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FORMULATION AND EVALUATION OF CELECOXIB LOADED EUGRADIT S100 NANOPARTICLES

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ABSTRACT

Celecoxib- A selective COX1 & COX2 inhinbitor has shown promising results for treating colon polyps but on the other hand may leads to complication in gastrointestinal region. In this study Celecoxib nanoparticles were prepared by loading the drug in a polymer "Eugradit ® S100". Drug-excipient compatibility was checked by FTIR spectroscopy. Celecoxib loaded Eugradit ® S100 nanoparticles were prepared by solvent extraction method. Four different formulation (F1, F2, F3 and F4) were prepared by taking different ratios of drug and polymer. Formulations were evaluated for % yield, entrapment efficiency, particle size determination etc. Dissolution study was performed and % drug release was compared with the marketed formulation. Melting point of celecoxib was found 157±0.5°C. drug showed maximum absorption at 255nm. Confirmation of functional groups (alcohol, nitro compound, alkyl halides & H-bonded alcohol) was successfully done by IR spectroscopy. From TEM images, prepared nanoparticles were found spherical with the range of 100.54±0.014 nm. Percentage yield of nanoparticles was found to be 80.68±0.69 %. Among four prepared formulations F1 was selected for dissolution studies and % drug release was found to be 60.01% which was better than marketed formulation (40.23%). It can be concluded from the study that the dose of celecoxib can be reduced which can eventually reduce side effect of the drug.

KEYWORDS: Drug delivery, Nanoparticle, Celecoxib, Eugradit ® S100, spectroscopy.

1. INTRODUCTION

Nanoparticle can be described as tiny particulate having size range of 10-1000 nm which may be either in solid form or in particulate dispersion form.[1] Matrix are used to disperse, entrapment or attach the drug to form matrix loaded nanaoparticles. Rate of drug release can also be achieved through these methods in the form of control and sustain release drug delivery system.[2]

Advantages of nanoparticle

1) Particle size and surface characteristics of nanoparticle can be achieved to obtain targeting of drug in active and passive manner after parenteral administration.
2) They can affect organ distribution, subsequent clearance of drug and may provide sustain and control effects of drug during drug residence in the body, eventually enhance drug therapeutic efficacy and decrease side effects.
3) By selecting the suitable matrix reservoir we can manage the drug release and particle degradation characteristics.
4) Various techniques such as magnetic targeting or attachment of targeting ligands to surface, can be used for specific sites.
5) Nanoparticles can be applicable to different routes of administration such as oral, nasal, parentral.[3,4]
6) Nanoparticles are available in wide range as Fullerenses[5], Solid lipid nanoparticles (SLNs)[6], Quantum dots (QD)[7], Dendrimers.[8]

Limitation of nanoparticles

1) Sometimes handling of nanoparticle are tough in liquid and dry forms due to aggregation between particles of small sized and higher surface area.
2) Burst release and reduction in drug loading can occur due to small particle size and larger surface area.[9]

2. EXPERIMENTAL WORK: Celecoxib is classified under the category of NSAID as selective cyclooxygenase inhibitor.[10] The Drug inhibit prostaglandin synthesis through inhibiting cyclooxygenase 1 & 2. Various study shown the potential use of celecoxib in the cancer therapy as chemopreventive agents.[11,12]

Preformulation studies

Drug characterization

A) Physical Appearance

The drug celecoxib was checked visually for its color and odor.

B) Determination of melting point

Melting point of the drug was found by the capillary fusion method. Mean of the triplicate reading was observed and matched with the literature value.

C) Quantitative analyses

Quantitative analysis or determination of drug sample was done by UV-visible spectrophotometry to find maximum wavelength. . λ max is determined by co-relating the highest value of absorbance with that of corresponding wavelength.

D) Preparation of calibration curves.

In Phosphate Buffer Saline (7.4)

Primary stock solution of 100 µg/ml was prepared in phosphate buffer saline. Dilution of different strength was made from this solution. The λ max of celecoxib was finalized by scanning suitable dilutions of stock in same solvent.

E) Solubility determination

The solubility of celecoxib in various solvents viz., water, 0.1N HCl, Phosphate buffer saline (6.8) and phosphate buffer saline (7.4) was determined. The samples were kept for 10 minute and then supernatant was diluted suitably and drug estimation was done by UV spectroscopy.

F) Determination of Partition coefficient.

The partition coefficient of celecoxib was determined using n-octanol and aqueous phase in a separating funnel. Then assay of both the aqueous and octanol phase was performed pre and post partition with UV spectrophotometer at suitable λ max to obtain partition coefficient. Three reading were observed and mean was calculated.

