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Research Article

Preparation and Characterization of Prednisolone Containing Nanoparticles for Treatment of Colon Disorder

Vitthal K Vijapure*[1, 2], Dr, Sunabee [2], Dr. Rakesh Kumar Jat [1]

[1] *Shree JJTU Institute of Pharmacy, Shri JJT University, Vidyanagari, Chudela, Jhunjhunu, Rajasthan-333010, India*

[2] *Shri Sharanabasaveshwar College of Pharmacy Vijayapura, Hanchinal, Karnataka 586103, India*

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*Address for Correspondence:

Vitthal K Vijapure, Assistant Professor, Department of Pharmaceutics, Shri Sharanabasaveshwar College of Pharmacy Vijayapura

Abstract

The point of flow research work is planning and portrayal of prednisolone containing nanoparticles by spray drying process using regular, semi engineered and manufactured polymers for treatment of colon problem. The pre-arranged Nanoparticles were assessed for Surface morphology, Medication entanglement effectiveness, differential filtering colorimetry, molecule size, Fourier change infrared spectroscopy, in-vitro drug release and X-beam diffraction studies. The pre-arranged Nanoparticles are smooth in surface and showing circular shape. The normal molecule sizes of the nanoparticles were tracked down in the scope of 523 nm to 901 nm. The medication exemplification effectiveness (EE) of the steroid containing nanoparticles were tracked down in the scope of 82.21%to 89.30%. Here the medication encapsulation efficiency of arranged nanoparticles were expanded with expansion in the fixation of the polymer. The X-beam diffractogram of drug has shown trademark serious top between the 2ɵ of 19.67 and 30 because of its translucent nature. Where as in the event of medication free Nanoparticles, no extreme pinnacles connected with drug. In drug stacked Nanoparticles peaks were saw between 2ɵ of 29.67 and 49. The in-vitro drug discharge information of the multitude of definitions were viewed as zero request and shown supported discharge over a time of 24hour.The FTIR Spectra of Nanoparticles detailing are contrasted and the spectra of unadulterated medication, there is no much deviation in the spectra's and not noticed any medication and polymer communications. The brief time frame dependability investigation of streamlined plan has done and exposed to sedate epitome effectiveness and In-vitro drug release studies, where results shown that there is no huge change in the detailing.

Keywords: Polymer, Steroids, FTIR, X-Ray, Prednisolone.

INTRODUCTION

Oral route is the most convenient and preferred route but other routes for CDDS may be used. Rectal administration offers the shortest route for targeting drugs to the colon. However, reaching the proximal part of colon via rectal administration is difficult. Rectal administration can also be uncomfortable for patients and compliance may be less than optimal.[1] Colon-designated drug conveyance is for sure a specific field that plans to improve the remedial impacts of prescriptions for conditions influencing the lower gastrointestinal plot. The difficulties related with traditional oral medication conveyance, early medication disintegration in the upper GI parcel. Can be addressed through different techniques intended to guarantee drug conveyance explicitly to the colon. Here are a few vital perspectives and approaches related with details are designed to endure drug discharge in the stomach and small digestive system, rather delivering the prescription explicitly in the colon. These details are frequently utilized for sicknesses or conditions influencing the colon, permitting the medication to be delivered explicitly in the colon. Intestinal coatings or pH-delicate polymers are frequently used to accomplish postponed discharge, as the pH in the colon is higher contrasted with the stomach. Drug delivery can be controlled in light of time, guaranteeing that the medication is delivered at a particular rate or in a pulsatile way after arriving at the colon. Time-subordinate details might utilize systems like osmotic siphons or time-subordinate coatings. Colon-explicit medication conveyance can be accomplished by taking advantage of the extraordinary climate of the colon, including the presence of explicit chemicals and microbial verdure. Prodrugs that are actuated by colonic proteins or plans that answer bacterial digestion are instances of microbial-set off frameworks. PH-delicate polymers can be utilized to deliver drugs in light of the changing pH levels along the gastrointestinal plot, with explicit focusing to the colon. Covering the medication with polymers that are impervious to gastric and gastrointestinal liquids however debase in the colon can be a successful strategy. Nanoparticles and liposomes can be intended to embody tranquilizes and work on their conveyance to the colon, offering controlled discharge properties. Using probiotics or prebiotics to improve drug conveyance to the colon by utilizing the harmonious connection between these parts and the colonic climate. Ligands or antibodies can be integrated into drug details to target explicit receptors or locales inside the colon, improving the accuracy of medication conveyance. Colon-designated drug conveyance is especially advantageous for drugs with low bioavailability, those helpless to debasement in the stomach, or medications requiring restricted treatment in the colon. By conquering the difficulties related with regular medication conveyance, these

