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Formulation and Evaluation of Starch Gelatin Complex Microspheres of Amoxicillin as Sustainedrelease Delivery System

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ABSTRACT
The purpose of this research was to design and develop starch gelatin complex microspheres of Amoxicillin Trihydrate by ionotropic gelation method with combination of two polymers to get best possible formulation out of them. The starch gelatin complex microspheres were prepared using Jackfruit starch and Hydroxy propyl methyl cellulose K4M as polymer to achieve an extended retention in upper GIT and there by improved bioavailability. The microspheres were evaluated for particle size analysis, Drug Entrapment Efficiency, Drug Loading Capacity, Micromeritic properties like Bulk Density, Tapped Density, Carr's Index, Hausner Ratio, Angle of repose, In-vitro release studies and surface morphology characterized by Scanning electron microscopy (SEM). The Microspheres have an average size range of 570±12.36 to 990±10.70µm. The entrapment efficiency was found to be in the range of 80.49±0.09 to 89.94±0.25. The In-vitro release studies of the drug from the best formulation F5 exhibit a sustained release of 88.96±0.94% as studied over 24hrs. Release was best explained by zero-order kinetic model and it shows that the drug release follows diffusion mechanism. FT-IR data revealed that, compatible and there was no interaction between the drug and excipients. The data obtained in this study suggest that the starch gelatin complex microspheres of Amoxicillin Trihydrate are promising for sustained drug delivery which can reduce dose frequency.
Keywords: Microspheres, Amoxicillin Trihydrate, Ionotropic Gelation Method, Hydroxy propyl methyl cellulose K4M

I. INTRODUCTION

Jackfruit (Artocarpus heterophyllus Lam) is a popular fruitcrop that is widely grown in Thailand and Southern partsofIndia.Theripefruitcontainswellflavoredyellowsweetbulbsandseeds.Seedshavehighcarbohydratesandproteincontent.Starchiswidelyusedasafoodadditive andhasverygoodlaxativeactivity.Alginateisacomplex polysaccharidewhosecompositionvariesonthebasisoftheproportionofmonomericunitsnamely,mannuronicacidandglucuronicacid.Itiswidelyusedfordrugdilutionsystem.[1,2]

Amoxicillin is the anhydrous form of a broad-spectrum, semisynthetic amino-penicillin antibiotic with bactericidal activity. Amoxicillin binds to and inactivates penicillin-binding proteins (PBPs) located on the inner membrane of the bacterial cell wall. Inactivation of PBPs interferes with the cross-linkage of peptidoglycan chains necessary for bacterial cell wall strength and rigidity. This interrupts bacterial cell wall synthesis and results in the weakening of the bacterial cell wall and causes cell lysis. The combination of amoxicillin and clavulanate is an oral antibiotic widely used in the treatment of mild-to-moderate bacterial infections including sinusitis, bronchitis, otitis media, cellulitis and community acquired pneumonia.[3-6]

Microspheres are small spherical particles, with diameters 1 µm to 1000 µm. They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. The Novel Drug Delivery System started the alternative means of delivering the drug in the form of microspheres. A unique pharmaceutical delivery system comprising a physiologically acceptable nonaqueous liquid such as an edible oil and a thickening agent such as colloidal silicon dioxide which together form a semi-solid having the consistency of a pudding is provided. Microspheres prepared with gelatin as the polymer have been found to be highly mucoadhesive and have been used for the controlledrelease of many drugs. Novel drug delivery system development is largely based on promoting the therapeutic effects of a drug and minimizing its toxic effects by increasing the amount and persistence of a drug in the vicinity of a target cell and reducing the drug exposure of nontarget cells. They are spherical free flowing particles consisting of proteins or synthetic polymers which are biodegradable in nature. There

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are two types of microspheres; microcapsules and micromatrices, which are described as, Microcapsules are those in which entrapped substance is distinctly surrounded by distinct capsule wall and micromatrices in which entrapped substance is dispersed throughout the matrix. Microspheres are sometimes referred to as microparticles. Microspheres can be manufactured from various natural and synthetic materials. Microsphere play an important role to improve bioavailability of conventional drugs and minimizing side effects.[7-13]

II. MATERIAL AND METHOD

Amoxicillin trihydrate is obtained as a gift sample from Astam healthcare limited Theda (HP). Jackfruit starch was obtained from jackfruit seeds which were purchased from local market Mandi, Himachal Pradesh, India. Sodium alginate is obtained from Sigma chemicals Pvt. Ltd. New Delhi, INDIA. Calcium chloride and HPMCK4M was obtained through Loba chemie Pvt. Ltd. Mumbai.

Isolation of Starch from Jackfruit Seeds

The extraction of starch from jackfruit seeds was done via aqueous and alkali extraction processes. About 5g of jackfruit seeds was added into 100ml distilled water and set aside for 6-8hours at room temperature with constant stirring. Then the slurry was filtered through sieve no. 212, and the remaining sediment was washed with distilled water for three times. The filtrates were collected and precipitated overnight at 4ºc. Then the supernatant was discarded and the crude starch was washed with distilled water. This step was repeated three times and the starch cake obtained was dried at 40ºc for 24 hours in a dryer. Then the starch was ground with a mortar and pestle. The starch was packed in air tight container and kept at room temperature until further use.

Prepration of amoxicillin microspheres by ionic gelation technique

The starch gelatin complex microspheres were formulated by using a well-established ionotropic gelation technique, to entrap with drug amoxicillin trihydrate for the production of microspheres. The microspheres were prepared by the different concentration of starch. Various concentration of polymer like Starch and HPMC K4M solution were prepared by mixing sodium alginate in distilled water to get proper mixing and distribution. Amoxicillin trihydrate were added to the above mixture and dispersed thoroughly with initial stirring and sonicated for 5 minutes in bath sonicator. The drug polymer dispersion was added manually drop wise with a syringe (21G) into 100ml calcium chloride solution by stirring with a magnetic stirrer, maintaining a specific height and pressure. Gelation time of 1hr was allowed to complete the curing reaction to produce spherical and rigid microspheres. The microspheres obtained were collected by decantation, washed with distilled water and dried at room temperature for 24hr.

Evaluation parameters for extracted starch

Physicochemical test for jackfruit powder and extracted starch

The raw jackfruit powder and starch extracts were subjected to phytochemical tests for the identification of carbohydrate, proteins, alkaloids, glycosides and steroids by various tests such as Molisch test, biuret test and Mayer test as shown in Table no.3.

Gelatinization temperature

For the determination of gelation temperature, the starch powder is moistened with water and transferred into capillary tube by means of intrusion.The temperature of gelling and the time from swelling to full gelatinization were recorded with a melting point apparatus. Theresultsaregiven in table no.4

Determination of pH

The pH value of 1% starch suspension were measured using digital pH meter as shown in table no.4

Viscosity

The viscosity of 1% starch suspension were measured using a viscometer. The results are given in table no.4

Swelling index

Swelling index Starch samples (200mg) were added to 10mL of water, and light liquid paraffin was taken in two different test tubes and mixed thoroughly. The dispersions were allowed to stand for 12hours. The volumes of the sediment in the tubes were recorded. The swelling index of the material was calculated as follows and shown in table no.4

$$SI\% = \frac{\text{volume of sediment in water} - \text{volume of sediment in light liquid paraffin}}{\text{volume of sediment in light liquid paraffin}}$$

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Table No.1: Composition and processing parameters of amoxicillin trihydrate microspheres

Formulation Code	Drug (mg)	Starch jackfruit seeds (mg)	HPMC K4M (mg)	Sodium Alginate (g)	Calcium Chloride (g)	Distilled water (ml)
F1	500	450	-	2	4	50
F2	500	450	-	2	4	50
F3	500	450	400	2	4	50
F4	500	500	450	2	4	50
F5	500	500	500	2	4	50
F6	500	500	550	2	4	50
F7	500	650	-	2	4	50
F8	500	650	-	2	4	50
F9	500	650	-	2	4	50

Evaluation Parameters of Microspheres formulation

Micromeritic Studies

The prepared microspheres are characterized by their micromeritic properties such as microsphere size, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose.

