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Research Article

FORMULATION AND IN VITRO EVALUATION OF RIVAROXABAN MICROSPHERES

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ABSTRACT:
Microsphere drug delivery methods have been utilized to boost effectiveness, reduce toxicity, and improve patient compliance. Additional benefits of using microspheres to deliver medications include controlled drug release, improved bioavailability, and targeted drug delivery to the desired location. In order to achieve the required therapeutic effect, Chitosan is encapsulated in a biodegradable microsphere delivery system and given orally. The benefit of microsphere formulations over traditional tablet or capsule formulations is that they increase the surface area exposed to the absorption site, boosting medication absorption and reducing drug dose frequency. An anticoagulant and the first orally active direct factor Xa inhibitor. Rivaroxaban microspheres were prepared by Ionotropic Gelation Technique using different ratios of Rivaroxaban and Sodium Alginate, along with polymers like HPMC K15M, Pectin and Chitosan. Rivaroxaban microspheres were evaluated for percentage yield, particle size. Surface morphology, flow properties, drug content and entrapment efficiency and were found to be within the acceptable range. Invitro dissolution studies of the microspheres revealed that the formulation F12 containing Chitosan as a polymer shows maximum drug release at the end of 12 hours, when compared with the other formulations. Drug release kinetics of the optimized formulation states that the formulation F12 follows zero order drug release with Super case II transport mechanism.
Key words: Rivaroxaban microspheres, Chitosan, Ionotropic Gelation Technique, SEM.

INTRODUCT ION

Microencapsulation is the process by which solids, liquids and gases are enclosed in microscopic particles by formation of wall coatings around the drug[1]. Microspheres are small spherical particles within the 1-100 µm range[2]. Microspheres can be characterized as a matrix system that allows the drug to be homogenously dispersed, dissolved or suspended[3]. There are different techniques involved in the production of microspheres. The solvent evaporation method is used were the polymer is dissolved in an organic solvent and the drug is either dissolved or dispersed in a polymer solution. The solution containing the drug is then emulsified into an aqueous phase containing suitable additive to form oil in water emulsion[4]. The ionotropic gelation method is based on the ability of the polyelectrolyte to cross link in the presence of counter ions in order to form beads[5]. The emulsion solvent diffusion method is the process were the drug is dissolved in the organic solvent and the solution is dispersed in the aqueous in the aqueous producing the emulsion droplets.[6]

MATERIALS & METHODS USED: Rivaroxaban API was procured from Dr. Reddy's Laboratories, and HPMC K 100M, Pectin were procured from Spectrum pharmalabs Hyderabad, Calcium Chloride, Sodium Alginate were procured from S D fine chemical Ltd, Mumbai, Chitosan was procured from Shreeji chemicals, Mumbai

Solubility study:

Excess drug was added carefully using a spatula to 10 ml of the different buffer solutions in a conical flask, while stirring until a heterogeneous system (solid sample and liquid) was obtained. The solution containing excess solid was then capped, and stirred at 150 rpm at room temperature for 24 hours. The solution containing excess solid was filtered using 0.45µm PVDF filter, appropriate dilutions were then made and analyzed using UV spectrophotometer at required nanometer range of drug. The same procedure was fallowed for all selected drugs. (Saturation solubility was carried out at 25^0C using required different buffers).

Determination of absorption maximum (λ-max):

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The wavelength at which maximum absorption of radiation takes place is called as λ max. This λ max is characteristic or unique for every substance and useful in identifying the substance. For accurate analytical work, it is important to determine the absorption maxima of the substance under study. Most drugs absorb radiation in ultraviolet region (190-390nm), as they are aromatic or contain double bonds.

Accurately weighed 10mg of drug was dissolved in 6.8 pH phosphate buffer taken in a clean 10ml volumetric flask. The volume was made up to 10ml with the same which will give stock solution-I with concentration 1000µg/ml. From the stock solution-I, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10ml using 6.8 pH phosphate buffer to obtain stock solution-II with a concentration 100µg/ml. From stock solution-II, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10ml using 6.8 pH phosphate buffer to get a concentration of 10µg/ml. This solution was then scanned at 200-400nm in UV-Visible double beam spectrophotometer to attain the absorption maximum (λ-max). The sample was analyzed by UV Spectrophotometer at 248 nm.

PREPARATION OF CALIBRATION CURVE

Procedure for standard curve in 6.8 pH phosphate buffer:

10 mg of drug was dissolved in 10 ml of 6.8 pH phosphate buffer by slight shaking (1000 µg/ml). 1 ml of this solution was taken and made up to 10 ml with 6.8 pH phosphate buffer, which gives 100 µg / ml concentration (stock solution). From the stock solution, concentrations of 0.5,1.0,1.5,2,2.5 and 3ml was withdrawn and add in 10ml volumetric flasks separately then we get 5, 10, 15, 20,25 and 30 µg/ml in 6.8 pH phosphate buffer were prepared. The absorbance of diluted solutions was measured at particular nanometer and a standard plot was drawn using the data obtained. The correlation coefficient was calculated.

