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Research Article

Formulation and Evaluation of Controlled Release Diacerein Microspheres Using Egg Albumin

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ABSTRACT

Diacerein is a new anti-inflammatory analgesic and antipyretic drug developed from especially for the treatment of osteoarthritis. The main objective of the study was formulated and evaluated controlled release Diacerein microspheres using egg albumin. Controlled release Diacerein microspheres were prepared by chemical cross-linking method using natural polymer as a egg albumin in different ratio. The Physicochemical compatibility study of drug and polymer was studied by FT-IR spectroscopy. Prepared microspheres evaluated for morphological analysis, entrapment efficiency, drug content, *in vitro* drug release studies and *in vitro* anti-inflammatory activity study. Among the prepared formulation containing F5 containing microspheres were found to be best formulation which showed the higher drug release, good entrapment efficiency, extent *in vitro* drug release and satisfactory anti-inflammatory activity.

INTRODUCTION

The Novel drug delivery system is to provide a therapeutic amount of drug to the appropriate site in the body to accomplish promptly and then maintain the desired drug concentration. The drug delivery system should deliver drug in rate-controlled manner in the body over a specific term of treatment [1]. Oral route has been the commonly adopted and most convenient route for the drug delivery. Oral route of administration has been received more attention in the pharmaceutical field because of the more flexibility in the designing of dosage form than drug delivery design for the other routes. In last two decades the drug delivery technology has been developed rapidly and many novel oral drug delivery systems have been invented [2]. Microsphere is a term used for small spherical particles, with diameters in the micrometer range (typically 1µm to 1000µm (1mm) and thus microspheres are sometimes referred to as micro particles. These are spherical free flowing particles consisting of proteins are synthetic polymers which are biodegradable in nature.

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Microsphere plays an important role to improve bioavailability of conventional drugs and minimizing side effects [3]. Egg albumin has a property of good protein binding and physical entrapment. It also supports passive as well as facilitated release of various types of incorporated drugs from the polymer matrix. So, the concept for the formulation of albumin-based microspheres to increase the bioavailability of the drugs to get a sustained release of drug, resulting in decrease in the dosing frequency came into existence. The accumulation of albumin in solid tumours forms the rationale for developing albumin-based drug delivery systems for tumour targeting. Thus, it has been used as a carrier for targeting drugs to tumours, and since the synovium of the rheumatoid arthritis patients shares various features observed in tumours, albumin-based delivery systems can be used to target drugs to the inflamed joint. Intravenous administration of the drugs coupled with albumin has been reported to improve the targeting efficiency of the drug to arthritic regions. The circulation half-lives of the drugs have been reported to dramatically increase when the drug is conjugated with albumin. Increasing the circulation half-life of the formulation by reducing its uptake by the reticulo endothelial system has been shown to

improve the targeting efficiency of the formulation to the arthritic paws of rats. Achieving higher concentrations of the drug at the arthritic joint and minimizing its distribution to the other tissues would minimize the side effects associated with the drug. Targeting drugs to the inflamed joints, in the treatment of rheumatoid arthritis, would reduce the amount of drug required to control the disease, with possible additional reduction or even elimination of adverse side effects [4, 5].

MATERIALS AND METHODS

Materials

Diacerein was collected as a gift sample from Ami life science Gujarat. Liquid paraffin, Tween 80, Span 80 was collected as a gift sample from Fourrts India PVT ltd, Chennai. Egg albumin and Glutaraldehyde was purchased from Merck Laboratories Mumbai and all other reagents were of analytical grade.

Methods

Preparation of Egg Albumin Microspheres of Diacerein

Microspheres were prepared the chemical cross-linking method. In this method, solutions of albumin (having different concentration) in 15 ml of distilled water was prepared, with the addition of 0.5% Tween 80 and kept overnight. Then after 10-15-minute stirring, the drug was added to the above albumin solutions. The formulation was carried out with (1:1, 1:1.5, 1:2, 1:2.5, 1:3.0, 1:3.5, 1:4:0, 1:4.5, 1:5.0) drug: polymer ratios. Then above drug-polymer solutions were slowly added drop wise by injection to a beaker containing 150 ml of liquid paraffin containing 1% of span 80, as an emulsifying agent preheated 60°C and stirred for 30 minutes at 250 rpm. The resulting microspheres were solidified using glutaraldehyde solution stirred for a period of 3 hours and add 5 ml of n-hexane were added. The microspheres were collected by decantation, then washed with petroleum ether and dried at room temperature. The details of formulations are given in the Table 1.

Calibration Curve for Diacerein

Preparation of Standard Graph in Phosphate Buffer pH 6.8

100 mg of Diacerein was transferred in to 100 ml of volumetric flask. The drug is dissolved 10 ml of dimethyl sulphoxide and then the volume was made up to 100ml with phosphate buffer pH 6.8, from this primary stock (1 mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 6.8. From this secondary stock 1, 2, 3, 4, 5 and 6 ml were taken separately and made up to 100 ml with phosphate buffer pH 6.8 to produce 1, 2, 3, 4, 5 and 6µg/ml respectively. The absorbance was measured at 258nm using a UV spectrophotometer [8].