Particle Size Determination

The particle size of the microspheres was determined by using optical microscopy method. Approximately 100 microspheres were counted for particle size using a calibrated optical microscope.

Morphological Study using SEM

The morphological study was carried out by Scanning Electron Microscope (SEM). Microspheres were scanned and examined under Electron Microscope HITACHI SU 1500, Japan connected with Fine coat, JEOL JFC-1100E Ion sputter. The sample was loaded on copper sample holder and sputter coated with carbon followed by Gold.

Drug Loading and Drug Entrapment

Microspheres equivalent to 50 mg of the drug were taken for evaluation. The amount of drug entrapped was estimated by crushing the microspheres and extracting with aliquots of 0.1N HCl (pH-1.2) repeatedly. The extract was transferred to a 100 mL volumetric flask and the volume was made up using 0.1N HCl (pH-1.2). The solution was filtered and the absorbance was measured after suitable dilution spectrophotometrically (UV 1900, Shimadzu, Japan) at 272 nm against appropriate blank. The amount of drug loaded and entrapped in the microspheres was calculated by the following formulas

$$\%\ \textbf{Drug loading} = \frac{\textbf{weight of drug loading in the microsphere (DC)}}{\textbf{Total weight of the microspheres}} \times 100$$

$$\%\textbf{Drug entrapment} = \frac{\textbf{Amount of drug actually present (DC)}}{\textbf{Theoretical drug loaded expected}} \times 100$$

DC = Actual drug content

In vitro drug release Study

The prepared microspheres were subjected to in vitro drug release sequentially in three different suitable dissolution media. USP type I dissolution apparatus was used. The dissolution medium for 8 hr. was 900 ml of 0.1 N HCl (pH 1.2). The temperature of dissolution medium was maintained at 37 ±0.5 °C and the basket was rotated at 50 rpm. An aliquot of 5 ml was withdrawn at predetermined time intervals and replaced with an equal volume of the fresh dissolution medium to maintain sink conditions. The samples were analyzed at 272 nm, for the percentage drug release using an UV Visible double beam spectrophotometer.

Release Kinetics

The matrix systems were reported to follow the Peppas release rate and the diffusion

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mechanism for the release of the drug. To analyze the mechanism for the release and release rate kinetics of the dosage form, the data obtained was fitted in to, Zero order, First order, Higuchi matrix, Peppas and Hixson Crowell model. In this by comparing the R-values obtained, the best-fit model was selected.

Stability Studies

Stability of a drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, light, and enables recommended storage conditions.

ICH guidelines the length of study and storage conditions:

Accelerated testing - 40°C/75% RH for six months.

The accelerated stability study of the best formulations was carried out as per the ICH guidelines.

III. RESULTS

The starch gelatin complex microspheres of Amoxicillin Trihydrate were prepared by Ionotropic Gelation Method. The results of the physico-chemical characterization of jackfruit starch are shown in Table no.3. The prepared microspheres were found to be discrete, spherical and free flowing. All batches show percent entrapment more than 80% and it is found that entrapment of drug increases with an optimum amount of the polymer. Higher amount of the starch and HPMC K4M leads to decrease entrapment of the drug. Formulation F5 shows maximum entrapment whereas formulation F9 shows minimum entrapment of the drug in the polymer. All batches showed a percentage yield of greater than 70%, Percentage yield is found to be higher with formulation F5. Angle of repose, Hausner ratio, and Carr's index were determined to predict flow ability. A higher Hausner ratio indicates greater cohesion between particles while a high Carr index is indicative of the tendency to form bridges. The prepared microspheres exhibited good flow properties. From the sieve analysis study, it was found that the formulations have the size range of 570µm-900µm. The particle size distributions of the formulations F1 to F9 are shown in table. Surface morphology characteristics were studied using SEM. SEM indicated that the prepared microspheres are spherical with smooth surface; distinct pores are evident on the surface of microspheres, which will be responsible for the release.

Determination of λmax in 0.1N HCl

The resultant solution was scanned from 200 to 400 nm and the spectrum was recorded to obtain the values of maximum wavelength i.e., 272nm. The UV spectrum is shown in Figure no.1:

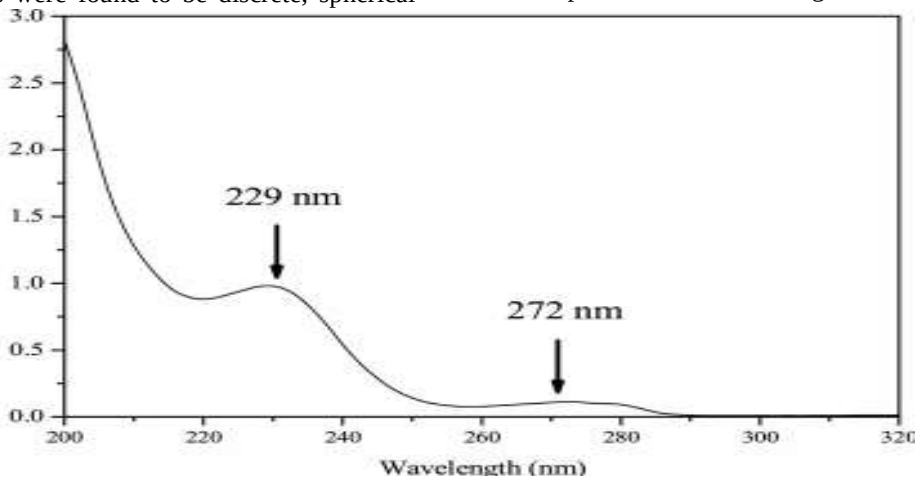

Figure No.1: λmax of Amoxicillin Trihydrate in 0.1N HCl

Preparation of Standard Calibration Curve of Amoxicillin Trihydrate

Fromthestocksolution1-10mlwerepipettedoutinto10mlvolumetricflask and were made up to the mark with 0.1 N HCl to obtain amoxicillinconcentrationof2-20µg/mlrespectively. The absorbance was measured in a UV spectrophotometer at 272 nm against 0.1N HCl. The absorbances of standard solutions of Amoxicillin Trihydrate ranging from 2-20 µg/ml so

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obtained were tabulated as in Table. Calibration curves were plotted and shown in Figure no.12 respectively. The curves were found to be linear in the range of 2-20 µg/ml at λmax 272 nm. The regression values were found to be 0.9991 respectively.