FORMULATION DESIGN

Table.1 Formulation design for Rivaroxaban microspheres using different ratios of drug and polymers

Formulation code / Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	20	20	20	20	20	20	20	20	20	20	20	20
Sodium alginate	100	100	100	100	100	100	100	100	100	100	100	100
Pectin	20	40	60	80	--	--	--	--	--	--	--	--
HPMC K15M	--	--	--	--	50	100	150	200	--	--	--	--
Chitosan	--	--	--	--	--	--	--	--	50	100	150	200
Calcium chloride	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
Distilled water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Preparation of Rivaroxaban microspheres

Method used: Ionic Gelation Technique:

Microspheres of Rivaroxaban were prepared by ionotropic gelation method using Drug & Sodium alginate, and Polymers like Pectin, HPMC K15M, Chitosan and calcium chloride.

Step 1: Add the weighed quantity of Sodium alginate was dissolved in 25ml of distilled water.

Step 2: Next to this, weighed quantity of drug and polymers were added to sodium alginate solution with stirring at about 800 rpm.

Step 3: The mixture was extruded through a 22G syringe needle into drop wise to 100 ml of calcium chloride (1%) solution under continuous stirring. Stirring was continued for 60 minutes. The obtained microspheres were filtered and washed with purified water and then dried for 12 hours at 40°C. Preparation of microspheres was optimized based on entrapment efficiency and release data

EVALUATION OF RIVAROXABAN MICROSPHERES

EVALUATION:

FTIR analysis:

The drug-polymer interactions were studied by FTIR spectrometer, Shimadzu 8400 S. 2% (w/w) of the sample, with respect to a potassium bromide (KBr; SD Fine Chem. Ltd., Mumbai, India) was mixed with dry KBr. The mixture was ground into a fine powder using mortar and then compressed into a KBr discs in a hydraulic press at a pressure of 10000 PSI. Each KBr disc was scanned 10 times at a resolution of 2 cm^{-1} using Happ-Genzel apodization. The characteristic peaks were recorded

MICROMERETIC PARAMETERS:

Bulk Density: Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. It is determined by pouring pre-sieved blend into a graduated cylinder via a large funnel and measure the volume and weight as is given by

Bulk density= weight of blend/Bulk volume of blend

Tapped density: Tapped density is determined by placing a graduated cylinder containing known mass of blends on a mechanical tapped apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed.

Tapped density=weight of blend/tapped volume of blends

Compressibility Index: The compressibility index of the granules was determined by Carr's compressibility index.

Carr's index (%) = [(TBD – LBD) × 100]/TBD

Hausner's ratio: Hausner's ratio was determined as the ratio between the tapped density to that of the bulk density.

H.R = Tap Density / Bulk Density

Angle of repose: The manner in which stresses are transmitted through a bed and beds response to applied stress is reflected in the various angles of friction and response. The most commonly used of these is angle of repose, which may be determined experimentally by a number of methods. The method used to find the angle of repose is to pour the powder in a conical heap on a level flat surface and measure the inclined angled with the horizontal pile.

$$\text{Tan } \theta = h/r$$

$$\theta = \tan^{-1}(h/r)$$

Particle Size

It is possible to use ordinary microscope for particle size determination in the range of 0.2 to above 100 μm to measure particle size of individual microsphere.[55]All the microspheres were evaluated with respect to their size and shape using optical microscope fitted with an ocular micrometer and a stage micrometer. Ocular micrometer was calibrated with the stage micrometer. Slides of dilute suspensions of microspheres in liquid paraffin were prepared and slides were placed on mechanical stage of microscope. The diameter of 100 microspheres was measured randomly by optical microscope and average particle size was determined.

Scanning electron microscopy (SEM)

In the pharmaceutical industry, SEM may be used as a qualitative tool for the analysis of drug substance and drug product in order to obtain information on the shape and surface structure of the material. SEM plays an important role in the characterization of nanoscale and sub-micron particles. It has been used to determine surface topography, texture and to examine the morphology of fractured or sectioned surfaces. The examination of the surface of polymeric drug delivery systems can provide important information about the porosity and microstructure of device.

Procedure for SEM Analysis:

Mounting: The dried samples were lightly sprinkled on a double adhesive carbon tape, which was stuck to analuminum stub.

Coating: Thin coating of an electron dense metal (platinum) was applied to the mounted sample using JEOL JFC-1600 Ion Sputter Coater which is having a vacuum chamber. The chamber was evacuated using a rotary pump and inert carrier gasargon was introduced to produce partial vacuum of 10^{-2} mmHg. The argon atmosphere ionized by electrodes located near platinum metal foil, thereby heavy metal atoms were ejected from the foil, covering the mounted sample with finely dispersed coating.