Partition coefficient of Celecoxib was determined from the given equation.

$$P = \frac{\text{Concentration of drug in oil phase } (C_o)}{\text{Concentration of drug in aqueous phase } (C_a)}$$

Drug excipients compatibility studies

FTIR spectra was determined to calculate the drug-excipient compatibility. Drug and

excipients were taken in the proportion of 1:1 and stored for the period of 1 month at 40°c and 75% RH for and room temperature.

Table 2.1: FTIR analysis of drug and excipients

Sr. No.	Excipients	Ratio
1	celecoxib + Eudragit S100	1:1

Formulation design

Celecoxib loaded nanoparticles were prepared by Solvent extraction method.[13] Polymer Eudragit S 100 was first dissolved in acetone with the drug celecoxib. And the specified amount of PVP was added in the distilled water it with continuous stirring and allow it to stir in a magnetic stirrer.

Then aqueous solution of Eudragit S100 was added dropwise in to solution containing PVP through syringe while stirring in a mechanical stirrer followed by sonication for half an hour. The turbid solution were then allowed to centrifuge for 1 hour. Centrifugal tube which were then washed with distilled water thrice. The nanoparticles recovered were then suspended in distlled water and were lyophilized. The nanoparticle in powder form were then stored for further evaluation.

Table 2.2: Formulation of celecoxib NPs using different polymer to drug ratio.

Sr. No.	Formulation code	Drug (mg)	Eudragit S 100 (mg)
1	F1	200	200
2	F2	200	400
3	F3	200	600
4	F4	200	800

Characterization of Celecoxib nanoparticles.

Percentage yield

Prepared freeze-dried nanoparticle from each preparation were weighed accurately and total yield was calculated by comparing nanoparticle obtained and the total weight of material.[14]

$$(\%\ \text{Yield}) = \frac{\text{Amount of nanoparticles obtained (mg)}}{\text{Total weight of solid material (mg)}} * 100$$

Determination of Entrapment Efficiency

Percentage drug entrapment was determined by the following formula.[15,16]

$$\text{Entrapment Efficiency } (\%) = \frac{\text{Total amount of drug in supernatant}}{\text{Total amount drug used}} * 100$$

Transmission electron microscopy

The shape of the nanoparticle was determined by the transmission electron microscope technique TEM.

***In-Vitro* Drug Release Study**

In vitro drug release from the individual nanoparticle formulations was evaluated in media of varying pH (pH 1.2, and 7.2) as per a reported procedure, with slight modifications. Briefly, nanoparticles, equivalent to 100 mg of celecoxib were transferred to dialysis. The formulations were dialyzed against 100 mL of individual media, at 37◦C, in a shaking water bath at 50 rpm. At specific time points, release of the individual drugs from all the formulations was determined using UV spectroscopy method.[17.18]

3. RESULT AND DISCUSSION

Preformulation Studies

Drug characterization

A) Physical appearance

Celecoxib was found to be odorless white crystals or powder.

B) Determination of melting point

Table 3.1: Comparative values of melting point used to identify the drug.

Method	Experimental value	Literature value.
Capillary Fusion Method	157˚C ± 0.5˚C	158˚C

The melting point of celecoxib was in the range of 158˚C ± 0.5˚C.

C) UV-visisble Spectrum of drug Celecoxib

UV spectra of the drug (100µg/ml) showed the maximum absorbance at wavelength 255 nm.

