

Investigation and Comparative Studies of Biodegradable Poly[Mannitol-co-Sebacic Citrate] and Poly[Sorbitol-co-Sebacic Citrate] Doped Hydroxyapatite Nano Composite

Rajakumar.T¹, Karunanidhi M², & Subhashini S³, Kesavan.A¹, Ravi A^{*}

1*.Department Of Chemistry, Government Arts College, Tiruvannamalai, Tamil Nadu, 606601

2.Department Of Chemistry, Government Arts College, Udumalpet, Tamil Nadu.

3.PG Department Of Zoology, Arulmigu Palaniandavar Arts College for Women, Palani Tamil Nadu.

ABSTRACT

The study of attention in biomaterials from biodegradable polymers, it offer ends in atop porcelain and metallic based biomaterials. It exhibits a drudgery compilation of mechanical degradation and physiochemical assets. Synthesis of nanocomposites, the utmost foremost manner is model of polymer grid consisting nano particle. The aliphatic polyester adapted with Nano hydroxyapatite, it augment their mechanical strength hugely. Here this study was carried out with the assist of synthesizing Poly [Mannitol-co-Sebacic Citrate]PMSC and Poly [Sorbitol-co-Sebacic Citrate]PSSC. The biocompatibilities of biodegradable aliphatic polyester, with catalyst free direct soften polycondensation and nano Hydroxy Apatite synthesised Sol-gel procedure. Nano hydroxyapatite-polymannitolcosebasiccitrate polymer nanocomposite were synthesised with extremely-sonication technique. Biodegradable copolyester and its nanocomposites have been acknowledged by spectral study like FT-IR, Farther UV- visible spectral observe. It also accomplished the nanohydroxyApaptite and polyester nanocomposite. Powder XRD and SEM assessment make spotless as regards the crystallinity and morphology of the nanocomposite and polyester. A fated quantity of commercially accessible drug loaded contained by the polyester nanocomposite and the drug liberating ability considered.

Keywords: *Nanohydroxyapatite, polymernanocomposite-nHA, nanodrugloader*

1. INTRODUCTION

Polymer becomes anticipated resources being in our routine life for quality and comfort. Their strength, lightness, durability, protection and low value is the reason for adaptable virtues of the compound. Plastics be used superior parts of venture and contain more or less paper, glass and wood in the bundle and construction swap. The contrary

massiveness compound extreme industries are a goods, electrical/ electronics, automobile agriculture, medical, pharmaceutical, physics and house appliance. Synthetic polymers confine to all or several types of degradation were originally developed for longevity, jointly by biodegradation. A quantity of these intrinsic worth of the compound contain at present happen to liability. It likely enormously obliging as of ecological stand intention. If these films be sturdy, rotten almost entirely assail of organisms in excess of an amount, state that few months or they will vigour an access fragment in order so as to they be doing not become injurious to the atmosphere. All polymers degrade however; in pertain, if a compound donot degrade amongst human life time it's usually consideration regarding not degradable. Present days the marketplace polyolefin microfilm like LDPE, HDPE and PP utilize in the manufacture of wrapping carry bags is extremely. Un doped polyolefins are evidence against damage by biological agents. On one occasion these polymers be combined by additives or plasticizers, the resulting compound is full of organisms in abundant degree. On the whole of today's plastics and non-natural polymers area units are produced from petrochemicals. Typical plastics build up contained by the atmosphere. For this reason plastic resources region thing a mainstream stores of ecological contamination, perhaps harm life, onto land and water. In seas, an illustration, plastic rubbish -as of rigging and nets as of brewage packs, chokes and entangles maritime mammals. Polymers encompass unfavourable impact on waste management and municipalities be reaching conscious to the a lot of of savings that area unit accumulate a range of 'wet' organic wastes in imaginary 'biobins' to be composted. For this basis, attainment the circumstances for replacement of non-degradable compounds by degradable polymers be foremost every to decision-makers and so the plastic trade. In the Tamil Nadu state, a receipt to ban non-recyclable plastic from being sold-out, stored, transported and used was bring in to the regime for authorization. The defect organize focus of this state is accessible consideration in general population on the danger of unfortunate transfer and in addition the favours of the choice. The high value of perishable plastics confines the market of typical artefact polymers. Significance aggressive perishable plastics be able to enlarge their market by the enlargement of a variety of biodegradable plastics by contradictory structures, properties and degradation behaviours, a diversity of without a doubt suitable application area unit as are increasing. Artificial polymers seem concerning sixty years have left and right away medical peoples expert that this new grouping of chemical compound materials be attention for numerous biomedical application. Since, numerous polymers are evaluated as candidate biomaterials. However solely variety of them have attained the stage of clinical purpose and industrial accessibility. Biomaterials be