Imaging: The sample were removed from the Ion Sputter and mounted on a sample holder of JEOL JSM-6360 SEM and scanned by an electron beam Scanning Microscope. These electrons were collected with detector which produced three dimensional images of the sample surface on TV screen attached to the microscope. The images were printed on photographic film using at various magnifications.

Actual drug content and encapsulation efficiency

10 mg of microspheres were accurately weighted and transferred in a 50 ml volumetric flask. Volume was adjusted with 1% SLS and microspheres were dissolved by ultra-sonication for 3 h at25 °C. The samples were filtered through 0.2 μm membrane filter. 5 ml from the sample solution was transferred to 50 ml volumetric flask and volume was adjusted to 50 ml with same medium and absorbance of samples was measured at 248 nm using UV-spectrophotometer. Actual drug content (AC)and encapsulation efficiency (EE) were calculated using following equations. All analyses were carried out in triplicate.

$$AC(\%) = \frac{Mact}{Mms} \times 100$$

$$EE(\%) = \frac{Mact}{Mthe} \times 100$$

Where,

M_{act}= Actual bosentan monohydrate content in microspheres

M_{ms}= Weighed quantity of microspheres

M_{the}= Theoretical quantity of Bosentan Monohydrate in microspheres calculated from the quantity added in the process.

In vitro Dissolution Studies:[88,89]

The dissolution test measures the amount of time required for certain percentage of the drug substance in a tablet to go into solution under a specified set of conditions. It describes a step towards physiological availability of the drug substance, but it is not designed to measure the safety or efficacy of the formulation being tested.

In-vitro release profile:

Medium : 6.8 pH Phosphate Buffer
Apparatus : USP I (Basket)
Speed : 75 rpm
Time : 1hr, for every 2hrs up to 12hr
Temperature : 37.5 °C
λ max : 248 nm

Perform the test on microspheres place in each dissolution vessel containing 900ml of 6.8 pH Phosphate Buffer maintained at 37 °C ± 0.5 °C. At specified time withdrawn required amount the sample and replace the same amount with (maintain sink conditions) phosphate buffer, then absorbance was taken and calculate percentage release.

RELEASE KINETIC MODELS:

One of the most important and challenging areas in the drug delivery field is to predict the release of the active agent as a function of time using both simple and sophisticated mathematical models. The importance of such models lies in their utility during both the design stage of a pharmaceutical formulation and the experimental verification of a release mechanism. In order to identify a particular release mechanism, experimental data of statistical significance are compared to a solution of the theoretical model. It is therefore clear that only a combination of accurate and precise data with models accurately depicting the physical situation will provide an insight into the actual mechanism of release.

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

Zero Order Kinetics: This model describes the system where the release rate is independent of the concentration of the dissolved species. Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly assuming that area does not change and no equilibrium conditions are obtained can be represented by the following equation-

$$\mathbf{WO\text{-}Wt = K\ t}$$

First Order Kinetics: The first order equation describes the release from systems where the dissolution rate is dependent upon the concentration of the dissolving species.

To study the first order release rate kinetics, the release rate data were fitted to the following equation.

$$\mathbf{\log Qt = \log Qo + K1t / 2.303}$$

Higuchi Model: Higuchi developed several theoretical models to study the release of water soluble and low-soluble drugs incorporated in semisolids and/or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion media. The Higuchi equation is

$$\mathbf{f_t = K_H \times t_{1/2}}$$

Korsemeyer-Peppas Model: Korsemeyer et al. developed a simple, semi-empirical model, relating exponentially the drug release to the elapsed time. To study this model the release rate data is fitted to the following equation

$$\mathbf{Ft = M_t / M_\infty = K.\ t^n}$$

RESULTS AND DISCUSSIONS

PREFORMULATION STUDIES

Solubility study:

Saturation solubility was carried out at 25^0C using 0.1N HCl, 6.8 phosphate buffer, and 7.4pH buffer.

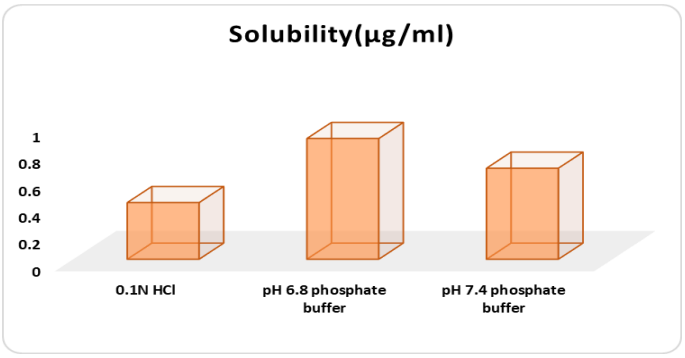

Figure 1. Solubility studies

Discussion: From the above obtained solubility studies we can say solubility of the drug is more in 6.8 pH Buffer than the other buffers.