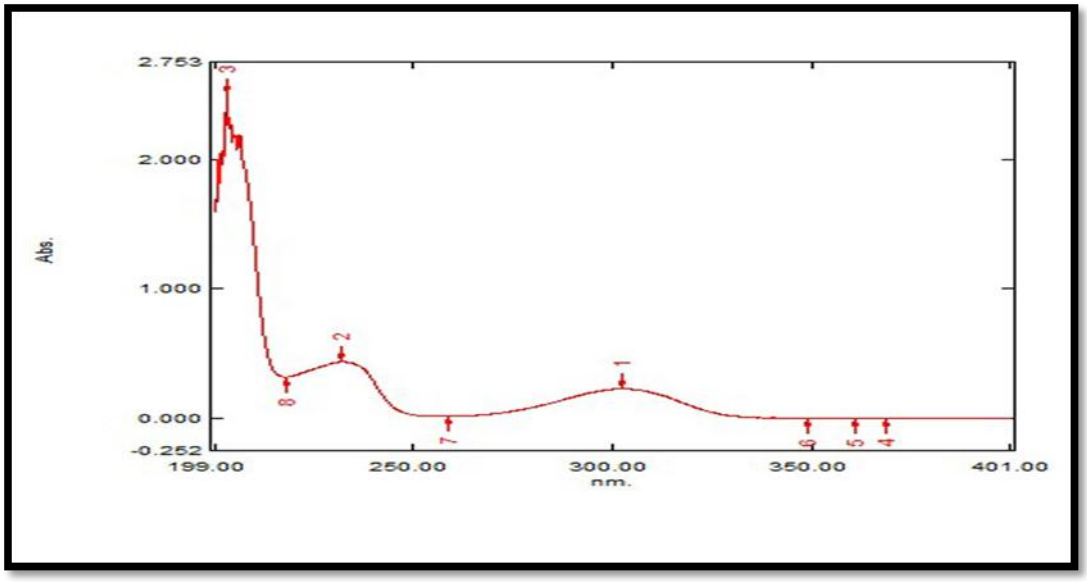

Fig 3.1: λ_{max} Scan of Celecoxib.

D) Callibration curve of Celecoxib.

i) In Simulated colonic fluid

Table 3.2: Absorbance data of Celecoxib at λ_{max} 255nm in SCF 7.4.

Sr. No.	Concentration (µg/ml)	Absorbance ± SD
1	0	0.000
2	10	0.101 ± 0.022
3	20	0.180 ± 0.024
4	30	0.272 ± 0.026
5	40	0.389 ± 0.021
6	50	0.482 ± 0.024
7	60	0.580 ± 0.026
8	70	0.642 ± 0.029
9	80	0.723 ± 0.024
10	90	0.810 ± 0.022

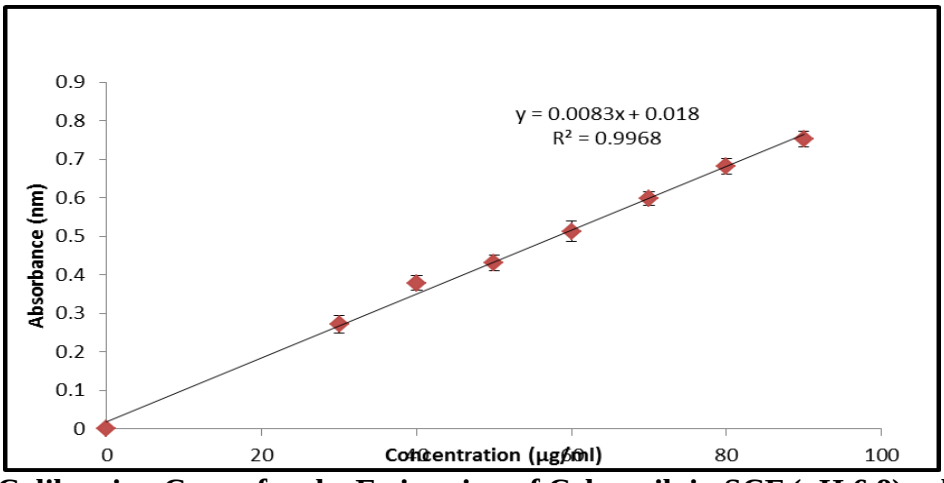

Fig. 3.2: Calibration Curve for the Estimation of Celecoxib in SCF (pH 6.8) colonic pH.

E) Solubility study

Table 3.3: Solubility data of Celecoxib at 25˚C in various solvents.

Solvents	Solubility Critera (BP)
Water	Poorly Soluble
Ethanol	Soluble
Phosphate Buffer (7.4)	Spraingly Soluble
Methanol	Soluble

F) Partition coefficient of the drug

Table 3.4: Partition coefficient of Celecoxibe.

Sr. No.	Drug	Experimental value Log P	Literature value Log P
1	Celecoxib	3.7 ± 0.5	3.9