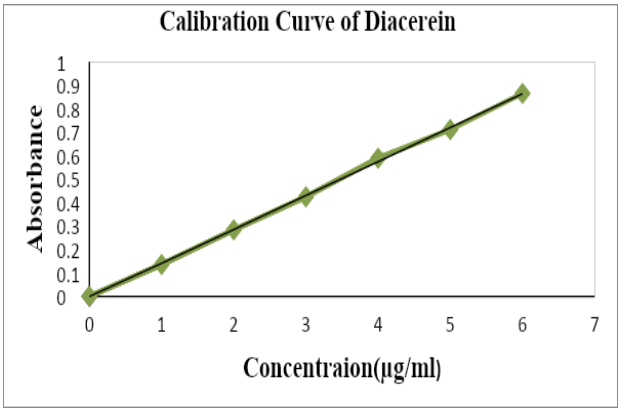

Figure 1: Calibration Curve for Diacerein in phosphate buffer pH 6.8

Table 1: Formulation Table

S.No.	Formulation code	Drug (g)	Polymer (g)	Drug: polymer Ratio	Light Liquid Paraffin (ml.)	Span 80	Glutaraldehyde (ml)
1	M1	1	1	1:1.0	150	1%	20
2	M2	1	1.5	1:1.5	150	1%	20
3	M3	1	2.0	1:2.0	150	1%	20
4	M4	1	2.5	1:2.5	150	1%	20
5	M5	1	3.0	1:3.0	150	1%	20
6	M6	1	3.5	1:3.5	150	1%	20
7	M7	1	4.0	1:4.0	150	1%	20
8	M8	1	4.5	1:4.5	150	1%	20
9	M9	1	5.0	1:5.0	150	1%	20

Evaluation of Microspheres

Surface Morphology [9]

The microspheres were coated with gold in vacuum at high voltage (800-1500V) using ion coater. Samples were examined with scanning electron microscope.

Particle Size Analysis [10]

Determinations of the average particle size of Diacerein loaded microspheres were determined with an optical microscope using a calibrated ocular and stage micrometer. Minute quantities of microspheres were spread on a clean glass slide with a drop of liquid paraffin and a cover slip is placed on it. The average particle size was calculated by measuring 100 particles of each batch.

$$dav = \Sigma\, nd/\Sigma n$$

Where, dav is the average diameter of particles (µm), n is number of particles per group, and d is the middle value (µm).

Percentage Yield [11]

The yield of the prepared formulations was calculated as the percentage of the weight of the dried product at room temperature compared to the theoretical amount. Product yield is calculated by using the following Equation:

$$Product\ Yield = \frac{\text{Weight of the product}}{\text{Weight of the raw material}} \times 100$$

Drug Content [12]

The various batches of the microspheres were subjected for drug content analysis. Microspheres containing 25 mg of Diacerein were transferred in to 100 ml of volumetric flask. 10 ml of dimethyl sulphoxide added to dissolve the drug and then the volume was made up to 100ml with phosphate buffer pH 6.8 (primary stock). The solution is filtered and 2 ml of filtrate was transferred to another volumetric flask and made up to 100 ml with phosphate buffer pH 6.8. The absorbance was measured at 258nm using a UV spectrophotometer.

$$\text{Drug content} = \frac{\text{Practical content}}{\text{Theoretical content}} \times 100$$

Entrapment Efficiency [13]

50 mg of microspheres were powdered and dissolved in phosphate buffer pH 6.8 in 50 ml volumetric flask and made up to the volume. The solution was kept for 1 hour with occasional shaking. Further 1 ml solution diluted up to 50 ml with phosphate buffer pH 6.8. The content was analyzed spectrophotometrically at 258 nm against phosphate buffer pH 6.8 as blank. The %EE of each formulation was calculated using the following equation.

$$\text{EE\%} = \frac{\text{Actual Drug Content}}{\text{Theoretical Drug Content}} \times 100$$

Evaluation of Flow Properties [14, 15]

Flow properties of microspheres were investigated by determining by following standard procedures. All studies were carried out in triplicate (n=3). The flow properties were determined by measuring the angle of repose, Carr's index, Hauser's ratio and bulk density.

Bulk Density

Bulk density was determined by taking known weight of dried microspheres in a measuring cylinder and tapping 3 times from 1-inch height at 2 Second intervals. The bulk volume is noted and the bulk density was calculated from following equation.

$$U = M/Vb$$

Where,

M = Mass of microspheres in gram

Vb = Bulk volume of microspheres (after three tapping).

Tapped Density

Tapped density is the ratio of mass of microspheres to the volume occupied by the same mass of the powder after a standard tapping of a measure. Weighed quantity of microspheres was taken in a cylinder and tapping 300 times from 1 inch at 2 second interval. The tapped volume is noted and the tapped density was calculated from the following equation.

$$b = m/vt$$

Where, m = mass of microspheres in gram

Vt= volume of microspheres (final tapped volume).

Carr's Index

The Carr index (Carr's Compressibility Index) is an indication of the compressibility of powder. The Carr's Index is calculated by the formula:

$$\text{Carr's Index} = \frac{(\text{Tapped Density} - \text{Bulk density})}{\text{Tapped density}} \times 100$$

Hausner's Ratio

The Hausner ratio is a number which is correlated to the flow ability of a powder or granules.

$$\text{Hausener's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Angle of Repose

A funnel was fixed to a stand and bottom of the funnel was fixed at a height of cm from the plane. Microspheres were placed in funnel and allowed to flow freely and the height and radius of the heap of microspheres was measured.

$$\theta = \text{Tan-1}(h/r)$$

Where, θ = Angle of Repose, h= height of the pile, r= radius of the pile formed.

***In Vitro* Drug Release Study of Microsphere Formulations in Phosphate Buffer pH 6.8 [12]**

In vitro drug release studies were performed using UPS test apparatus I (basket type). The dissolution studies were performed in 900 ml dissolution medium phosphate buffer pH 6.8 at 75 rpm maintained at 37ºc ± 0.5ºc. 10ml of sample were withdrawn at specific time interval for 24 hours. The sample volume was replaced by an equal volume of fresh medium.4 ml of filtrate diluted with 100 ml using 6.8 phosphate buffer. The concentration was determined spectrophotometrically at 258nm.