Table No.2: Prepration of Calibration Curve of Amoxicillin trihydrate In 0.1N HCl

Sr. No.	Concentration	Absorbance
1.	2	0.078
2.	4	0.142
3.	6	0.220
4.	8	0.289
5.	10	0.350
6.	12	0.449
7.	14	0.508
8.	16	0.579
9.	18	0.653
10.	20	0.729

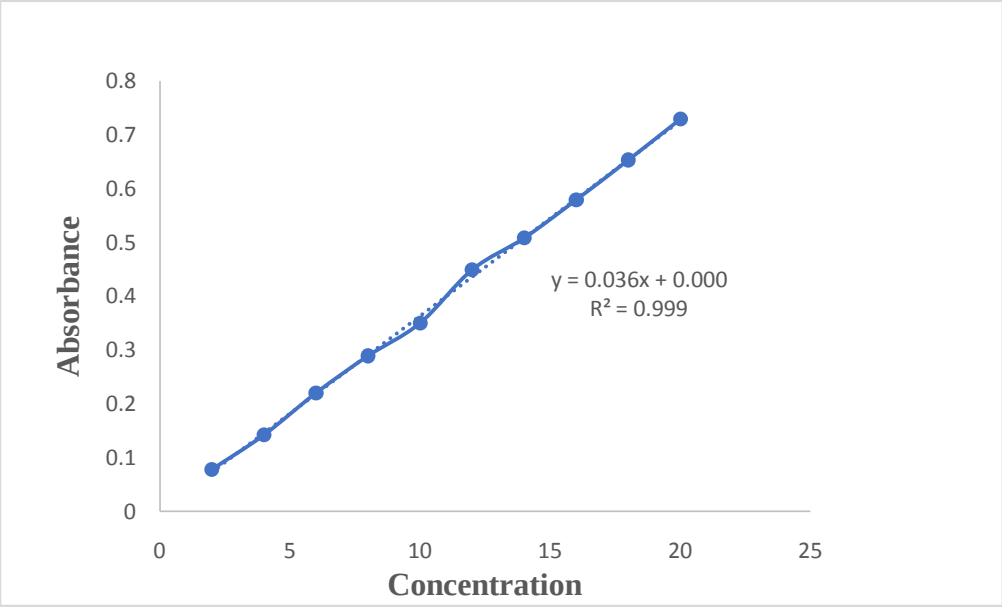

Figure No.2: Standard calibration curve of Amoxicillin Trihydrate in 0.1N HCl

Compatibility Studies
Interpretation of FTIR Spectrum

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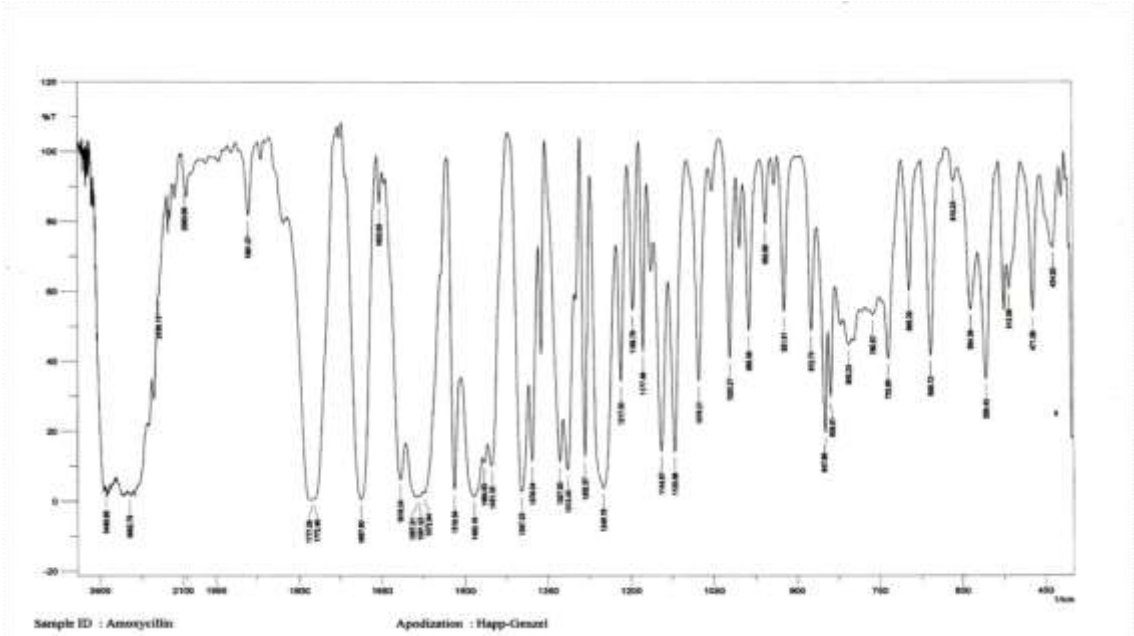