G) ATR-FTIR

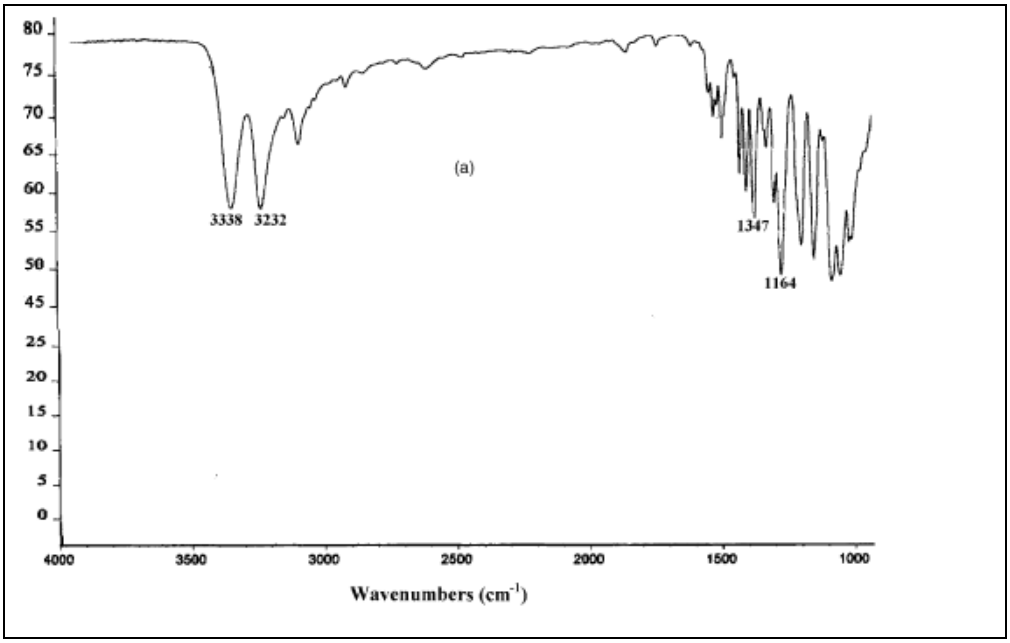

Fig 3.3: ATR-FTIR.

Table 3.5: ATR-FTIR.

Frequency cm–1	bond	functional group
3500–3200 (s)	O–H stretch, H–bonded	Alcohols
1360–1290 (m)	N–O symmetric stretch	nitro compounds
1300–1150 (m)	C–H wag	alkyl halides
3500–3200 (s)	O–H stretch	H–bonded alcohols

In this ATR-FTIR spectra, pure Celecoxib showed major peaks at 3338, 3232, 1347 and 1164. The following were observed which is due to the presence of different groups of Celecoxib.

7.2 Evaluation of Celecoxib Nanoparticles

7.1.2 Percentage yield

Table 3.6: Percentage yield.

S.No.	Formulation code	Percentage yield
1	F1	80.68±0.69
2	F2	76.59±0.82
3	F3	71.39±0.71
4	F4	60.63±0.55

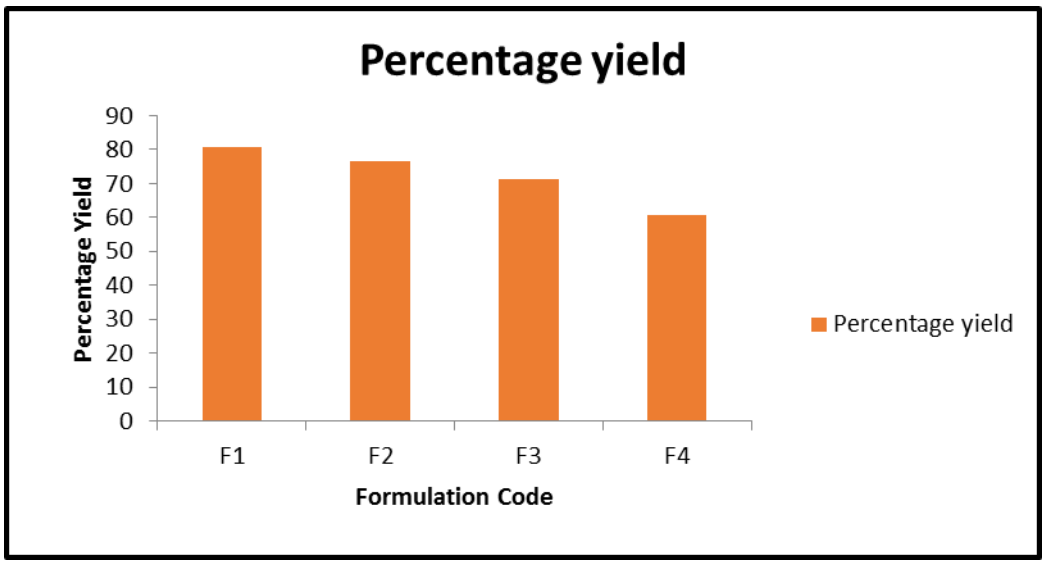

Fig. 3.4: Percentage Yield.