specific details add to worked on restorative results for colonic sicknesses. colon focusing on drug conveyance is a promising methodology for further developing the treatment results of colonic sicknesses and lessening unfavorable impacts related with fundamental medication openness., explicitly the colon. This designated approach is significant for the limited therapy of different colonic illnesses, including peevish entrail condition, fiery gut infection (like Crohn's sickness and ulcerative colitis), and colon disease. Customary oral dose frames frequently bring about drug retention in the stomach or digestive liquid, a cycle impacted by the medication's physicochemical properties. Be that as it may, these traditional structures may not be reasonable when a medication needs insurance from the brutal upper gastrointestinal climate or when nearby conveyance to the colon is important. Plans intended for colon-designated conveyance ordinarily include postponed discharge measurements structures. These definitions are designed to give either a "Burst discharge" or maintained/delayed discharge explicitly after arriving at the colon. Accomplishing fruitful medication conveyance to the colon includes utilizing different methodologies, adding to the adequacy of treatment for colonic infections.[2]

MATERIAL AND METHODS

Prednisolone drug received a gift sample from the arathi Pharmaceuticals Mumbai, Pectin(Himedia Lab Pvt ltd, Mumbai), Chitosan(Himedia Lab Pvt ltd, Mumbai) , others solvents and additives required for the preparation obtained from college store.

Method:-

Nanoparticles loaded with Prednisolone were prepared by using spray-drying technique using a laboratory spray dryer (Model SPD-P-111; Techno search Instruments, India) using a standard 0.7 mm nozzle. Different batches of Nanoparticles were prepared by dissolving the different ratios of Chitosan and pectin polymer with drug in glacial acetic acid solution under constant stirring at 500 rpm for 2 h using a magnetic stirrer. Required quantities of glutaraldehyde (GA) and 0.1 N HCl were added to the drug-polymer solution just before spray drying. When the drug-polymer aqueous solution was flowed through nozzle with a peristaltic pump, by the force compressed air atomization occurred, by spraying the aqueous solution into droplets. The droplets, together with hot air, were blown into the drying chamber, where the solvent in the droplets was evaporated and discharged out through an exhaust tube. The Nanoparticles were collected from cyclone1 and cyclone 2, washed with distilled to remove surface adhered drug and further dried completely in oven at 40 °C for overnight & store in closed container. [3, 4] The processing conditions of the spray drying were:

Inlet Temperature: 120 °C

Outlet temperature: 100 °C

Feed pump rate: 2ml/min

Spray pressure atomization: 2X105 PC.

Evaluation of Prepared Nanoparticles

The prepared Nanoparticles were evaluated by following parameters

A. Characterization

1. Particle size and Zeta potential analysis
2. Scanning electron microscopic studies
3. Differential scanning calorimetric analysis
4. Fourier transform infrared spectroscopy analysis
5. X-ray diffraction studies

B. Evaluation parameter of Nanoparticles

6. Drug encapsulation efficiency
7. *In-vitro* drug release study
8. Stability study

1. Particle size and Zeta potential analysis

The particle size and particle size distribution of SPIONs were measured with a Malvern instrument. The particle size distribution is reported as polydispersity index. The samples were placed in the analyzer chamber and readings were performed at 25°C with a detected angle of 90°. The zeta potential of SPIONs was measured with a Malvern instrument. The samples were diluted with pH 7.4 buffer and placed in electrophoretic cell and measured in the automatic mode.[5]

2. Scanning electron microscopic studies

The morphology of the prepared NPs was observed by means of a scanning electron microscope (JSM-T330A, Nihon Denshi, Japan) The samples were prepared on aluminum stubs and coated with gold prior to examination. A drop of the nanoparticle suspension was placed on a graphite surface. Observation was performed at 25 kV.[6]

3. Differential scanning calorimetric analysis.

DSC measures the heat flow into or out of a sample as a function of temperature or time. It compares the heat flow to a reference material under controlled heating conditions. The temperature at which changes in the sample occur, such as phase transitions, chemical reactions, or crystallization, is detected as peaks or troughs in the DSC curve. A typical DSC instrument consists of two sample pans, one containing the sample and the other the reference material. Both pans are subjected to the same controlled temperature program. The heat difference between the sample and reference pans is continuously monitored and recorded.[7]

4. Fourier transform infrared spectroscopy analysis

FTIR spectra of the samples were obtained using an FTIR spectrometer (model FTIR-2000, Perkin Elmer,Waltham, MA, USA). A small amount of each sample was triturated with a proper amount of potassium bromide (KBr) and the disks were formed under pressure. The spectra were collected in the range of 400 to 4000 cm-1 at a resolution of 4 cm−1 using 16 co-added scans and the baseline was corrected and converted into absorbance mode.[8]

