"Formulation and Evaluation of Floating Microspheres of Dexrabeprazole Sodium"

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Abstract:

The aim of any drug delivery system is to offer a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. Oral drug administration is by far the most preferable route for taking medications. Oral route has been received more consideration in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for other route. However, most of the oral dosage forms possess several physiological limitations such as variable gastrointestinal transit, variable gastric emptying lead to nonuniform absorption profiles, incomplete drug release and shorter residence time of the dosage form in the stomach. In vitro studies formulation F1- F7 release studies of the formulation gradually increase as the time passes while considering all the formulation F1 formulation Graph of Zero order release kinetics of F-1 Graph of First order release kinetics of F-1, Graph of First order release kinetics of F-1 Graph of Higuchi release Kinetics, Graph of Higuchi order release kinetics of F-1 Graph of Korsemayer – Pappas Kinetics. Release Kinetics of Optimized Formulation F-1The *In-vitro* drug release data of the optimized formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, Higuchi's and Korsmeyer's models in order to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of Korsmeyer's was maximum i.e 0.928 hence indicating drug release from formulations was found to follow Higuchi kinetics.

Keywords: Microsphere, Release Kinetics, Dexrabeprazole,

INTRODUCTION

New applications of microparticles necessitate successful technology transfer, industrial scaleup, and reliable investigation methods also in preformulation and in formulation steps.[1] Design of experiment (DOE). Optimization with factorial based designs and analysis of the response surfaces is a powerful, efficient and systematic tool that shortens the time required or the development of dosage forms and improves research and development work.180,181 DOE aids the evaluation of the results of the measurements mentioned below. Rheological measurements. It can be carried out to investigate the viscosity of the: (i) solvent mixture; (ii) aqueous and oil phases; and (iii) simple/multiple emulsions. Morphological study. The microparticles can be studied for appearance and the emulsions for droplet type using SEM and optical microscopy, respectively. Particle size analysis. Microparticles could be sieved with a combined sieving system.[2] One of the commonly used techniques for assessing the PS distribution, SSA and SPAN appeared to be laser diffractometry. Photon correlation spectroscopy (PCS), the Coulter® Multisizer II equipment31 and light or electron microscopy can also be used. Drug entrapment (E) and encapsulation efficiency (EE). Very common method to measure the drug entrapment, when microparticles are dissolved with applicable solvent, then filtered and analysed with UV-spectrofotometry. Protein and peptide content could measure with protein assay: HPLC-method, and Bio-Rad microassay. IgG and IgA levels can be monitored by LISA method. DSC and XRD and EDXRF also were used to measure the actual E value.[3] Evaluations of the potential of EDXRF apparatus in microparticles have been performed,[I] its application for our purpose can be considered a novelty.[4] Thermoanalytical measurements (TA). TA is a useful tool in investigating e.g. the solubility of the drug in the polymer. However it should be emphasized that such a solubility is determined at the melting point of the drug and not at ambient temperature.[5] The 'Heat-cool-reheat' technique when after the 1st heating step the sample is cooled and reheated to delete the disturbing effect of the adsorbed water, so the Tg characteristic to the polymer can be measure clearly.[6] Raman spectroscopy (RS). Based on the measurement of Raman-scattering by a molecule,[7] RS, FT-Raman, and surface-enhanced Raman (SERS) are used for the structural analysis of molecules, the vibrational characterization of drugs, the characterization of drug stability, the quantification of complex mixtures, furthermore to confirm the possible interactions, and to differentiate crystalline forms of the materials. FTIR measurement. It can also be used to characterize the parameters mentioned in connection with RS, often together with other techniques (FTIR + TGA + DSC). Analysis of residual organic solvents and cosolvents.[8] Manufacturers are required to remove residual solvents completely or keep them below acceptable limits, as complete removal is often not possible.[9] Few reports of residual solvent effects are available, such as the effect of residual CH2Cl2 on the crystallinity of the drug. Cumulative drug release and release profile studies.[10] The knowledge of the BCS characteristics of a drug can also be

utilized by the formulator to develop a more optimized dosage form based on fundamental mechanistic, rather than empirical information.[11] The in vitro dissolution rates of the microparticles can be measured at defined rpm in 37±1 °C buffer solution/deionized water mixture of defined pH according to the USP Drug Release Test 2 criteria.[12] Dissolution in the GI tract takes place under heterogeneous conditions, this is one of the reasons why different buffer solutions (citrate, acetate, phosphate or other) are used, although most of them do not correspond to the physiological situation in the human GI-tract.[15] The use of surfactants in the dissolution systems has physiological significance also as natural surfactants like bile salts (wetting, micellar solubilization, and/or deflocculation). Gastric juice has a relatively low surface tension, (42.7 dyn·cm-1) compared with water (70 dyn·cm-1) which aids in the wetting of both hydrophobic and hydrophilic particles.[13]

PREPARATION AND CHARACTERIZATION

Preparation of floating microsphere of Dexrabeprazole

Floating microsphere containing dexrabeprazole was prepared using emulsion solvent diffusion technique. The drug to polymer ratio used to prepare the different formulations was 1:7. The polymer content was a mixture of Ethyl cellulose Hydroxy propyl methyl cellulose (HPMC) as shown in table no.1. The drug polymer mixture is dissolved in a mixture of ethanol (8 ml) and dichloromethane (8 ml) was dropped in to 0.75% polyvinyl alcohol solution (200 ml). The solution was stirred with a propeller-type agitator at 40□C temperatures for 1 hour at 300 rpm. The formed floating microspheres were passed through sieve no.12 and washed with water and dried at room temperature in a desiccator. The various batches of floating microsphere were prepared as follows.