divided into together main category in line with considered necessary lifetime, mainly bio stable and perishable. Biostable materials are employed for an extended time for every enduring and time-restricted application. Biodegradable schemes be capable of nice attention for therapeutic applications of surgery, medicine, tissue engineering and drug delivery. The main perishable artificial compound was poly (glycolic acid). This compound was surplus owing to poor thermal and hydrolytic stabilities so as to unsuccessful to allow it to be a daily plastic material and it's not connected with natural polymers. Polymer composed modest recurrence units with long-chain molecules. Their unit is natural (DNA, proteins, polyose and starch) and artificial (PVC, PE, PP, PMMA, etc.) polymers. Since they will be simply factory-made and attain several forms as fibres, textiles, films, rods, and viscous liquids little straight forward chemical units referred to as compounds Artificial chemical compound materials draw attention in bioscience.

Polymers collected by the tiny and simple chemical units which is known as monomers and which molecule of large in their size. These monomers are may linearly or by branching arrange with covalent bond to form a macromolecule [1-8].

The majority part, bifunctional compounds provide direct items poly utilitarian mixes by surplus of two practical congregations provide a cross-associated or prolonged compound item. Polymeric material encompass of more than one sort of monomer is a copolymer [9-11]. Copolymerization on soothing point, synthetic and warm security flexibility and rapidly have been consider in detailed [12-14]. Polymerization is a procedure where a enormous numbers of little particles (called monomers) join to frame a major atom (called a polymer) with or lacking end of little particles like water.

2.MATERIALS

Merck samples of Calcium Nitrate tetrahydrate, Phosphoric Acid, Ammonia Sebacic acid,Citric Acid, D-Sorbitol 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 apredetermined amount of citric acid, 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 up to 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 desiccator

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-NH₃ solution, At that point, the solution was stirred well for 2hr with 1200rpm at room temperature. The gel obtained was dried at 65°C for 24h in a dry oven. The resultant powder was calcined in at 500°C for 30 min in an muffle furnace and cooled and kept in a desiccator for further usage.

2.3 SYNTHESIS OF POLYESTER HYDROXYAPATITE NANO COMPOSITE

Synthesis of HAp polyester nanocomposites was done by sonication by using ultrasonicator. Predetermined amount of polyester fine powder in 1, 4-Dioxane at 50±2 °C. To this solution 4 wt. % of nHAp powder was mixed and it is allowed to 30 minutes of ultrasonication (25 kHz, 65°C, 61amp). 60 vol. % NaCl (Merck, with the size of 212-250 µm) was 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 THE 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 PMSC were analyzed by solubility, viscosity measurements, and spectral analysis such as IR, UV, and XRD. The Hydroxyapatite polyester nano composites PMSC and PSSC using sonication method by ultra-probe sonicate. 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

4.1 SOLUBILITY MEASUREMENTS

It is a necessary property of a compound to be considered in its synthesis. First solvent particles gradually diffuse into the polymer to produce a swollen gel. Secondly the swollen gel becomes 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.