***In Vitro* Anti-Inflammatory Test [16]**

1 ml of sample solution was withdrawn during *in-vitro* drug release study at every one-hour interval, thereafter subjected to *in-vitro* anti-inflammatory analysis. For the purpose of control, equal volume of distilled water was used. To each reaction mixture, 1 ml of bovine albumin (1% in distilled water) was transferred and pH was adjusted to 6.3 using small amount of 0.1 N HCl. Samples were incubated for 30 min at 37ºC in the dark followed by incubation at 57ºC for 5 min. Reaction tubes were then cooled under running tap water and turbidity of all the samples were recorded spectrophotometrically at 660 nm. Percentage inhibition of albumin denaturation was calculated by using,

$$\text{Percentage inhibition} = \frac{\text{Abs Control} - \text{Abs Sample}}{\text{Abs Control}} \times 100$$

Kinetic Analysis [17]

To analyze the *in vitro* drug release data various kinetic models were used to describe the release kinetics.

1. Zero order-order kinetic model-cumulative %drug release versus time.
2. First order –Kinetic model-Log cumulative percent drug remaining versus time.
3. Higuchi's model –cumulative percentage drug released versus square root of time.
4. Korsmeyer equation / Peppa's model-Log cumulative %drug released versus log time.

RESULTS

Preformulation Study

Preformulation studies are primarily done to investigate the physiochemical properties of drug and to establish its compatibility with other excipients used.

FT-IR Compatibility Studies

FTIR spectra of pure drug formulation with other ingredients were recorded. The FTIR spectra of pure Diacerein drug and polymer were compared with the FTIR Spectrum of drug.

The peaks observed in the FTIR spectrum of physical mixture of DCN and egg albumin showed no shift and no disappearance of characteristic peak of drug as well as polymer. This suggests that there is no interaction between drug and polymer. Hence it can be concluded that the drug maintain identity without undergoing any chemical interaction with egg albumin.

Scanning Electron Microscopy

The shape and surface morphology of optimized microspheres (F5) was observed in SEM. It shows that the microspheres were almost spherical.

Evaluation of Microspheres

From the above results, it is found that particle size distribution is in the range of 54.62 µm to 131.60 µm. This reveals that as drug: polymer ratio increases the particle size increases. This is because the viscosity of polymer solution increases with increasing polymer concentration resulting in enhanced interfacial tension, which in turn decreases the stirring efficiency, which results in increased particle size. After the preparation of microspheres practical yield and percentage yield was determined. It was found that percentage yield was in the range of 96.4%

to 99.3%. The percentage entrapment efficiency calculated for all microspheres range from 55.5 % to 94.6 %. The highest entrapment efficiency is found for the formulation F5 is 94.6%. After the preparation of microspheres drug content were calculated. It was found in the range of 95.8% to 99.2%. The highest drug content is found for the formulation F5 is 99.2% (Table 2).

Evaluation of Flow Properties

The bulk density was found to in the range of 0.352 g/ml to 0.535 g/ml. The tapped density was found in the range of 0.461 g/ml to 0.625 g/ml. The Hausner's ratio of the formulation was found in the range of 1.1 to 1.3 (Table 3).