Table No. 1: Formulation of the floating microspheres prepared

Sr. No	Formulation Code	Dexrabeprazole (gm)	EC (gm)	HPMC (gm)
1	**F_1**	0.1	0.8	0.1
2	F_2	0.1	0.7	0.2
3	F_3	0.1	0.6	0.3
4	F_4	0.1	0.5	0.4
5	F_5	0.1	0.4	0.5

6	F_6	0.1	0.3	0.6
7	F_7	0.1	0.2	0.7
8	F_8	0.1	0.1	0.8

Evaluation of microspheres

Particle size analysis:

Particle size analysis plays an important role in determining the release characteristics and floating property. The sizes of floating microspheres were measured by using an Horiba nano particle analyzer, and the mean particle size was calculated by measuring nearly 200 particles with the help of a calculated ocular micrometer.

Floating behavior of floating microsphere:

100 mg of the floating microsphere were placed in 0.1 N HCI. The mixture was stirred with paddle at 100rpm. The layer of buoyant microspheres was pipetted and separated by filtration at 1, 2, 4 and 6 hours. The collected microspheres were dried in a desiccator overnight. The percentage of microspheres was calculated by the following equation:

$$\% \text{ floating microsphere} = \frac{\text{Weight of floating microsphere}}{\text{Initial weight of floating microsphere}} \times 100$$

Drug entrapment

The various formulations of the floating microspheres were subjected for drug content. 50 mg of floating microspheres from all batches were accurately weighed and crushed. The powdered of microspheres were dissolved with 10ml ethanol in 100ml volumetric flask and makeup the volume with 0.1 N HCl. This resulting solution is than filtered through what man filter paper No. 44. After filtration, from this solution 10 ml was taken out and diluted up to 100 ml with 0.1 N HCl. The absorbance was measured at 260.0 nm against blank. The percentage drug entrapment was calculated as follows.

$$\% \text{ Drug entrapment} = \frac{\text{Calculated drug concentration}}{\text{Theoretical drug concentration}} \times 100$$

Percentage yield

The prepared microspheres with a size range of 609-874 µm were collected and

weighed from different formulations. The measured weight was divided by the total amount of all non-volatile components which were used for the preparation of the microspheres.

$$\% \text{ Yield} = \frac{\text{Actual weight of product}}{\text{Total weight of drug and polymer}} 100$$

Shape and surface characterization of floating microspheres by scanning electron microscopy:

From the formulated batches of floating microspheres, formulations (F_4) which showed an appropriate balance between the buoyancy and the percentage release were examined for surface morphology and shape using scanning electron microscope JEOL, JSM-670F Japan. Sample was fixed on carbon tape and fine gold sputtering was applied in a high vacuum evaporator. The acceleration voltage was set at 3.0 KV during scanning. Microphotographs were taken on different magnification and higher magnification (500X) was used for surface morphology.

***In-vitro*release studies**

The drug release rate from floating microspheres was carried out using the USP type II (Electro Lab.) dissolution paddle assembly. A weighed amount of floating microspheres equivalent to 100 mg drug were dispersed in 900 ml of 0.1 N HCI (pH 1.2) maintained at 37 ± 0.5°C and stirred at 100 rpm.

Drug release kinetic data analysis

Several kinetic models have been proposed to describe the release characteristics of a drug from matrix. The following three equations are commonly used, because of their simplicity and applicability.

Zero order equation: When a graph of the cumulative percentage of the drug released from the matrix against time is plotted, zero order release is linear in such a plot, indicating that the release rate is independent of concentration.

$$Q_t = k_0.t \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where $Q_{t\ is}$ the percentage of drug released at time t and k_0 is the release rate constant; First order equation:

$\ln (100-Q_t) = \ln 100 - k_I.t$ ..... (2)

Where k_I is the release rate constant;

Higuchi's equation:

$Q_t = k_H.t^{1/2}$ .....(3)

Where K_H is the Higuchi release rate constant

Physical appearance

The drug Dexrabeprazole sodium powder was examined for its organoleptic properties like colour and odour.

Table No. .3: Physical appearance of Drug

Color	: White
Odor	: Odorless
Form	: powder

Solubility

Solubility of DEX was freely soluble in ethyl acetate, chloroform and ethanol, insoluble in n-hexane and ether, soluble in water and methanol. The melting point and partition coefficient of DEX was found to be 220-223°C and 1.17 respectively Table No.4: Solubility of Dexrabeprazole sodium

S. No.	Solvent	Solubility
1.	Water	Very soluble
2.	Methanol	Very soluble
3.	Ethanol	Freely soluble
4.	Chloroform	Freely soluble
5.	Ethyl acetate	Freely soluble
6.	Ether	Insoluble
7.	n- hexane.	Insoluble

Melting Point:

It is one of the parameters to judge the purity of drugs. In case of pure chemicals, melting points are very sharp and constant. Since the drugs contain the mixed chemicals, they are described with certain range of melting point.

Procedure for determine melting point:

Table No. 5: Melting point of drug

S. No.	Method	Literature Melting Point	Practically Melting Point
1.	Capillary fusion method	220-223 °C	220-223°C

Drug Partition Studies

Partition coefficient is a measure of drug lipophilicity and an indication of its ability to cross biomembrane. For drug delivery, hydrophilic lipophilic balance (HLB) is an important factor. It is also useful in screening of some biologic properties. Partition coefficient of Dexrabeprazole sodium was determined in octanol:water. Accurately weighed amount of drug (10mg) was taken in a glass stoppered test tube containing 10ml of n-octanol and 10ml of water. The mixture was shaken on a wrist action shaker for 24hr. Both the phases were separated using separating funnel and the drug concentration in aqueous and octanol phase was determined by spectrophotometrically at 258.0.0 nm.