4.2 VISCOSITY OF COPOLYESTER

The inherent viscosities of these random co polyesters were measured in 1,4 Dioxane at 32°C at the concentration of 0.2g these values are given below the table-4.2.1

TABLE-4.2.1

INHERENT VISCOSITY OF RANDOM COPOLYESTERS

S.No	Co polyesters	Inherent Viscosity (g/dl)
1.	PMSC	0.357
2.	PSSC	0.349
3.	PMSC-HA _p	0.438

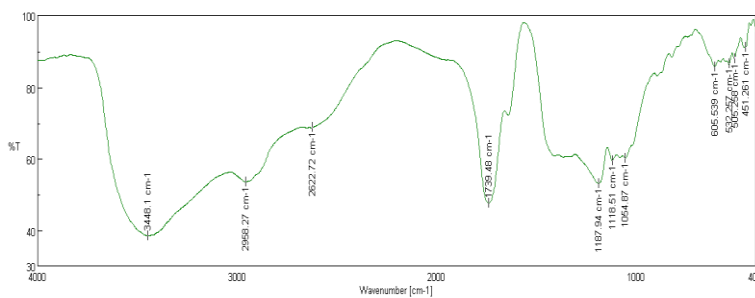
4.	PSSC-HA _P	0.441
----	----------------------	-------

Among the above polyesters PMSC,PSSC,PMSC-HA_P, and PSSC-HA_P has a maximum viscosity. The polymer PMSC and PSSC show nearly the same value of inherent viscosity because both polymers contain aliphatic C-H stretching in their structure. The relatively high viscosity of the compound indicates that it may have high molecular weight.

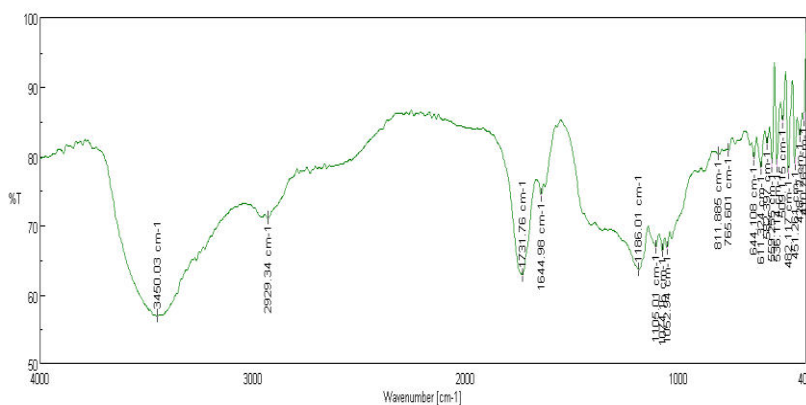
4.3 FT-IR SPECTRAL STUDIES

Figure 4.3.1 (a), 4.3.2(b), 4.3.3(c), 4.3.4(d), shows the FTIR spectra of PMSC, PSSC, and PMSC-HA_P,PSSC-HA_P. In spectra 4.3.1(a) shows a characteristic absorption band at around 1735 cm^{-1} which exhibits the carbonyl stretching vibration that indicating the polyester chain present in all polymers. The absorption band around at 2922 cm^{-1} and 2956 cm^{-1} were assigned to C-H stretching vibration for the diols/diacids and C-O-C stretching vibration shows at 1057 cm^{-1} .In spectra 4.3.2 (b) shows a stretching vibration band at around 1733 cm^{-1} , which shows carbonyl functional groups present in the polyester. The absorption band around at 2927 cm^{-1} and 2969 cm^{-1} were indicates C-H extending vibration for the diols/diacids and C-O-C extending vibration appears at 1057 cm^{-1} .the characteristic band for C=C appears at 1634 cm^{-1} .

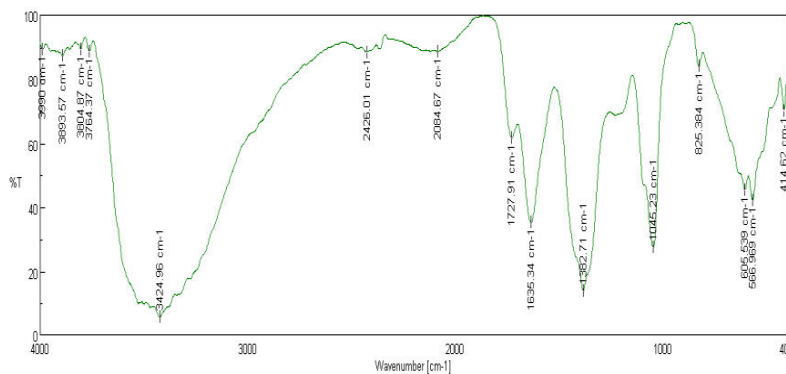
In spectra 4.3.3 (c) and 4.3.4 (d) a strong band of PO_3^{4-} group was seen at 1047 cm^{-1} due to symmetric stretching vibration. The spectra possessed a broad band ranging between 3350 cm^{-1} and 3554 cm^{-1} shows the presence of -OH group. The pronounced peaks at 1729 cm^{-1} suggest the presence of carbonyl (C=O) groups from the ester bond. The bands cantered at around 2422 cm^{-1} were assigned to methylene (-CH₂-) groups for diacids/ diols. The retention band at 1635 cm^{-1} , which is trademark ingestion of C=C extending vibration