The observed Percentage yield of celecoxib in formulations was found to be in range of 80.68±0.69 which was considered as the best as it represents higher percentage yield.

7.2.2 Percentage drug entrapment

The drug content determination measures the actual weight of Celecoxib inside the Nanoparticles. The drug content was measured by deviation from theoretical weight.

Table 3.7: Drug content of Celecoxib Nanoparticles.

S.No.	Formulation	Drug Content (%)
1	F1	72.73 ± 0.68
2	F2	62.25 ± 0.12
3	F3	52.25 ± 0.25
4	F4	69.25 ± 0.62

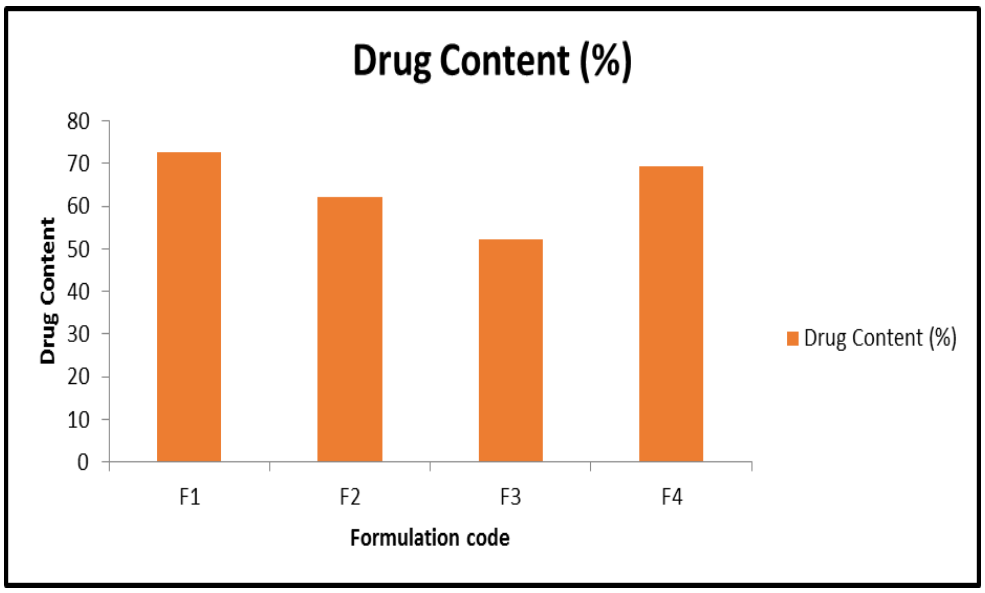

Fig. 3.5: Drug Content.

Percentage Drug entrapment of formulation F1 found to highest was 72.73 ± 0.68 and hence considered as the best.

7.2.3 Particle Size Determination

Particles size and size distribution are critical factors were determined through TEM.

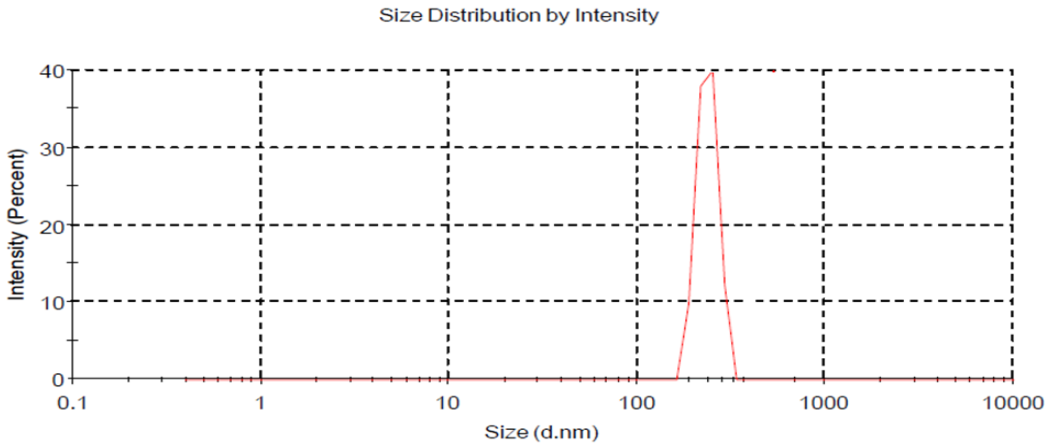

Fig. 3.6: Particle size of F1 formulation.