The partition coefficient of drug found to be in n-octanol: water by using following equation:

$$\text{The partition coefficient, } K = \frac{\text{Amount of drug in organic layer}}{\text{Amount of drug in aqueous layer}}$$

Table No. 6: Partition Coefficient Values of Drug

S. No	Medium	Partition Coefficient (Log P)
1.	n – octanol : Water	1.17

Standard curve of dexrabeprazole sodium

The absorption maximum of dexrabeprazole sodium was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer (Chitlange *et al.,* 2010).

Procedure:

100 mg equivalent weight of dexrabeprazole sodium drug sample was dissolved in 100 ml of Distilled water in a volumetric flask. 5 ml of this solution was taken and diluted to 50 ml. The resulting solution was serially diluted to obtain drug concentrations of 5-25 µg/ml. The absorbances of the solutions were measured three time (Rep-1, 2, & 3) against in distilled water as blank at 258.0 nm using the UV spectrophotometer. The plot of mean absorbance vs. concentration was plotted and the Beer's range was determined.

λmax. of Dexrabeprazole sodium

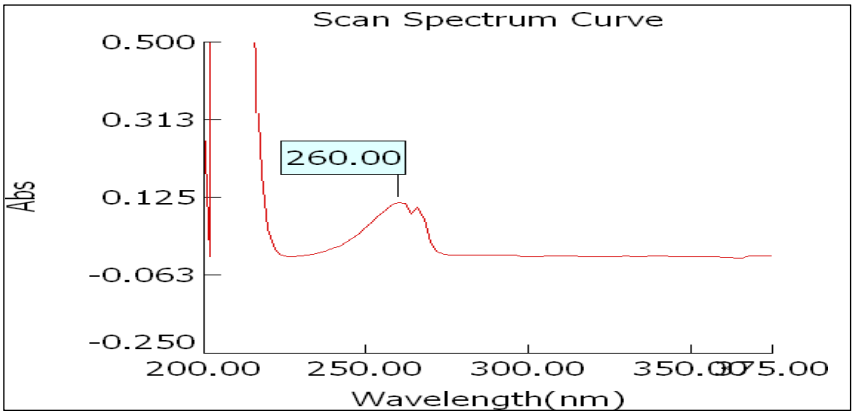

Fig no. 4: λmax of dexrabeprazole sodium

Table No. 7: Linearity of dexrabeprazole sodium

Conc. µg/Ml	0	5	10	15	20	25
Replicate-1	0	0.256	0.516	0.743	0.985	1.214
Replicate-2	0	0.257	0.516	0.741	0.984	1.215
Replicate-3	0	0.256	0.517	0.742	0.985	1.214
Mean	0	0.256	0.516	0.742	0.985	1.214
S.D.	00	0.001	0.001	0.001	0.001	0.001
R.S.D%	000	0.225	0.112	0.135	0.059	0.048

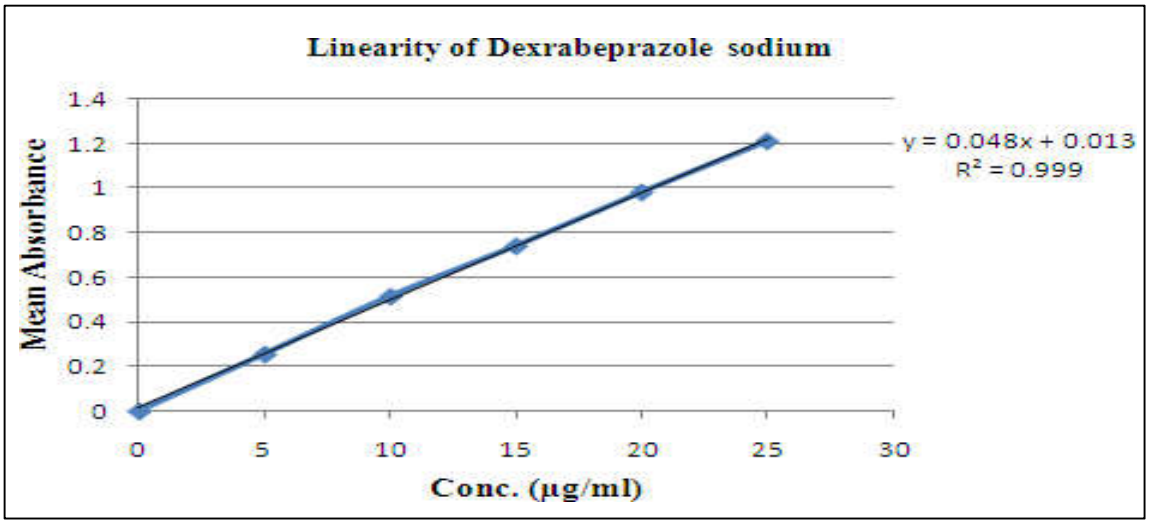

Fig no. 5: Calibration curve of standard Dexrabeprazole sodium

Regression Equation

Y= mx +c,

Slope- M= 0.048 Intercept -C= 0.013 r^2= 0.999

Optical parameter:-

Table No. 9: Result of optical parameter of Dexrabeprazole sodium

S. No.	Parameters	Observation
1	□ max	258.0 nm
2	Beer's law limit (µg/mL)	5-25
3	Regression equation	Y = 0.048 x +0.013
4	Correlation Coefficient (r2)	0.999

FTIR Spectroscopy:

Infra- red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. The region from 0.8 µ to 2.5 µ is called Near Infra-red and that from 15 µ to 200 µ is called Far infra-red region. Identification of Dexrabeprazole sodium by FTIR Spectroscopy with respect to marker compound. Dexrabeprazole sodium was obtained as White or almost white crystalline powder. The FT-IR spectrum was performed from SIRT-Pharmacy Bhopal using Bruker- alpha instrument. It was identified from the result of IR spectrum as per specification.

