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Synthesis and Characterisation of Hydroxyapatite based Poly[Mannitol-co-Citric Glutarate] Coployester for Drug Loaded Application

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ABSTRACT

Synthesis of nanocomposites, the most dominant procedure is adaptation of nano particle in polymer grid. The researchers gave special attention in biomaterials obtained from biodegradable polymers. The capability to regulate the physical, chemical and biological properties of polymers, the enormous supremacy of nanoparticles assimilation in the polymer is useful in drug acquit significance in medicine. The adaptation of Nano hydroxyapatite to aliphatic polyester, it grows their mechanical power extensively. Current study was execute by synthesizing Poly [Mannitol-co-Glutarate Citrate] PMGC, biodegradable aliphatic polyester utilizing catalyst free direct melt polycondensation and nano Hydroxy Apatite exploiting Sol-gel process. Nano hydroxyapatite-polymannitolcoCitrate polymer nanocomposite synthesised with ultra sonication method. Biodegradable polyester and its nano composites were identified by spectral studies like FT-IR, Farther UV- visible spectral study also executed for the nanohydroxyApaptite and polyesternano composite. Powder XRD and SEM analysis make clear regarding the crystallinity and morphology of the nanocomposite and polyester. Predestined quantity of commercially obtainable drug loaded in the polyester nano composite and the drug releasing competency calculated. The high releasing capability of polyester nanohydroxy apatite composite contrast to normal polyester Poly mannitolco citrate.

Keywords: *nanodrugloader , polymernanocomposite-nHA, biodegradable polymers*

1. INTRODUCTION

Polymers are extremely large molecules that are essential to our very existence. They are a main constituent of our food (starch, protein, etc.), our clothes (polyester, nylons, etc.), our houses (wood cellulose, paints, etc.), and our bodies (poly(nucleic acids), proteins, etc.). Hence, it is reasonable to assume the education of every chemist should, at least, include an introduction to their chemistry and properties. [1-6]

Polymers form a very important class of materials without which the life seems very difficult. They are all around us in everyday use; in rubber, in plastic, in resins, and in adhesives and adhesives tapes. The word polymer is derived from greek words, poly= many and mers= parts or units of high molecular mass each molecule of which consist of a very large number of single structural units joined together in a regular manner. In other words polymers are giant molecules of high molecular weight, called macromolecules, which are build up by

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linking together of a large number of small molecules, called monomers. The reaction by which the monomers combine to form polymer is known as polymerization. The polymerization is a chemical reaction in which two or more substances combine together with or without evolution of anything like water, heat or any other solvents to form a molecule of high molecular weight. The product is called polymer and the starting material is called monomer. [7-11]

Transpire the bias of the modern research in Nano drug bearer with biodegradable nature of polymers. This work attention on, synthesis and characterization of new random polyesters with diol moiety. The Hydroxy apatite is the gifted biomaterial which is used in a lot of biomedical fields. Nanocomposite biodegradable drug carrier synthesis with promising candidate for intention drug delivery. [12-14]

2.MATERIALS

Merck samples of Calcium Nitrate tetrahydrate, Phosphoric Acid, Ammonia Glutataric acid, Citric Acid and D-mannitol areused without further purification. The phosphate buffer solution was used for biodegradation analysis (P^H 7.0±0.01).

2.1 POLYMERISATION PROCEDURE

The aliphatic co-polyesters were prepared by the polycondensation of a diol incorporate with diacid. A three-necked glass is fitted with a mechanical stirrer and was heated with a predetermined amount of citric acid,sebacic acid and D-mannitol in oil trap. The reaction mixture temperature raised to 150°C for 20 minutes, thenceforth the temperature was rice to 10°C at regular intermittently up to 210°C. This circumstance was retained up to two hours for remove the water from the esterification product. The mixture was retained upto under these circumstances for 24 hours. In general, when the viscosity of the reaction mixture is increased the reaction was stopped.

After all the viscous sludge was cooled in the reactor below the room temperature; the copolyesters were collected in methanol and warmed in an oven at 150°C eight hours to enlarge the polymer weight then the polyester stored in vacuum dessicator

2.2 SYNTHESIS OF NANO HYDROXYAPATITE

Nano-hydroxyapatite (n-HAp) was formulated by sol-gel method. 0.25M Phosphoric acid (PA) solution was mixed with the ammonia solution A solution of 1M Calcium nitrate tetrahydrate was gradually added to the PA-NH_3 solution, At that point, the solution was stirred well for 2hr with 1200rpm at room temperature. The gel obtained was dried at 65ºC for 24h in a dry oven. The resultant powder was calcined in at 500ºC for 30 min in an muffle furnace and cooled and kept in a desicator for further usage.