5. X-ray diffraction analysis (XRD):

PXRD patterns were obtained using X'Pert PRO MRD® (analytical Ltd., Almelo, and the Netherlands) with Cu Kα radiation generated at 200 mA and 45 kV. The samples were placed on a silicon plate at room temperature and 2θ scans were collected from 5° to 60°C. [9]

6. Drug entrapment efficiency (DEE):

Weighed amount of Nanoparticles (100mg) with phosphate buffer pH 7.4 (10 ml) was added in a vial. The solution was stirred vigorously for 24 hours with mechanical stirrer. Supernatant was collected by centrifugation and drug content in supernatent was determined by using UV spectrophotometer at wavelength 244.8nm. Efficiency of drug entrapment is calculated by the following formula.[10]

DEE= absorbance ×dilution factor

Slope= concentration × dilution factor DEE = drug content ×

100 Label claim.

7. *In-vitro* drug release study

The *in-vitro* release studies of drug-loaded Nanoparticles were carried out in simulatedgastric fluids. Nanoparticles (100 mg) were weighed accurately and gently spread over the surface of 900 ml of dissolution medium (SGF). The content was rotated at 100 rpm at 37±0.5°C. Perfect sink condition was maintained during drug dissolution study period. The simulation of GI transit condition was achieved by altering the pH of dissolution medium at different time intervals. The pH of dissolution medium was maintained at 1.2 for 2hrs. Using 0.1N Hcl and then 3 hrs using pH 6.8 phosphate buffer. The release study was observed by adjusting the pH 2nd hour the pH of the dissolution medium was adjusted to 7.4 and maintained up to 24 hours. A 5-ml sample was withdrawn from the dissolution medium at various time intervals using a pipette and analyzed drug release using a UV–Visible spectrophotometer at 244.8nm. The receptor volume was maintained constant by replacing with equivalent volume of buffer after each withdrawal.[11]

Stability Study:-

The purpose of stability study is to provide evidence on how the quality of the drug substanceor drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. The Budesonide loaded Nanoparticles formulation was filled in tightly closed glass vials and subjected to short term stability testing according to the international conference on Harmonization (ICH), guidelines for zone 3 and 4. The packed containers of Nanoparticles were kept at room temperature (25±2ºc) and acceleration condition (40±2ºc/75±5%RH) in a hot air oven for a period for one month. The sample (n=9) were analysed at 45 days and evaluated for drug content.[12,13,14]

RESULTS AND DISCUSSION

Nanoparticles.

