CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.21264764

Available online at: http://www.iajps.com Research Article

PREPARATION AND EVALUATION OF NANOGEL BY SOLVENT EMULSION DIFFUSION TECHNIQUE

B.Chaitanya[1]*, Chitikela Nandhini[2], Gajula Nikhitha[2], Gujarwar Priyanka[2], Mallepu Sumathi[2], Mode Nandini[2]

[1]Assistant Professor, Department of Pharmaceutics, Joginpally B.R Pharmacy College, Moinabad, Ranga Reddy, Telangana.

[2]Student, Joginpally B.R Pharmacy College, Moinabad, Ranga Reddy, Telangana.

Abstract:

The objective of the present study was to formulate and evaluate an optimal stable nanogel formulation of Diacerein with an aim to increase its bioavailability. To formulate Nano gel, the selected formulation of Diacerein nanogel has been integrated into a gelling agent. The components for the formulation of nanogel were surfactants namely Tween 80 were selected. The nanogel was prepared using a biocompatible polymer, which formed a stable gel matrix. The nanogel exhibited excellent drug loading capacity and sustained release properties. The prepared nanogel was evaluated for particle size, zeta potential, electron Scanning Microscopy (SEM), percentage of encapsulation efficiency (EE) and in vitro drug release. Besides, pH, homogeneity, spread ability, viscosity. Nanogel was successfully formulated by using Diacerein dispersion. The average sizes of nanogel were found to be 122±18.7nm, zeta potential study reveals that formulation was stable. The resulting shave found F4 was best formulation among all batches and has transformed into topical Nanogel.

Keywords: *Diacerein, FTIR studies, Polymers, surfactants, Emulsion solvent diffusion technique, In vitro drug release studies*

Corresponding author:

B.Chaitanya,
Assistant Professor,
Department of Pharmaceutics,
Joginpally B.R Pharmacy College,
Moinabad, Ranga Reddy, Telangana.

QR CODE

Please cite this article in press ***B.Chaitanya*** *et al.,* ***Preparation And Evaluation Of Nanogel By Solvent Emulsion Diffusion Technique****, Indo Am. J. P. Sci, 2026; 13(07).*

INTRODUCTION:

Nanogels are three-dimensional hydrogel materials in the nanoscale size range formed by crosslinked swellable polymer networks with a high capacity to hold water, without actually dissolving into the aqueous medium. Nanogels can be composed of a variety of naturally occurring polymers, synthetic polymers or a combination thereof.[1] Nanogels can be a versatile platform for the incorporation of various small drug molecules through the combination of electrostatic and hydrophobic interactions as well as hydrogen-bond formation. They have advantages over macro-sized networks because their size enables them to interact with cells in a more specific fashion and even be internalized and due to their soft nature behave differently from solid and self-assembled polymer-based drug delivery systems, including polymer-based nanoparticles, micelles, and liposomes.[2] Development of nanogels that can carry, protect, target and release therapeutic agents in spatially and temporally controlled manner is actively ongoing and their rational design can provide a platform for multiple applications.[3] Diacerein (DCN) is a good chondroprotective agent involved in active component list of anti-arthritic drugs. It is basically di- acetylated derivative of rhein. It belongs to analgesic, antipyretic and anti-inflammatory category. Anthraquinone ring composing rhein is the active metabolite and it inhibits the production of interleukin- 1β and down regulates interleukin 12 and tumor necrosis factor α (TNF α).[4,5] This study was prepare and evaluate diacerein nanogel prepared by using solvent emulsion diffusion technique.

MATERIALS AND METHODS:

MATERIALS

Diacerein procured from Hetero Labs, HYD. HPMC, Carbopol and Tween 80 was obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY

IR spectroscopy:

The physical form of isolated bio-material was solid so the KBr disc method was employed for IR spectroscopy, and in this technique about 1mg of the solid sample was mixed with about 100 mg of pre dried and desiccated solid KBr. The mixture was finely ground in a mortar, preferably under an IR lamp to exclude any Purified Water vapors. The finely ground mixture was pressed under pressure of about 10 tons using a hydraulic pump to form a small pellet about 1-2mm in diameter. The resulting KBr disc was removed from the KBr die and is positioned in a special holder into the path of the IR radiation and its spectrum is recorded. The resulting IR.[6]

Formulation development

Table-1: Composition of Diacerein nanogel

F.no	Drug (mg)	HPMC (mg)	Carbopol 934 (mg)	Glycerin (ml)	Dichloromethane (ml)	Tween 80 (ml)	Methyl paraben (ml)	Water
F1	50	50	-	10	10	1	0.1	q.s
F2	50	100	-	10	10	1	0.1	q. s
F3	50	-	50	10	10	1	0.1	q.s
F4	50	-	100	10	10	1	0.1	q. s

Preparation of Diacerein loaded Nano dispersion:

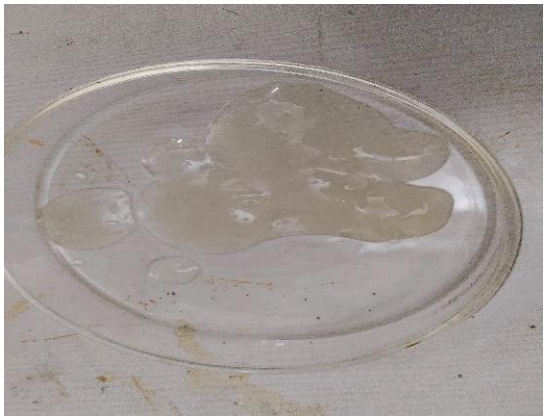
The Nano dispersion of the Diacerein was prepared by modified emulsification-diffusion method 50 mg of Diacerein was weighed and dissolved in 10 ml dichloromethane containing polymer. This organic phase containing drug polymer mixture was added into the 30ml of aqueous phase containing Tween 80, with constant stirring at 5,000-10,000 rpm using high speed homogenization When the emulsion is dispersed into nanodroplets by the ultrasonic homogenizer, an o/w emulsion is produced.

Addition of organic phase was done with the help of syringe positioned with needle directly into the aqueous stabilizer solution at the rate of 0.5 ml/min. The resulting dispersion was stirred for 6 min at

10,000-25,000 rpm and was subjected to the sonication for 5- 10 min. Then double distilled water was added slowly to the dispersion with subsequent stirring for 1 hour to induce diffusion of organic solvent into the continuous phase and leading to the formation of Nano dispersion.30

Preparation of a Diacerein nanogel:

Gels of the Nano dispersion were prepared by dispersing a gel forming agents such as Carbopol 934 and HPMC in the Nano dispersion of Diacerein by using high speed stirrer. The pH was adjusted to the 7.0 by using triethanolamine to form the gel and Diacerein enriched gels were stored at room temperature.[7]



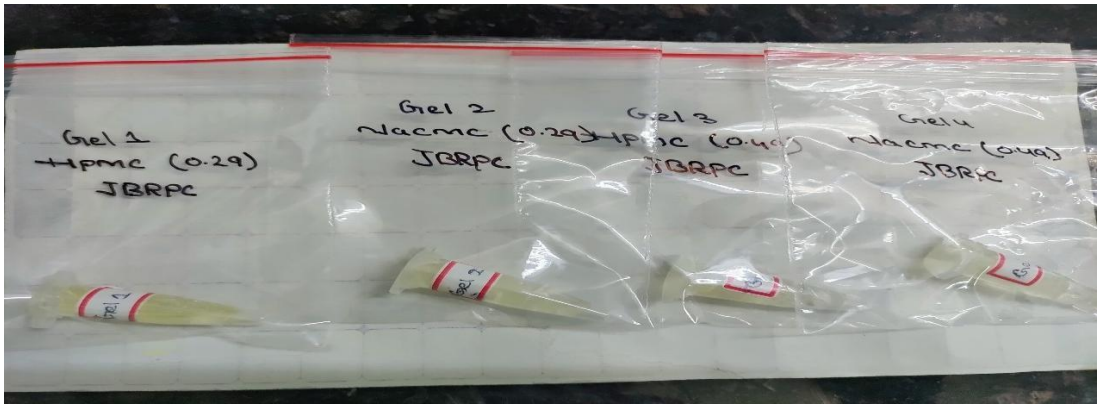


Fig-1formulations of gel

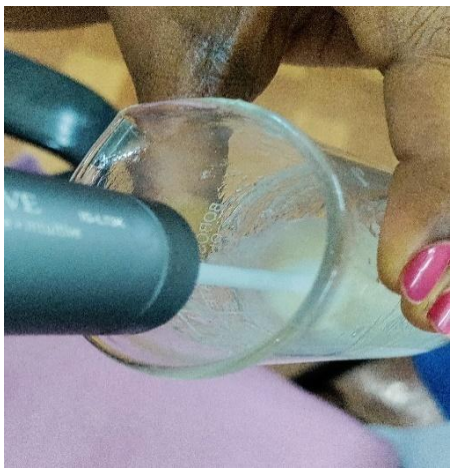


Fig-2: Homogenizing of nanogel

CHARACTERIZATION

Particle size and zeta potential: The particle size and size distribution of the drug loaded nanoparticles was characterized by photon correlation spectroscopy (PCS) using a Zetasizer 2000 Malvern Instruments, UK. Nano preparation was diluted with filtered (0.22µm) ultra-pure Purified Water and analyzed using Zeta sizer. The surface charge determination was performed using an aqueous dip cell in an automatic mode by placing diluted samples (with ultra-purified Purified Water) in the capillary measurement cell and cell position was adjusted.[8]

SEM Analysis: The external morphology of isolated biomaterial was analyzed by scanning electron microscopy (SEM). The biomaterials were fixed on supports, and coated with gold under an argon atmosphere using a gold sputter module in a high vacuum evaporator. Samples were then observed with the scanning electron microscope at 200 kV.[9]

Drug entrapment efficiency: Drug entrapment efficiency study was performed by centrifugation method. Accurate quantity of nanogel was taken in centrifuge tube with 10 ml of phosphate buffer pH 7.4. The amount of drug presented in clear supernatant after centrifugation for 30 min at 12,500 rpm was determined by UV spectroscopy. The amount of drug in supernatant was then subtracted from the total amount of drug added during preparation of nanoparticle (W). Effectively (W-w) will give the amount of drug entrapped.[10]

Determination of pH: The value of pH of topical nanogel was measured by using digital pH meter (Lab India Sab 5000 pH meter) at the room temperature.[11]

Measurement of viscosity: Viscosity of different formulations was measured with the viscometer at different speeds and temperature, using spindle PF.