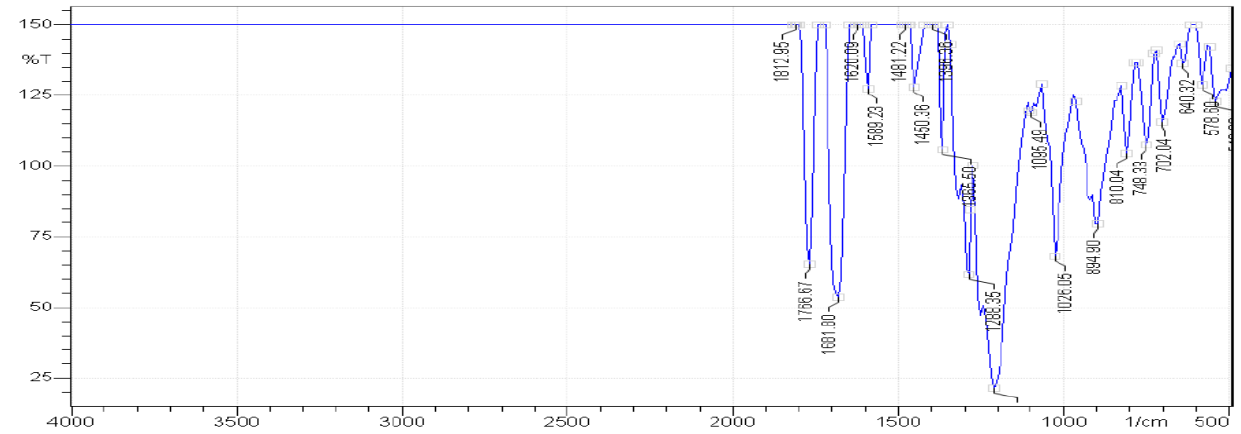

Figure 2: FI-IR spectrum of Diacerein

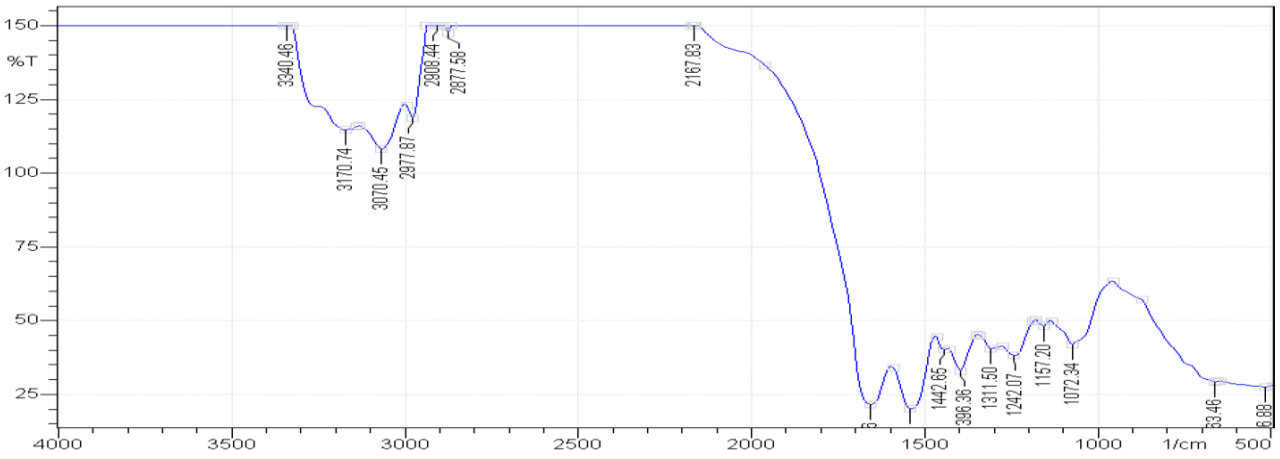

Figure 3: FI-IR spectrum of Egg Albumin

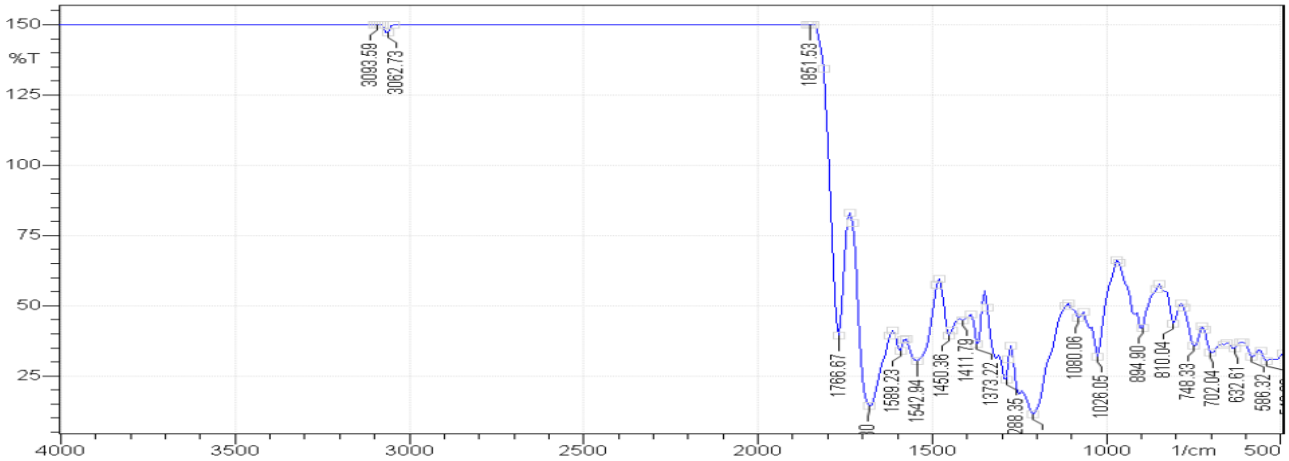

Figure 4: FI-IR spectrum of Diacerein and Egg Albumin

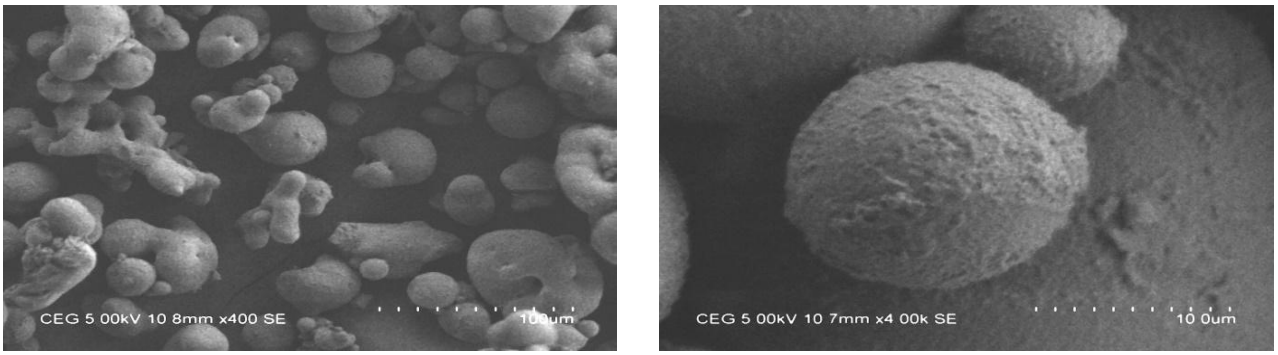

Figure 5: Scanning Electron Microscopy of F5

Table 2: Average Particle Size, Percentage Yield, Entrapment Efficiency (%), Drug Content (%)