UV SPECTRUM OF RIVAROXABAN

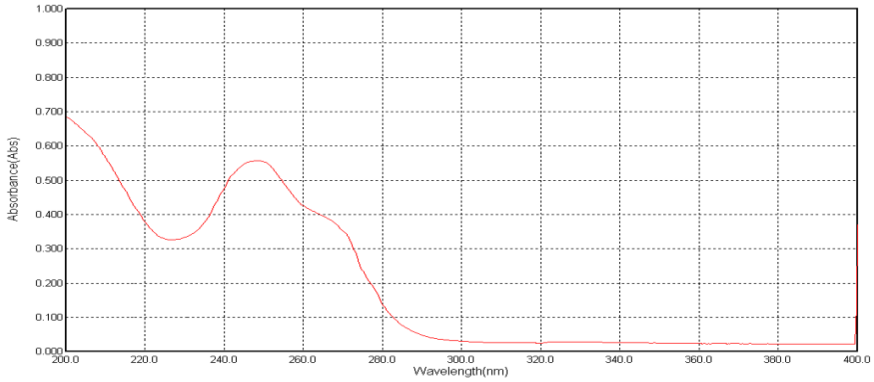

Figure.2 UV spectra of Rivaroxaban at 248 nm

Discussion:

The maximum absorbance of the Rivaroxaban was found to be at 248 nm. Hence the Wavelength of 248 nm was selected for analysis of drug in dissolution media.

STANDARD CALIBRATION CURVE

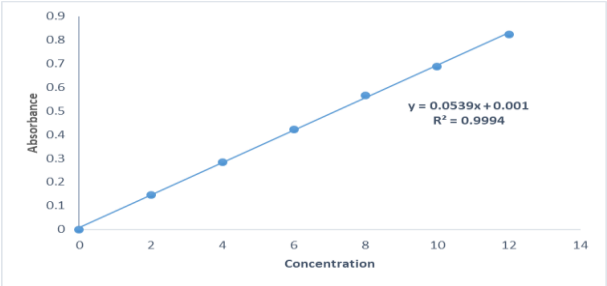

Figure.3 Standard calibration data of Rivaroxaban in 6.8 pH Buffer

EVALUATION OF RIVAROXABAN MICROSPHERES

Drug polymer interaction (FTIR) study

From the spectra of Rivaroxaban, physical mixture of Rivaroxaban and polymer, Rivaroxaban microspheres and blank microspheres, it was observed that all characteristic peaks of Rivaroxaban were present in the combination spectrum, thus indicating compatibility of the Rivaroxaban and polymer. IR Spectra shown in Figures below.