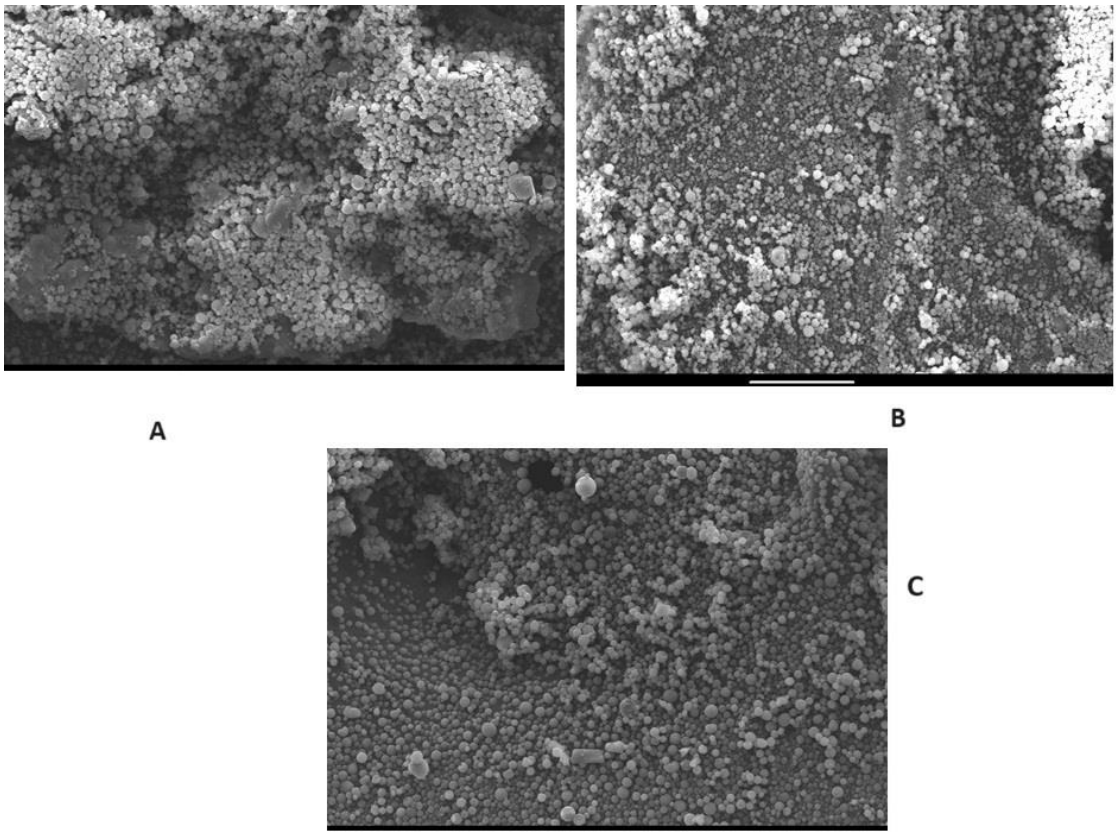

Figure 1: Scanning electron microscopic photographs of PRDS4 (A), PRDS8(B), PRDS9(C)

Table 1: Average size and drug entrapment efficiency (DEE) of Prednisolone Nanoparticles.

Serial. No	Nanoparticles code	Average size (nm)	DEE (%)
1	PRDS1	3.479	87.85±0.89
2	PRDS2	3.481	95.41±0.92
3	PRDS3	4.354	84.62±1.10
4	PRDS4	5.017	86.10±0.98
5	PRDS5	2.169	88.23±1.21
6	PRDS6	3.586	94.7±0.78
7	PRDS7	4.354	88.78±0.88
8	PRDS8	5.168	88.11±0.92
9	PRDS9	2.169	93.98±1.21

The values are average of three determinations. ± indicates SD values

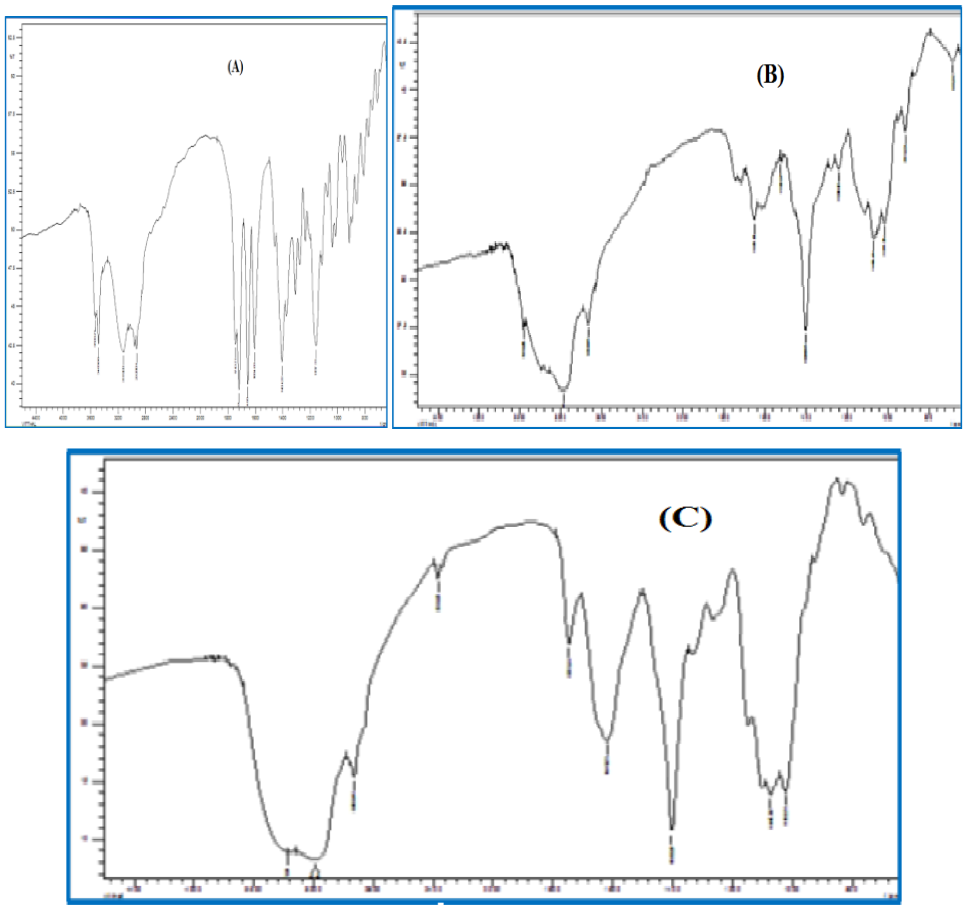

Figure 2: FTIR spectra of Prednisolone (A), FTIR spectra of combination of Pectin & Chitosan (1:1) (B), FTIR spectra of formulation (PRDS9) (C).

