



Research Article

Polymeric Intercalated Silicate Nanocomposites: An Approach to Controlled Drug Delivery

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*Keywords:*Intercalation,
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Nanocomposite of 2-Ethyl hexylacrylate(EHA) and acrylic acid(AA) intercalated with sodium silicate (SS) was prepared by emulsion technique using benzoyl peroxide (BPO) as reaction initiator. The transmittance electron microscopy showed the well dispersion of the polymer nanocomposite into the intercalated silicate layers. The novel nanocomposite was further characterized by NMR, IR, TGA and exhibited excellent properties of higher thermal stability and superabsorbency for use as high performance materials. P(EHA-co-AA)/silicate nanocomposite was found to have better swelling capacity in simulated intestinal fluid. So the nanosystem is expected to be useful as controlled drug delivery device in future.

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INTRODUCTION

Polymer-layered silicate represents a new class of biomaterial with high performance and is of great academic and industrial interest. The improved properties of these nanocomposites include mechanical [1], thermal, [2,3] properties and are related to the dispersion and nanostructure of the layered silicate in the polymer. There are four methods to make nanocomposites: exfoliation-adsorption^[4], *in-situ* intercalative polymerization, melt intercalation^[5] and template synthesis^[6]. With favorable interactions between the polymer and silicate, two types of structures, intercalated and exfoliated, are generally possible. The intercalation of polymer chains results in the finite expansion of the silicate layers being disturbed. Therefore intercalated structures consist of well-ordered multi-layers of polymer and silicate layers a few nanometers thick. Exfoliated structures however are formed because of extensive penetration of polymer into the silicate layers. Acrylic polymers currently dominate the other pressure sensitive medical markets, due to their low level of allergenicity.

Acrylic pressure sensitive adhesives are designed for skin clean removal, low rates of chemical and mechanical irritation and acceptance resistance to cobalt and ethylene oxide sterilization. Previously, acrylic acid has been combined with montmorillonite [7], kaolinite [8], mica [9] to prepare nanocomposites. In the field of drug delivery, due to the pH sensitivity behavior, acrylic acid is now used for controlled and targeted drug delivery in the form of nano carriers [10-14].

So the present study aims at developing P(EHA-co-AA)/silicate nanocomposite and finding its suitability as a controlled drug delivery device.

MATERIALS & METHODS

Monomers, 2-Ethyl hexylacrylate and acrylic acid were purchased from SRL India Ltd., Benzoyl peroxide (BPO) from Himedia India Ltd. and Sodium silicate was a gift sample from PQ Corporation, Netherlands.

Preparation of nanocomposite

The polymerization reaction was carried out in a specially designed reaction vessel equipped with magnetic stirrer and an inlet nitrogen gas supply. Distilled EHA and AA were dispersed (v/v ratio as shown in Table 1) in deionised water via stirring with sorbitol (surfactant). Silicate solution was prepared by weight percentage basis (2 % w/v sodium silicate) for the suitability

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of the experiment. The mixture was slowly heated to 80°C and the initiator benzoyl peroxide (BPO) in acetone was added as per suitability of the polymerization. Emulsion polymerization was carried out with a constant stirring speed at 80° C. After a total of 3h of reaction, polymerization was terminated by the addition of a 0.1M solution of ferrous ammonium sulfate solution. The coagulated products were purified by washing with distilled water and other solvents and then dried at 45°C.

Table 1: Preparation of P(EHA-Co-AA)/ Silicate Nanocomposites at different monomer ratio and 2% W/V Sodium silicate

Sample	Monomer Ratio (v/v) (EHA:AA)
S1	100:00
S2	80:20
S3	60:40
S4	50:50
S5	40:60
S6	20:80
S7	00:100

Water absorbency Studies

The pH-dependent equilibrium swelling of P(EHA-co-AA)/silicate was studied both in the simulated gastric and intestinal pH conditions using 0.1 N HCl and phosphate buffer (0.1M, pH 7.4), respectively. Nanocomposite was allowed to swell completely for about 24 h to attain equilibrium at room temperature. Adhered liquid droplets on the surface of the particles were removed by blotting with tissue papers and the swollen polymer was weighed and dried in an oven at 60 °C for 5 h until there was no change in the dry mass of the samples. From the equilibrium mass%, M_1 of the sample, water uptake, S was calculated by measuring the dry mass, M_0 using the equation:

$$\%S = [(M_1 - M_0) / M_0] \times 100$$

Degradation study in biological medium

The degradation of P(EHA-co-AA)/silicate (S5) was studied on weight loss basis with slight modifications¹¹ taking about 1.0 g weight, over a period of 24h. They were conditioned to minimum weight at 37±1 °C in an oven containing desiccant prior to being immersed into 100 ml of a simulated intestinal fluid (SIF)

