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Research Article

# Rectorite Nanocomposite Beads As Drug Delivery Carrier: Intercalation and *In Vitro* Release of Diclofenac Sodium

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## ABSTRACT

**Aim**: The present study aimed at the formulation development of rectorite nanocomposite beads as drug delivery carrier and its evaluation.

**Methods**: SA/OR/DS nanocomposite beads were prepared by gelation technique. All the prepared samples were characterized and compared simultaneously by PXRD, SEM, FT-IR, and PSA (zeta sizer).

**Results**: For all batches of nanocomposite beads, there was no variation of the bead size. The large size of wet beads suggested high swelling and water retention capability. The average particle diameter of the optimized nanocomposite beads was found to be 68.8 nm, where as polydispersity index of particles was found to be 0.284. The crystallite size of the nanocomposite beads was found to be around 87 nm from the calculations done by applying Scherrer equation. From the in vitro release study, it is confirmed that addition of clay decreases the release of drug at pH 7.4. It also confirmed that prepared biopolymer/clay nanocomposite beads exhibited extended release period of drug as compared to the pristine biopolymer sodium alginate.

**Keywords:** Nanocomposites, organic rectorite, clay

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**Conflict of Interest:** None declared

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## INTRODUCTION

Rectorite is an interstratified clay mineral having structural and functional similarity with montmorillonite. It is made of regular 1:1 stacking of dioctahedral mica-like layer (non-expansible) and dioctahedral montmorillonite-like layer (expansible). It has the property to form cleavage easily between smectite-like interlayers, forming monolithic rectorite layers of 2 nm thick. The interlayer cations can also be exchanged easily by either organic or inorganic cations. Rectorite possesses water swelling properties like other clay minerals, which makes it possible to prepare biopolymer/rectorite nanocomposites by solution-mixing technique. As pure rectorite is hydrophobic in nature, so the affinity between rectorite and biopolymer is not enough. To overcome this, it must be modified for increasing the affinity (Wang et al, 2007).

Some of the impressive and recent applications of sodium alginate as polymer have been in the area of biomedical sciences. It is a natural polymer that possesses certain properties such as biocompatibility, biodegradability. Biocompatibility means it will not show any adverse effect inside the body where as biodegradability means its degradation products or materials are metabolizable in the body. Alginate, a linear, naturally occurring polysaccharide extracted from brown sea algae contains D-mannuronic (M) and L-gulcuronic (G) acids which are arranged in homo polymeric MM or GG blocks separated by blocks with an alternating sequence. Sodium alginate can act as drug carriers by controlling the release rate of drug initially loaded in the application

of drug delivery systems. The ability of alginate to form two types of gel dependent on pH, i.e., an acid gel and an ionotropic gel, gives the polymer unique properties compared to neutral macromolecules. Alginate shrinks at low pH (gastric environment) and the encapsulated drug. Thus much interest has been shown in its practical prospective as a potential matrix of biodegradable composite which could be synthesized from renewable sources at a very low cost and should be eco friendly ( Murata *et al.,* 2007; Gombotz *et al.,* 1998; Mladenovska *et al.,* 2007; Sarmento *et al.,* 2007).

Diclofenac sodium is a potent NSAID with analgesic and antipyretic properties. It is used for the treatment of chronic musculoskeletal pain, chronic inflammatory conditions, and for treatment of degenerative joint diseases like rheumatoid arthritis, and osteoarthritis. It has a short half life (< 2 h), which necessitates multiple dosing for maintaining therapeutic effect throughout the day. For such conditions, an effective sustained release formulation would be preferred, especially if it provides an initial burst of drug to facilitate rapid onset of action and then maintain a constant plasma level for a prolonged period of time. Such a formulation will not only avoid systemic accumulation of drug and related side effects, but will also decrease dosing frequency (Madan *et al.*, 2011).

In the present study attempts have been made to intercalate biopolymers like SA into the interlayers of the silicate (organically modified rectorite); meanwhile, exhibiting this technique to develop new nanocomposites for drug delivery applications.

## EXPERIMENTAL

### Materials

Sodium alginate (low viscosity) was obtained from Research-Lab Fine Chemicals Industries, Maharashtra State, India. Calcium rectorite was purchased from Hubei Mingliu Inc. Co, China. Diclofenac sodium was purchased from Sigma-Aldrich, USA. Cetyltrimethyl ammonium bromide (CTAB) was supplied by Xinrui Science and Technology Inc. Co., China. All of the used chemical reagents in experiment were analytical grade, and solutions were prepared with double distilled water. All chemicals were used without further purification.