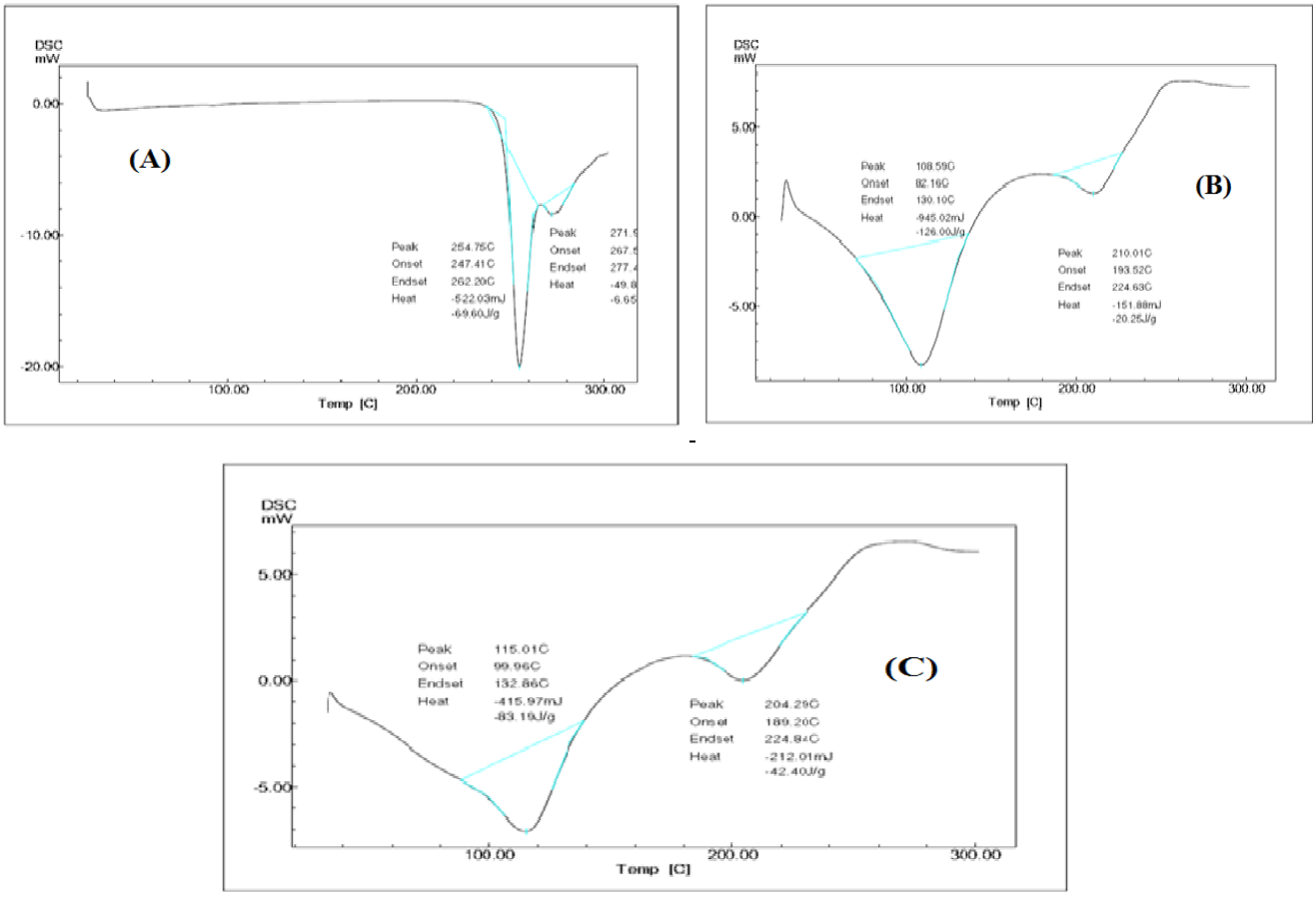

Figure 3: DSC thermograms of Prednisolone (A), Dummy of PRDS9(B) and drug loaded PRDS9 Nanoparticles (C).