Spreadibility study: Glass slide and wooden block measuring tools were used to determine it. The time it took for the upper slide to completely disengage from the fixed slides was timed after adding a weight to the pan of about 20g.[12]

After that, spreadability was determined using the following formula: S= M. L/T

S stands for spreadability, M for weight to the upper slide, and L for glass slide length.

T is the amount of time needed to completely separate the slides from one another

In vitro drug diffusion studies: Dialysis membrane diffusion technique was used to study in-vitro diffusion of drug from the prepared nanogel formulations. The receptor medium used was freshly prepared phosphate buffer pH 7.4. Dialysis membrane (Molecular weight cut off- > 12, 000, Hi media) previously soaked overnight in the receptor medium was on the Franz's Diffusion cell assembly. Prepared formulation was placed in the donor compartment and the assembly was kept on the multi station diffusion study apparatus (make Orchid Scientific) at 37°C±2°C and stirred at 700 rpm. Aliquots of 1 ml were withdrawn at pre-determined time intervals and immediately replaced by same volume of the fresh medium. The aliquots were suitably diluted with the dissolution medium and analyzed by UV-Vis Spectrophotometer at appropriate wavelength. The data obtained from the in vitro diffusion studies were fitted to various kinetic equations to find out the mechanism of drug release from the Nano gel formulation.[13]

Kinetics of drug release studies [14] The quantitative elucidation of the values obtained in the dissolution study is facilitated by the usage of a generic equation that mathematically translates the diffusion curve in function of some parameters related to the nanogel. For understanding the mechanism of drug release and release rate kinetics of the drug from dosage form, the Invitro drug dissolution data of optimized formulations obtained was fitted to various mathematical models such as zero order, First order, Higuchi matrix and Korsmeyer-Peppas models.

Zero order kinetics

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly can be represented by the following equation:

$Q0 - Qt = K0t$

Arrangement of equation yields: $Qt = Q0 + K0t$

Where Qt is the amount of drug dissolved in time t, Q0 is the initial amount of drug in the solution (most times, Q0 = 0)

and K0 is the zero-order release constant expressed in units of concentration/time.

To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time.

First order Kinetics

The equation for first order release is given below

$Log\ Qt = log\ Q0 + K1t/2.303$

Where Qt is the amount of drug released in time t, Q0 is the initial amount of drug in the solution and K1 is the first order release constant.

A graph of the decimal logarithm of the released amount of drug versus time will be linear. Nanogel following this diffusion profile release the drug in a way that is proportional to the amount of drug remaining in its interior, in such way, that the amount of drug released by unit of time diminishes.

Higuchi model

Higuchi described drug release as a diffusion process based on the Fick's law, square root time dependent. The simplified Higuchi equation is represented as

$Qt = Kt^{½}$

Where Qt = amount of drug released in time t,

K = Higuchi's constant

A linear relationship between amount of drug released (Q0 versus square root of time ($t^{½}$) is observed if the drug release from the nanogel is diffusion controlled.

Korsmeyer-Peppas model

This mathematical model, also known as the Power Law, has been used, very frequently; to describe the drug release from several different pharmaceutical modified release dosage forms. The Korsmeyer-Peppas model relates drug release exponentially to time. It is described by the following equation

$Mt/M\infty = atn$

Where 'a' is a constant incorporating structural and geometric characteristics of microspheres, 'n' is the release exponent, indicative of the drug release mechanism, and the function of 't' is Mt/ M∞ (fractional release of drug).

Stability study: Stability studies of prepared nanogel were carried out, by storing optimized formulation at 4°C ±1°C and 30°C ± 2°C in stability chamber for 90 days. The samples were analyzed at 0, 1, 2, and 3 months for their drug content, drug release rate (t50%) as well as any changes in their physical appearance (ICH Q1A (*R*2) 2003).[15]

RESULTS AND DISCUSSION:

Drug - excipient compatibility studies

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. This indicates that the drug was compatible with the formulation components.