2.3 SYNTHESIS OF POLYESTER HYDROXYAPATITE NANO COMPOSITE

Synthesis of HAp polyester nanocomposites was done by sonication by using ultra-sonicator. Predetermined amount of polyester fine powder in1, 4Dioxane at 50±2 °C. To this solution 4 wt. % of nHAp powder was mixed and it is allowed to 30 minutes of ultra-sonication (25 kHz, 65°C, 61amp). 60 vol. % Nacl (Merck, with the size of 212-250 μm) was

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added to mix and stirred for 30 minutes. Following 48 hours of room drying, tests were dried in an oven under vacuum for 24 hours. For salt leaching, the contents were washed for with deionized water in an orbital shaker and after that dried in vacuum drier at 48 hours

2.4 DRUG LOADING INTO HYDROXY APATITE- POLYESTER NANOCOMPOSITES

Drug loading in Synthesised HAp polyester nanocomposites was done by sonication method using ultra-sonicator.0.5g of Hydroxyapatite polyester nanocomposite powder is dissolved in a suitable solvent. 0.1g of drug (ciprofloxacin) is added to this mixture. Then the mixture was allowed to sonication by ultra-sonicator. It can be done by Following 30 minutes of ultra-sonication (25 kHz, 65°C, 61amp). Then the samples were allowed to dry for solvent evaporation at room temperature,it is stored in a desiccator for further studies.

3. CHARACTERISATION OF POLYESTERS

The synthesized PMGC were analyzed by solubility, viscosity measurements, and spectral analysis such as IR, UV, and XRD. The Hydroxyapatite polyester nano composites PMGC,(PMGC-Hap) and (PMGC-Hap) with D using sonication method by ultra-probesonicate. The entrapment efficiency of drug was calculated by using UV- visible spectrophotometry analysis. The structure morphology of nanocomposite and drug loaded HAp-nanocomposites polyesters was studied by SEM analysis.

4 RESULTS AND DISCUSSION

4.1SOLUBILITY MEASUREMENTS

It is a necessary property of a compound to be considered in it synthesis. First solvent particles gradually diffuse into the polymer to produce a swollen gel. Secondly the swollen gel become soluble and gets a clear solution.

All the co-polyesters and nanocomposites are soluble in polar solvents like 1, 4 Dioxane and acetone. Another significant perception made is that the copolyesters combined from the aliphatic diols are generally unreservedly dissolvable in like manner natural solvents.

4.2VISCOSITY OF COPOLYESTER

The inherent viscosities of these random co polyesters were measured in1, 4 Dioxane at 32^0c at the concentration of 0.2g these values PMGC, PMGC-HA_P and PMGC-HA_P with D 0.435 dL/g ,0.443 dL/g and 0.494dL/g respectively.

4.3 FT-IR SPECTRAL STUDIES

Figure 4.3. (a), 4.3.(b), and 4.3,(c) shows the FTIR spectra of PMGC and PMGC-HA_P and PMGC-HA_P with D .FT-IR spectra of 4.3 (a) shows a characteristic absorption band at around 1722 cm^{-1} which exhibits the carbonyl stretching vibration that indicating the polyester chain present in the polymer. The absorption band around at 2927cm^{-1} was assigned to C-H stretching vibration for the diols/diacids and C-O-C stretching vibration shows at 1052 cm^{-1}. In spectra 4.3 (b) a strong band of PO_3^{4-} group was seen at 1045 cm^{-1} due to symmetric stretching vibration. The spectra possessed a broad band range 3580 cm^{-1} shows