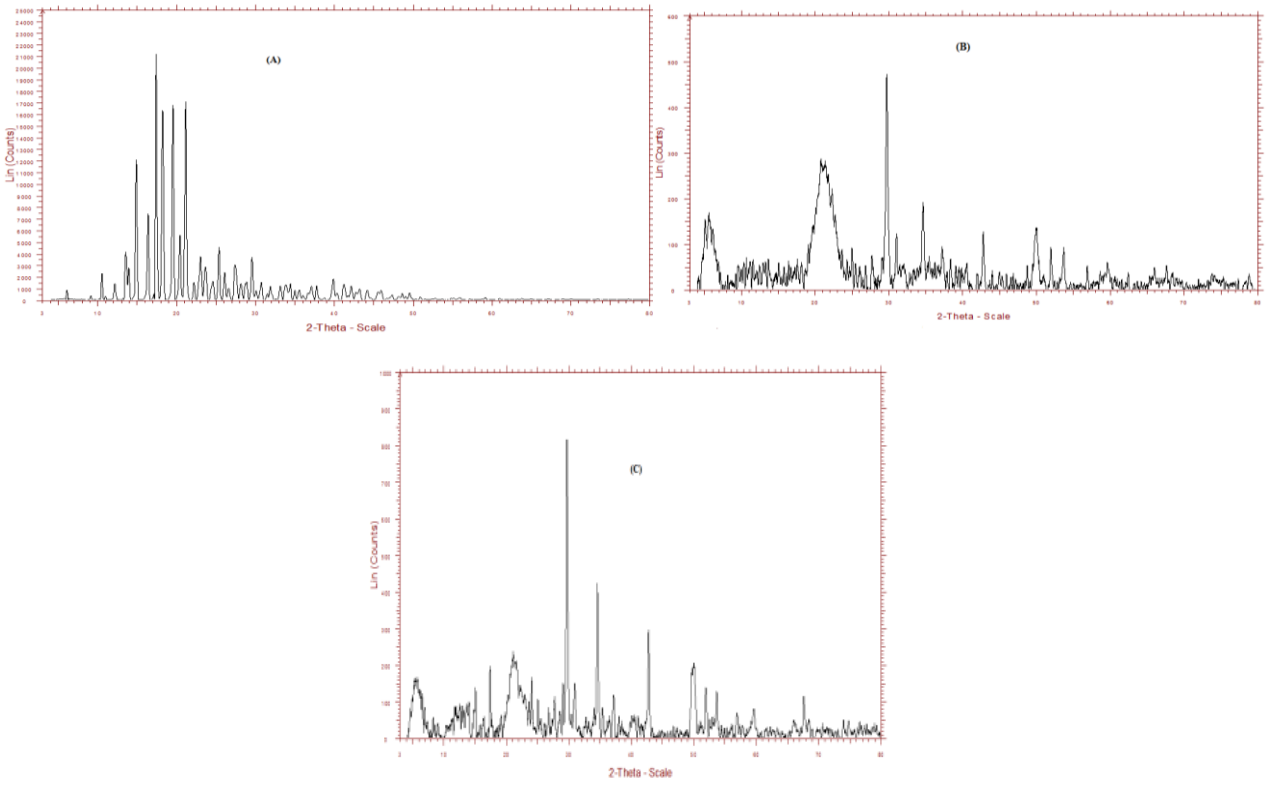

Figure 4: X-Ray Diffractograms of Prednisolone (A), Dummy PRDS9 (B), and drug loaded PRDS9 (C) Nanoparticles.

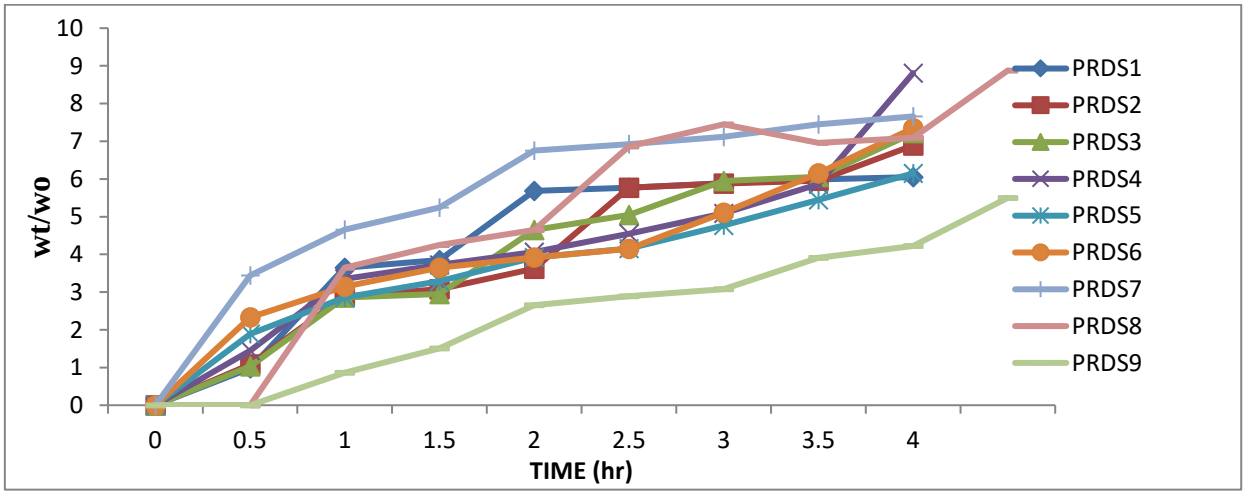

Figure 5: Swelling index pattern of colon specific Nanoparticles containing Prednisolone.