### Preparation of organically modified rectorite (OR) from raw calcium rectorite

Calcium rectorite was modified first in order to increase the affinity between biopolymer and clay. Modification of calcium rectorite was done by cation exchange. First, 20gm of calcium rectorite was dispersed in double distilled water to form clay suspension using a magnetic stirrer (1500 rpm speed) for 1 hr, and kept it for 24 h for swelling. After that, 10 gm of CTAB was dissolved in 100 ml of double distilled water, and then poured slowly into the clay suspension at $60^0$ C under magnetic stirring for 2 hours. After stirring, the product was washed several times with double distilled water and filtered. Washing was performed to ensure the complete removal of bromide ions. The final product was dried at $60^0$ C to get organically modified rectorite and kept in powdered form for further studies (Wang et al., 2006).

### Preparation of DS-OR hybrid

DS-OR hybrid material was obtained by mixing the DS solution with the swelled organic rectorite with vigorous stirring (2500 rpm)with initial DS-OR weight ratios of 1:1,1:2,1:3,and 1:4. In order to establish DS incorporation efficiency (IE) in organic rectorite, the resulting suspension was centrifuged, and the drug concentration in the supernatant was determined by UV-Vis spectroscopy at $\lambda$ max=276 nm (the amount of the drug incorporated in the clay was calculated as the difference between the initial amount of DS and the amount of DS in the supernatant). The optimised hybrid was dried and powdered.

Optimization of DS/OR ratio with regard to percentage drug entrapment was done and recorded.

### Preparation of SA/OR/DS nanocomposite beads

SA/OR/DS nanocomposite beads were prepared by gelation technique. Firstly 2% w/v sodium alginate (SA) solution was prepared at $50^0$ C temperature and 1000 rpm by using double distilled water. After complete dissolution of sodium alginate, DS/OR hybrid was added slowly into the sodium alginate aqueous solution and stirred for 5 hour with vigorous stirring to obtain a homogenous suspension. SA/OR/DS nanocomposite beads were prepared by adding the above prepared solution into 500 ml of 100 mM calcium chloride solution, with gentle agitation with a magnetic stirrer. This suspension was dropped using a peristaltic pump with helps of a 20-guage hypodermic needle fitted with a rubber tubing (falling distance 2 cm, pumping rate 1.5 ml/min). The beads were allowed to settle in solution for 30 min for curing, then collected by filtration and were washed thrice with distilled water and then dried at 60 $^0$C. In the similar method, pristine sodium alginate beads, SA/DS beads and SA/OR beads were also

prepared. The amount of drug loss during the formation of bead was measured by UV absorption of the filtrate.

The encapsulation efficiency of the beads was calculated using the formula given below;

EE%= (Weight of DS fed – Weight of DS in the supernatant/ Weight of DS fed) x 100

**Characterizations**

All the prepared samples were characterized and compared simultaneously by PXRD, SEM, FT-IR, and PSA (zeta sizer). The powder X-ray diffraction (XRD) analysis was performed using a powder diffractometer with Cu target and Kα (λ=0.154056nm) at 40 kV with a slow scan of 0.3 degree/s in 2θ range 10-50 degree at room temperature. The crystallite size of the nanocomposite was determined from the XRD study by the Scherrer Equation.

$t = 0.9\,\lambda / B.\cos\theta$

Where, t = thickness of crystallite, λ = x-ray wavelength, B = (2θ High) – (2θ Low)

The intercalation of DS and SA into interlayer of OR was also examined by PXRD analysis. Fourier transforms infrared (FT-IR) spectra were recorded on Perkin Elmer Spectrum Version 10.03.02 as KBr pellet over the wavelength range 4000–400 $cm^{-1}$. UV/Vis absorbance of DS solutions was measured at a characteristic λmax = 276 nm by UV/Vis spectrophotometer equipped with a quartz cell having a path length of 1 cm. Thermal analysis (TG-DTA) was conducted using a differential thermal analyzer Shimadzu DTG-TA 51H (30 - 1000ºC temperature range and 10ºC/min heating rate). The intensity of distributions, average diameter, and polydispersity index of particles in the nanocomposite were determined by Particle size analyzer (LS230, Beckman Coulter, USA). The surface morphologies and surface topography were obtained using a scanning electron microscope (SEM).