Formulation	Average Particle Size(µm)	Percentage yield (%)	Entrapment Efficiency (%)	Drug content (%)
F1	54.62	98.5	55.5	96.1
F2	79.28	96.4	75.3	97.6
F3	83.19	97.3	78.0	95.8
F4	105.18	98.6	90.4	98.2
F5	115.38	98.5	94.6	99.2
F6	120.48	98.0	84.8	97.6
F7	123.19	98.6	87.7	96.8
F8	128.00	98.2	88.7	96.2
F9	131.60	99.3	86.9	97.9

Table 3: Flow Properties of Diacerein Microsphere

F. Code	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose(º)	Hausner ratio	Compressibility index %
F1	0.413	0.496	20. 806	1.2	16.7
F2	0.502	0.615	17.832	1.2	18.3
F3	0.521	0.561	24.259	1.1	7.1
F4	0.485	0.625	15.944	1.3	22.4
F5	0.463	0.518	20.735	1.1	10.6
F6	0.432	0.487	23.814	1.1	11.2
F7	0.535	0.601	21.810	1.1	10.9
F8	0.445	0.482	24.546	1.1	7.6
F9	0.352	0.461	27.367	1.3	23.6

The compressibility index was found in the range of 7.1 to 23.6. The angle of repose was found in the range 15.944° to 27.367°. The flow properties of the formulated microspheres are found to be excellent.

In Vitro Drug Release Study

F1, F2, and F3 formulations showed *in vitro* drug release of 79.54%, 85.92%, and 88.27% respectively at the end of 24 hours. F4, F5, F6 formulations showed *in vitro* drug release of 92.32%, 98.56%, and 86.12% respectively at the end of 24 hours. F7, F8, F9 formulations showed *in vitro* drug release of 81.31%, 82.41%, and 80.34% respectively at the end of 24 hours. From the *in vitro* drug release data formulation F5 showed higher drug release of 98.56% at the end of 24 hours, when compared to the other formulation. Hence formulation F5 was chosen as the optimized formulation.

Pure drug of DCN showed 99.33% drug release at the end of 11 hours. Optimized formulation (F5) prolonged the release of the DCN to 24 hours. Formulation of DCN in the form of albumin microspheres extended the drug release.

Evaluation of Optimized Formulation
Preformulation Studies of the Pure Drug and Optimized Formulation F5
The flow property of pure drug is found to be good. Excellent flow property is observed in F5 microspheres.

Preparation of Capsule
The optimized microspheres were filled in to 0 size HPMC capsule each containing 100 mg of DCN.

***In Vitro* Drug Release Study of C5 Capsules**
From the *in vitro* drug release data formulation C5 showed higher drug release of 98.45% at the end of 24 hours [9].

***In Vitro* Anti Inflammatory Activity**
In vitro anti inflammatory activity by albumin denaturation method showed that the formulation C5 inhibited 87.80 % for 24 hours. Thus C5 exhibits anti-inflammatory activity.

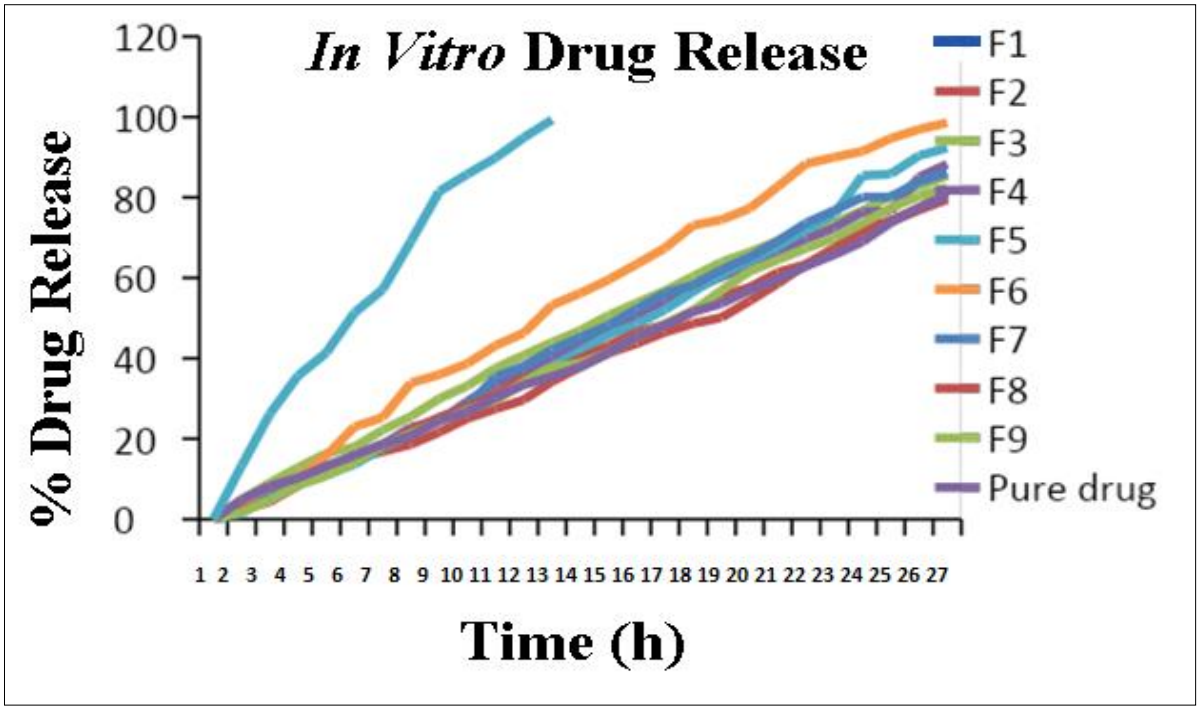

Figure 6: *In Vitro* Drug Release

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***In Vitro* Anti Inflammatory Activity**
In vitro anti inflammatory activity by albumin denaturation method showed that the formulation C5 inhibited 87.80 % for 24 hours. Thus C5 exhibits anti-inflammatory activity (Table 7).