Figure No.3: FTIR spectra of Amoxicillin Trihydrate

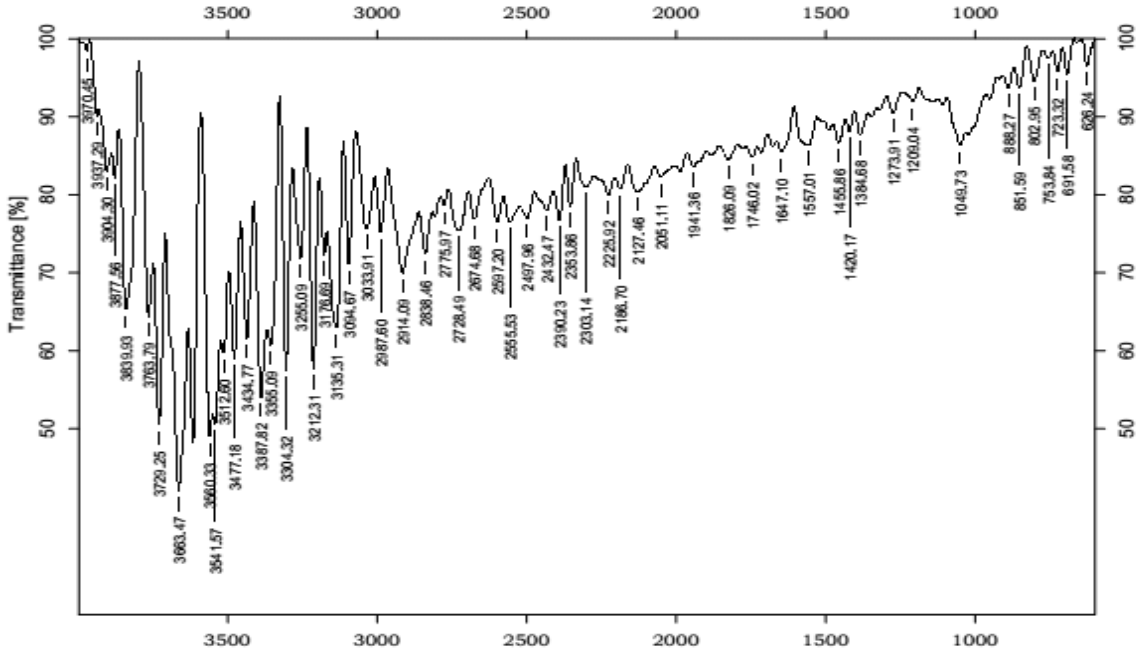

Figure No.4: FTIR spectra of HPMC K4M

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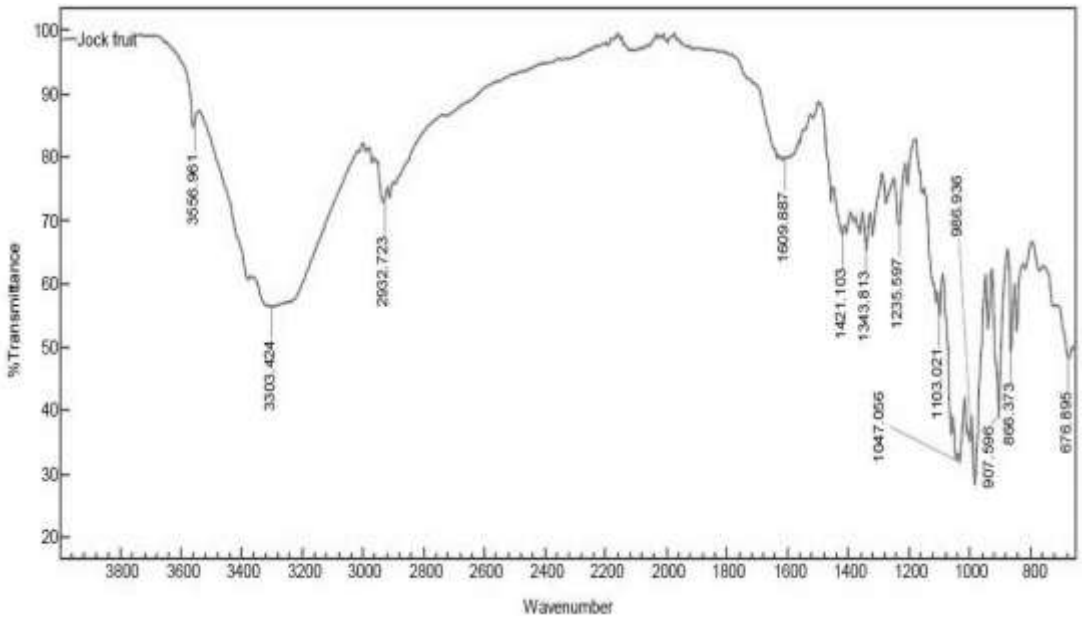

Figure No.5: FTIR spectra of jackfruit seed starch

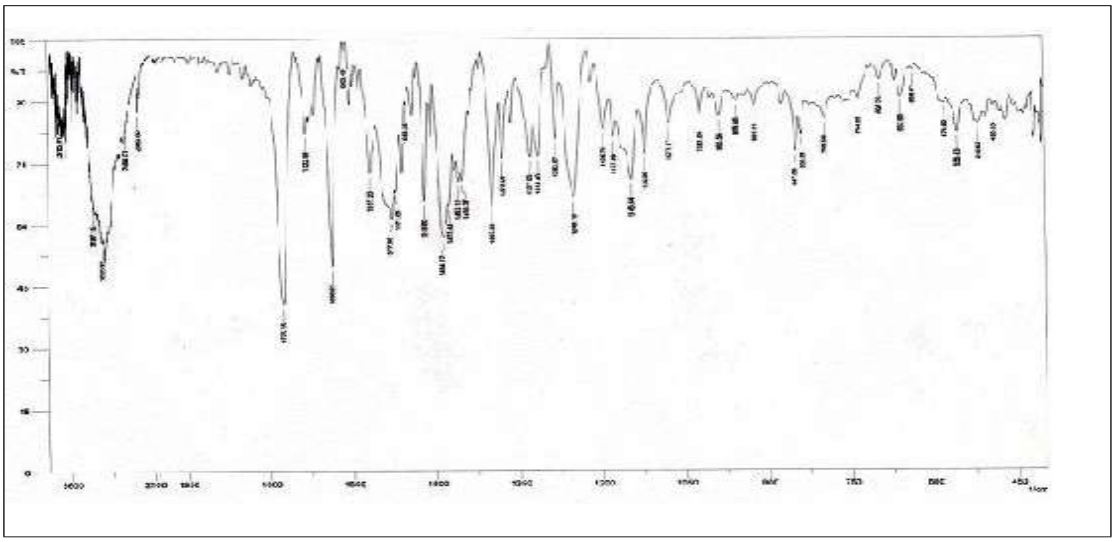

Figure No.6: Combine FTIR spectra of Amoxicillin Trihydrate with Jackfruit starch+ HPMC K4M

Phytochemical test and evaluation of jackfruit starch

Table No.3: Phytochemical tests for jackfruit seed powder extracted starch

Chemical test	Name of test	JFSP1	JFS1
Tests for carbohydrates	Molisch test	+ve	+ve
	Benedict's test	+ve	+ve

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	Barfoed test	+ve	-ve
Test for polysaccharides	Iodine test	+ve	+ve
Test for proteins	Biuret test	+ve	-ve
Test for alkaloids	Meyer's test	+ve	-ve
Test for glycosides	Killer – killani test	+ve	-ve
Test for flavanoidsw	Ferric chloride test	-ve	-ve

Where, JFSP1: jackfruit seed starch extracted by using water, JFSP: jackfruit seed powder

Table no.4: Evaluation of physicochemical properties of JFSP and extracted starch

Sr. No.	Parameter	JFSP	JFSP1
1.	Gelation temperature	66-70	65-70
2.	pH	6.75	6.89
3.	Viscosity	1.056cps	2.077cps
4.	Swelling index (%)	80	158

Where JFSP is jackfruit seed powder, JFSP1 is jackfruit seed starch extracted using water

Evaluation of powder blend

The results of all formulations F1 to F9 of Amoxicillin Trihydrate microsphere are shown in Table no.5, which were evaluated for variable parameters such as bulk density, tapped density, Compressibility index, Hausner's ratio and angle of repose. The % Compressibility index was in the range of 11-19 for all the formulations F1 to F9 indicating good flow property. The values of angle of repose for all the formulations was found to be in the range of 25-28 which indicated the good flow potential. Amoxicillin trihydrateisin powder form were investigated for various physical parameters. The result revealed that it has better flow property, bulk density, tapped density and the compressibility and Hausner ratio confirmed its better flow property. Amoxicillin trihydrate and excipients in the blend state had evaluated for its Preformulation property. They showed better flow property and compressibility and Hausner- ratio had showed its better suitability for the prepration of microspheres.

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Table No.5: Evaluation of powder blend

Formulation Code	Bulk Density ($g/cm^{3)}$	Tapped Density ($g/cm^{3)}$	Angle of Repose	Hausner's Ratio	Compressibility Index (%)
F1	0.724 ±0.30	0.944 ±0.12	25.53 ±0.21	1.116±0.11	17.70±0.22
F2	0.754±0.33	0.927±0.31	25.10±0.25	1.031±0.15	11.36±0.32
F3	0.818±0.32	0.948±0.22	25.20±0.23	1.65±0.16	18.51±0.33
F4	0.840±0.32	0.879±0.34	26.81±0.12	1.012±0.13	19.55±0.33
F5	0.608±0.13	0.829±0.32	28.33±0.20	1.163±0.18	16.50±0.36
F6	0.610±0.39	0.860±0.43	28.11±0.27	1.93±0.17	15.06±0.38
F7	0.735±0.37	0.850±0.37	25.40±0.32	1.172±0.12	14.30±0.35
F8	0.810±0.34	0.928±0.35	25.90±0.25	1.137±0.16	15.33±0.32
F9	0.812±0.09	0.833±0.32	25.13±0.21	1.134±0.15	14.37±0.38

Average particle size

Average particle size of microspheres as determined by optical microscopy by using stage micrometer are shown in Table no 6 and in Figure no.7. The mean particle size for the formulation F1 to F4 containing jackfruit starch was found to be in range from 460±12.40µm to 930±7.14µm. For formulation F5 to F9 containing jackfruit starch and HPMC k4m the mean particle size was found to be in range from 740±12.34µm to 990±10.70µm respectively. With increase in polymers concentration in the microspheres from F1 to F9, the particle size of microspheres increases respectively. This is because the viscosity of the polymer solution increases with increasing polymer concentration, which in turn decreases the stirring efficiency.