Particle size of F3 was found to be 298.76nm and PDI was found to be 0.381.

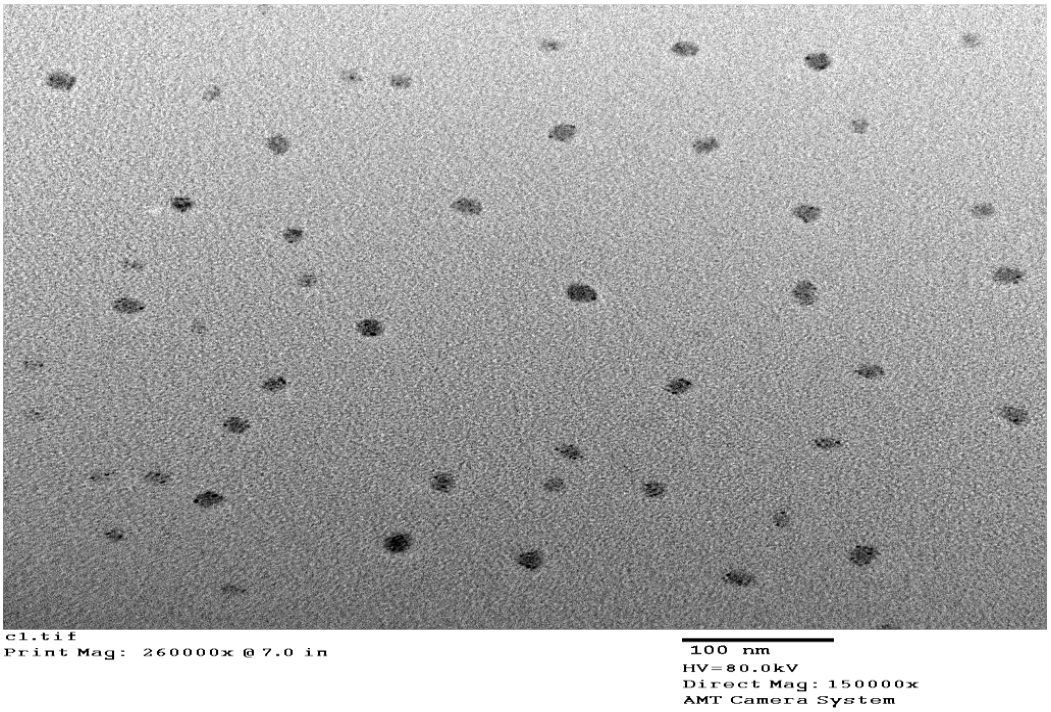

Fig. 3.7: Transmission Electron Microscopy of Celecoxib Nanoparticles.

From TEM image it was found that nanoparticle was spherical in shape and range is 100.54±0.014 nm.

7.2.4 FTIR analysis of Celecoxib Nanoparticles

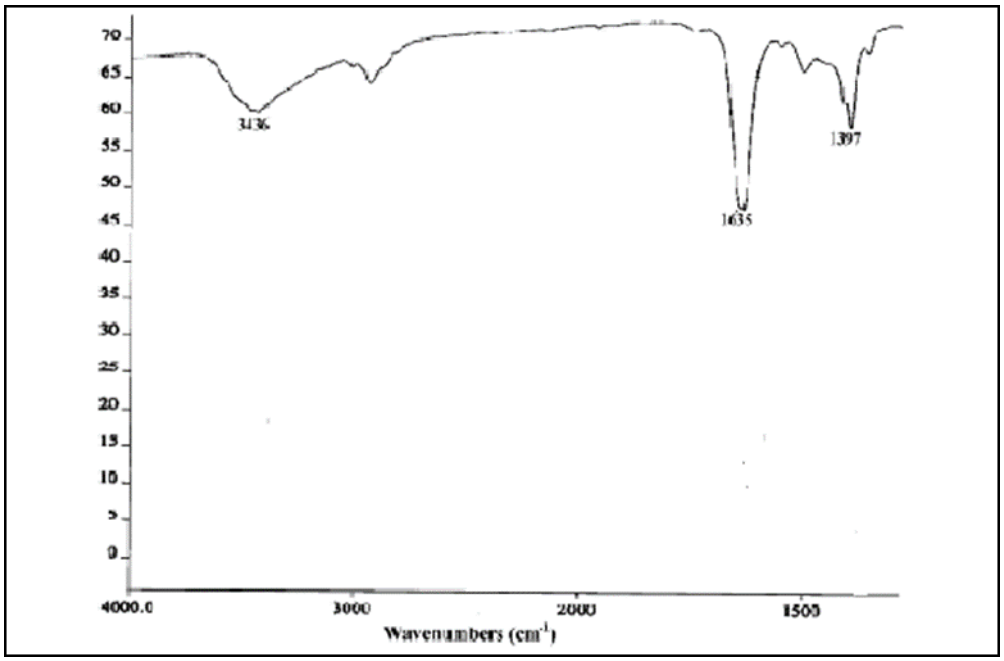

Fig. 3.8: FTIR spectrum of Nanoparticles.