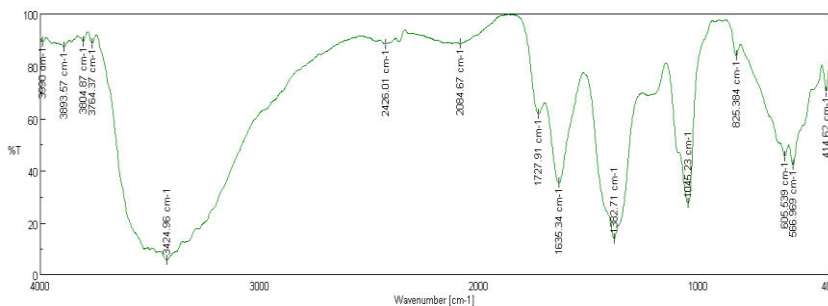
4.3.1 (a) IR Spectrum of PMSC



4.3.2(b) IR Spectrum of PSSC



4.3.3 (c) IR Spectrum of PMSC-HAP



4.3.4 (d) IR Spectrum of PSSC-HAP

4.4 UV-VISIBLE SPECTRAL STUDIES POLYESTER AND NANOCOMPOSITES

The UV visible of PMSC, PSSC, PMSC-HA_p and PSSC-HA_p nano composites are shown in figure 4.4.1 (a), 4.4.2(b), 4.4.3(c), 4.4.4(d). The UV spectra of HA_p clearly shows a red shift in comparison with the UV spectra of pure HA_p nanoparticles ($\lambda_{\text{max}} \sim 225 \text{ nm}$), when HA_p nanoparticles were functionalized with PMSC ($\lambda_{\text{max}} \sim 229 \text{ nm}$) and PSSC ($\lambda_{\text{max}} \sim 224 \text{ nm}$). The polyesters are combined with the HA_p nanoparticles, a further red shift is observed ($\lambda_{\text{max}} \sim 211 \text{ nm}$) and ($\lambda_{\text{max}} \sim 228 \text{ nm}$). The UV spectrum of HA_p nanoparticles shifts to the higher wavelength due to the bonding of PMSC on its surface.