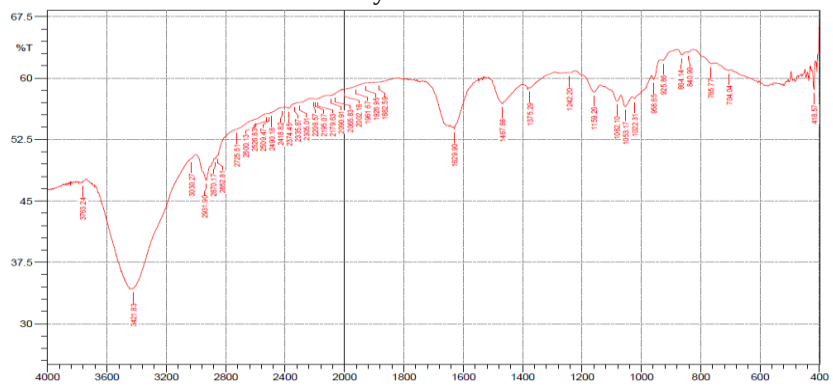


Fig-3: FTIR Studies of Diacerein

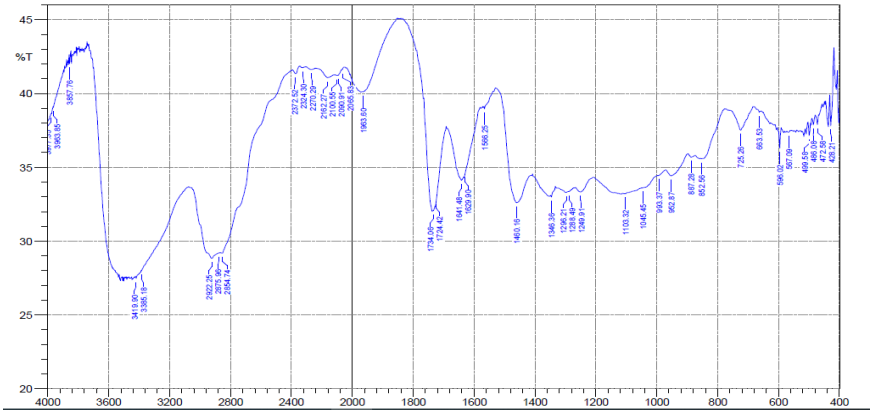


Fig-4: FTIR Studies of physical mixture of Diacerein+Tween 80+Carbopol 934

EVALUATION PARAMETERS:

P^H and Viscosity

Table-2: PH and Viscosity values of all formulations

F. code	pH	Viscosity (cps)
F1	7.6±0.07	162±7.57
F2	7.1±0.32	173±5.25
F3	7.3±0.37	169±0.75
F4	6.9±0.12	175±3.25

Spread ability

Table-3: Spread ability values of all formulations

F. code	Spread ability(sec)
F1	16.12±0.13
F2	15.55±0.29
F3	15.36±0.10
F4	14.98±0.27

Spread ability of the formulated diacerein nanogel was assessed using the sliding plate method, and the spread ability time was found to be range of 14.98±0.27– 16.12±0.13 seconds. This result suggests that the nanogel possessed good flow and spread characteristics, enabling easy application.

Entrapment Efficiency:

Table-4: Drug entrapment efficiency of all formulation

F.no	Drug entrapment efficiency (%)
F1	72.21±0.53
F2	77.85±0.43
F3	80.16±0.58
F4	84.65±0.46