[15] prepared by dissolving 6.8 g of monobasic potassium phosphate in 250 ml of water, then adding 190 ml of 0.2 N NaOH, 400 ml of water and 10 g of pancreatin, and finally adding 0.2 N NaOH to adjust the pH to 7.5, and then diluting with water to 1000 ml. The specimens were removed at regular intervals, 2, 4, 8, 12, 16, 20, 24h being taken out of the solution, blotted on filter paper to remove surface solution and dried in an oven at 50°C to constant weight in order to determine eventual weight loss, taking an average of two readings.

Scanning electron microscopy

To study the surface morphology and biodegradation of the prepared nanocomposite, the SEM of P(EHA-co-AA)/silicate before and after biodegradation were recorded by Scanning electron microscope- JEOL JSM-5000, Japan at 20 kV.

Transmission electron microscopy (TEM)

Nanoscale structure of the prepared nanocomposite i.e., P(EHA-co-AA)/SS was examined by means of transmission electron microscopy (TEM) (H-7100, Hitachi Co.), operated at an accelerating voltage of 100 kV. The ultra thin section (the edge of the sample sheet perpendicular to the compression mold) with a thickness of 100 nm was microtomed at -80°C.

¹H Nuclear Magnetic Resonance (NMR) studies

The ¹H NMR of the composite P(EHA-co-AA)/SS was measured at temperature 296 K with a Jeol, GSX 400 with 250 Hz/cm using THF (deuterated) as the solvent.

Fourier Transformed Infrared (FTIR) spectrophotometry

The FTIR spectra of PEHA, PAA, P(EHA-co-AA) and P(EHA-co-AA)/silicate in the form of KBr pellets were recorded in the Perkin-Elmer model Paragon-500 FTIR spectrophotometer for proof of copolymerization.

Thermo gravimetric analysis (TGA)

Thermal properties of the samples were measured by using a Shimadzu DTA-500 system. It was carried out in air, from room temperature to 6000 C at a heating rate of 10°C/min.

X-ray diffraction (XRD) studies

The insertion of PEHA into the silicate layer was confirmed by using XRD, monitoring diffraction angle 2θ from 1.50 to 10° on a Philips PW-1847 X-ray crystallographic unit equipped with a Guiner focusing camera.

RESULTS AND DISCUSSION

Water absorbency studies

From the Fig. 1, it is found that on increasing the monomer (AA) content in the copolymer, the water absorbency increases and then gradually decreases. The increase of water absorbency from S1 to S5 is due to the fact that the hydrophilic part of the polymer enhances the water absorption and also sodium silicate plays an important role i.e., as a crosslinker to increase the water content by forming large number of rooms in the composite. But from S5 to S7 the samples shows a decreased trend of swelling, as the formation of excess of crosslinked density, which results in the less water absorption due to the unavailability of free space in the composite.

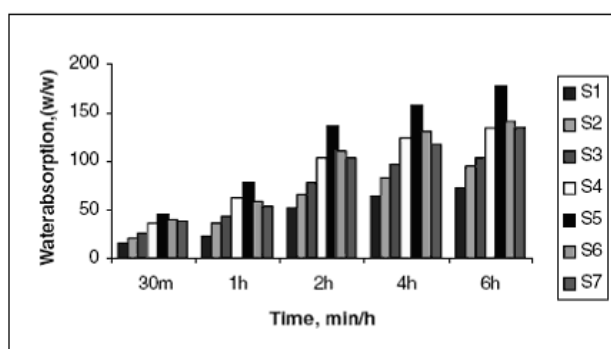


Figure 1: Swelling studies of P(EHA-co-AA)/SS (S1-S7)

Degradation studies in biological media

The degradation studies of the prepared nanocomposite (S5) were studied on the basis of % weight loss in simulated intestinal fluid containing enzyme pancreatin at regular intervals, 2, 4, 8, 12, 16, 20, 24h. From the degradation study over a period of 24h (Fig.2), it was found that as the immersion time increases, the weight loss also increases to become stabilized after about 20h and extend up to 24h. So the present system is expected to be useful as a controlled drug delivery device owing to its degradation characteristics in biological media.