Sample of pure Dexrabeprazole sodium

The IR spectrum of sample drug shows the peak values which are characteristics of the drug and the graph were shown in figure.

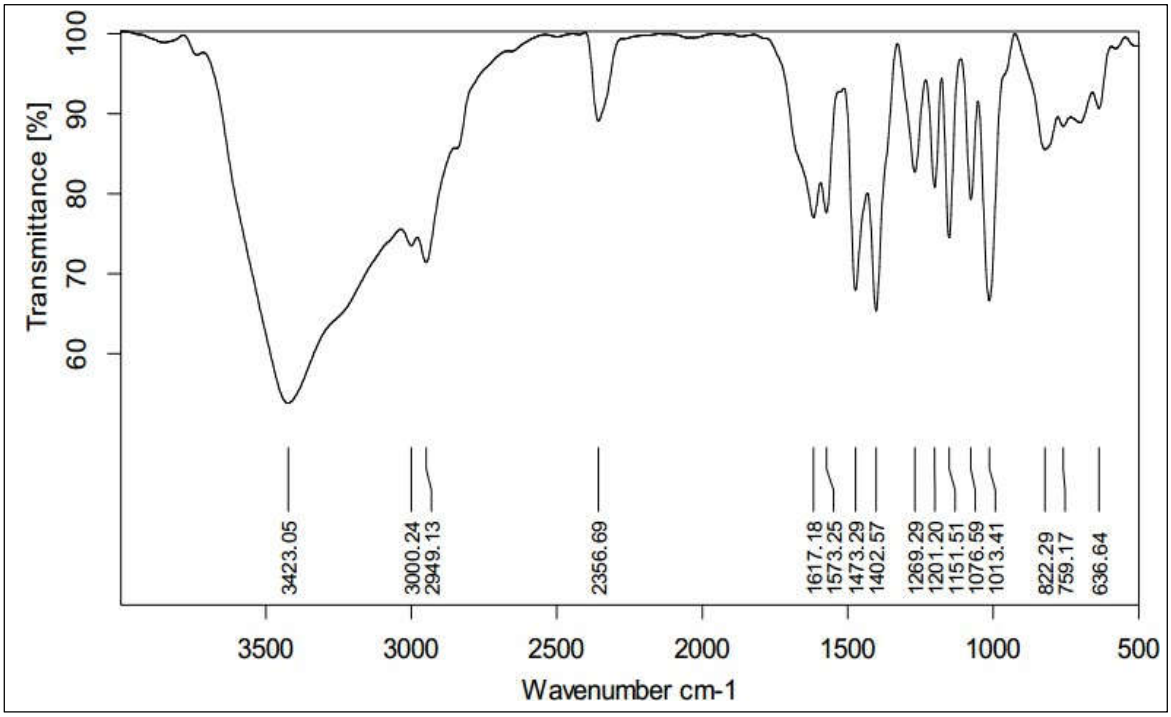

Fig no. 6: FT-IR Spectrum of Pure Drug (Dexrabeprazole sodium)

Table No. 10: IR Spectrum Peaks of Pure Drug (Dexrabeprazole sodium)

S. No.	Functional group	Peak wave number(cm^{-1})	
		Experimental	Theoretical
2	C-H Stretch (aromatic)	3423.05	3600-3400
3.	N-H Stretch	3175.14	3200-3300
5.	S=O stretch	1473.29	1400-1600
6.	C=H Str.	1617.18	1500-1700

Loss on Drying (LOD)

Procedure: Loss on drying directly measuring by IR moisture balance. Firstly calibrate the instrument by knob then take 5.000 gm sample (powder) and set the temp at 100°C to 105°C for 5 minutes and constant reading set the knob and check % moisture.

The percentage of loss on drying was found to be **1.56 %w/w**.

Determination of pH (1□ w/v solution in water):

Procedure

1gm of the Powder was taken and dissolved in 100ml of distilled water with sonication and filtered, pH of the filtrate was checked with standard glass electrode.

The pH determination of Dexrabeprazole sodium was done by Digital pH meter and found to be **3.67.**

Flow property of Dexrabeprazole sodium powder: (Lachman, 1991)

A. Bulk properties

Bulk density is defined as the mass of powder divided by the bulk volume. Bulk density largely depends on particle shape, as the particles become more spherical in shape, bulk density is increase. In addition as granules size increase, bulk density decrease. Bulk properties such as particle size, bulk density etc. of a solid form, are likely to change during process development. Therefore, comprehensive characterization of all preformulation lots is necessary to avoid misleading predictions.

Bulk density is determined by measuring the volume of a known mass of powder sample that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup.

Procedure:

A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit. Calculate the bulk density, in gm per ml gm/cc, by the formula

Bulk Density = Bulk mass/Bulk Volume

Table No. 11: Bulk Density of Dexrabeprazole sodium

S. No.	DENSITY	RESULT
1.	Untapped Density	**0.269 g/cc**
2.	Tapped Density (after 50 tapping)	**0.356 g/cc**

B. Compressibility index (Carr's index) :

Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material.