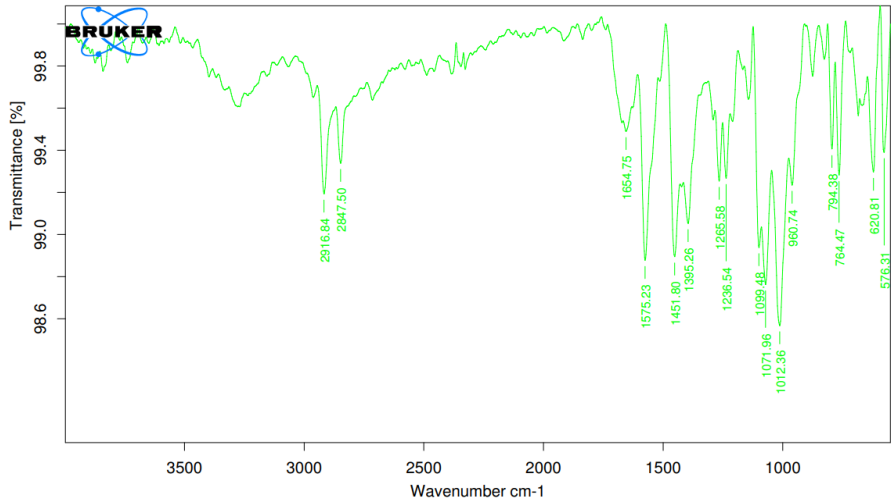

Figure.4 IR spectra of pure Rivaroxaban

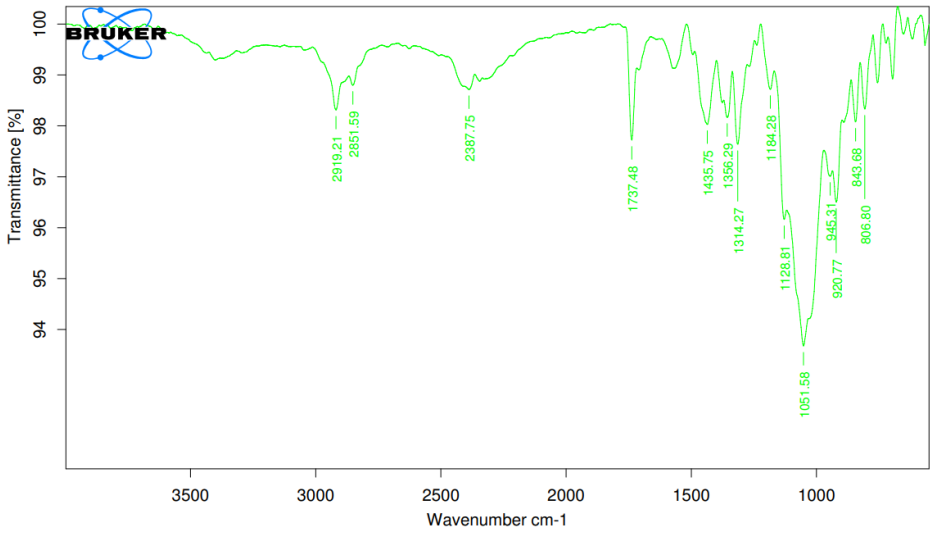

Figure.5 IR spectra of optimized formulation

Discussion:

From the drug excipient compatibility studies we observed that there are no interactions between the pure drug (Rivaroxaban) and optimized formulation (Rivaroxaban+ excipients) which indicates there are no physical changes.

Flow Properties:

Table .2 Flow Properties of Rivaroxaban (pure drug):

FLOW PROPERTIES	VALUES
Angle of Repose	27˚45
Bulk Density	0.392 g/ml
Tapped Density	0.451 g/ml
Hausner's Ratio	1.17
Carr's Index	15.26%

Discussion:

From the Flow Properties studies we found that the, angle of repose of Rivaroxaban (pure drug) was 27˚45. The bulk density of Rivaroxaban (pure drug) was 0.392 g/ml The tapped density of Rivaroxaban (pure drug) was 0.451 g/ml. The Hausner's ratio of Rivaroxaban (pure drug) was 1.17. The Carr's index of Rivaroxaban (pure drug) was 15.26%

FLOW PROPERTIES

Characterization of Rivaroxaban microspheres:

Table.3 Characterization of Rivaroxaban microspheres

Parameter	Bulk density (gm/cc)	Tapped density (gm/cc)	Hausner's ratio	Compressibility index
F1	0.429±0.06	0.535±0.05	1.21±0.02	19.47±1.12
F2	0.434±0.09	0.541±0.09	1.18±0.01	17.25±1.09
F3	0.421±0.05	0.526±0.11	1.16±0.03	16.36±1.08
F4	0.410±0.09	0.543±0.09	1.15±0.02	16.84±1.14
F5	0.445±0.08	0.538±0.10	1.20±0.01	20.62±1.15
F6	0.464±0.07	0.575±0.09	1.18±0.02	19.41±1.19
F7	0.409±0.07	0.568±0.07	1.16±0.03	17.18±1.12
F8	0.412±0.04	0.586±0.10	1.14±0.01	16.47±1.18
F9	0.438±0.03	0.535±0.09	1.17±0.02	15.48±1.12
F10	0.452±0.05	0.578±0.07	1.15±0.01	13.42±1.16
F11	0.448±0.01	0.495±0.05	1.13±0.02	14.24±1.11
F12	0.465±0.05	0.589±0.07	1.11±0.01	12.42±1.18

Discussion: The formulations F1 to F12 found to have varying bulk density, tapped density, compressibility index and Hausner's ratio which ranged from 0.409±0.07gm/cc to 0.465±0.05gm/cc, 0.495±0.05gm/cc to 0.589±0.07 gm/cc, 12.42±1.18% to 20.62±1.15% and 1.11±0.01 to 1.21±0.02 respectively. The observed values were within I.P limits and also demonstrate good flow property for the developed formulation (Table).

Table.4 Particle size, Drug Entrapment Efficiency of Rivaroxaban microspheres

Formulation Code	Particle Size (µm)	% Yield	Entrapment Efficiency	Drug Content
F1	214.15±1.33	92.18±1.21	53.25±1.92	94.56±0.63
F2	226.74±0.81	94.24±1.14	59.18±1.11	95.48±0.91
F3	208.78±1.12	95.29±1.29	61.26±1.85	96.59±1.97
F4	207.15±1.14	96.42±1.35	65.45±1.25	97.64±1.01
F5	214.15±0.18	93.85±1.29	56.26±2.74	93.46±1.22
F6	205.18±1.29	95.36±1.55	60.48±2.15	94.78±1.46
F7	217.62±1.18	96.75±1.97	64.25±1.36	96.11±1.18
F8	226.78±1.74	97.19±1.01	69.16±1.84	98.46±1.26
F9	203.18±0.74	94.28±1.18	63.18±1.45	96.15±1.42
F10	209.62±1.26	96.84±1.26	67.24±1.84	97.36±1.85
F11	204.45±1.85	97.25±1.45	69.74±1.24	98.47±1.24
F12	200.00±1.68	98.86±1.12	75.26±1.95	99.45±1.58

Discussion: The formulations F1 to F12 found to have varying particle size, percentage yield, entrapment efficiency and drug content which ranged from 200.00±1.68 µm to 226.78±1.74µm, 92.18±1.21% to 98.86±1.12%, 53.25±1.92% to 75.26±1.95% and 94.56±0.63% to 99.45±1.58% respectively.