Scanning electron microscopy

A standard method for the observation of surface morphology is the scanning electron microscopy (SEM). From Fig.3 it is clear that the surface are mostly communicating with large amount of silicates in the mixture, making the polymer matrix more porous. Further, the SEM of the P(EHA-co-AA)/SS before and after biodegradation clearly confirmed the extent of

biodegradability as the plane surface in Fig. 3(a) became rough in Fig. 3(b).

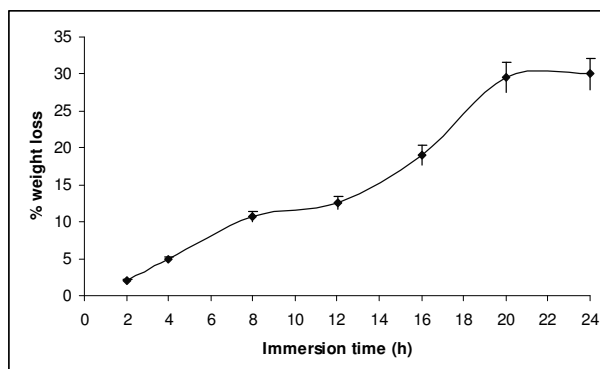


Figure 2: Degradation of P(EHA-co-AA)/SS (S5) in simulated intestinal fluid by weight loss

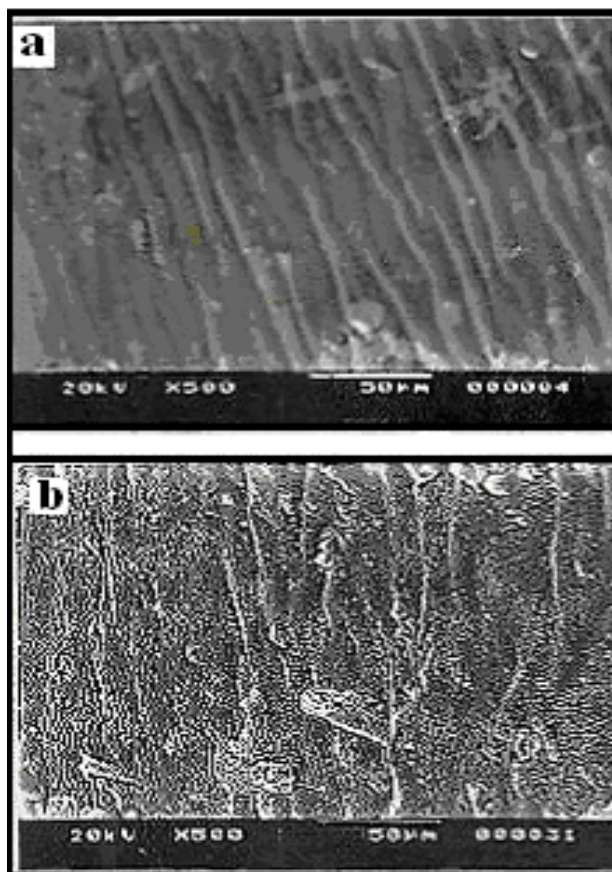


Figure 3: SEM of P(EHA-co-AA)/SS (S5) before (a) and after (b) biodegradation

Transmission electron microscopy (TEM)

The dispersion microstructure of the intercalated silicate layers is being examined by means of TEM. TEM image of P(EHA-co-AA)/silicate (Fig.4) demonstrates that the silicate layers are structured in good order and are well dispersed in the polymer matrix. The periodic alternating dark and light bands represent the layers of silicate and interlayer respectively. The

smaller interlayer spacing in the figure indicates the intercalation not exfoliation. Finally, the images confirm that the synthesized composite is a nanoscale material and the particle size is found to be 50 nm.