It can be calculated as per given formula:

$$C.I. = \frac{100\,(V0-Vf)}{V0} \quad \text{OR} \quad C.I. = \frac{\text{Tapped density- Bulk density}}{\text{Tapped density}} \times 100$$

Table No. 12: Carr's index range

S. No.	% Comp. Index	Properties
1.	5-12	Excellent
2.	12-16	Good
3.	18-21	Fair – passable
4.	23-25	Poor
5.	33-38	Very Poor
6.	>40	Extremely poor

The compressibility index of Dexrabeprazole sodium was found to be **25.69%.**

C. Hausner ratio:

It indicates the flow properties of the powder and is measured by the ratio of tapped density to bulk density.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk Density}}$$

Table No. 13: Hausner ratio and flow property characteristics

S. no.	Hausner ratio	Property
1.	0.0 - 1.2	Free flowing
2.	1.2 - 1.6	Cohesive powder

Standard value of hausner ratio is 1.334

D. Angle of Repose

Flow properties determination of powder or granules is the unique tools to avoid the weight variation of tablet Angle of repose, Carrs index, Hausner ratio are some technique by which we can estimate the flow properties of powder.

- The angle of repose is a relatively simple technique for estimating the flowability of a powder through a funnel and fall freely onto a surface. The height and diameter of the resulting cone is measured and using the following equation, the angle of repose can be calculated.

Tan □ = h/r

Where h, r is the relatively height and radius of the powder cone.

For most pharmaceutical powders, the angle of repose values range form 25 to 45, with lower values indicating better flow characteristics. Values of angle of repose > 30 usually indicate a free flowing material and angle □40 suggest a poorly flowing material.

Table No. 14: Angle of repose (θ) and flow property characteristics

S. No.	Angle of repose (θ)	Flow Property
1.	25-45	Better flow
2.	> 30	Free flow
3.	>40	Poorly flow

Procedure: The angle of repose is a relatively simple technique for estimating the flow ability of a powder through a funnel and fall freely onto a surface. The height

and diameter of the resulting cone is measured and using the following equation, the angle of repose can be calculated. Weigh 10 gm of Dexrabeprazole sodium powder accurately, and pass through the fennel height up to10 cm from surface and measure the height and diameter by scale.

Tan □ = h/r

Where h, r is the relatively height and radius of the powder cone.

1. The Angle of repose of Dexrabeprazole sodium was found to be **33.0** degree.

2. Particle size pass through 40# was found to be **100 (%w/w).**

Moisture by Karl-Fischer Apparatus (KF)

The titrimetric determination of water is based upon the quantitative reaction of water with an anhydrous solution of sulphur dioxide and iodine in the presence of a buffer that reacts with hydrogen ions.

In the original titrimetric solution, known as Karl Fisher Reagents, the sulfur dioxide and iodine was dissolved in pyridine and methanol. The test specimen may be titrated with the reagent directly, or the analysis may be carried out by a residual titration procedure. The stoichiometry of the reaction is not exact, and the reproducibility of a determination depends upon such factors as the relative concentration of the reagent ingredients, the nature of the inert solvent used to dissolve the test specimen, and the technique used in the particular determination. Therefore, an empirically standardized technique is used in order to achieve the desired accuracy. Precision in the method is governed largely by the extent to which atmospheric moisture is excluded from the system. The titration of water is usually carried out with the use of anhydrous methanol as the solvent for the test specimen; however other suitable solvents may be used for special or unusual test specimens. (Note: Now-a-days pyridine free KF reagents are coming in which pyridine is replaced by the imidazole, because pyridine has carcinogenic effects).

The Moisture Content was found to be **1.019%.**

RESULT AND DISCUSSION

Evaluation of dexrabeprazole floating microspheres

Particle size analysis

Particle size was determined by optical microscopy method. It plays important role in floating ability and release of drug from microsphere. If size of microspheres is less than 500 □m release rate of drug will be high and floating ability will reduce, white microspheres ranging between 200□m - 500□m, the floating ability will be more and release rate will be in sustained manner.

The mean particle size of dexrabeprazole sodiummicrosphere was in range 210 - 264 µm as shown in Table -15.

Mean particle size of different batches of dexrabeprazole sodiummicrosphere

Table No. 15: Mean particle size

S. No	Formulation code	Mean particle size (µm)
1.	F_1	212±12
2.	F_2	225±21
3.	F_3	264±23
4.	F_4	236±25
5.	F_5	242± 24
6.	F_6	244±40
7.	F_7	210±23

Floating behavior of microsphere:

Dexrabeprazole sodiumMicrosphere was dispersed in 0.1 HCl as simulate gastric fluid. Floating ability of different formulation was found to be differed according to EC and HPMC ratio. F_1-F_4 formulations showed best floating ability (91.47-72.97%) in 6 hours. F_5-F_7 formulation showed less floating ability (66.12-45.09%) as showed in Table-16. The floating ability of microsphere is decreased by increasing the HPMC ratio. Percentage buoyancy for different formulation

Table No. 16: Percentage Buoyancy for Different Formulation

Formulation	1 hour	2 hours	4 hours	6 hours
F_1	98.41	97.08	93.23	91.47
F_2	98.11	95.58	92.17	87.34
F_3	98.54	95.64	85.34	78.45
F_4	99.54	92.49	80.57	72.97
F_5	98.72	91.95	73.49	66.12
F_6	98.45	86.62	65.14	57.76
F_7	88.34	75.41	56.04	45.09

Drug Entrapment:

The drug entrapment efficacies of different formulations were in range of 48.47 -

74.19 % w/w as shown in Table No-7.8. Drug entrapment efficacy slightly decrease with increase HPMC content and decreased EC ratio in Microspheres. This is due to the permeation characteristics of HPMC that could facilitate the diffusion of part of entrapped drug to surrounding medium during preparation of Dexrabeprazolesodium microspheres. Drug entrapment for different formulation

Table No. 17: Drug Entrapment for Different Formulation

Formulation	Drug entrapment (% w/w)
F_1	76.19
F_2	70.59
F_3	66.23
F_4	64.76
F_5	61.01
F_6	57.38
F_7	48.47

Percentage Yield:

Percentage yield of different formulation was determined by weighing the Microspheres after drying. The percentage yield of different formulation was in range of 56.84 - 82.87% as shown in Table-18.