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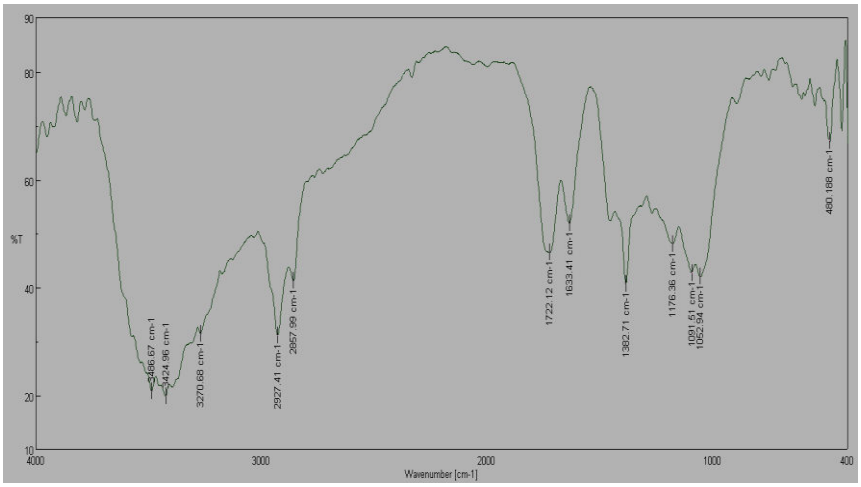
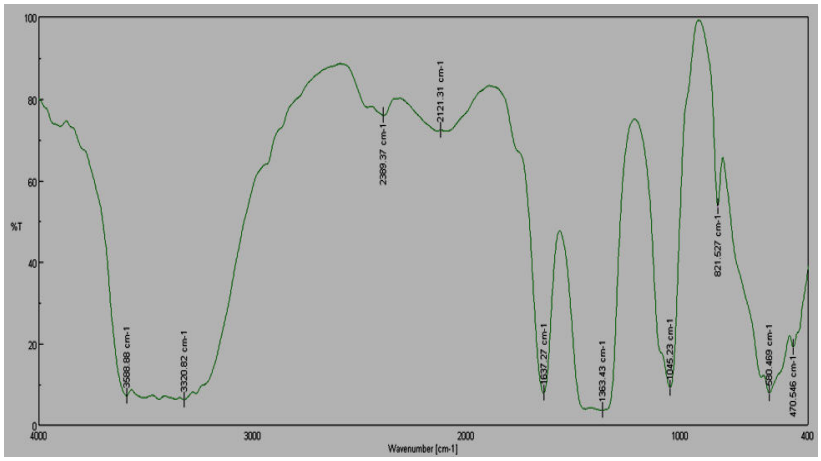
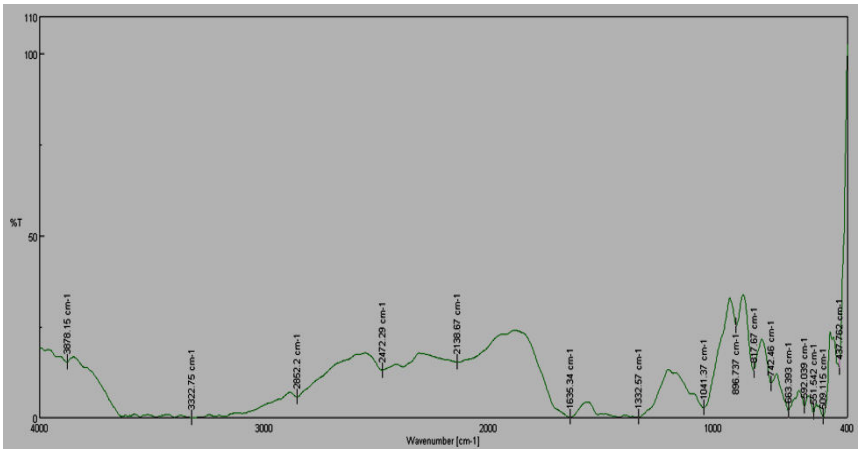
the presence of –OH group. 4.3,(c) The peaks at 1704 cm^{-1}attributed to the presence of carbonyl (C=O) groups from the ester bond. The bands at around 2923 cm^{-1} due to Aliphatic C-H Stretching vibration groups. The band at 1452 cm-1 coin to the NH bending vibration