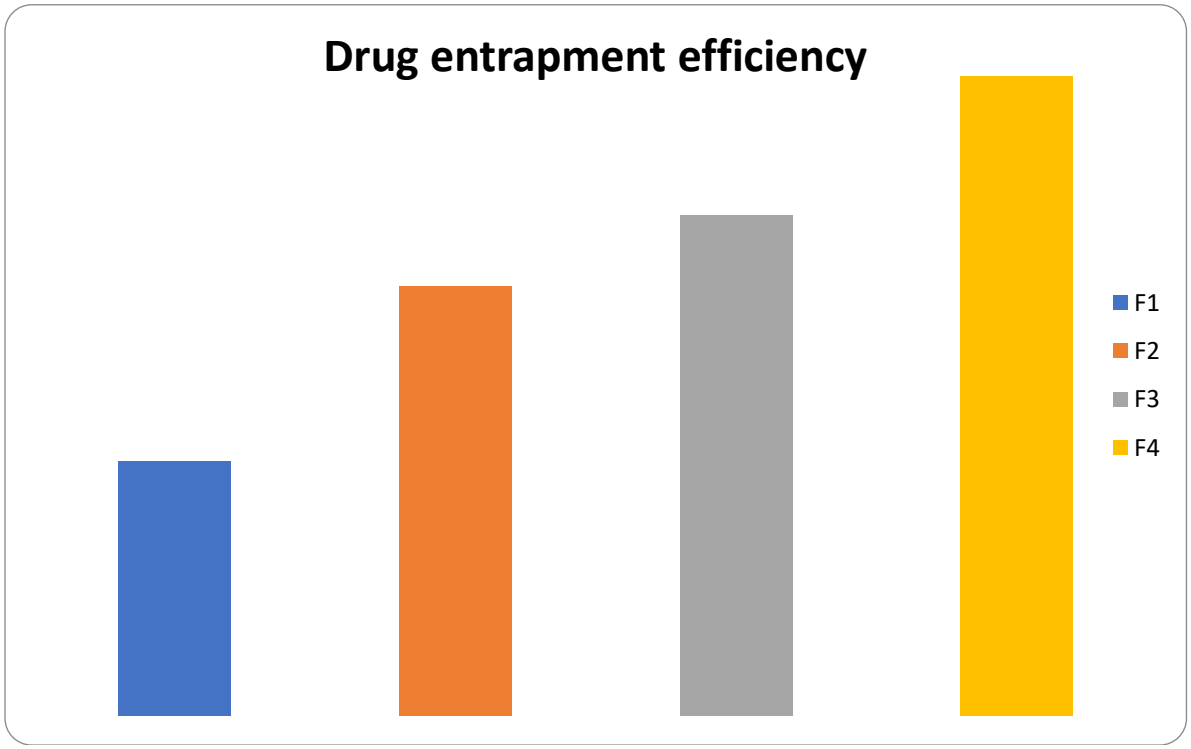


Fig-5: Drug entrapment efficiency of all formulations

The entrapment efficiency for the prepared formulation was in the range of 72.21±0.60 to 84.65±1.66 %. The entrapment efficiency increased progressively with increasing the concentration of polymers which could be attributed to the formation of larger nanogel that entrapped more amount of drug. Nanogel were found to be the finest among all with a entrapment efficiency of 84.65±1.66 %.

Determination of Vesicle morphology and Size

sample was coated with gold and allowed the SEM to capture the images at a temperature of - 1200c and voltage of 5kV.

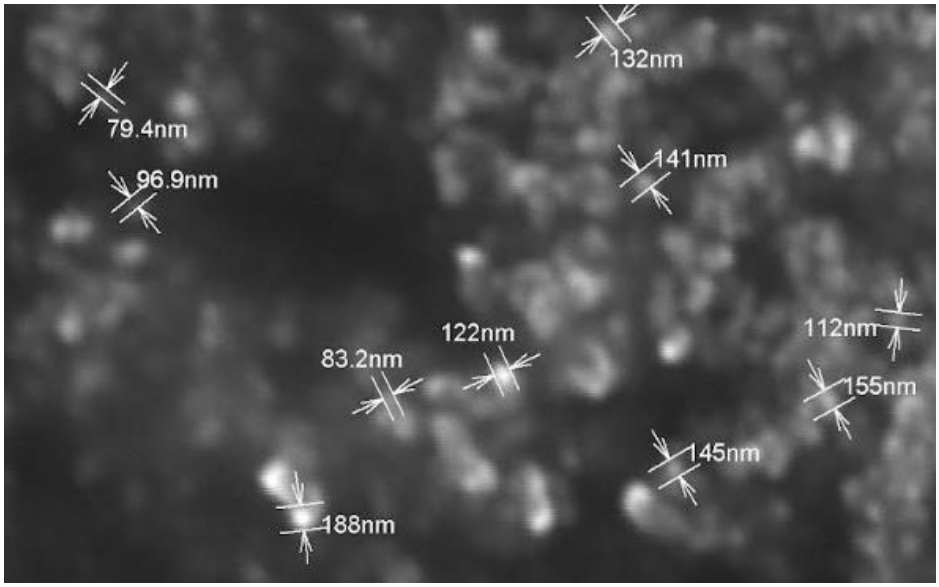


Fig-6: SEM analysis of Optimized Nanogel

Particle size

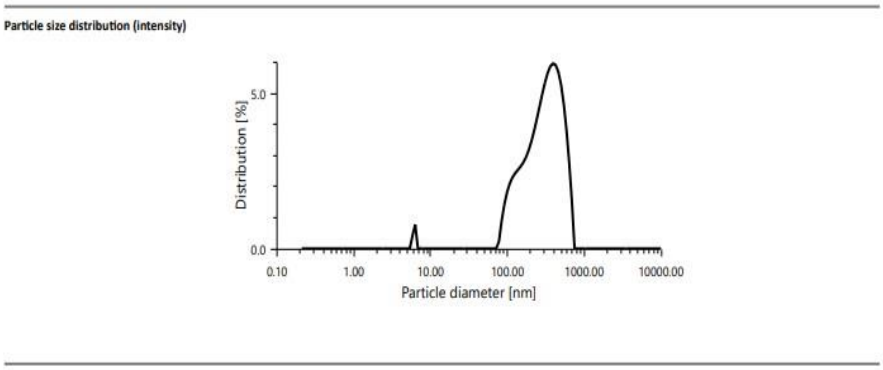


Fig-7: Particle size of optimized formulations

Zeta potential

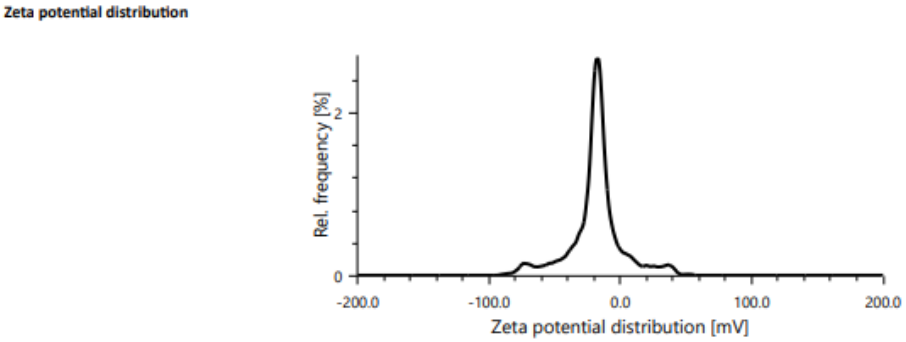


Fig-8: Zeta potential of optimized formulation

Table-5: Evaluation Studies of Diacerein Nanogel particle size and Zeta potential