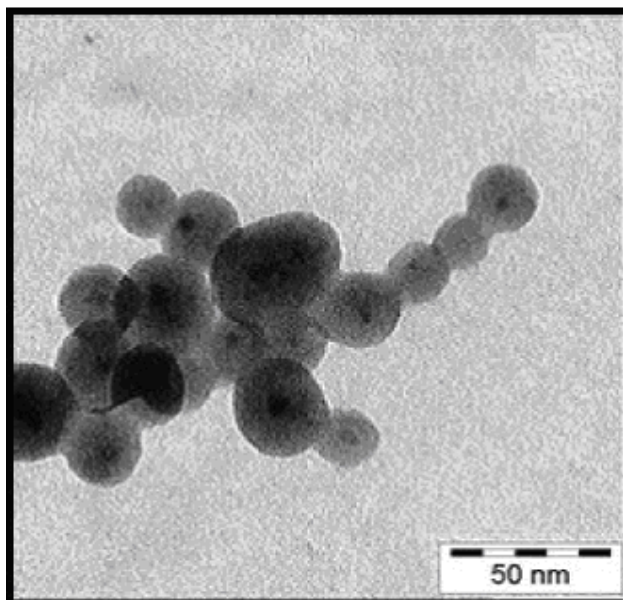


Figure 4: TEM of (PEHA-co-AA)/SS COMPOSITES (S5)

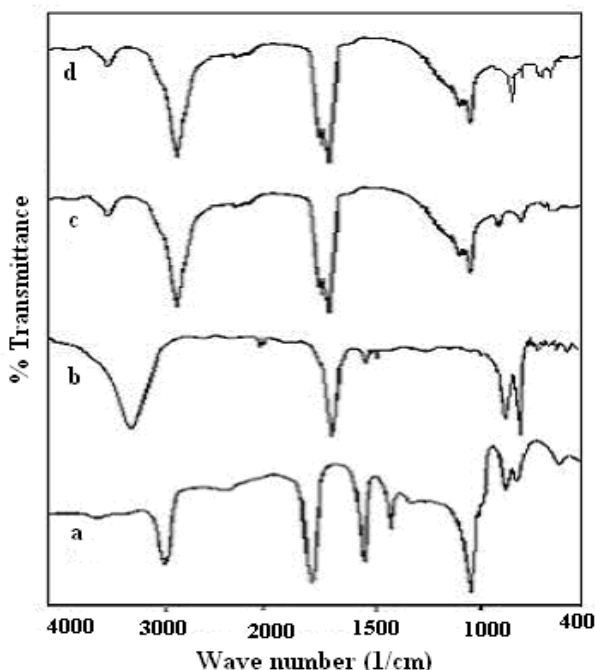


Figure 5: FT-IR spectra of (a) PEHA, (b) PAA, (c) P(EHA-co-AA), (d) P(EHA-co-AA)/SS

FTIR spectrophotometry

Fig. 5 shows comparative FTIR spectra of PEHA, PAA and P(EHA-co-AA). Absorption bands at 1545, 1406 and 1015 cm^{-1} , assigned to the carbonyl group of the carboxylate of PEHA (Fig. 4a). In PAA (Fig. 4b), peak at 1715 cm^{-1} is due to $-\text{COOH}$ acid group. The absence of absorption peak at 1630 cm^{-1} region due to $\text{C} = \text{C}$ bond confirms the absence of monomer impurities in the copolymer. For the copolymer, P(EHA-co-AA) as shown in the Fig 5c, the characteristic peaks for both EHA and AA are present with little shifting of position. Again the presence of peak in the region 618 cm^{-1} and 900-1100 cm^{-1} confirms that there is Si-O-Si bonding due to silicate in the polymer matrices.

Nuclear Magnetic Resonance (H^1)

From the H^1 NMR spectra of the sample P(EHA-co-AA), the absence of any peak at 5-6 ppm indicates that the copolymer is completely pure (i.e., without any impurities) as shown neatly in Fig. 6. The peaks are explained as below. (a) For EHA, the peaks appear at 0.85 – 2.25 ppm and also at 3.9 ppm. Peaks for two $-\text{CH}_3$ groups appear at 0.85 and 0.91 ppm and peaks for fourth $-\text{CH}_2$ group and one methine proton appear at 1.28 and 1.40 ppm respectively. The protons of backbone vinyl group, (i.e., for methylene and methine) show peaks at 1.55 and 2.25 ppm respectively. The peak for the pendant $-\text{CH}_2$ group appears at 3.9 ppm. (b) For the AA, a doublet peak is found at 1.1 ppm for $-\text{CH}_2$ group, a triplet at 1.9 ppm for methine group of the backbone and a weak peak appears at 12.1 ppm for the carboxylic proton. Hence, the H^1 NMR spectra shown in Fig. 6 confirms the formation of the copolymer i.e., P(EHA-co-AA).