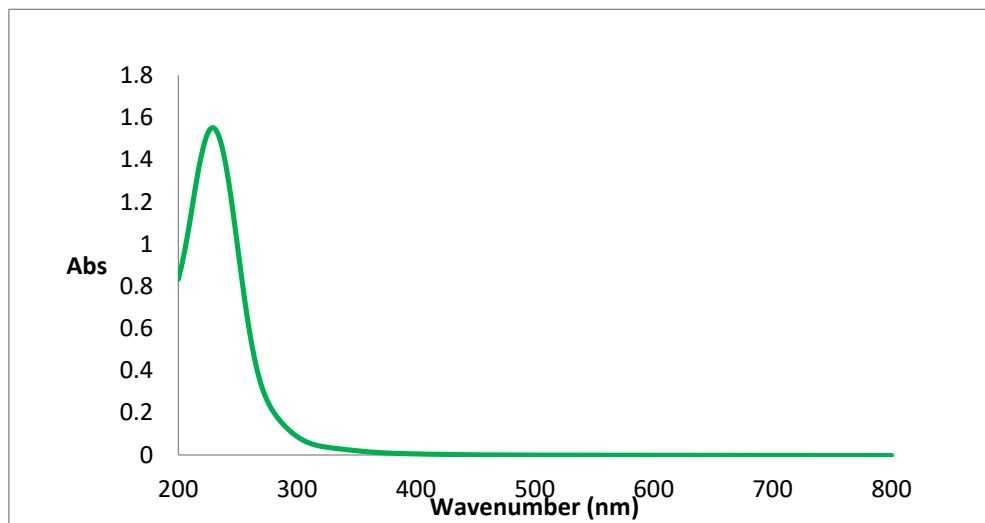


Fig 4.4.1 (a) UV SPECTRA OF PMSC

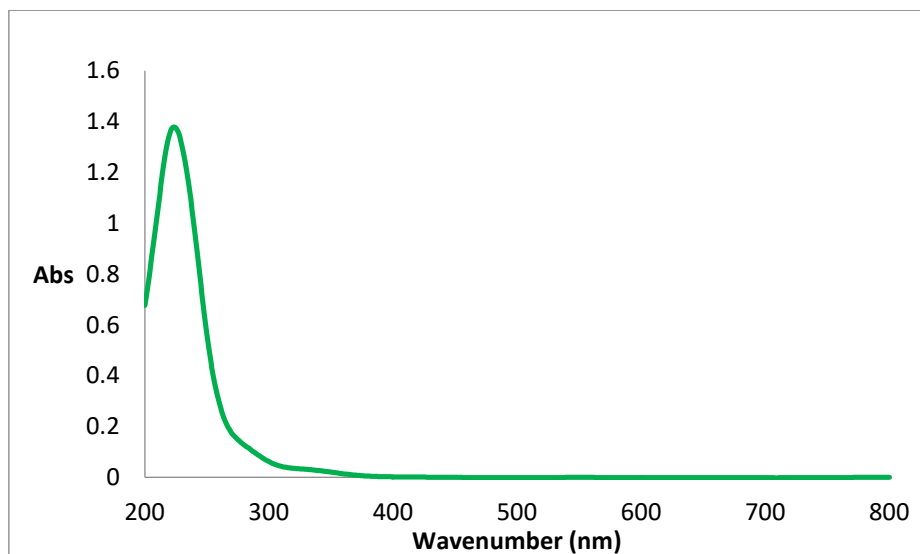


Fig 4.4.2 (b) UV SPECTRA OF PSSC

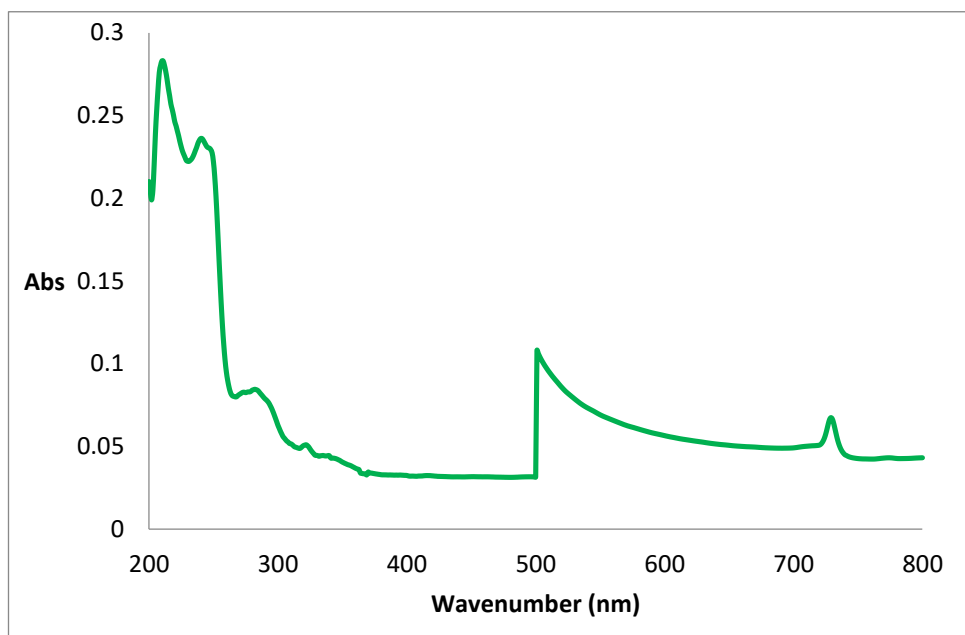


Fig 4.4.3 (c) UV SPECTRA OF PMSC-HA_p NANOCOMPOSITE

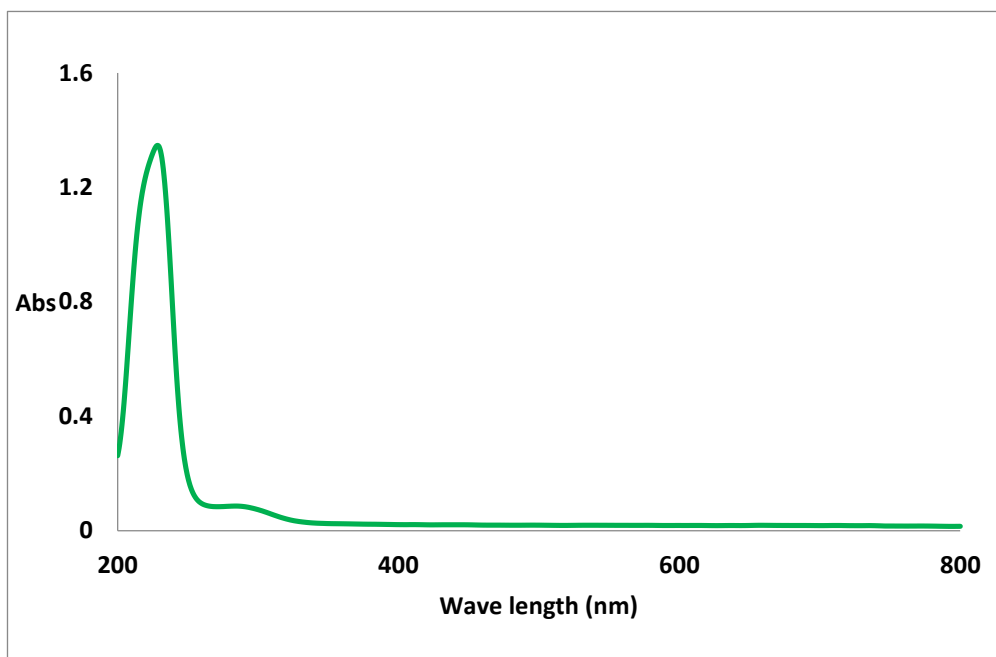


Fig 4.4.4 (d) UV SPECTRA OF PSSC-HA_p NANOCOMPOSITE

4.5 XRD SPECTRAL STUDIES

The X-Ray Diffractograms of PMSC, PSSC, and PMSC-HAP, PSSC-HAP nano composites and drug loaded nano composites were appeared in the figure 4.5.1 (a), 4.5.2(b), 4.5.3(c), and 4.5.4(d). 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 example is exposed to a collimated X-Ray beam, with location of the type and power of dispersing by stacked parallel nuclear planes of the example, at explicit points. Qualities of the dispersing X-beams demonstrate the structural arrangement in the crystalline material, utilizing Bragg's Law: $2d \sin\theta = n\lambda$, where n is a whole number, λ is the wavelength, θ is the dispersing point, and d is the interplanar separation. As indicated by Bragg's law, at a decided wavelength, the dispersing angle is conversely corresponding to the interplanar distance.

XRD can be utilized to distinguish the crystalline stage, crystallinity degree and direction, nature of the compound (in contrast with a known standard), and size of the crystallites. Sharp and wide diffraction are observed for crystalline and shapeless materials, individually, with littler crystallites delivering more extensive diffraction tops. In the event that it is expected that peak widening is basically because of size impacts, the normal nanocrystallite 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.