Table 4: Preformulation parameters of pure drug and microspheres

F.code	Bulk density (g/ml)	Tapped density (g/ml)	Carr's Index (%)	Hausner's ratio	Angle of repose (Θ)
Pure drug	0.348(±0.015)	0.759(±0.012)	15.8 (±0.02)	0.90 (±0.04)	31º.247 (±0.59)
F5	0.467(±0.011)	0.530(±0.011)	11.8(±0.018)	1.135(±0.024)	20º.992(±0.63)

*Mean±SD (n=3)

Post Formulation Studies of Optimized Capsule C5

Table 5: Evaluation parameters of optimized capsule

Formulation	Average weight of capsule (mg)	Drug content of capsule	Disintegration Time
C5	401.0±0.06	98.2 ±1.18	20 min 10 sec

Table 6: *In vitro* drug release study of capsule C5

S.No	Time (Hrs)	% Drug release
1	0.30	3.04 (±0.182)
2	1	7.54 (±0.370)
3	2	10.23 (±0.217)
4	3	15.65 (±0.282)
5	4	22.87 (±0.416)
6	5	25.72 (±0.361)
7	6	33.66 (±0.223)
8	7	35.71 (±0.226)
9	8	40.16 (±1.722)
10	9	43.39 (±0.537)
11	10	45.88 (±0.824)
12	11	53.26 (±0.345)
13	12	55.74 (±0.437)
14	13	59.95 (±0.506)
15	14	63.38 (±0.183)
16	15	67.08 (±0.414)
17	16	72.69 (±0.367)
18	17	74.77 (±0.909)
19	18	77.51 (±0.303)
20	19	82.33 (±0.478)
21	20	87.97 (±0.894)
22	21	89.78 (±0.667)
23	22	91.82 (±0.420)
24	23	94.37 (±0.405)
25	23.50	96.88 (±0.531)
26	24	98.45 (±1.523)

Table 7: *In vitro* anti inflammatory activity of C5 Formulation and Pure drug

Time	C5 Formulation	Pure drug
0	0	0
0.30	0.73	43.54
1	0.58	52.68
2	1.88	56.74
3	4.49	62.11
4	10.15	67.34
5	14.07	72.42
6	17.27	80.11
7	22.35	83.45
8	24.96	84.47
9	27.72	87.80
10	30.91	-
11	34.54	-
12	37.73	-
13	44.84	-
14	45.71	-
15	51.81	-
16	54.86	-
17	57.03	-
18	60.81	-
19	64.15	-
20	66.90	-
21	70.10	-
22	74.16	-
23	76.92	-
23.50	82.00	-
24	84.32	-

Mean±SD(n=3)

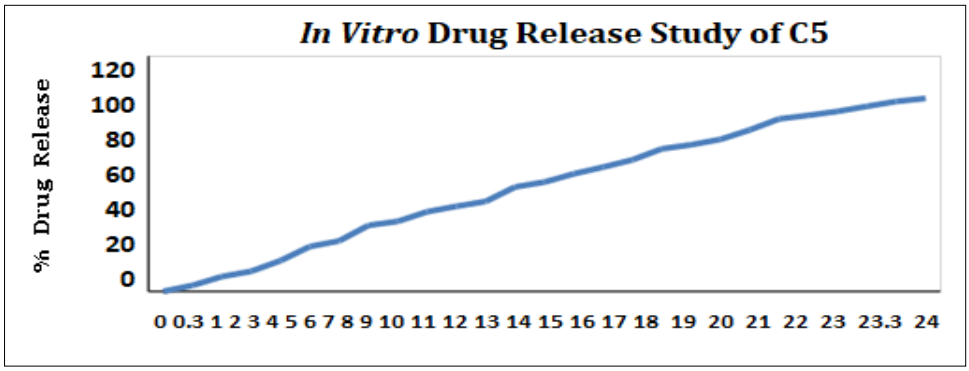

Figure 7: *In vitro* drug release study of C5

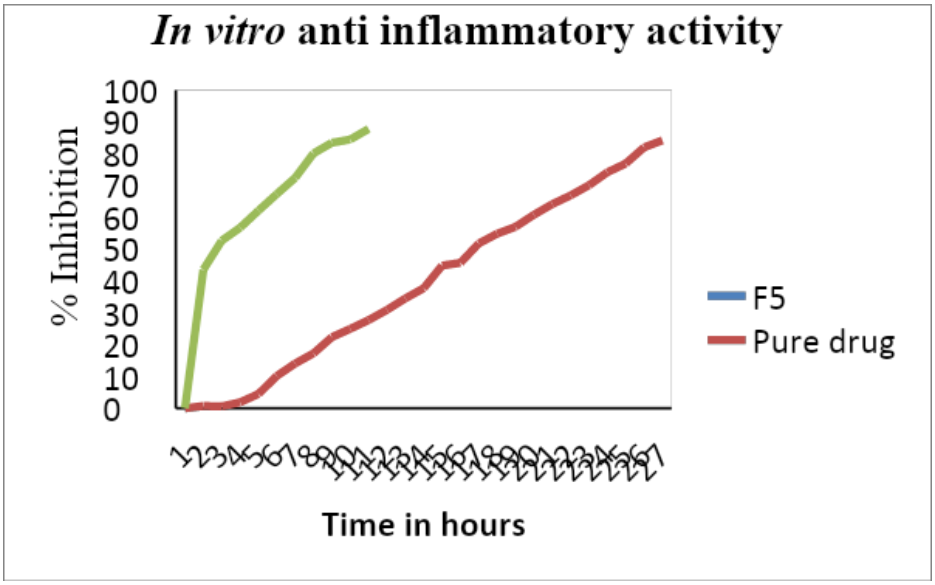

Figure 8: *In vitro* anti inflammatory activity C5 and Pure drug

Release Kinetics of the Optimized Formulation [17]