4.3 (a) IR Spectrum of PMGC



4.3 (b) IR Spectrum of PMGC-HA$_P$



4.3 (c) IR Spectrum of PMGC-HA$_P$ with D

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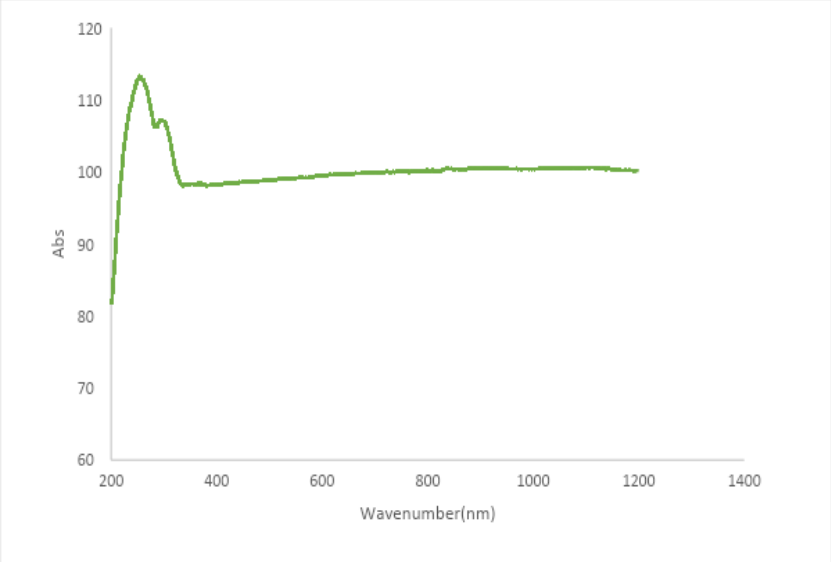
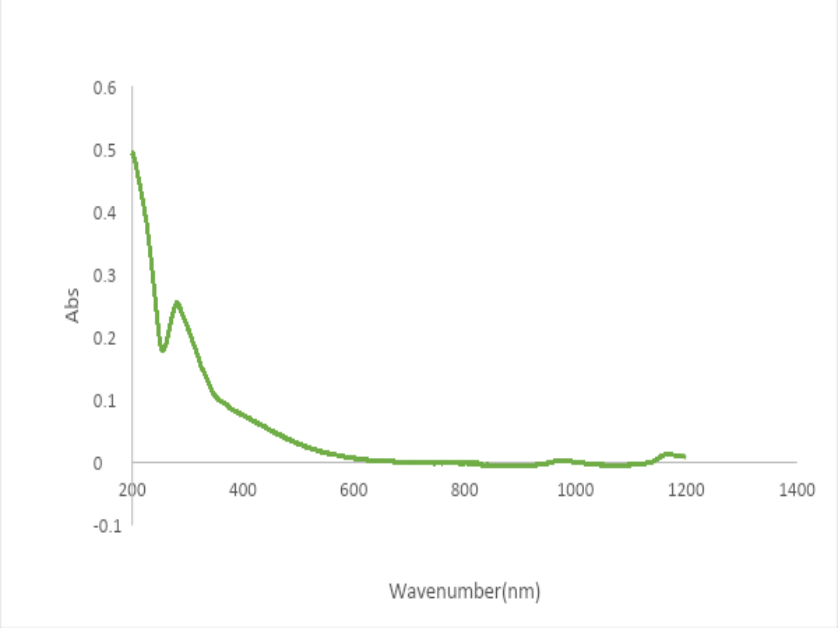
4.4 UV-VISIBLE SPECRAL STUDIES POLYESTER AND NANOCOMPOSITES

The UV visible of Polyester,PMGC, PMGC HAp and its Drug, Nanocomposite PMGC HAp with Drug are shown in fig,4.4.(a) , 4.4.(b), and 4.4.(c). The UV spectra of pure drug observed red shift (λ_{max}~349 nm), The UV spectra of HAp nanoparticles were functionalized with PMGC (λmax ~ 255 nm). The UV spectrum of HAp nanoparticles shifts to the higher wavelength due to the bonding of PMGC on its surface. The presence of HAp in the polyester if, the wavelength is shift to higher wavelength. When Polyester and nanocomposites are loaded with drug the red shift is observed ((λmax~334 nm) and (λmax~353) respectively.



4.4 (a) UV SPECTRA OF PMGC



4.4 (b) UV SPECTRA OF PMGC-HA$_P$ NANOCOMPOSITE

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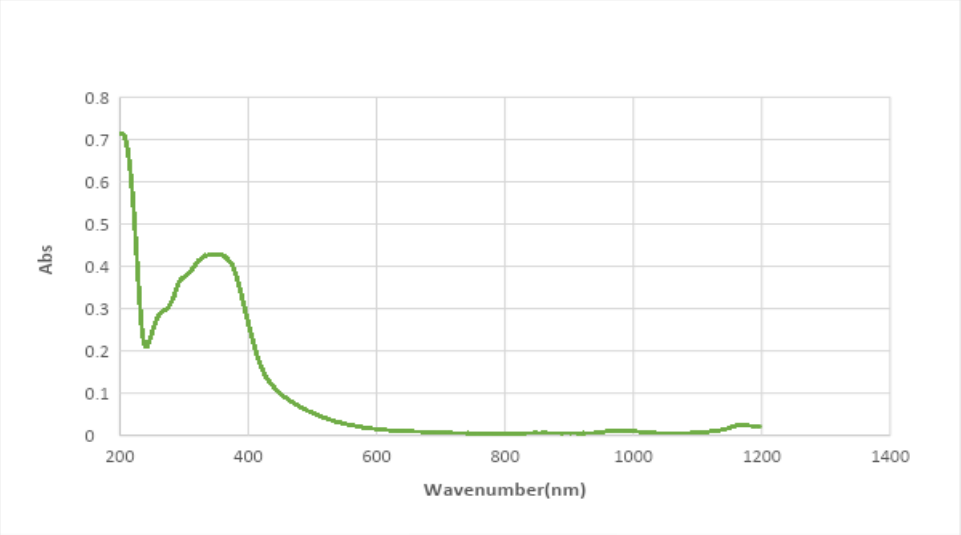
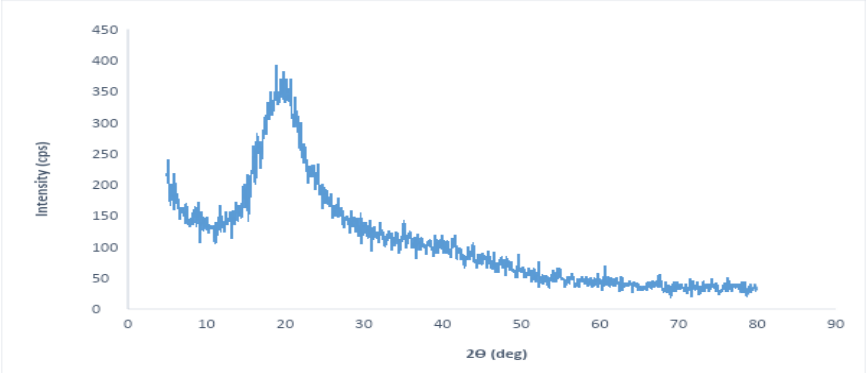