Scanning electron microscopy analysis (SEM)

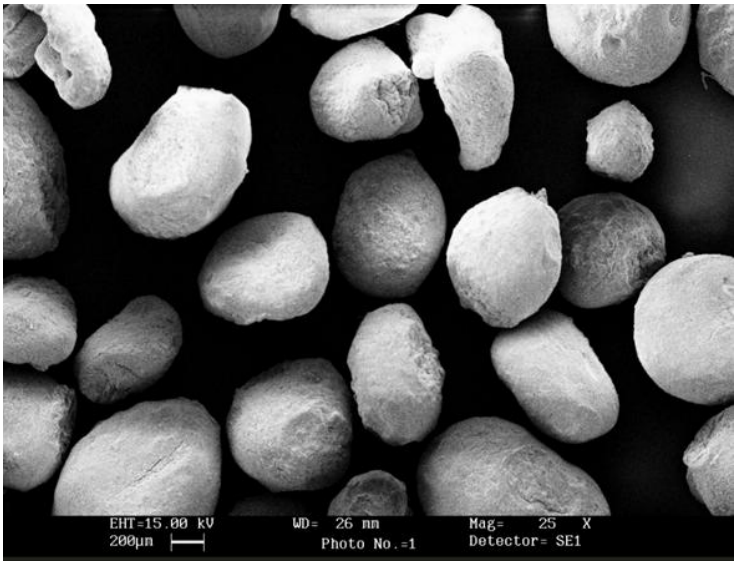

Figure.6 Scanning electron microscopy analysis (SEM)

Discussion: The optimized formulation was evaluated for its surface morphology by using Scanning electron microscopy. The outer surface of the microspheres was found to be smooth. The surface topography revealed a spherical surface for all the formulations and a round cavity enclosed by an outer shell composed of the drug and polymer. The particle size was found to be 200µm.

***In vitro* dissolution studies of Rivaroxaban:**

Table.5 Dissolution profile of Rivaroxaban formulations (Mean ± SD; n=1)

Time(hr)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	25.64±1.25	27.58±1.36	32.84±1.15	18.75±1.47	24.54±1.18	26.15±1.70
2	31.14±1.26	47.15±1.54	45.85±1.43	25.64±1.98	36.84±1.4	32.26±1.21
4	38.45±1.89	66.84±1.67	54.98±1.26	32.38±1.45	50.14±1.48	46.42±1.85
6	69.45±1.87	79.85±1.59	75.23±1.75	49.75±1.19	65.28±1.70	56.26±1.61
8	86.28±1.56	91.45±1.65	87.55±1.10	63.78±1.47	79.74±1.35	78.45±1.31
10	98.74±1.25	98.28±1.45	97.81±1.78	78.98±1.54	98.48±1.75	86.26±1.05
12				98.12±1.23		

Table.6 Dissolution profile of Rivaroxaban formulations (Mean ± SD; n=1)

Time(hr)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
1	29.25±1.17	28.64±1.74	38.47±1.98	42.45±1.25	18.19±1.77	25.48±1.98
2	35.42±1.55	34.98±1.44	45.81±1.84	52.67±1.24	25.86±1.15	36.48±1.75
4	49.19±1.33	41.45±1.51	59.61±1.24	63.48±0.98	42.84±1.09	58.71±1.85
6	58.25±1.60	48.42±1.78	75.64±1.02	77.51±1.65	55.74±1.48	65.24±1.24
8	75.36±1.74	64.45±1.30	85.24±1.24	89.54±1.21	69.85±1.70	72.48±1.26
10	98.19±1.49	78.98±1.19	98.64±1.84	99.61±1.74	79.69±1.36	89.64±1.74
12		98.41±1.07			98.27±1.22	99.11±1.42

