends upon the various factors like the solubility of drug and the excipients, swelling of polymeric matrix and the relative ratio of drug and polymer used in the formulation of tablets.

CONCLUSION

Poly vinyl alcohol grafted locust bean gum was synthesized by microwave assisted technique using ceric ammonium nitrate. The grafted gum was biocompatible and biodegradable in nature. As this was again formulated in a sustained release tablet form, the polymer showed the desired release. Hence, it can be concluded that PVA-g-LBG can be used as a rate controlling hydrophilic polymer for controlled release application.

LIST OF ABBREVIATIONS

Ceric ammonium nitrate (CAN)
Differential scanning colorimetry (DSC)
Fourier transform infrared spectroscopy (FTIR)
Grafting efficiency (% GE)
Locust bean gum (LBG)
Percent drug release (%DR)
Percent grafting (% G)
Percentage conversion (%C)
Poly vinyl alcohol grafted locust bean gum (PVA-g-LBG)
Poly-vinyl alcohol (PVA)
Satranidazole (STZ)
Scanning electron microscopy (SEM)
Thermal gravimetric analysis (TGA)
X-Ray Diffraction (XRD).

REFERENCES

1. Pawar H.A., Kamat S.R., Choudhary. PD an Overview of Natural Polysaccharides as Biological Macromolecules: Their Chemical Modifications and Pharmaceutical Applications. Bio Med (Aligarh), 2015; 6: 224. doi.org/10.4172/0974-8369.1000224.
2. Rohit R. Bhosale, H.V., Gangadharappa, Afrasim Moin, D.V., Gowda and Riyaz Ali M. Osmani. Grafting Technique with Special Emphasis on Natural Gums: Applications and Perspectives in Drug Delivery. The Natural Products Journal, 2015; 5(2): 124-139. doi.org/10.2174/2210315505021507021422228.
3. Stannett V. Grafting. Radiant Phys Chem., 1981; 18: 215–222.
4. H.E., Batal, A. Hasib, A. Ouatmane, A. Boulli, F. Dehbi, A. Jaouad, J. Mater. Yield and composition of carob bean gum produced from different Moroccan populations of carob (Ceratonia siliqua L.) Environ. Sci., 2013; 4: 309–314. https://www.jmaterenvironsci.com/Document/vol4/vol4_N2/38-JMES-319-2013-Elbatal.pdf.
5. Hassan CM, Peppas N.A., Structure and applications of polyvinyl alcohol hydrogels produced by conventional crosslinking or by freezing/ thawing methods. Advances in Polymer Science, 2000; 153: 37-65. doi.org/10.1007/3-540-46414-X_2.
6. Mahesh S Sakhare, Hrishikesh H Rajput Polymer. Grafting and Applications in Pharmaceutical Drug Delivery Systems - A Brief Review. Asian J Pharm Clin Res., 2017; 10(6): 59-63. doi.org/10.22159/ajpcr.2017.v10i6.18072.
7. Szwarc, M. Living polymers: Their discovery, characterization and properties. J. Polym. Sci. Polym. Chem. A., 1998; 36: 09-15. doi/10.1002/(SICI)1099-0518(19980115)36:1.
8. Liu Z, Xu Z. Surface modification of polypropylene microfiltration membranes by graft polymerization of N-vinyl-2-pyrrolidone surface modification of polypropylene microfiltration membranes by graft polymerization of N-vinyl-2-pyrrolidone. Eur Polym J., 2004; 40: 2077-2087. doi.org/10.1016/j.eurpolymj.2004.05.020.
9. Kaith B.S., Kalia S. Preparation of microwave radiation induced graft copolymers and their applications as reinforcing material in phenolic composites. Polymer Composites, 2008; 29: 791-797. doi.org/10.1002/pc.20445.
10. Kumar R, Setia A, Mahadevan N. Grafting Modification of the Polysaccharide by the use of Microwave irradiation- A review. Int. J. Rec. Adv. Pharm. Res., 2012; 2: 45-53. https://www.researchgate.net/publication/308311952_Grafting_modification_of_the_polysaccharide_by_the_use_of_microwave_irradiation_-_A_review#citations.
11. S. Deepu, Molly Mathew and Ms. Shamna. Controlled Drug Delivery System. Int. J. Pharm. Sci., 2014; 3:3; 636-641. DOI: 10.36713/epra2013.