4.4 (c) UV SPECTRA OF NANOCOMPOSITE WITH DRUG (PMGC-HA$_P$ (D)).

4.5 XRD SPECTRAL STUDIES

The X-Ray Diffractograms of PMGC and PMGC-HAp and PMGC-Hap with D nano composites were exhibited in the figure 4.5.(a), 4.5.(b),4.5(c) X-Ray diffraction studies are used to determine size of the particles was done by Scherrer equation. XRD can be utilized to study polycrystalline materials. In this analysis, the sample is exposed to a collimated X-Ray beam, with location of the type and power of dispersing by stacked parallel nuclear planes of the sample, at explicit points.

XRD can be utilized to distinguish the crystalline stage, crystallinity degree and direction, nature of the compound, and size of the crystallites. Sharp and wide diffraction are observed for crystalline and shapeless materials, individually, with littler crystallites delivering more extensive diffraction pattern. If it is expected that peak widening is basically because of size impacts, the normal nanocrystalline size can be utilizing the Debye–Scherrer formula: $D = \kappa\lambda/\beta\cos\theta$, where D is the particle size, κ is a Scherrer constant. (Shape factor), λ is the X-beam wavelength, β is the full-width-at-half-limit of a diffraction peak, and θ is the diffraction angle.



4.5 (a) XRD SPECTRA OF PMGC

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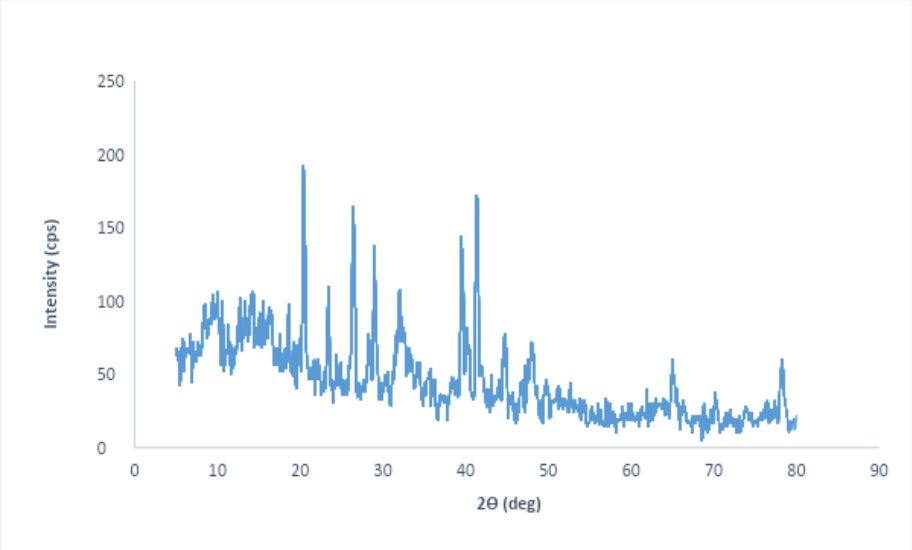
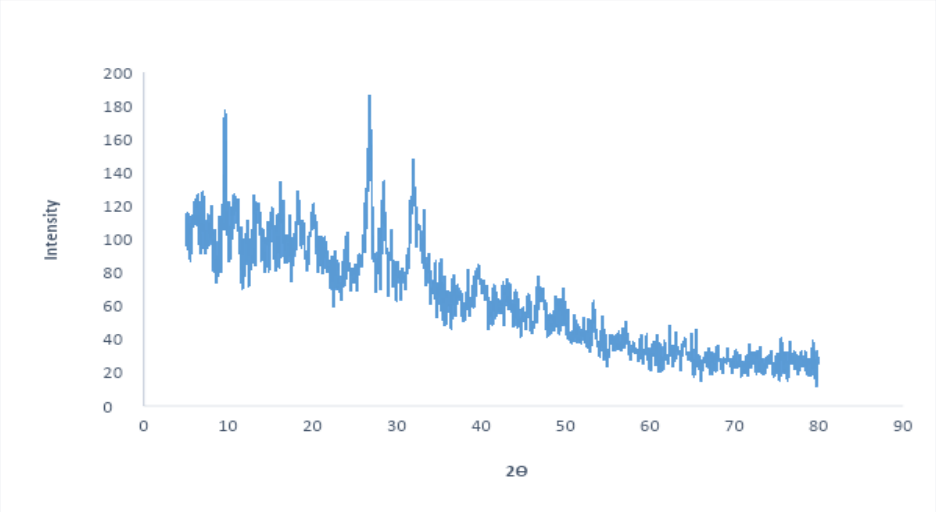