**Drug release study *(in vitro)***

Buffer solution of pH 7.4 (simulated intestinal fluid) was prepared for release behaviour study. *In vitro* release studies were performed using USP six stage dissolution rate test apparatus by using dialysis bag technique. The dialysis sac was equilibrated with the dissolution medium for few hours prior to experiments. 250 mg of DS loaded composite beads suspended in 5 ml of dissolution medium was taken in a dialysis bag and sealed at both ends. Dialysis bag was dipped into 500 ml of dissolution medium, stirred at 100 rpm at 37±1º. At time intervals of 30 minutes, 5 ml of the dissolution medium was taken and the DS concentration was determined by UV/Vis spectrophotometer at λmax = 276 nm. These studies were performed in triplicate for each sample and used in data analysis.

Same method was also used for the release study of drug from DS/SA hybrid.

**RESULTS**

**Morphology of the nanocomposite beads**

Generally, the wet beads were spherical with a diameter of around 4 mm and possessed a smooth surface. After air drying, the diameter of test beads decreased to about 2 mm but still kept the spherical shape. For all batches of nanocomposite beads, there was no variation of the bead size. The large size of wet beads suggested high swelling and water retention capability. The average particle diameter of the optimized nanocomposite beads was found to be 68.8 nm, where as polydispersity index of particles was found to be 0.284. From the intensity of distribution table, it is found that the diameters of 10% particles are below 23 nm, 50% particles are below 78.10 nm, 90% particles are below 233.90 nm.

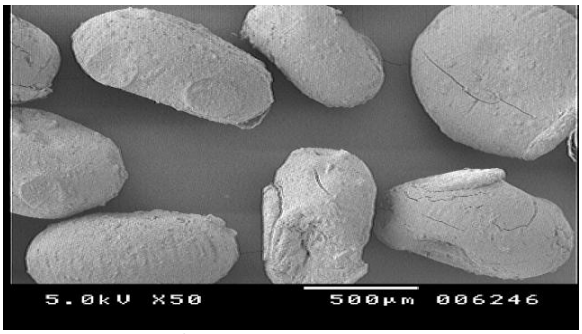


**Figure1a:** SEM of nanocomposite

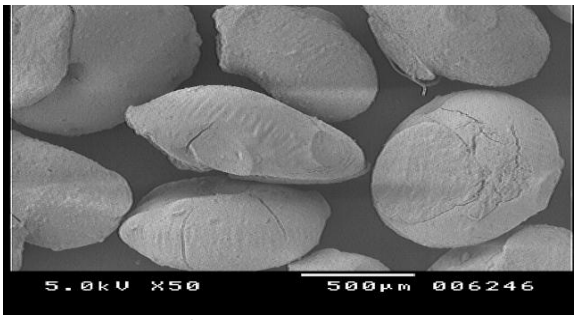


**Figure 1b:** SEM of nanocomposite

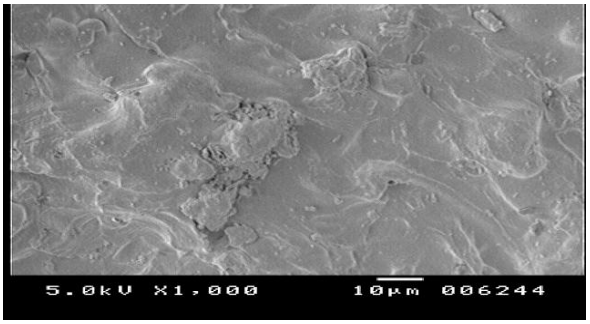


**Figure 1c:** SEM of DS/OR hybrid

| Formulation type | polydispersity Index | Diffusion Const. ($cm^2$/sec) | Mean Particle size(D) in nm | D (10 %) in nm | D (50 %) in nm | D (90%) in nm |
|---|---|---|---|---|---|---|
| SA/OR/DS | 0.284 | 7.149 e-008 | 68.8 | 23.00 | 78.10 | 233.90 |
| SA/OR | 0.176 | 1.495 e-008 | 329.1 | 34.40 | 118.50 | 773.40 |
| SA/DS | 0.296 | 8.002 e-009 | 614.7 | 72.80 | 191.00 | 6556.90 |
| Pristine SA | 0.349 | 6.044 e-009 | 813.9 | 237.40 | 294.10 | 15,237.60 |