F. No	Particle size (nm)	Zeta potential
F1	155±0.25	-21.36
F2	145±14.2	-23.20
F3	141±4.25	-25.49
F4	122±18.7	-27.63

In vitro drug release studies:

Table-6: Results of Diacerein Nanogel of all formulations

Time(hours)	F1	F2	F3	F4
0	0	0	0	0
1	12.12±35.5	15.16±36.9	16.96±35.9	17.90±33.5
2	22.38±25.9	24.33±26.5	27.41±36.8	28.96±32.6
3	35.10±23.5	39.12±32.1	36.15±30.5	39.15±28.7
4	42.15±27.8	46.46±35.5	44.82±29.8	48.36±25.7
5	53.32±26.5	58.39±30.8	55.62±27.5	59.25±31.6
6	61.20±25.7	69.65±25.6	70.30±32.1	74.21±27.4
7	70.25±32.5	77.53±34.6	85.26±33.8	87.31±29.6
8	78.65±32.9	83.53±32.5	91.25±34.9	96.38±35.1

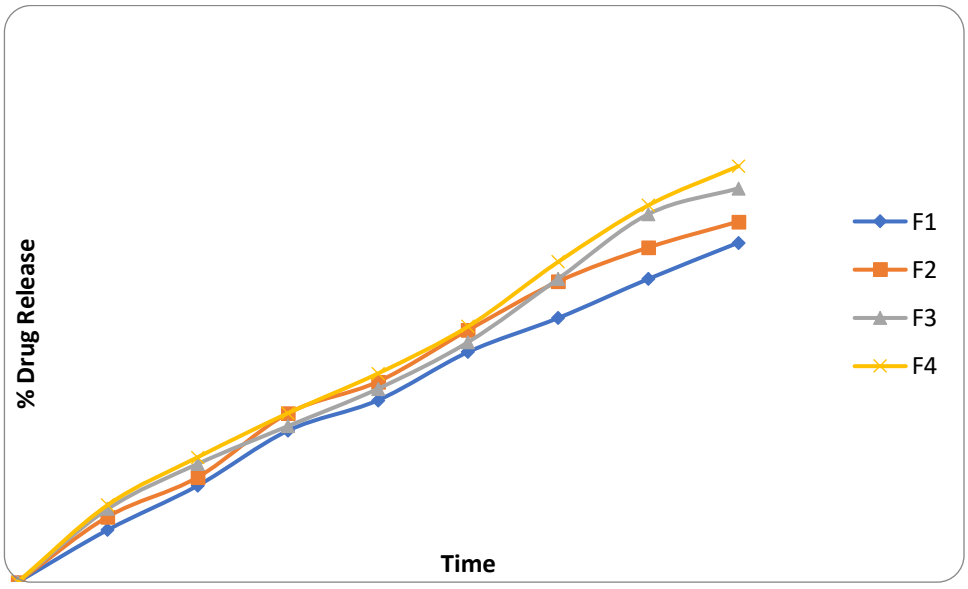