4.5 (b) XRD SPECTRA OF PMGC-HA$_P$ NANOCOMPOSITE



4.5 (c) XRD SPECTRA OF NANOCOMPOSITE WITH DRUG (PMGC-HAp (D))

The average crystal size of pure poly mannitol-co-sebacic citrate (PMGC), hydroxyapatite (HAp) and poly mannitol-co- sebacic citrate - hydroxyapatite (PMGC-HAp) nanocomposites ,and (PMGC-HAp) with drug was determined using scherrer equation and its tabulated in Table 4.5.1

TABLE 4.5.1

Average crystal size of samples using Scherrer equation

S.No	Co polyesters	Average Crystal Size(nm)
1.	PMGC	7.24

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2.	PMGC-HA_P	21.54
3.	PMGC-HA_P with D	13.22

The polyester nano composite PMGC-Hap shows less crystalline size compared to drug loaded polyester nanocomposite. This may be due to the polyester nanocomposite binding with drug more compared with normal one. Drug loaded polymer nanocomposite releasing also changed according to their crystalline nature. Entrapment efficiency of this PMGC Hap polyester nanocomposite is more with this drug, It is visible in the XRD data also.

4.6 SEM ANALYSIS

Scanning Electron Microscopy studies of the polyester and nanocomposites to study the structure morphologies. The SEM electron micrograph of Hydroxyapatite, polyesters (PMGC) polyester nanocomposites (PMGC-HAp) and (PMGC-HAp) with drug (ciprofloxacin) loaded nanocomposites in fig4.6.1, 4.6.2, and 4.6.3 indicates mono dispersed with a relatively nano distribution. The particle has smooth surface, moreover drug loaded nano composites and normal nanocomposites SEM micrographs clearly express the different structure morphologies.

SEM micrographs of drug loaded nanocomposite clearly indicate different morphology change compare with normal nanocomposites and polyesters.

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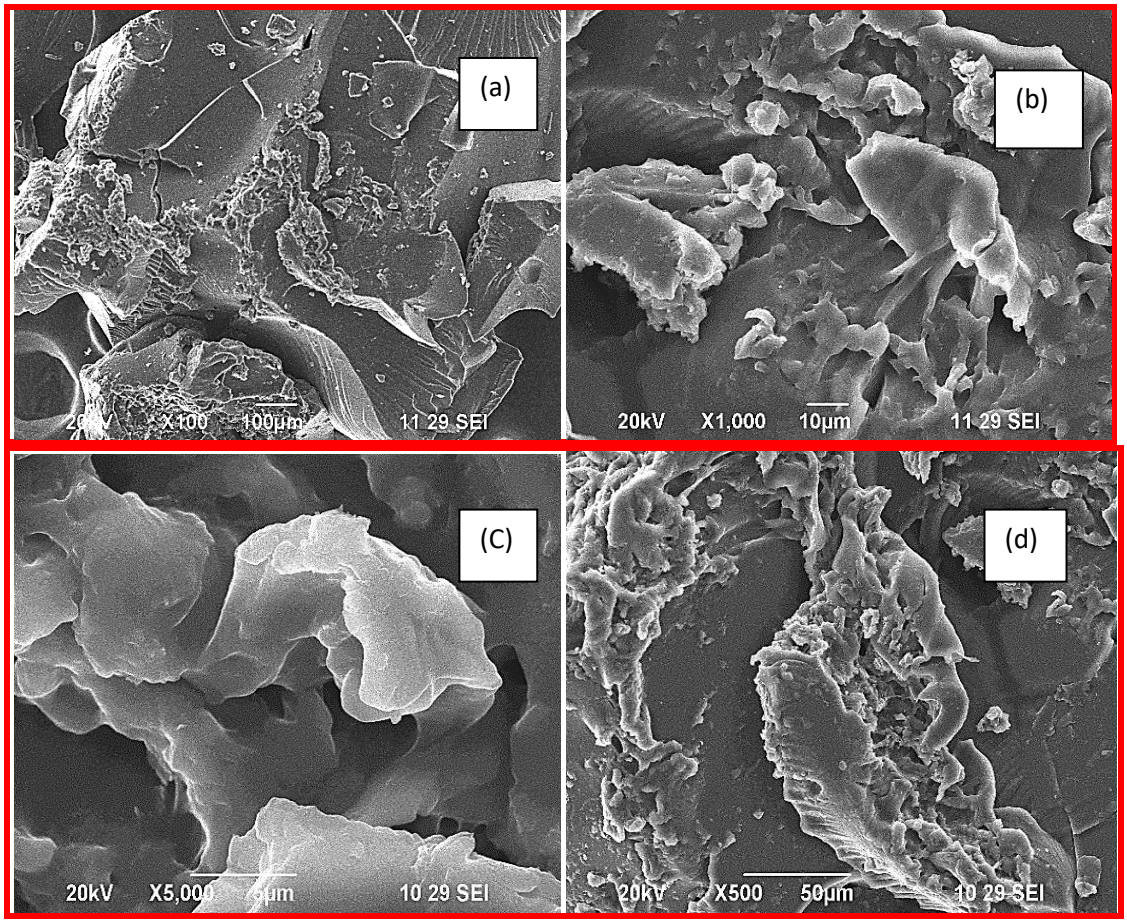