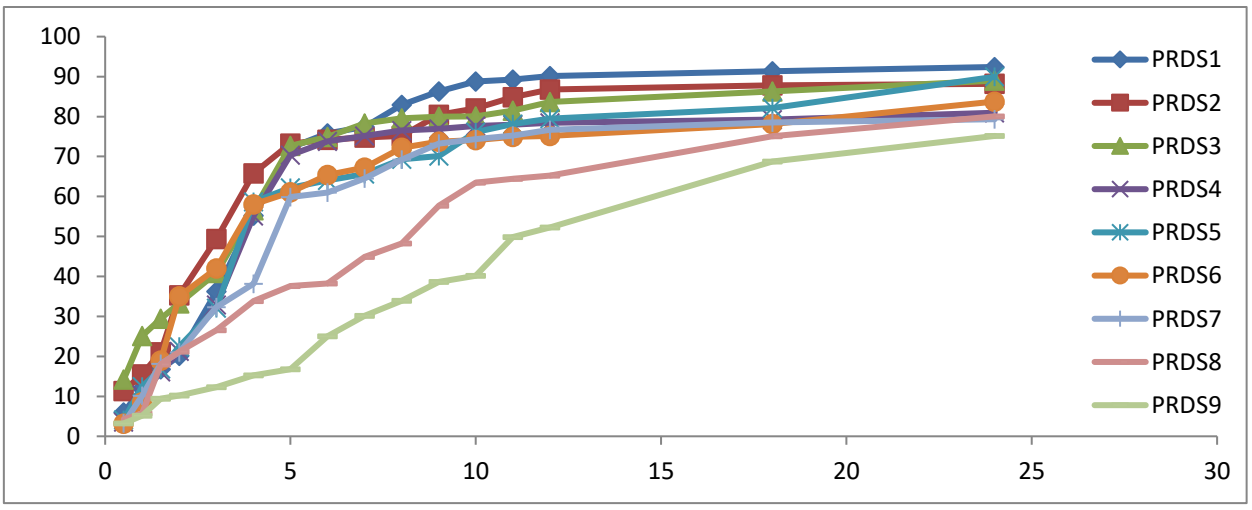

Figure 6: In-vitro release profile of Prednisolone from colon targeted spray dried Nanoparticles in gastric and intestinal fluids.

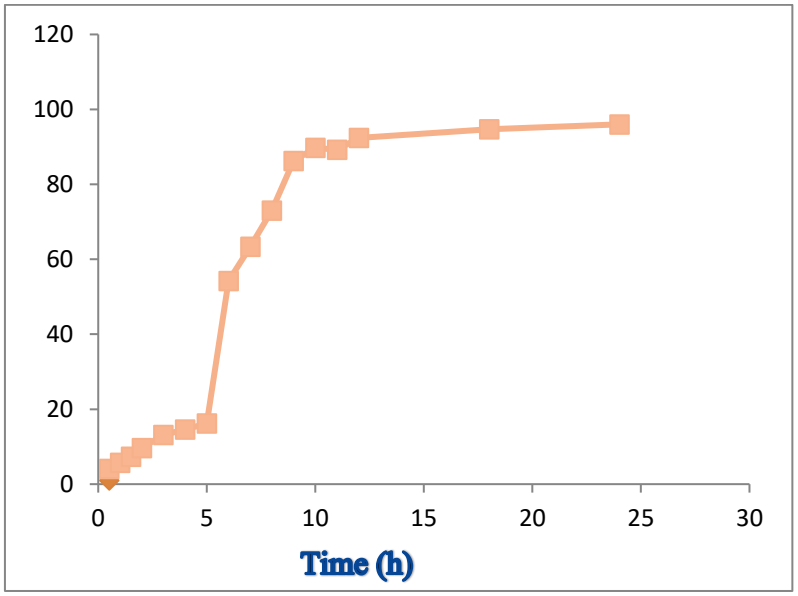

Figure 7: In-vitro drug release profile of Prednisolone from colon targeted Nanoparticles (PRDS9) in the presence of rat caecal content.

Table 2: Kinetic values of spray dried Nanoparticles of Prednisolone

Nanoparticles code	Zero order Equation		Higuchi model		Korsemeyer's Equation	
	N	R	N	R	N	R
PRDS1	4.245	0.954	26.29	0.846	0.752	0.911
PRDS2	3.529	0.991	21.94	0.875	0.574	0.909
PRDS3	3.286	0.964	19.94	0.922	0.453	0.965
PRDS4	3.158	0.947	20.83	0.952	0.723	0.970
PRDS5	3.214	0.944	21.95	0.966	0.645	0.971
PRDS6	3.145	0.947	22.58	0.957	0.862	0.960
PRDS7	3.443	0.941	19.40	0.979	0.797	0.982
PRDS8	3.279	0.975	20.54	0.976	0.816	0.969
PRDS9	3.396	0.977	18.81	0.961	0.870	0.975

DISCUSSION

The colon specific spray dried Nanoparticles of Prednisolone prepared by using chitosan and pectin. These formulations are spherical in shape and freely flowing. The surface morphologic study was examined by scanning electron microscopy studies (SEM). The SEM microphotographs showed that prepared Nanoparticles are smooth surface & spherical in shape, Figure 01.