Fig-9: Drug release studies of all formulation

Zero order kinetics

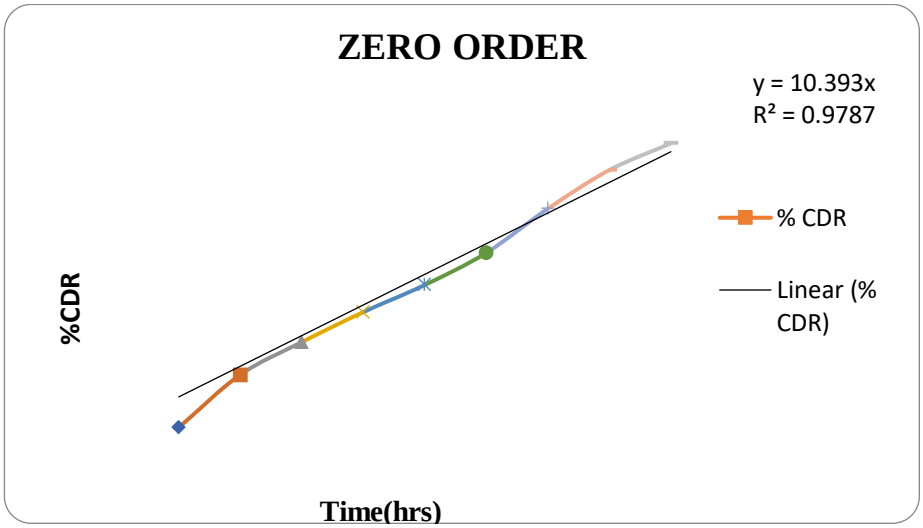


Fig-10: Zero order kinetics of optimized formulation

First order kinetics

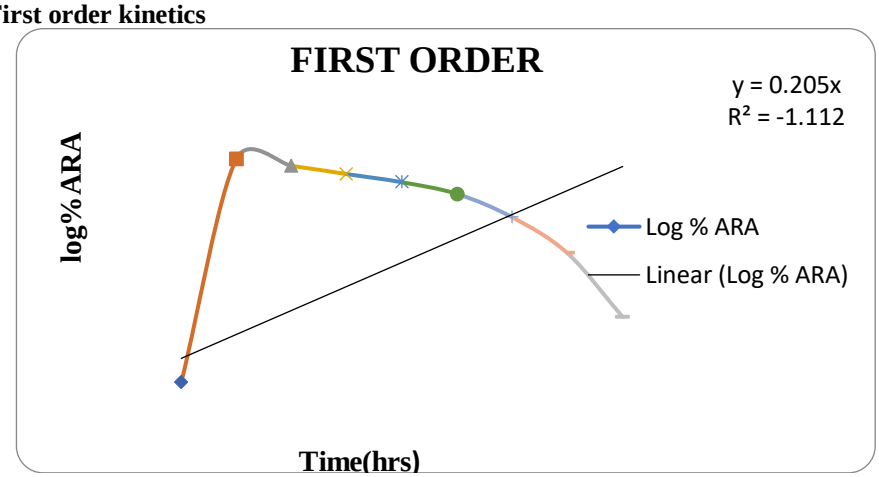


Fig-11: First order kinetics of optimized formulation

Higuchi

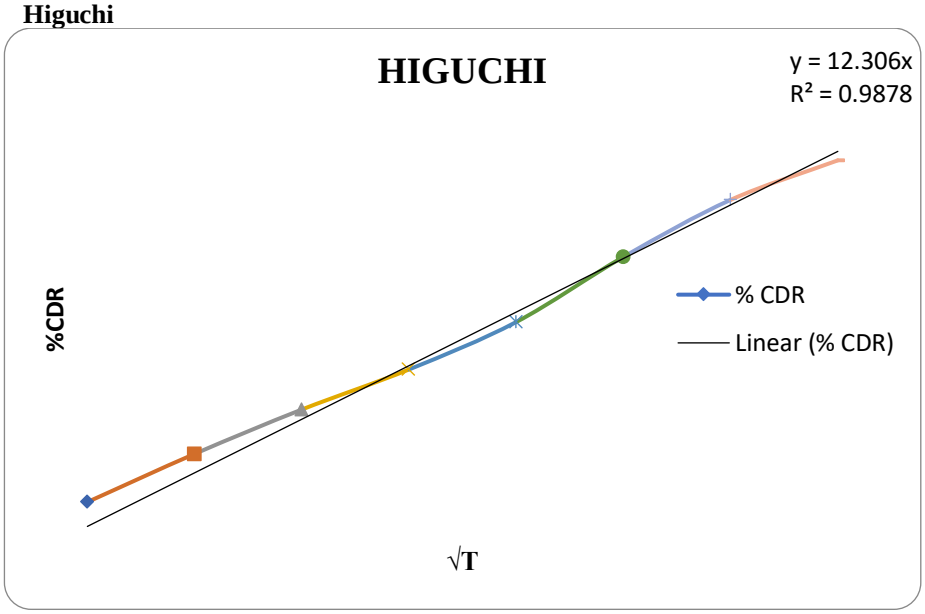


Fig-12: Higuchi model of optimized formulation

Korsmeyer peppas

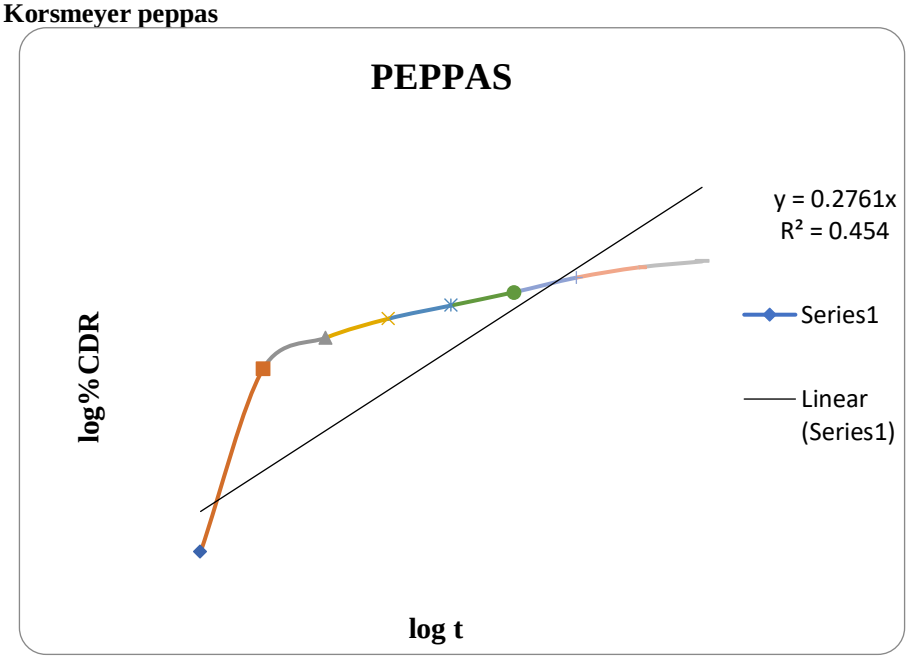


Fig-13: Korsmeyer peppas of optimized formulation

Stability studies

There was no significant change in physical and chemical properties of the nanogel of formulation F-4 after 90 days. Parameters quantified at various time intervals were shown.