**Table 1:** Average particle size (d), diffusion const., polydispersity index of prepared formulations

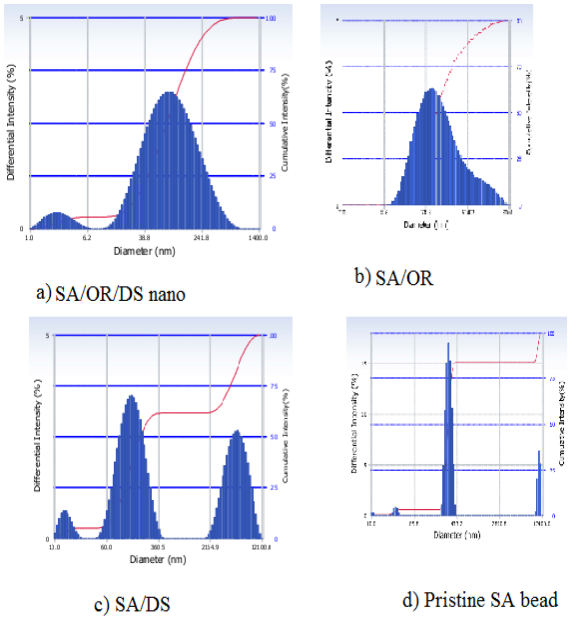


**Figure 2[a,b,c,d]:** Intensity of particle distributions

## Powder X-ray diffraction Analysis

XRD patterns of polymer-clay nanocomposite beads are shown in figure 8.3. The XRD result confirms the formation of nanocomposite beads. The crystallite size of the nanocomposite beads was found to be around 87 nm from the calculations done by applying Scherrer equation which is somewhat similar with the particle size determined by particle size analyzer (zeta-sizer).

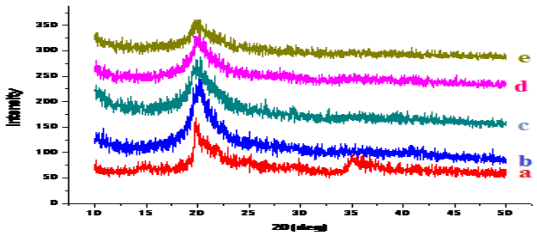


**Figure 3.** XRD pattern of (a) SA, (b) DS, (c) SA-DS, (d) DS/OR (e) SA/OR/DS

## Drug encapsulation efficiency

The EE (%) is given in Table 2. The EE of the beads increased with the amount of OR and SA added. The encapsulation of drug in beads without clay was 52.79, whereas the corresponding entrapment in the clay and sodium alginate containing beads varied from 67.34 to 91.22.

| Nanocomposite code | EE (%) |
|---|---|
| F1 | 52.79 ± 3.23* |
| F2 | 67.34 ± 4.25* |
| F3 | 77.05 ± 3.21* |
| F4 | 91.22 ± 2.21** |

**Table 2:** Drug Encapsulation Efficiency of Formulations Significantly different at ** $p < 0.01$ and * $p < 0.05$

## *In vitro* drug release study

*In vitro* release profile of the SA-DS and SA-DS-OR beads are shown in figure 4.

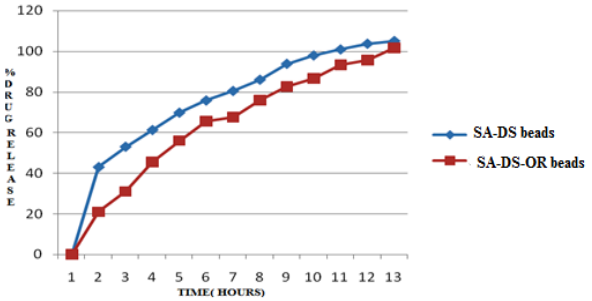


**Figure 4:** Release profile of drug at ph 7.4

## DISCUSSION

This paper represents the formulation development of rectorite nanocomposite beads as drug delivery carrier. The morphology study and surface topography study of beads revealed the preparation of nanocomposite. XRD investigation showed an intermolecular interaction between clay and polymer. It is clearly observed that the particle size of the nanocomposite beads is around 70 nm. From the in vitro release study, it is confirmed that addition of clay decreases the release of drug at pH 7.4. It also confirmed that prepared biopolymer/clay nanocomposite beads exhibited extended release period of drug as compared to the pristine biopolymer sodium alginate. This study provides a platform for further research on the polymer-clay nanocomposites for drug delivery and biomedical applications.

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