4.6.1. SEM MICROGRAPH IMAGES OF POLYESTER (PMGC)

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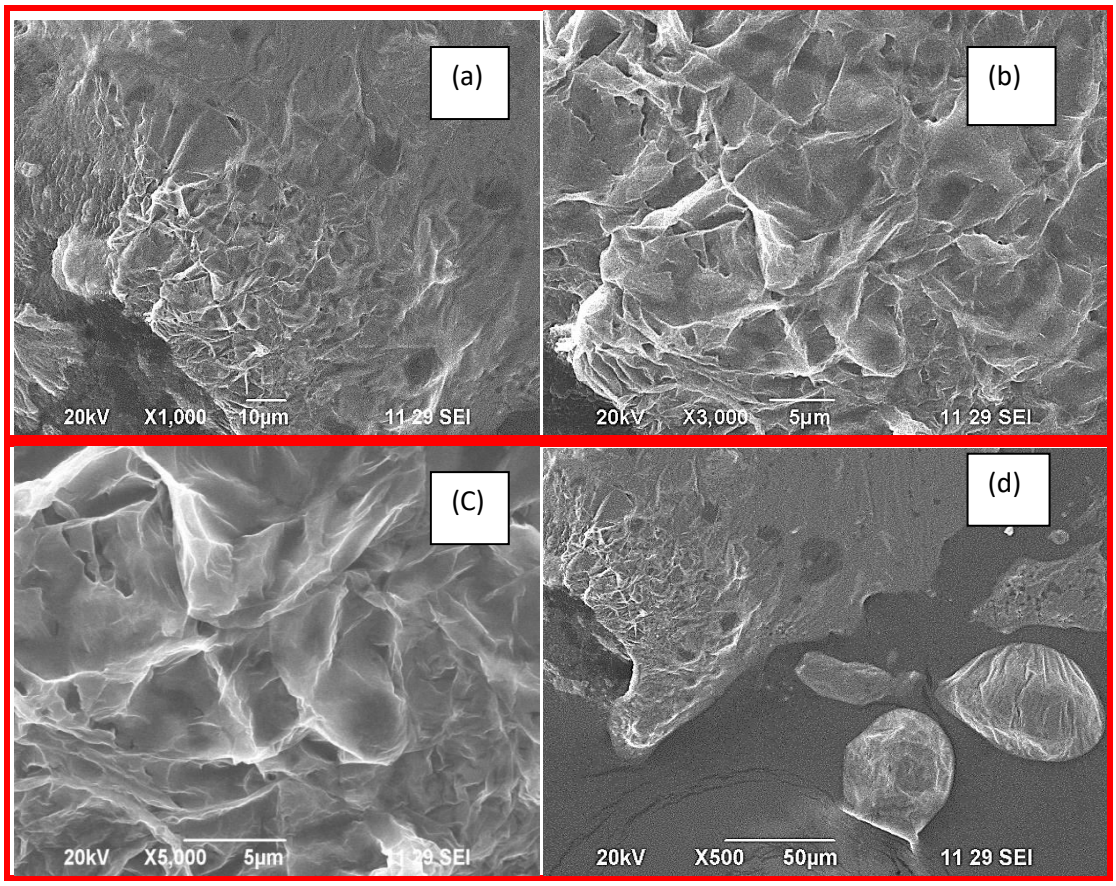
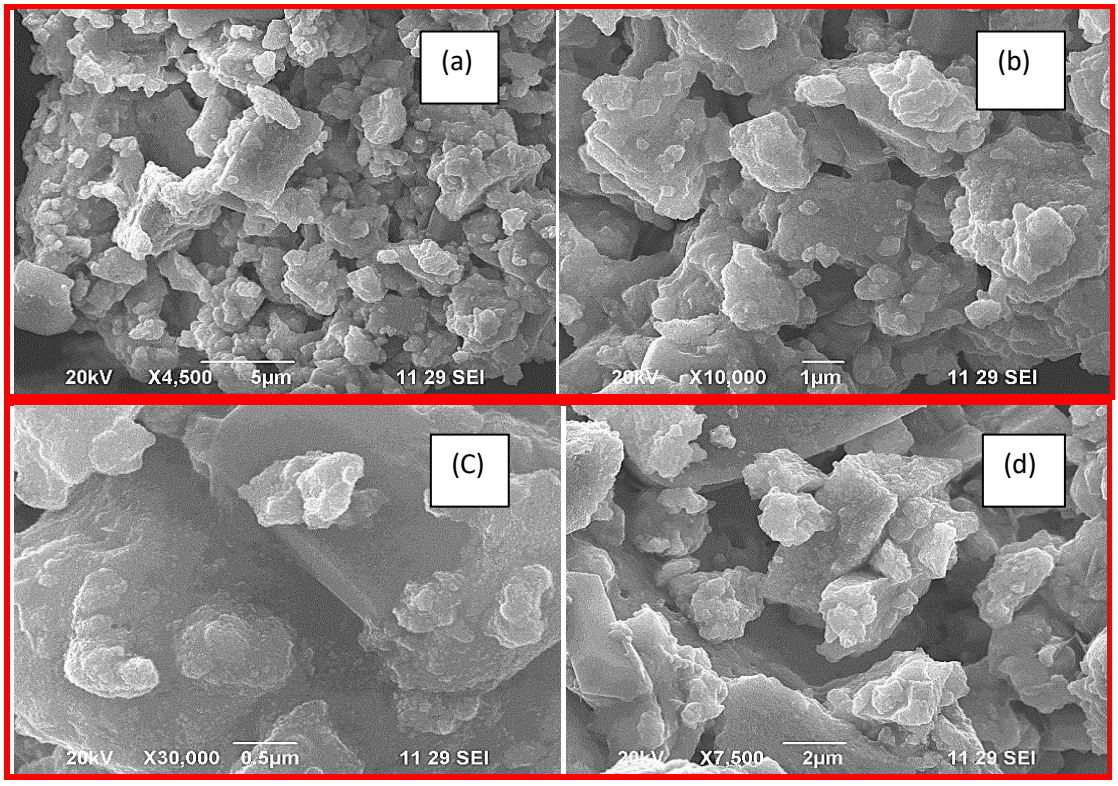


4.6.2. SEM MICROGRAPHS OF NANOCOMPOSITE (PMGC- HAp)



4.6.3 SEM MICROGRAPHS OF NANOCOMPOSITE WITH DRUG (PMGC-HAp (D))

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5. CONCLUSION

Synthesized aliphatic polyesters PMGC, PMGC-HAp and PMGC-HAp with D combined with sonication method and converted into its Nanocomposites. Nanocomposites were loaded with commercially available huge spectrum antibiotic drug ciprofloxacin predetermined quantity by using the usage of ultra sonication approach. The shape of the repeating unit of the synthesized polyesters PMGC and PMGC-HAp, drug loaded NCs had been expected through IR, and UV-Visible spectral studies. The IR spectra of polyester PMGC and PMGC-HAp,and PMGC-HAp with D nano composite suggests feature absorption frequencies due to the ester carbonyl stretching vibrations. The UV spectrum of HAp, Nanocomposites and drug loaded nanocomposites provide an explanation for approximately the drug entrapment performance and drug liberating capability.The morphology of polyesters, PMGC, PMGC-HAp and PMGC-HAp with D Nanocomposites, and drug loaded Nanocomposites become studied by way of SEM. The morphology trade of Nanocomposites and drug loaded Nanocomposites was obviously determined from SEM that's coincide with X-Ray Diffractograms. Contrast with the synthesised PMGC polyester PMGC-HAp nano Composite having high green candidate for drug shipping agent.

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