Table 3.8: FTIR interpretation of Celecoxib Nanoparticles.

Frequency cm–1	bond	Functional group
3500–3200 (s,b)	O–H stretch, H–bonded	alcohols, phenols
1710–1665 (s)	C=O stretch	α β–unsaturated aldehydes ketones
1400–1350 (m)	C–H rock	Alkanes

From the IR data, it was observed that functionality of the drug have remained unaffected, including intensities of the peak. So there was no compatibility issue between drug and excipients.

***In vitro* drug permeation study**

The percentage yield and the percentage drug entrapment of F1 formulation was selected for in vitro drug permeation study.

Table 3.9: Percentage drug release of F1 formulation.

Time(Hr.)	Percentage drug release of nanoparticle
0	0±0
1	0.68±0.25
2	1.62±0.52
3	10.55±0.9
4	20.15±0.71
5	27.98±0.88
6	35.45±0.3
7	44.25±0.48
8	54.75±0.68
9	60.01±0.14

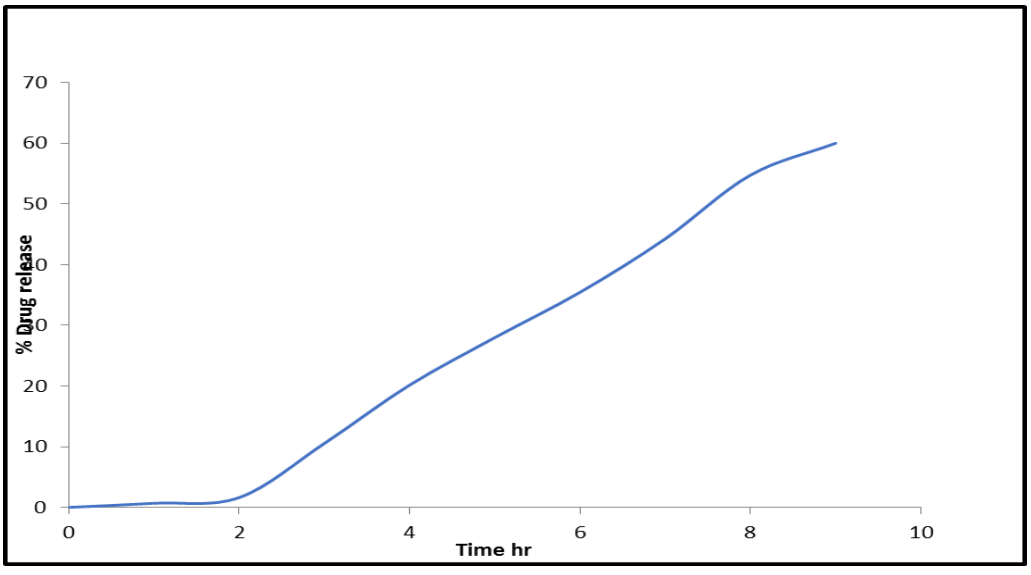

Fig. 3.9: Percentage release of F1 nanoparticle.

4. CONCLUSION: In this project work, Eudragit ® S100 nanoparticles containing Celecoxib were successfully prepared by using Solvent extraction method. The Celecoxib nanoparticles were then characterized with various parameters. Such as, Particle size, Drug encapsulation efficiency and in vitro release. Among the four formulation prepared (F1, F2, F3, F4), F1 showed better characterstics as compare to the others. Thus preparation of Celecoxib nanoparticle by ionically cross-linking cationic Eudragit S100 with PVP was particularly successful. Eudragit S100 nanoparticles produced by ionic crosslinking with PVP increased the drug loading efficiency in the Eudragit S100 nanoparticles and also prolonged the release period. Thus, it can be concluded that the formulation of Celecoxib loaded Eudragit S100 nanoparticles be used for the treatment of colon diseases.[19]