Percentage yield for different formulation

Table No. 18: Percentage Yield for Different Formulation

Formulation	Percent Yield (%)
F_1	82.87
F_2	78.53
F_3	76.47
F_4	71.56
F_5	69.31
F_6	66.03

F_7	56.84

Scanning Electronic Microscopy: Shape and surface characteristic of Dexrabeprazole sodiummicrospheres examine by Scanning Electronic Microscopyanalysis. Surface morphology offormulation examines at different magnification, which illustrate the smooth surface of floating Microspheres.

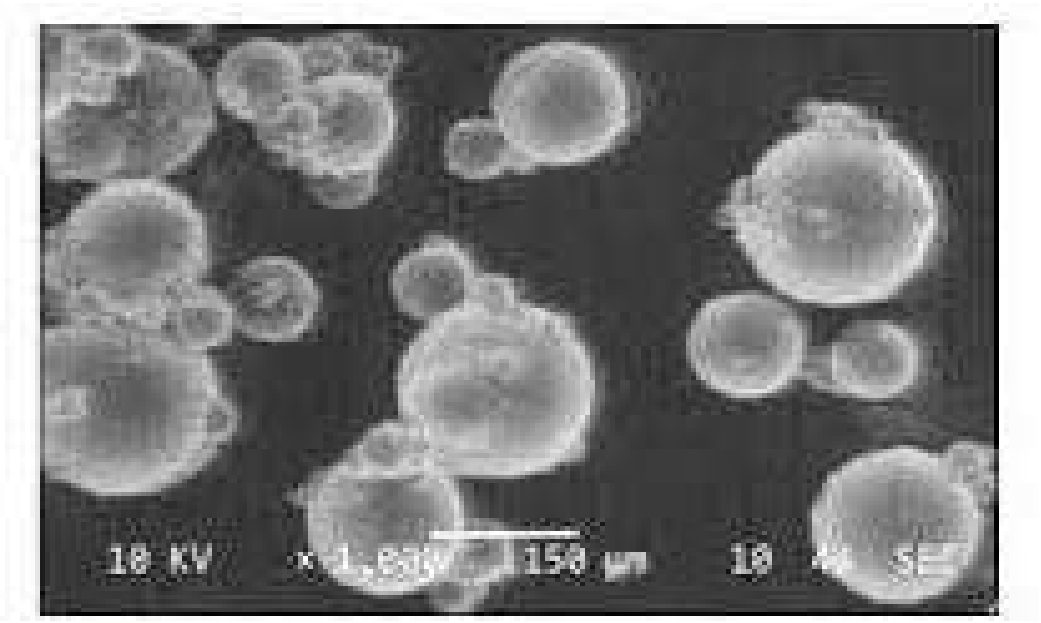

Fig no. 7: Scanning Electronic Microscopy Image of Optimized Formulation F-1

***In-vitro* drug release study:**

1. Drug Release Studies

In vitro drug release study of dexrabeprazolesodiumloaded Floating Microsphere

Table No. 19: Release study of Formulation F1- F7

Time	F1	F2	F3	F4	F5	F6	F7
0.5	16.429	15.000	13.571	14.286	17.857	16.429	14.286
1	25.714	17.857	17.143	17.857	27.143	25.000	22.143
1.5	28.571	25.714	22.857	25.714	32.143	29.286	32.143
2	53.571	30.000	28.571	30.000	40.000	40.000	35.714
3	65.000	55.714	41.429	36.429	55.714	49.286	53.571
4	72.143	70.000	46.429	46.429	62.857	70.000	48.571
6	82.143	75.000	70.000	63.571	66.429	82.143	55.714
8	82.857	75.714	74.286	75.000	80.000	84.286	80.143