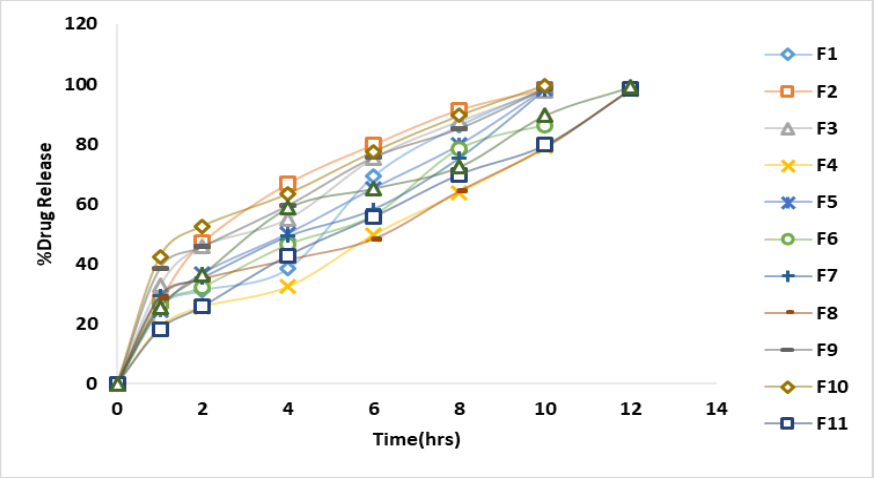

Figure.7 *In vitro* dissolution profile of Rivaroxaban formulations F1-F12

Evaluation of drug release kinetics of optimized formulation (F12):

ZERO ORDER PLOT

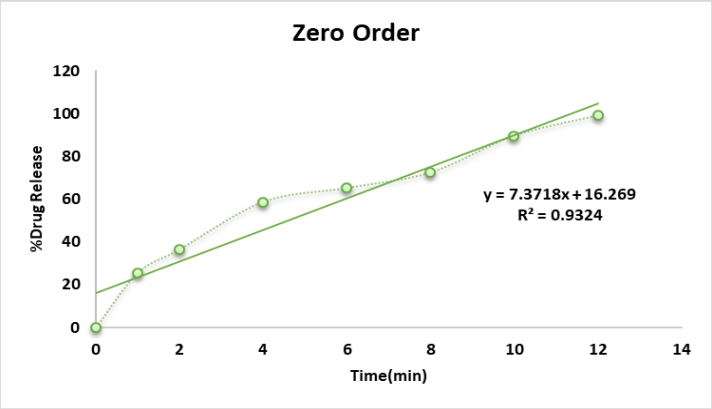

Figure.8 Optimized formulation zero order plot of Rivaroxaban (F12)

FIRST ORDER PLOT

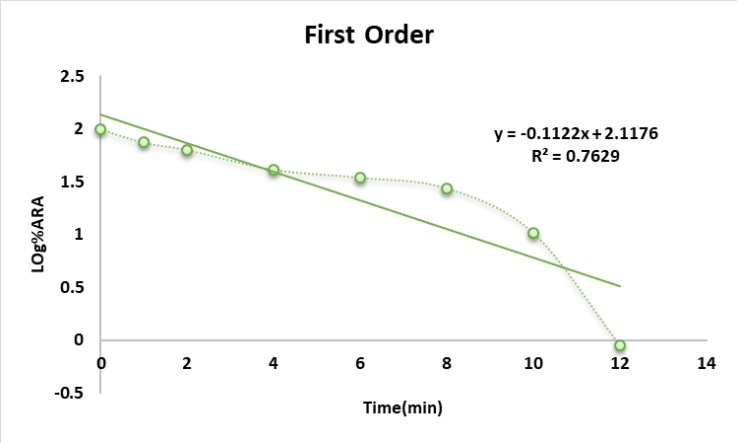

Figure.9 Optimized formulation first order plot of Rivaroxaban (F12)

HIGUCHI PLOT

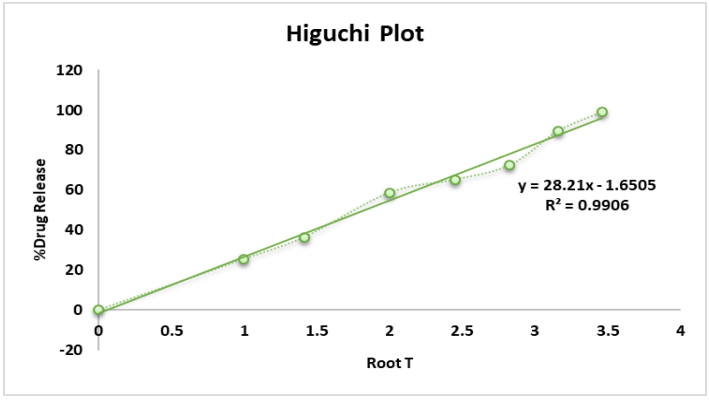

Figure.10 Optimized formulation Higuchi plot of Rivaroxaban (F12)

PEPPAS PLOT

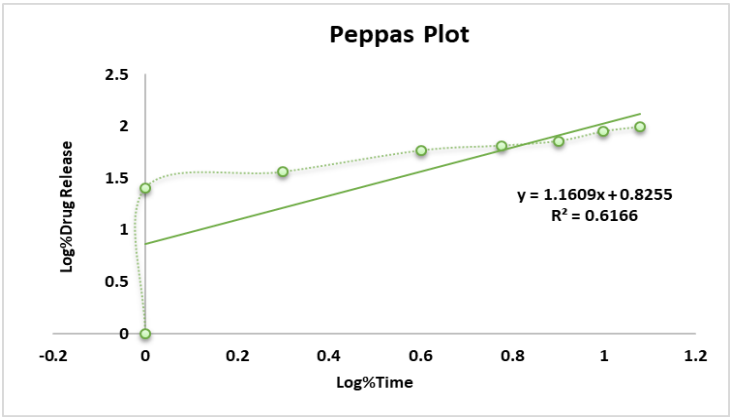

Figure.11 Optimized formulation Peppas plot of Rivaroxaban (F12)