REFERENCES

1. E. Walter, K.S. Soppimath, T.M. Aminabhavi, A.R. Kulkarni. Biodegradable polymeric nanoparticle as drug delivery devices. Journal of Controlled Release, 2001; 70: 1-20.
2. Saha partha, Goyal Amit K, Path Goutam. Formulation and evaluation of chitosan based Ampicilin trihydrate Nanoparticles. Tropical journal of pharmaceutical Research, 2010; 9(5): 483-488.
3. Kayser.O, Lemke.A, N.Hernandez-Trejo. The impact of nano biotechnololgy on the development of new drug delivery systems. Current Pharmaceutical Biotechnolgy, 2005; 6(1): 35.
4. Jong W.H.D, Borm P.J.A, Drug delivery and nanoparticles. Applications and hazards. International Journal of Nanomedicine, 2008; 3(2): 133-149.
5. Sano. N, Wang. H, Chowalla.M, I. Alex androv, G.A.J Amaratung. Synthesis of carbon onion in water. Journal of Pharmaceuticals, 2001: 506-507.
6. Muhlen Zur. A, Bassler N, Von Elverfeldt.D, Neudorfer I, Steitz B, Petri-fink.A, Hofmann.H, Bode C, Peter K. Super paramagnetic iron oxide binding and uptake as imaged by magnetic resonance is mediated by the integrin receptor mac-1 (CD11b/CD18). Implication on imaging of athero scleratic plaques, Atherosclerosis, 2007; 193(1): 102-111.
7. Das S, Wai Kiong Ng, Reginald B.H. Are nanostructured lipid carriers (NLCs) better than solid lipid nanoparticles (SLNs): Development, characterizations ad comparative evaluations of clotrimazole-loaded SLNs and NLCs? European Journal of Pharmaceutical sciences, 2012; (72): 139-151.

8. Grayson S.M, Frechet J.M. Convergent dendrons and dendrimers: From synthesis to Application. Chem. Rev, 2001; 101(12): 3819-3868.
9. Das S, Wai Kiong Ng, Reginald B.H. Are nanostructured lipid carriers (NLCs) better than solid lipid nanoparticles (SLNs): Development, characterizations ad comparative evaluations of clotrimazole-loaded SLNs and NLCs? European Journal of Pharmaceutical sciences, 2012; (72): 139-151.
10. Gong L, Thorn CF, Bertagnolli MM, Grosser T, Altman RB, Klein TE: Celecoxib pathways: pharmacokinetics and pharmacodynamics. Pharmacogenet Genomics, 2012 Apr; 22(4): 310-8. doi: 10.1097/FPC.0b013e32834f94cb.
11. Hawkey CJ: COX-1 and COX-2 inhibitors. Best Pract Res Clin Gastroenterol, 2001 Oct; 15(5): 801-20. doi: 10.1053/bega.2001.0236.
12. http: //www.drugbank.ca/drugs/DB002484.
13. Sailaja A.K, Amareshwar P, Chakravarty P. Different techniques used for the preparation of nanoparticles using natural polymers and their application. International Journal Pharm Science, 2011; 3(2): 45-50.
14. Ping Li, Ya-Ni Dai, Jun-Ping Zhang, Ai-Qin Wang, Qin Wei. Naoparticles as a Novel Drug Delivery System for Nifedipine. International Journal of Biomedical Science, 2008; (4): 221-228.
15. Zhu Aiping, Chen Tian, Yuan Lanhua, Wu Hao, Lu Ping. Synthesis and Characterization of N-Succinyl-Chitosan and its self-assembly of nanospheres. Carbohydrate Polymers. 2006; (66): 274-279
16. Sailaja A.K, Amareshwar P, Chakravarty P. Different techniques used for the preparation of nanoparticles using natural polymers and their application. International Journal Pharm Science, 2011; 3(2): 45-50.
17. Makhlof A, Tozukaa Y, Takeuchia H. Design and evaluation of novel pH-sensitive chitosan nanoparticles for oral insulin delivery. European Journal of Pharmaceutical Sciences, 2011; (12): 445-451.
18. Angelo Viscido, Annalisa Capannolo, Giovanni Latella, Renzo Caprilli, Giuseppe Frieri. Nanotechnology in the treatment of Inflammatory bowel Disease. Journal of Chron's and colitis, 2014; (8): 903-918.
19. Angelo Viscido, Annalisa Capannolo, Giovanni Latella, Renzo Caprilli, Giuseppe Frieri. Nanotechnology in the treatment of Inflammatory bowel Disease. Journal of Chron's and colitis, 2014; (8): 903-918.