Graph of release study of formulation F1-F7

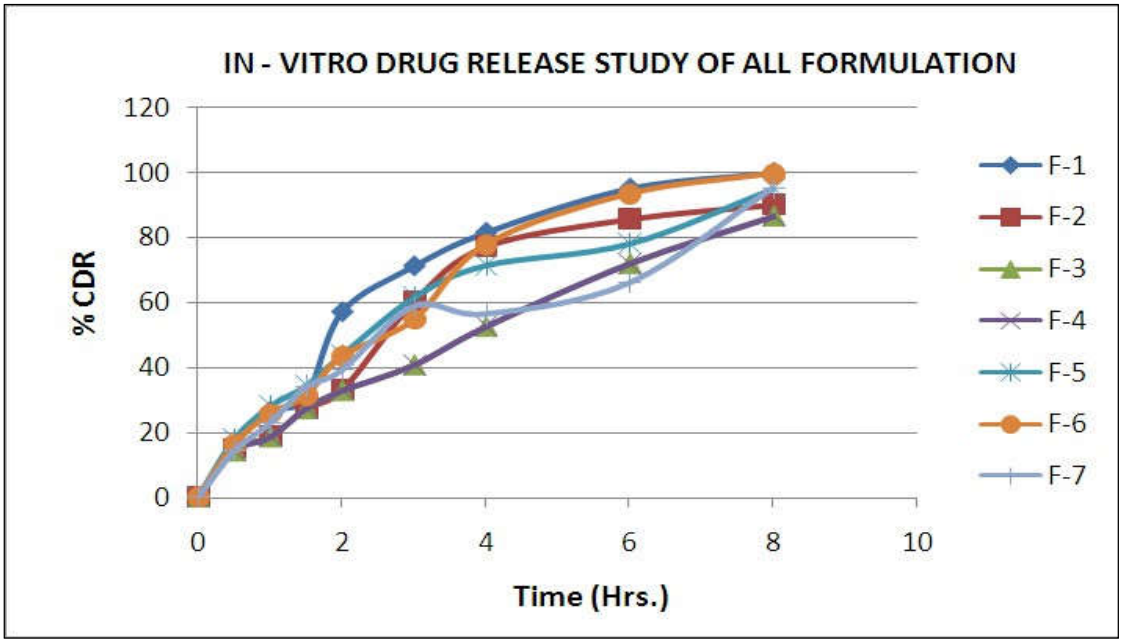

Fig no. 8: Graph of release study of formulation F1-F7

Release Kinetics of Optimized Formulation F-1

Table No. 20: Release Kinetics of Optimized Formulation F-1

Time (Hrs.)	% CDR	Log T	Root T	Log % cum. drug remain to be release	Log cum. % drug release	cum. % drug remain to be released
0.5	16.429	-0.30103	0.70710678	1.9220556	1.2156111	83.571
1	25.714	0	1	1.87090697	1.4101696	74.286
1.5	28.571	0.176091259	1.22474487	1.85387457	1.4559254	71.429
2	53.571	0.301029996	1.41421356	1.66678933	1.7289298	46.429
3	65	0.477121255	1.73205081	1.54406804	1.8129134	35

4	72.143	0.602059991	2	1.44493434	1.8581942	27.857
6	82.143	0.77815125	2.44948974	1.2518085	1.9145706	17.857
8	82.857	0.903089987	2.82842712	1.23408683	1.9183292	17.143

Graph of Zero order release kinetics of F-1

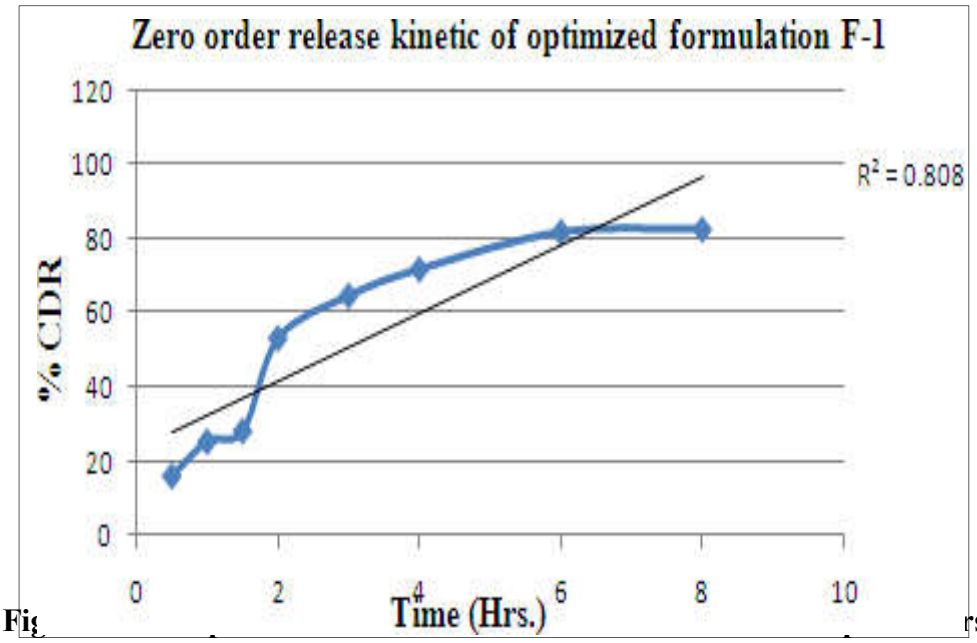

Fig rst order release kinetics of F-1

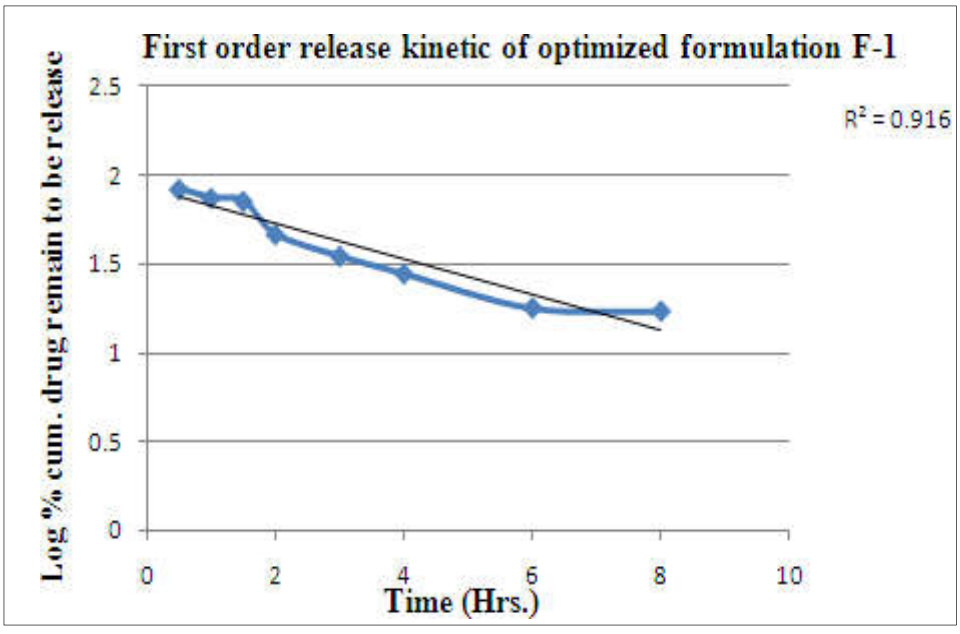

Fig no. 10: Graph of First order release kinetics of F-1 Graph of Higuchi release Kinetics