Table-7: Stability studies of F4 formulations

F.no	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-4	25^{0}C/60%RH	96.38±35.1	95.82±33.6	94.68±32.8	93.61±34.7	Not less than85 %
F-4	30^{0}C/75% RH	96.38±35.1	95.71±32.7	94.31±32.1	93.52±34.9	Not less than
F-4	40^{0}C/75% RH	96.38±35.1	95.28±31.9	94.29±31.9	93.10±31.2	Not less than

CONCLUSION:

Diacerein, an anthraquinone derivative used in the treatment of osteoarthritis, suffers from poor aqueous solubility and limited bioavailability when administered orally. To overcome these limitations and enhance topical delivery, diacerein-loaded nanogels were formulated and evaluated. The nanogel system combines the benefits of nanotechnology and gel-based delivery to improve drug permeation through the skin and ensure sustained release. In this study, diacerein nanogel was prepared using a suitable nanocarrier system followed by incorporation into a gel base (such as Carbopol 934 and HPMC). The formulation was characterized for particle size, zeta potential, entrapment efficiency, pH, viscosity, spread ability, drug content, and in vitro drug release. The in vitro study revealed that the Diacerein nanogel can be a useful means for the targeted delivery of drug.

REFERENCES:

1. Rolland JP, Maynor BW, Euliss LE, Exner AE, Denison GM, DeSimone JM. Direct fabrication and harvesting of monodisperse, shape-specific nanobiomaterials. J Am Chem Soc. 2005;127:10096–10100.
2. Vinogradov SV. Colloidal microgels in drug delivery applications. Curr Pharm Des. 2006;12:4703–4712
3. F. Danhier, E. Ansorena, J.M. Silva, R. Coco, A. Le Breton, V. Préat PLGA-based nanoparticles: an overview of biomedical applications J. Contr. Release, 161 (2012), pp. 505-522, 10.

4. S. Khandavilli, Nanoemulsions as versatile formulations for paclitaxel delivery: peroral and dermal delivery studies in rats,J. Investig. Dermatol.(2007)
5. V. Giannellini, A validated HPLC stability-indicating method for the determination of diacerhein in bulk drug substance, J. Pharm. Biomed. Anal. (2005)
6. Wu SY, Debele TA, Kao YC, Tsai HC. Synthesis and characterization of dual-sensitive fluorescent nanogels for enhancing drug delivery and tracking intracellular drug delivery. International journal of molecular sciences, 2017 May; 18(5): 1090.
7. Kumar GS, Vishnupriya D, Chary KS, Patro TU. High dielectric permittivity and improved mechanical and thermal properties of poly (vinylidene fluoride) composites with low carbon nanotube content: effect of composite processing on phase behavior and dielectric properties. Nanotechnology, 2016 Aug 11; 27(38): 385702.
8. Vania Rachael Fonseca, Prashan Jivaji, Bhide, Madhusudan Purushottam Joshi. Formulation, development, and evaluation of Etoricoxib nanosize microemulsion based gel for topical drug delivery, Indian Journal of Pharmaceutical Education and Research, 2019;53(4):60-65.
9. Swati Talele, Preetam Nikam, Braja Ghosh, Chaitali Deore, Ashwini Jaybhave, Anil Jadhav. A Research Article on Nanogel as Topical Promising drug Delivery for Diclofenac sodium, Indian Journal of Pharmaceutical Education and Research, 2017;51(4S):80-86.
10. Phatak Atul A, Chaudhari Praveen D. Development and evaluation of nanogel as a carrier for transdermal delivery of Aceclofenac, Asian journal of pharmaceutical technology, 2012;2(4):125-132.
11. Chopade swapnil, Khabade Sheeba, Patil Ajit and Powar Sayali. Formulation development and evaluation of anti-inflammatory potential of topical Tenoxicam nanogel on animal model. International Journal of Recent Scientific Research, 2018;9(12): 29951-29957.
12. Inamdar Yashadri, Rane Bhushan, Jain Ashish. Preparation and Evaluation of Beta Sitosterol Nanogel: A Carrier Design for Targeted drug Delivery system, Asian Journal of Pharmaceutical Research and Development, 2018;6(3):81-87.
13. Anasuya Patil, Pranoti kontamwar.Formulation and Evaluation of Antifungal nanogel for topical drug delivery system. Asian Journal of Pharmaceutical and Clinical Research, 2021;14(10):127-134. doi: 10.22159/ajpcr.2021.v14i10.42436.
14. Muniraj S N, Yogananda R, Nagaraja T S, Bharathi D R. Preparation and Characterization of Nanogel Drug Delivey System Containing Clotrimazole an antifungal drug. Indo American Journal of Pharmaceutical Research, 2020;10(7):24-31
15. Oh JK, Drumright R, Siegwart DJ, Matyjaszewski K. The development of microgels/nanogels for drug delivery applications. Progress in Polymer Science, 2008 Apr 1; 33(4): 448-77