Table.7 Co-efficient of determination and 'n' values of optimized formulation (F12)

	R2 values				n values
Formulations	**Zero order**	**First order**	**Higuchi**	**Korsmeyer-peppas**	**Korsmeyer-peppas**
F12 Optimized	0.932	0.762	0.990	0.616	1.160

Discussion: The optimized formulation F9 has coefficient of determination (R2) values of Zero order, First order, Higuchi and Korsmeyer Peppas of 0.932, 0.762, 0.990 and 0.616 respectively. A good linearity was observed with the zero order. The slope of the regression line from the Higuchi plot indicates the rate of drug release through mode of diffusion, and further confirms the diffusion mechanism. The data fitted into the Korsmeyer Peppas equation which showed linearity with slope n value of 1.160 for optimized formulation F12. This n value indicates the coupling of (swelling, polymer relaxation) diffusion and erosion mechanism. Thus, it indicates the drug release from the tablet follows Super case transport mechanism. The presence of swelling and cross linked polymers within the matrix structure might be responsible for the drug release controlled by more than one process. Thus, with regarded to release kinetics, the optimized batch F12 follows best fitted for zero order drug release with Super case II transport mechanism.

CONCLUSION:

The goal of present work is to provide a therapeutic amount of (Rivaroxaban) to the proper site in the body and also to achieve and maintain the desired Rivaroxaban concentration. An attempt was made to prepare microspheres of Rivaroxaban ionic gelation techniques by using polymers like HPMC K100M, Chitosan and

Pectin achieve an oral controlled release of the Rivaroxaban. In the present study nine formulations were formulated by using HPMC K100 M, Chitosan and Pectin in various concentrations. In pre formulation study, estimation of Rivaroxaban was carried out by Microprocessor UV-VIS Single beam Spectrophotometer (YIS-294) spectrophotometer at λ max 248 nm using 6.8 pH Buffer as buffer, which had a good reproducibility and this method was used in entire study. All the formulations were subjected for evaluation. Results of pre formulation studies, FTIR, % yield, drug content, buoyancy time and entrapment efficiency, in vitro dissolution and release kinetics shown satisfactory results. The FTIR Spectra revealed that, there was no interaction between polymers and Rivaroxaban. Entrapment efficiency was increased with increased polymer concentration. From the results it can be inferred that there was a proper distribution of Rivaroxaban in the microspheres and the deviation was within the acceptable limits. On the basis of release data and graphical analysis formulation F12 showed a good Sustained release profile with maximum entrapment efficiency because of high polymer concentration. The co-efficient of determination indicated that the release data was best fitted with zero order kinetics. The diffusion exponent 'n' values of Korsemeyer- Peppas model was found to be in the range of 1.160 for the Rivaroxaban microspheres prepared with drug and chitosan indicating Super case II transport mechanism of drug through Rivaroxaban microspheres. Hence, from the above obtained data it can be summarized that it is possible to formulate controlled release microspheres of Rivaroxaban by ionic gelation technique using polymers like HPMC K15M, Pectin and Chitosan and the optimized formulation occur by using drug and polymer ration as Rivaroxaban : Chitosan(F12) in 1 : 4 ratio.

BIBLIOGRAPHY:

1. Wheleham M, Marison, 2011 microencapsulation using vibrating technology. J Microencapsul. 28:669-688.
2. Peanparkdee M, Iwamoto S, Yamauchi, R. (2016). Microencapsulation: A Review of Applications in the Food and Pharmaceutical Industries. Rev Agric Sci. 4:56-65.
3. Kesharvani S, Jaiswal PK, MukerjeeA, Singh AK. (2020). Floating Microspheres; Formulation and Evaluation of Metformin Hydrochloride Loaded Floating Microspheres. Int J Pharm Pharm Sci. 12(2):74-82.
4. Singh B, Kanouji J, Pandey M, Saraf SA. (2010). Formulation and Evaluation of Floating Microspheres of Famotidine. Int J PharmTech Res. 2(2):1415-1420.
5. Pramod S, Shiv G, Prateek P, Ajay P. (2014). Hollow Microspheres: An Emerging Approach in the Field of Gastroretentive Drug Delivery System. International Journal of Universal Pharmacy and Bio Sciences. 3(4):305- 315.
6. Kapil K, Rai AK. (2012). Floating Microsphere: An innovative Approach for Gastro Retention. Journal of Pharmacy Reasearch. 5(2):883-886.