Table No.6: Average Particle Size of Amoxicillin Trihydrate Microspheres

Formulation code	Average particle size(µm)±SD
F1	835±6.35
F2	830±11.20
F3	460±12.40
F4	930±7.14
F5	990±10.70
F6	740±12.34

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F7	760±8.62
F8	890±11.63
F9	570±12.36

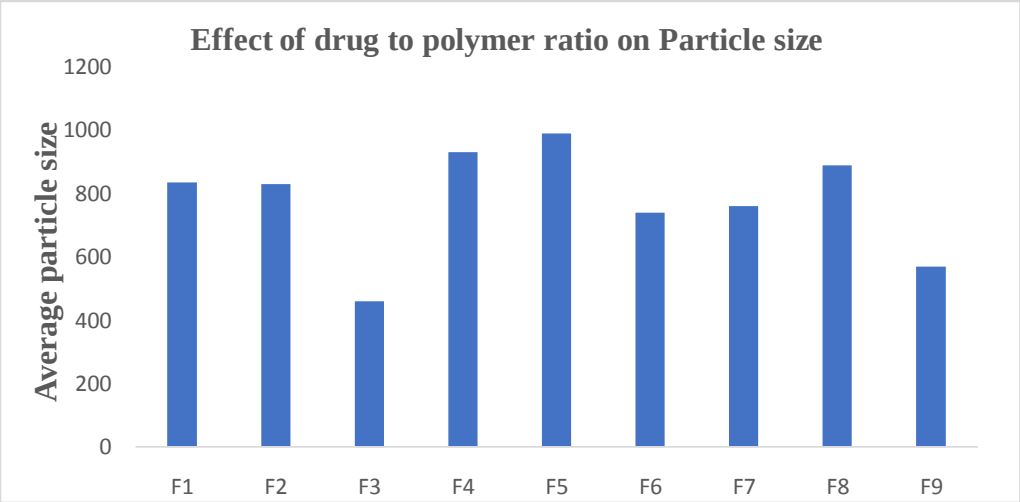

Figure No.7: Effect of drug to polymer ratio on Particle size

Scanning electron microscopy

The determination of shape and surface morphology was done by scanning electron microscope. SEM analysis of the samples revealed that all microspheres prepared were spherical in shape. The microspheres of amoxicillin trihydrate with starch were smooth, spherical and slightly aggregated particles when compared with the microspheres of HPMCK4M which were porous, grossly, discrete spherical. Scanning electron photomicrographs of the formulations F5 are shown in figure no.8

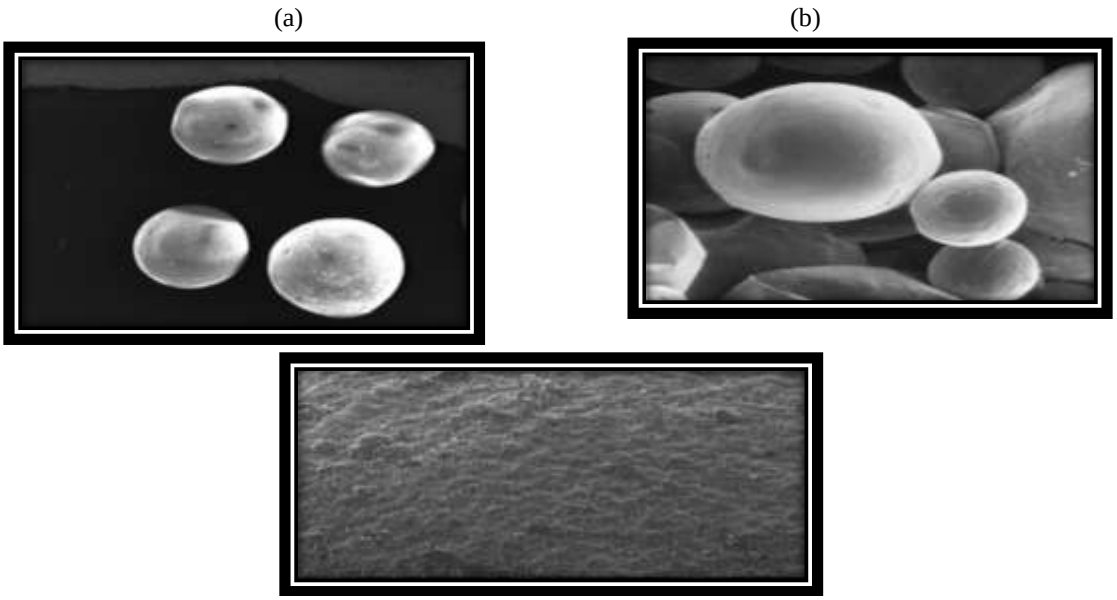

Figure No.8: SEM of spherical microspheres of Amoxicillin Trihydrate

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Percentage yield

Percentage yield of microspheres of all the formulations was in the range of 72.84% to 80.64% shown in the Table no.7

Table No.7: Percentage yield of Amoxicillin Trihydrate Microsphere

Sr. no.	Formulation code	%age yield
1.	F1	76.46±2.70
2.	F2	74.49±1.39
3.	F3	72.84±0.80
4.	F4	78.30±0.90
5.	F5	80.64±1.12
6.	F6	75.40±2.75
7.	F7	77.39±2.39
8.	F8	78.40±0.95
9.	F9	72.89±0.88

Values are mean ± SD, n=3

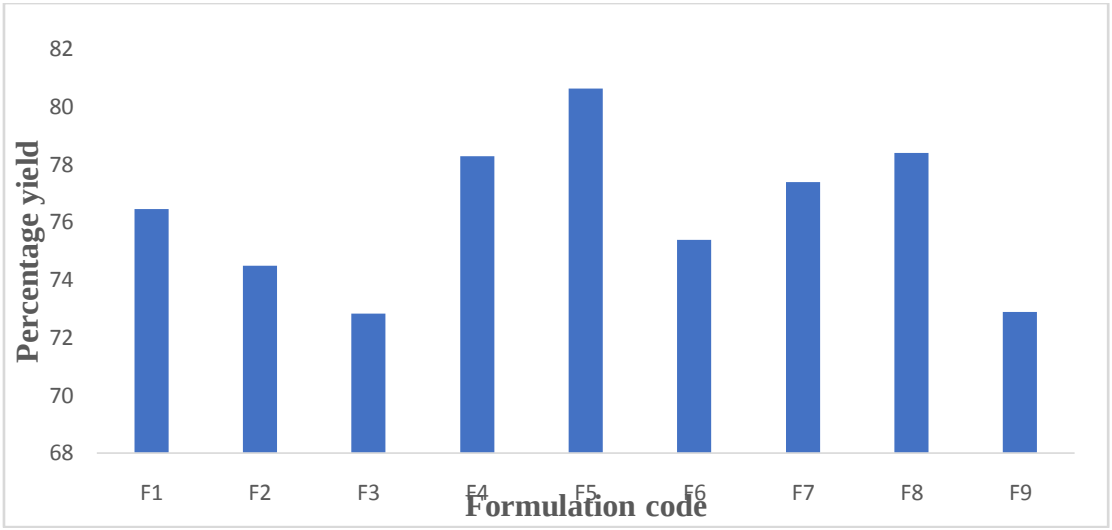

Figure No.9: Comparision of percentage yield

Determination of Drug content

The % determination of drug content was in the range of 83.79 to 92.75 respectively shown in Table no.8:

Table No.8: %age Drug Content of Prepared Microsphere

Sr.no.	Formulation code	Drug content
1.	F1	87.50±0.60
2.	F2	90.50±0.42
3.	F3	88.84±0.65
4.	F4	88.89±0.75
5.	F5	92.75±0.45
6.	F6	89.35±0.09
7.	F7	86.71±0.29
8.	F8	85.53±0.08
9.	F9	83.79±0.88

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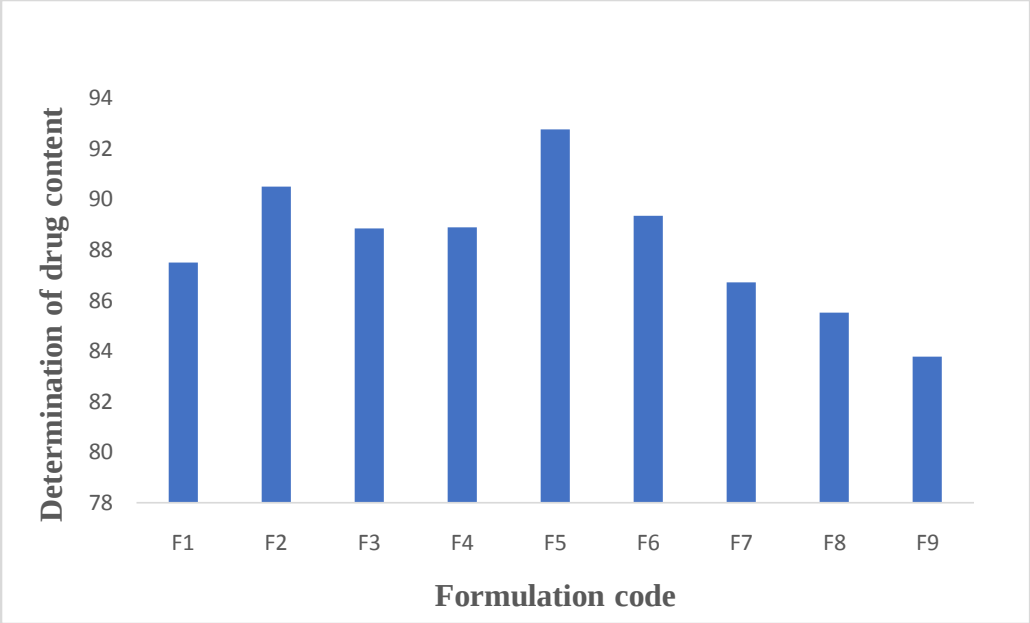

Figure No.10: Comparision of % Drug content of prepared microspheres

Percentage Drug Entrapment Efficiency

The % Drug entrapment efficiency was in the range of 80.49 to 89.94 respectively shown in Table no.9:

Table No.9: Drug Entrapment of Amoxicillin Trihydrate Microspheres

Sr. no.	Formulation	% Entrapment efficiency
1.	F1	81.70±0.05
2.	F2	82.60±0.55
3.	F3	81.70±0.66
4.	F4	84.89±0.77
5.	F5	89.94±0.25
6.	F6	88.44±0.21
7.	F7	81.33±0.68
8.	F8	80.49±0.09
9.	F9	84.78±0.79

Values are mean ± SD, n=3

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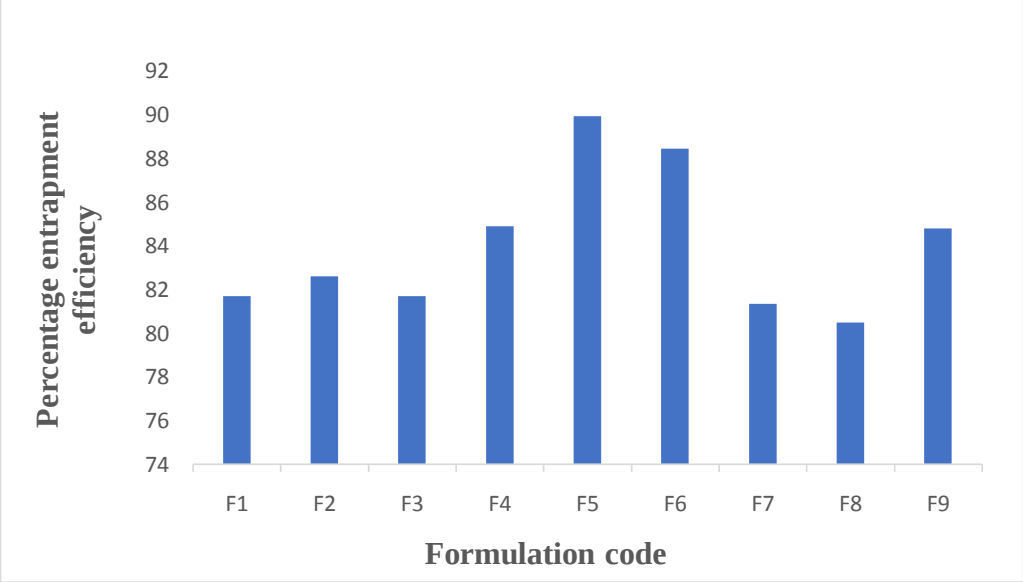

Figure No.11: Comparision of percentage entrapment efficiencyof prepared microsphere

In-vitro Drug Release Study

Dissolution studies on all the nine formulations of Amoxicillin Trihydrate microspheres were carried out using a USP dissolution apparatus Type I 0.1N HCl (pH 1.2) was used as the dissolution medium. The in-vitro drug release data of different formulations are shown in Table no.10and Figure no.12. The cumulative percentage drug release after 24hours was found to be in the range of 85.89, 83.11, 82.33 and 80.46% for the formulations F1, F2, F3 and F4 respectively whereas, cumulative percent drug release after 24hours was 88.96, 84.78, 81.04, 76.29, 79.80% for formulations F5 to F9 respectively. The cumulative drug release significantly decreased with increase in polymer concentration. The increased density of the polymer matrix at higher concentrations results in an increased diffusional path length. This may decrease the overall drug release from the polymer matrix. Furthermore, smaller microspheres are formed at a lower polymer concentration and have a larger surface area exposed to dissolution medium, giving rise to faster drug release.