The Kinetics of Drug Release for Optimized DCN Loaded Egg Albumin Microspheres C5 in Phosphate Buffer pH 6.8

Table 8: Release kinetics of the optimized formulation (C5)

Time (Hrs)	Cumulative % drug release	cumulative % drug remaining	Log cumulative % drug remaining	Square root of time	Log time	Log % cumulative drug release	Cube root of cum % drug remaining
0	0	100	∞	∞	∞	2	4.6415
1	7.54	92.46	0.8773	1	0	1.9659	4.5218
2	10.23	89.77	1.0098	1.414	0.301	1.9531	4.4775
4	22.87	77.13	1.3592	2	0.602	1.8872	4.2567
6	33.66	66.34	1.5271	2.449	0.778	1.8217	4.0481
8	40.16	59.84	1.6037	2.828	0.903	1.7769	3.9113
10	45.88	54.12	1.6616	3.162	1	1.7333	3.7825
12	55.74	44.26	1.7461	3.464	1.079	1.6460	3.5372
16	72.65	27.35	1.8612	4	1.204	1.4369	3.0129
20	87.97	12.03	1.9443	4.472	1.301	1.0802	2.2913
24	98.45	1.55	1.9932	4.898	1.380	0.1903	1.1572

The coefficient of determination (R^2) was taken as criteria for choosing the most appropriate model. The R^2 values of various models are given in Table 9.

Table 9: R^2 Values of various kinetics models

Kinetic models	Coefficient of determination (R^2)
Zero order	0.9915
First order	0.8331
Higuchi	0.9534
Korsemeyer -peppas	0.9921
Hixon crowell	0.9474

The *in vitro* drug release of the optimized formulation C5 was best explained by zero order kinetics as the plots showed linearity (**R^2** = 0.9915) .This zero order kinetics explains the controlled release of the prepared microspheres over the period of time. The 'n' value of Korsemeyer Peppas equation was found to be 0.9921.From this it was concluded that the drug release follows non-fickinian diffusion. Drug can be released from microspheres by the mechanism of diffusion. It was observed from that the mechanism governing the release of DCN from egg albumin based drug delivery system is predominantly drug diffusion.