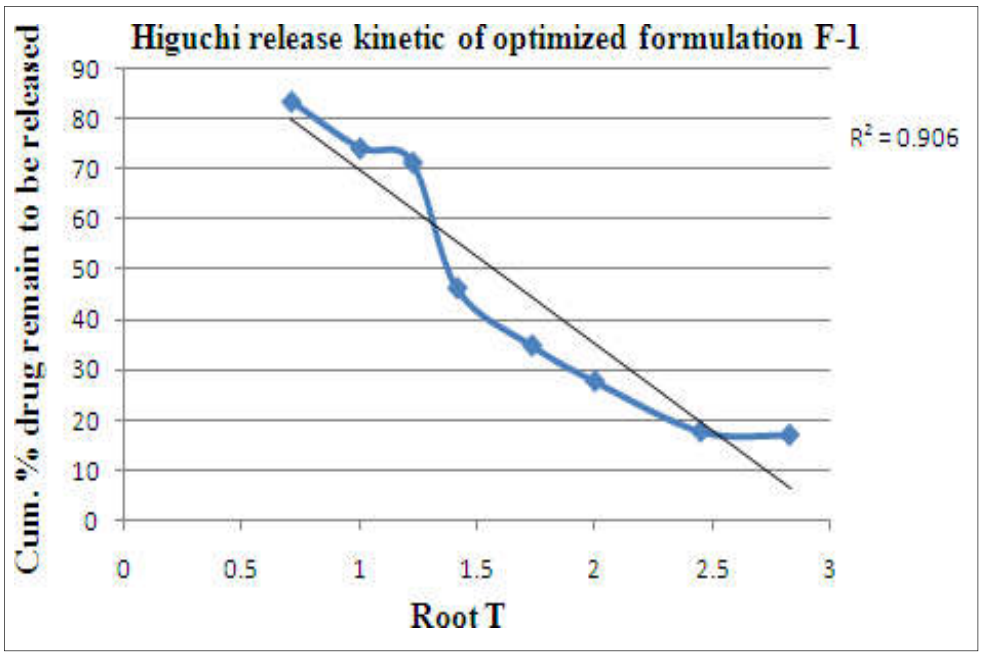

Fig no. 11: Graph of Higuchi order release kinetics of F-1 Graph of Korsemayer – Pappas Kinetics

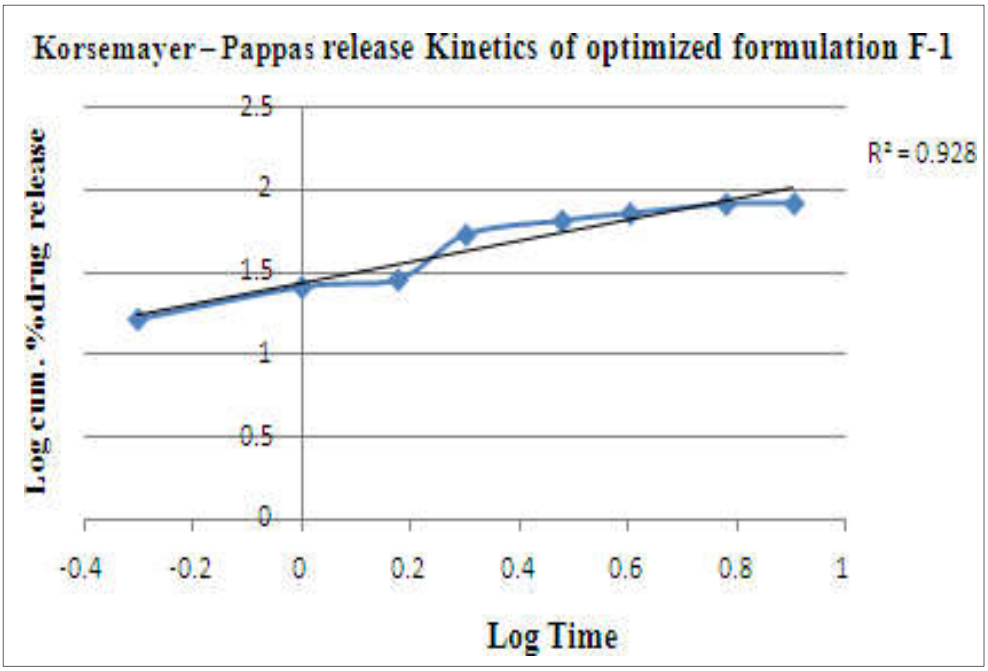

Fig no. 12: Graph of Korsemayer – Pappas release kinetics of F-1

Table No. 21:Comparative study of regression coefficient for selection of optimize Formulation F-1

Zero order		First order	Higuchi	Korsmayer
r^2	0.808	0.916	0.906	0.928

The *In-vitro* drug release data of the optimized formulation was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, Higuchi's and Korsmeyer's models in order to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of Korsmeyer's was maximum i.e 0.928 hence indicating drug release from formulations was found to follow Higuchi kinetics.

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