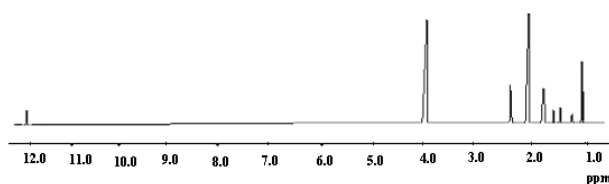


Figure 6: H^1 NMR spectra of P(EHA-co-AA) with a monomer feed ratio of 40:60

Thermogravimetry analysis

The thermal behaviors of PEHA, PAA and P(EHA-co-AA) are studied at room temperature at 28°C by comparing their thermogram (TGA) curves as shown in Fig.7. From the curves, the temperatures of decomposition (TD) are found to be 130 °C for PEHA, 185 °C for PAA and 225°C

for P(EHA-co-AA)/SS. The nanocomposites P(EHA-co-AA)/SS exhibit higher thermal stability due to the higher decomposition onset temperature than that of PEHA and PAA which can be attributed to the nanoscale and silicone penetration onto the matrix.

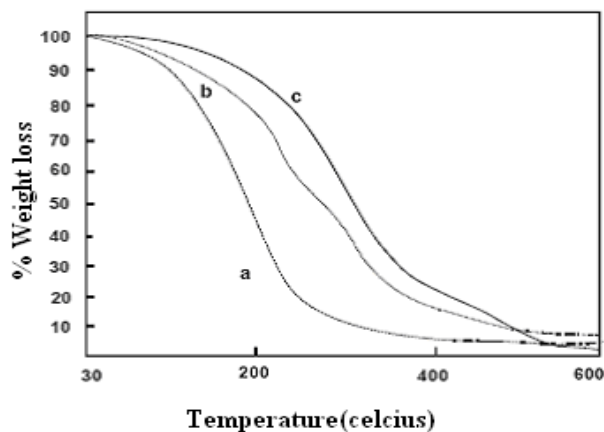


Figure 7: TGA thermogram of (A) PEHA, (B) PAA, (C) P(EHA-co-AA)/SS

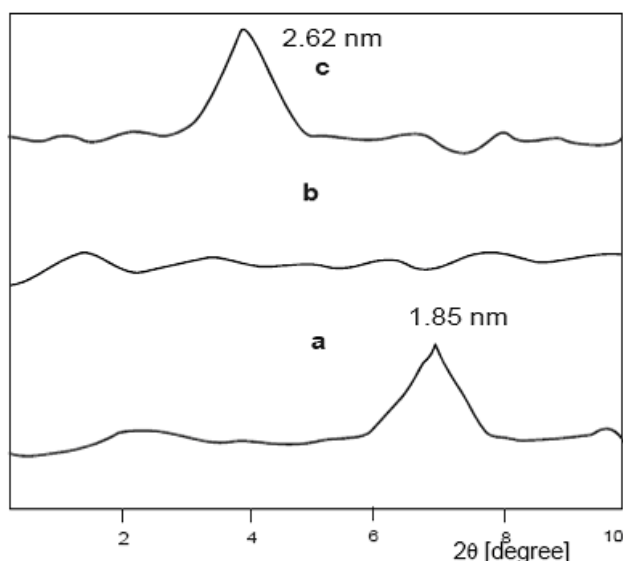


Figure 8: XRD curve of (A) Sodium Silicate, (B) P(EHA-co-AA), (C) P(EHA-co-AA)/Silicate

X-ray Diffraction studies

From XRD pattern of the polymers, the d-spacings are calculated from Bragg formula, at peak positions. Due to the intercalation of P(EHA-co-AA) into the galleries via emulsion polymerization, the d-spacing of P(EHA-co-AA)/silicate nanocomposites increases from 1.85 nm to 2.62 nm in the dry state, even though the interlayer distances of the PEHA / silicate

exhibits small deviation (Fig.8). This is a strong indication that, there is no trace for the occurrence of the de-lamination or exfoliation. The XRD patterns suggest that sample P(EHA-co-AA) is being inserted into the galleries of the hydrophilic silicate through emulsion polymerization.