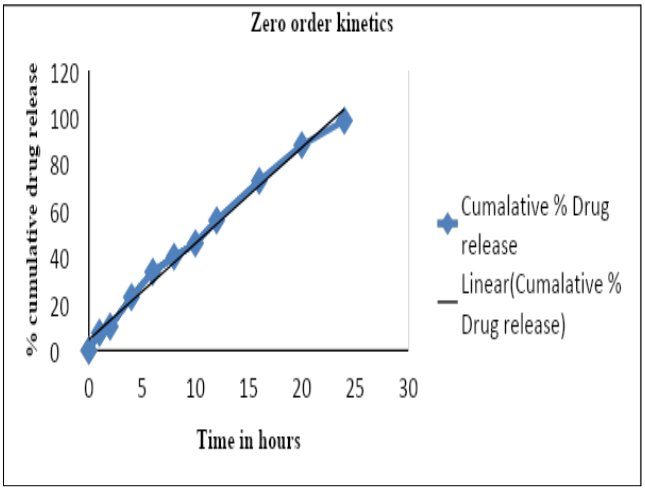

Figure 9: A Plot of Zero order kinetics

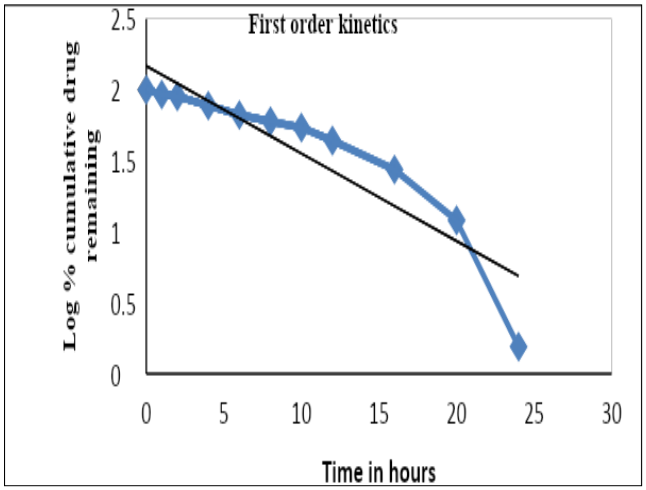

Figure 10: A Plot of First order kinetics

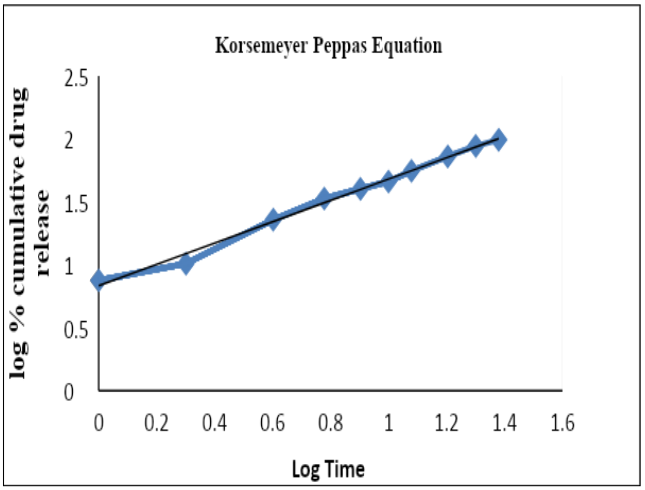

Figure 11: A Plot of Krosemeyer Peppas kinetics

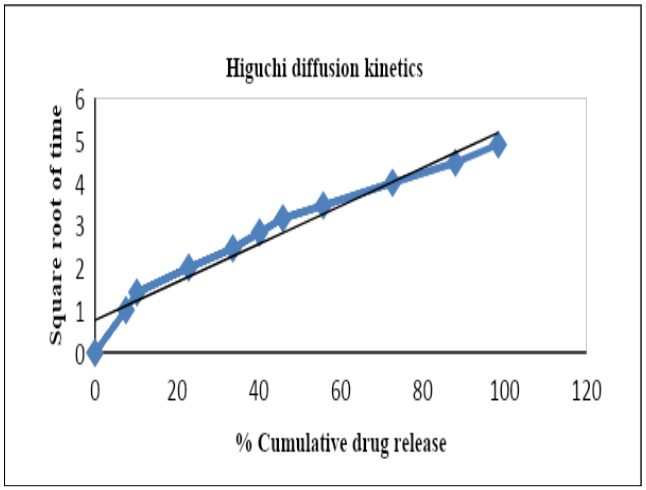

Figure 12: A Plot of Higuchi diffusion kinetics

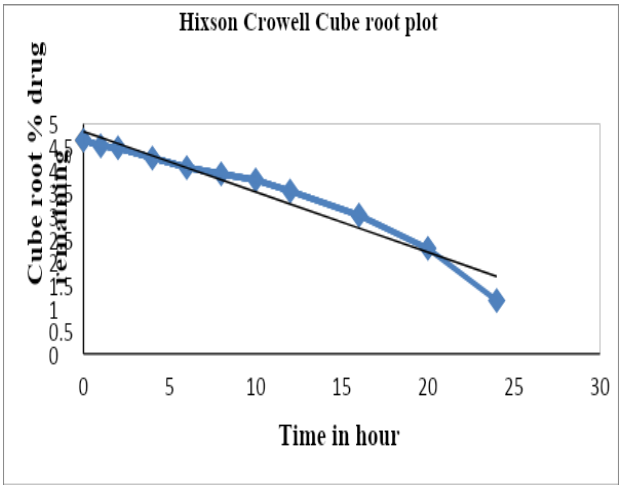

Figure 13: A Plot of Hixson Crowell kinetics

DISCUSSION

Diacerein is a poorly soluble drug with short half-life, thus selected for MDDS to release the drug in a controlled manner. Diacerein is formulated as Microspheres by Chemical cross-linking method. Compatibility studies were performed for drug and excipients. Physical compatibility study showed drug and excipients were physically compatible with each other. Chemical compatibility study (FT-IR) was carried out. It revealed no interaction between the drug and excipients. Standard graph was drawn for

Diacerein and it was found that the solutions showed linearity (R2=0.999) and obeyed Beer Lambert's law. In the present study F1 to F9 formulation were prepared using egg albumin as a natural polymer (1:1, 1:1.50, 1:2.0, 1:2.50, 1:3.0, 1:3.50, 1:4.0, 1:4.50, 1:5.0) in nine different ratios. The effect of polymer as well as increasing concentration of egg albumin on microsphere was studied by subjecting all the formulations to various evaluation parameters. The morphology of optimized formulation was studied by SEM analysis and found that shape of microspheres was almost spherical and found to be satisfactory. The mean particle size studies were carried out using microscopic analysis and in the range for all formulation were in 54.62 µm to 131.60 µm due to change in drug and polymer ratio. The entrapment efficiency of all the formulations was found to be in the range of 55.5% to 94.6 %. The formulation F5 had the highest entrapment efficiency of 94.6%. The *in vitro* release was carried out for all the formulations. The formulation F5 containing 1:3 drug: polymer (Egg albumin ratio) released 98.56% at the end of 24 hours. Therefore, C5 was selected as optimized formulations. The polymer ratio increases, production yield drug content and mean particle diameter increased. *In-vitro* anti-inflammatory activity by albumin denaturation method showed that the optimized formulation C5 inhibited approximately 84.32 % in 24h which clearly indicates that C5 also has a satisfactory anti-inflammatory activity. Preformulation study was carried out for drug and F5 microsphere. It revealed that the flow property of pure drug was good, but the microsphere has excellent flow. Post formulation parameters of capsules were evaluated and found to comply with the official specifications. The dissolution data of the C5 was fitted to various kinetic models and the formulation C5 fitted best to Zero order kinetics. It is concluded that C5 formulation containing 1:3 drug: polymer ratio with Egg albumin produced Controlled release.

CONCLUSION

The controlled microsphere of Diacerein were prepared by chemical cross liking method using natural polymer (Egg albumin) by varying polymer concentration the drug release was controlled. The evaluation parameters like morphological analysis, entrapment efficiency, *in vitro* drug release studies and *in vitro* anti-inflammatory activity studies was found to be satisfactory. The comparative study with the pure drug of DCN result showed that the F5 microsphere formulation had a controlled release up to 24 hours. The result of the study revealed that the use of natural polymer Egg albumin is an effective strategy for the designing and development DCN loaded controlled microspheres for easy and effective oral controlled drug delivery for treatment of Osteoarthritis.

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