Table No.10: Comparative Invitro drug release of Microsphere Formulations

Time (hrs.)	Cumulative % Drug Release of Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	17.21	16.56	14.40	13.92	18.15	16.90	16.55	14.14	13.93
2	22.43	21.47	19.18	17.10	25.78	22.37	21.67	18.98	18.76
3	28.40	25.60	24.40	22.53	35.78	25.56	26.51	20.32	22.80
4	34.10	32.43	31.44	29.33	42.06	36.16	31.84	23.45	27.31
5	47.37	38.39	37.73	31.87	49.92	38.11	40.71	30.29	37.28
6	58.00	49.39	53.71	51.80	64.98	51.63	54.69	48.15	55.79
7	63.90	55.97	59.75	58.65	71.89	62.09	60.49	53.99	61.79

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8	69.32	68.33	67.66	63.55	76.31	69.51	66.31	59.69	65.78
12	81.73	77.91	76.89	71.66	82.46	80.82	72.22	69.13	73.38
24	85.89	83.11	82.33	80.46	88.96	84.78	81.04	76.29	79.80

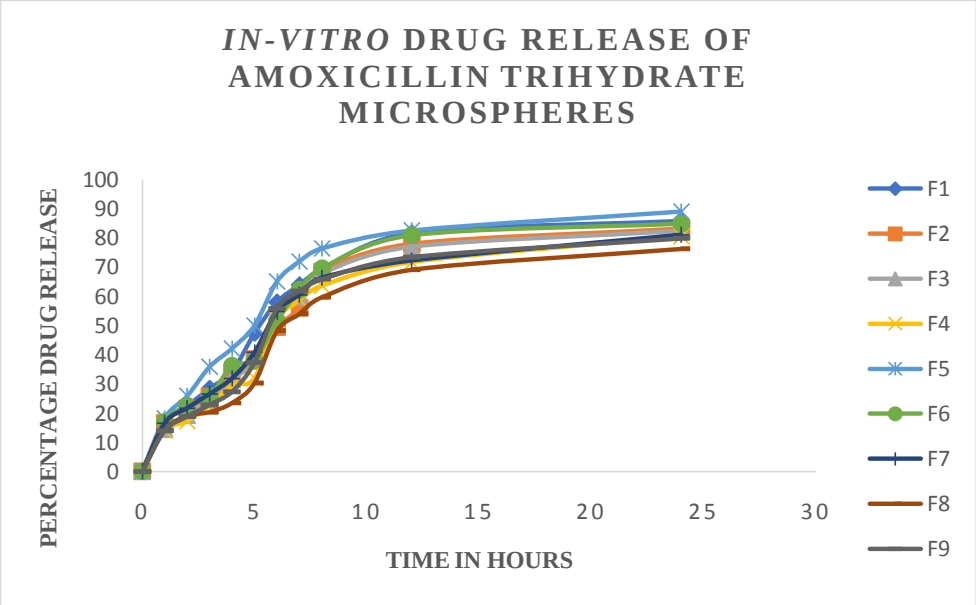

Figure No.12: Comparative In-vitro Dissolution Profile of Amoxicillin Trihydrate Microspheres

Release Kinetics

The results obtained from in-vitro drug release were plotted adopting five different mathematical models of data treatment as follows:
% 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 √T (root time). (Higuchi model) Log % Cum. Drug Release vs. Log Time (Peppas exponential equation). Hixson-Crowell's erosion equation, (% Cum. Drug Retained)1/3 Vs. Time.

The curve fitting results of the release rate profile of the designed formulation are shown in the Figure no. 13-17 which gave an idea on the release rate and the mechanism of release.
The values were compared with each other for model and drug equation as shown in Table no.11 based on the highest regression values (R^2), fitting of the release rate data to various models revealed that all the formulations (F1 to F9) follow zero order release kinetics with regression values ranging from 0.9785 to 0.9915.

Table No.11: Model Fitting Release Profile of Amoxicillin Trihydrate Microspheres

Formulation code	**Mathematical models (kinetics)**					**Best fit order**
	Korsmeyer	**Higuchi**	**Hixon Crowell**	**First order**	**Zero order**	
	R^2	**R^2**	**R^2**	**R^2**	**R^2**	
F1	0.6906	0.9384	0.7392	0.6694	0.9915	Zero order
F2	0.6972	0.9065	0.7554	0.6864	0.9835	Zero order

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F3	0.7270	0.9104	0.7704	0.7084	0.9894	Zero order
F4	0.7275	0.8918	0.7766	0.7172	0.9829	Zero order
F5	0.6641	0.9628	0.7047	0.6304	0.9782	Zero order
F6	0.6953	0.9084	0.7522	0.6825	0.9825	Zero order
F7	0.6899	0.9345	0.7376	0.6685	0.9904	Zero order
F8	0.7269	0.8744	0.7409	0.7352	0.9781	Zero order
F9	0.7344	0.9052	0.7767	0.7767	0.9865	Zero order

Korsmeyer-Peppas model for prepared Microspheres F5

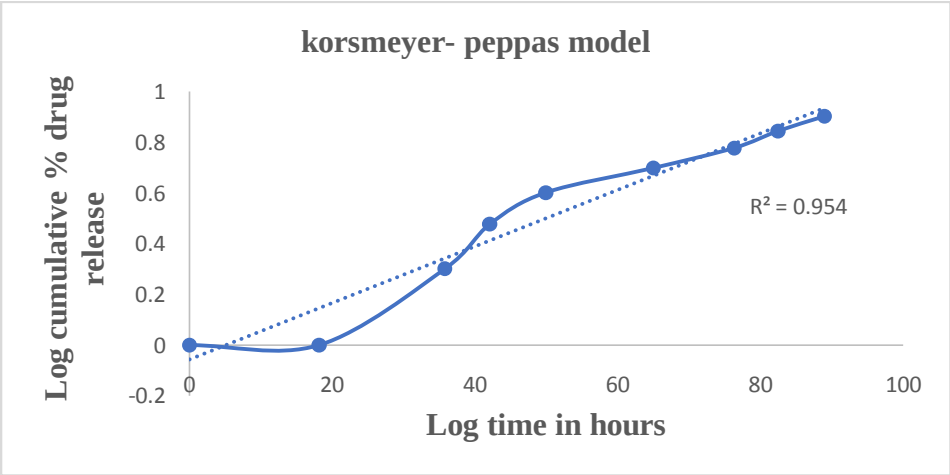

Figure No.13: Korsmeyer-Peppas release Kinetics for prepared microspheres F5

Higuchi model for prepared microspheres F5

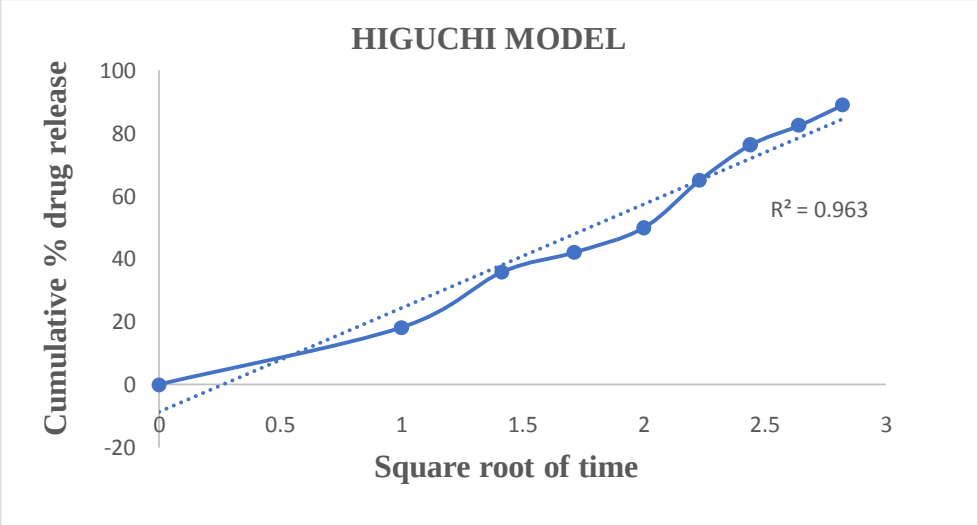

Figure No.14: Higuchi release kinetics for prepared microspheres F5

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Hixson-Crowell model for prepared microspheres F5