The Nanoparticles size was determined using particle size analyzer (Malvern,UK) and recorded in table 01. The average Nanoparticles size was found to be in the range of 1.07 to 4.00 µm. As the concentration of polymers increases the size of Nanoparticles increased. The drug encapsulation efficiency (DEE) of the spray dried formulations in the range of 85.42% to 95.75%. The DEE was decreased as concentration of polymer increased in spray dried Nanoparticles. Which may be due to increased polymer weight ratio, as a result the drug entrapment efficiency decreases. The drug polymer compatibility was studied using FTIR spectroscopy. The FTIR spectra obtained is predicted in Figure 02. Prednisolone shows broad peak at 3993 Cm^{-1} due to –OH groups. Large peak observed from 29945 cm^{-1} is due to –CH stretching for $-CH_2$ and CH3 groups. Absorption peaks at 1720 cm^{-1} & 1666 cm^{-1} Are the peaks of –C=O groups corresponding to ketonic group. A strong absorption peak due to C-O-C of ether. When Prednisolone was incorporated with chitosan and pectin, the same charecterstics peaks related to Prednisolone were seen with slight changes, concluding that there was no interaction between the drug-polymer; hence the drug is stable in formulations.

The Differential scanning colorimtry analysis of plain Prednisolone, dummy Nanoparticles and drug entrapped Nanoparticles was carried out and the results are shown in Figure 03. The without drug Nanoparticles have shown an endothermic peak at 115 ^0C and 204 ^0C, where as Prednisolone loaded Nanoparticles shown a peaks at 108 ^0C and 210^0C. The plain Prednisolone has showed an endothermic peaks at 254^0C due to melting of drug, but this peak is not seen in the drug loaded formulations. This indicates that the drug was amorphously or uniformly distributed in amorphous forms in formulations.

The X-ray diffractograms of pure prednisolone, drug free Nanoparticles and drug loaded Nanoparticles are shown in Figure 04. Prednisolone has showed characterstic intense

peaks between the 2Θ of 14^0 and 67^0 due to its crystalline forms. Whereas, in case of drug free Nanoparticles and drug loaded Nanoparticles, no intense peaks related to drug were noticed between the 2Θ of 14^0 and 67^0 and both of two diffractograms are identical. This indicates the amorphous dispersion of the drug after encapsulation into Nanoparticles. The swelling index study of Nanoparticles was shown in figure 05. When concentration of polymer is increased the rate of swelling decreases. The formulation number PRDS9 gives less swelling property due to the cross-linking agents.

The in vitro drug release study was performed using dissolution rate test apparatus in gastric (0.1 N HCl P^H1.2) and intestinal (phosphate buffer P^H 7.4) fluids with and without rat ceacal contents. The dissolution profiles of Prednisolone are given in Figure no 06; data are presented in Figure 06 shows results of in vitro drug release studies without rat caecal contents. A 92.4, 88.18, 88.98, 80.95, 89.95, 83.75, 79.33, 80.05, and 75.15 of drug was released from PRDS1, PRDS2, PRDS3, PRDS4, PRDS5, PRDS6, PRDS7, PRDS8, and PRDS9 formulations respectively at the end of 24th hour, while a 72.16, 73.25, 72.65, 70.35, 62.15, 61.08, 59.85, 37.57 and 16.75 of drug was released from PRDS1, PRDS2, PRDS3, PRDS4, PRDS5, PRDS6,PRDS7, PRDS8 And PRDS9 formulations respectively at the end of 5th h in the gastric environment. The Nanoparticles prepared with both TPP and Formaldehyde retarded the drug release in a more controlled manner and targeted the drug to colon.

Figure 07 represents the drug release profile in the presence of rat ceacal content medium. A 16.15% of drug was released from PRDS9 formulation at the end of 5th hour. But there was a large difference in the amount of drug released in presence or absence of rat ceacal content from PRDS9 formulation; this clearly indicates that sudden increased in drug released after 5th hour is due to presence of colonic bacterial enzymes. Thus, it was seen that the polymer was degraded in presence of colonic bacteria which resulted in increased drug release. A 96.01 % of drug was directly targeted to colon from PRDS9 formulation at the end of 24th hour.

The release data were fitted according to zero order release, Higuchi's equation and Korsemeyer's equation and the mechanism of drug release was calculated according to Peppas equation. The value has been shown in table 02.

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