CONCLUSIONS

Novel P(EHA-co-AA)/SS nanocomposite was prepared by emulsion technique with layer silicate. The TEM showed the well dispersion of the polymer nanocomposite into the intercalated silicate layers and the drug molecule may be adsorbed physically in the nanocomposite. The novel nanocomposite was further characterized by NMR, IR, TGA and exhibited excellent properties of higher thermal stability and superabsorbency for use as high performance materials. From this study, the nanocomposite system (S5) is expected to be useful as a controlled drug delivery device in future, which is in progress in our laboratory.

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REFERENCES

- [1] Burnside SD, Giannelis EP. Synthesis and properties of new poly(dimethylsiloxane) nanocomposites. *Chem Mater.* 1995; 7: 1597-1600.
- [2] Giannelis EP. Polymer Layered Silicate Nanocomposites. *Adv Mater.* 1996;8:29-35.
- [3] Wang W, Hu Y, Song L, Chen Z, Fan W. Preparation and thermal properties of ABS/montmorillonite nanocomposite. *Polym Degrad Stab.* 2002; 77: 423-26.
- [4] John PL, Jinghe W, Christopher O, Michael ML. Preparation of nanocomposites containing poly(ethylene oxide) and layered solids. *Electrochimica Acta.* 1995; 40: 2245-9.
- [5] Pourabas B, Raeesi V. Preparation of ABS/montmorillonite nanocomposite using a solvent/non-solvent method Behzad Pourabas, Vahid Raeesi. *Polymer.* 2005; 46: 5533-40.
- [6] Hidenobu A, Atsushi F, Yuzuru S, Shinji I, Noriaki S, Yoshiaki F, Masaru I. Template synthesis and characterization of gold nano-wires and -particles in

- mesoporous channels of FSM-16. J Mol Catalysis A: Chemical. 2003; 199: 95-102.
- [7] Ping-Sheng L, Ning-Lin LZ, Shao-Hua JZ, Synthesis and properties of a poly(acrylic acid)/ montmorillonite superabsorbent nanocomposite. J Appl Polym Sci. 2006; 102:5725-30.
- [8] Zhang B, Li Y, Pan X, Jia X, Wang X. Intercalation of acrylic acid and sodium acrylate into kaolinite and their *in situ* polymerization. J Phys Chem Solids. 2000; 68:135-42.
- [9] Jianming L, Jihuai W, Zhengfang Y, Minli P. Synthesis and Properties of Poly(acrylic acid)/Mica Superabsorbent Nanocomposite. Macromol Rapid Comm. 2001; 22: 422-4.
- [10] Ray D, Mohapatra DK, Mohapatra R, Mohanta GP, Sahoo PK. Synthesis and colon specific drug delivery of a poly(acrylic acid-co-acrylamide)/MBA nanosized hydrogel. J Biomat Sci Polym edn. 2008; 19:1487-502.
- [11] Muller JJ, Lukowski G, Kroeber R, Damaschun G, Dittgen M. Acrylic acid copolymer nanoparticles for drug delivery: structural characterization of nanoparticles by small-angle x-ray scattering. Colloid Polym Sci 1994; 272:755-69.
- [12] Tommy T, Timo N, Annika S, Bror Sr, Johanna H, Petteri P et al. Drug release from poly(acrylic acid) grafted poly(vinylidene fluoride) membrane bags in the gastrointestinal tract in the rat and dog. J Control Rel. 2000; 66:19-26.
- [13] Chakraborty S, Somasundaran P. Sequestration of drugs using poly(acrylic acid) and alkyl modified poly(acrylic acid) nanoparticles. Soft Mat 2006; 2:850-54.
- [14] Yong H, Yin D, Dan D, Mingjie S, Leyang Z, Xiqun J, Changzheng Y. Hollow Chitosan/Poly(acrylic acid) Nanospheres as Drug Carriers. Biomacromolecules. 2007; 8:1069-76.
- [15] Lee SS, Lim CB, Pai CM, Lee S, Park I, Seo MG, Park H. Composition and pharmaceutical dosage form for colonic drug delivery using polysaccharides. United States Patent: 6413494, Appl. No. 318579, 1999.