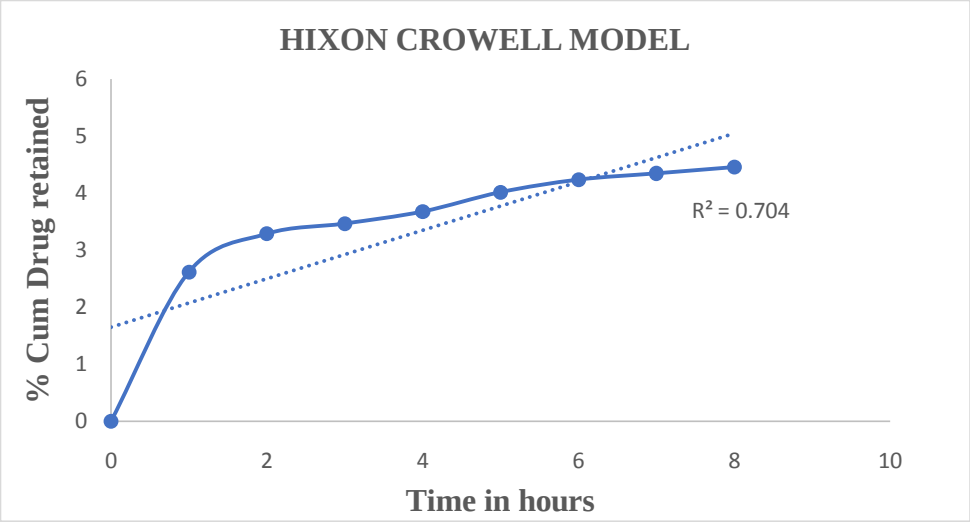

Figure No.15: Hixon-Crowell release kinetics for prepared microspheres F5

First order Model for prepared microspheres F5

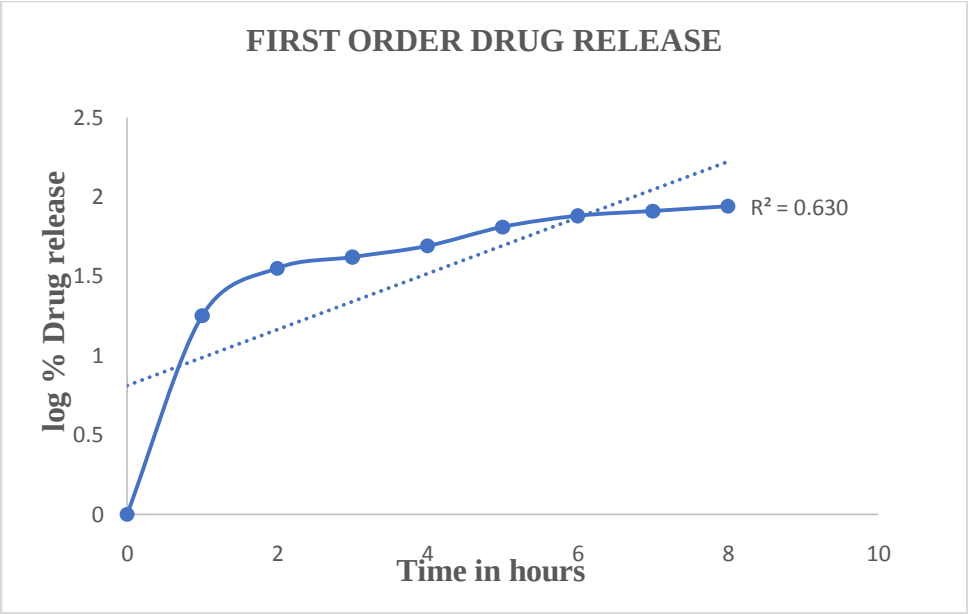

Figure No.16: First order release kinetics for prepared Microspheres F5

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Zero order for prepared microspheres F5

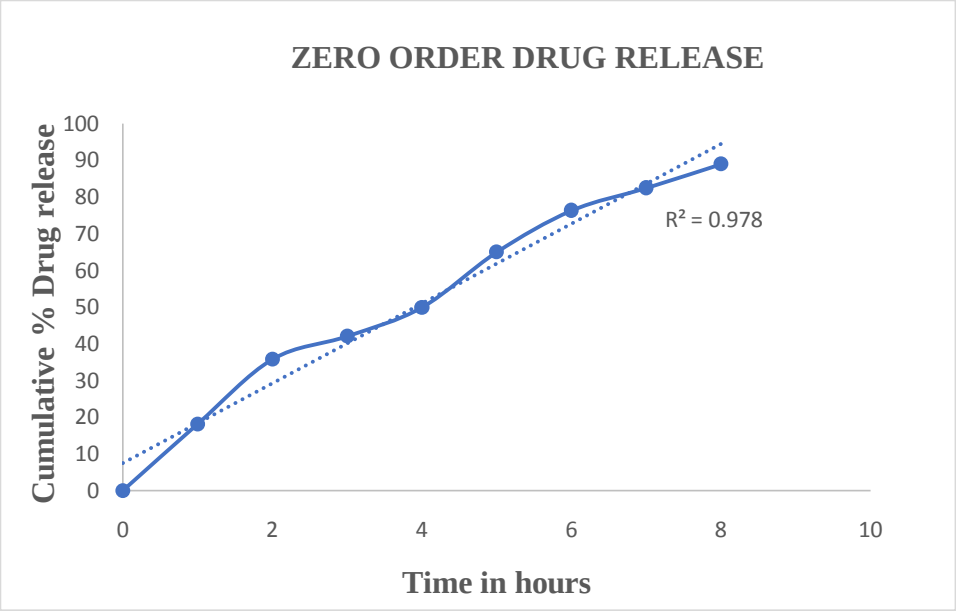

Figure No.17: Zero order release Kinetics for prepared Microspheres F5

Stability study

Stability study was conducted for the prepared amoxicillin trihydrate microspheres of formulation F5 at 40°C/75% RH respectively for a period of 60 days. Then, the sample F5 was analyzed for physical appearance, entrapment efficiency, and drug release studies of the microsphere at the end of 15,30,45,60 days.

The results of stability studies are given in the Table no.12.There was no significant change in the physical appearance, drug entrapment, and in-vitro release study of the microspheres.

Table No.12: Stability Studies for Formulations Stored at 40ºC/75% RH

Tested after days	% Drug entrapment	%CDR
	F5	F5
15	78.33	82.51
30	77.45	82.14
45	77.29	81.13
60	78.26	81.07

IV. CONCLUSION

The starch gelatin complex microspheres of Amoxicillin Trihydrate were prepared successfully using jackfruit starch in combination with HPMC K4M, Sodium alginate, Calcium chloride as copolymer in different proportions. Among all the formulations F5 showed better drug entrapment and sustained drug release than the other formulations. The formulated microspheres of Amoxicillin trihydrate via ionic gelation method enhance drug retention in stomach and increasing bioavailability of drug. It reveals that the prepared polymer system could be used in the drug delivery studies in future.

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