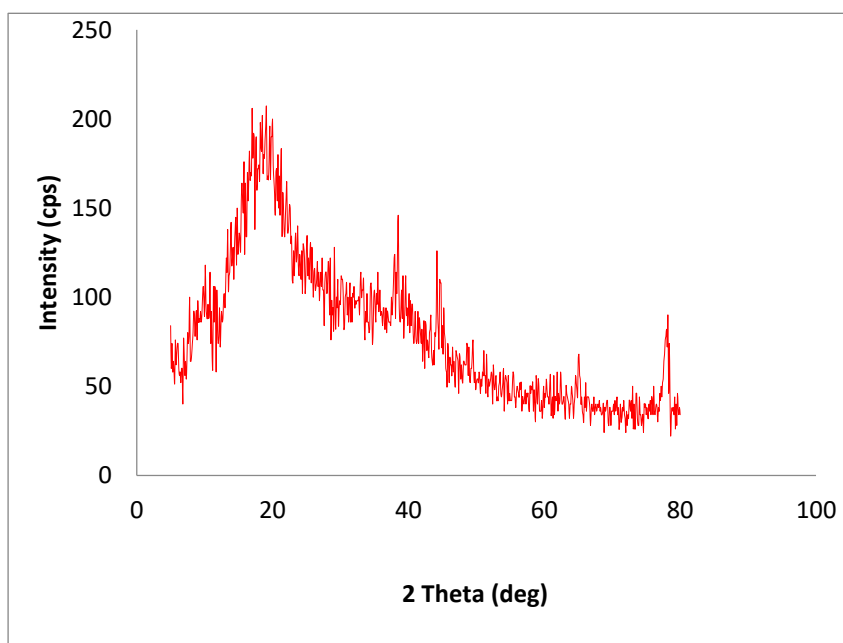


Fig 4.5.1 (a) XRD SPECTRA OF PMSC

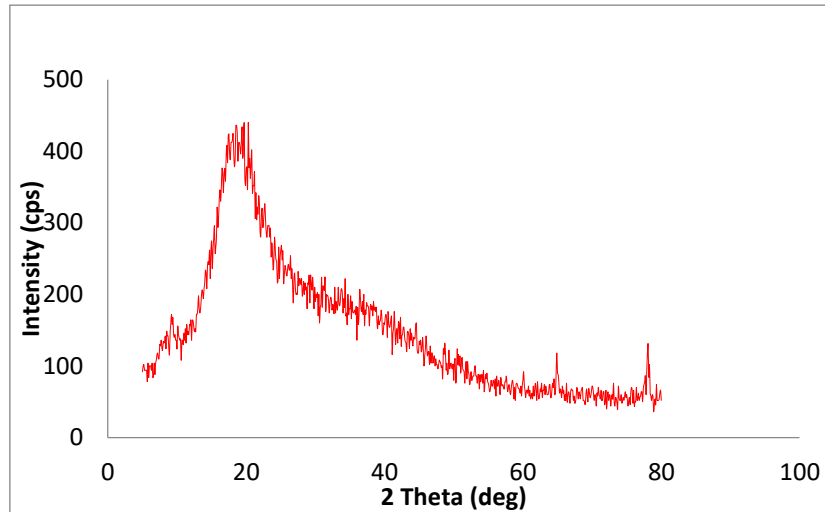


Fig 4.5.2 (b) XRD SPECTRA OF PSSC

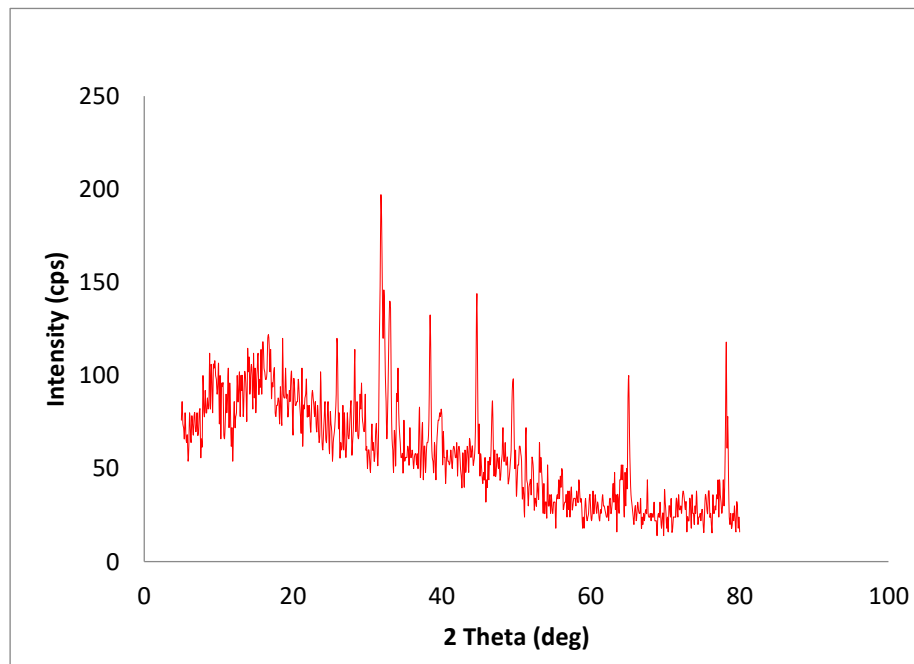


Fig 4.5.3 (c) XRD SPECTRA OF PMSC-HA_p NANOCOMPOSITE

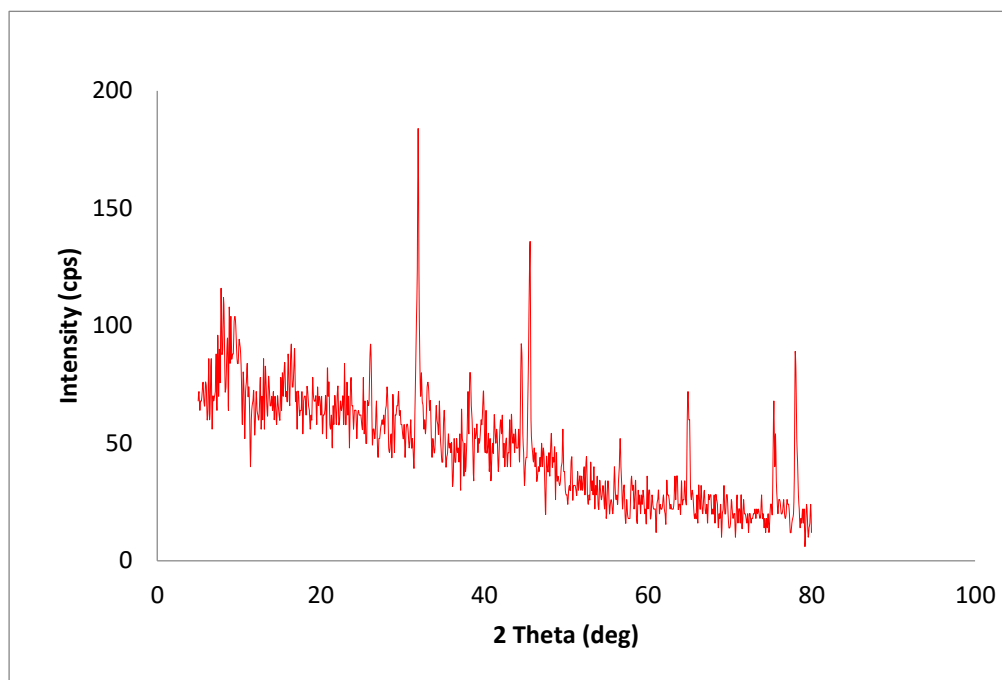


Fig 4.5.4 (d)XRD SPECTRA OF PSSC-HA_p NANOCOMPOSITE

4.6 BIODEGRADATION ANALYSIS

The synthesis polyester thin films of area $10 \times 10 \text{ mm}^2$ and about $200 \mu\text{m}$ thickness were placed in a petridish containing 10ml of phosphate buffer solution. After a particular time of incubation the films were expelled from dish, washed with distilled water and dried weighed till steady weight. The produced was repeated for every chosen time interval.

The weight loss percentage of co polyester PMSC, PSSC as a function of time is plotted against weight loss percentage plotted in 4.6.1. PMSC exhibit higher weight loss than PSSC. The weight loss percentage to polyester PMSC, PSSC during hydrolysis by phosphate buffer is presented in the following table 4.6.1.

TABLE 4.6.1

WEIGHT LOSS PERCENTAGE OF CITRIC ACID SERIES

S.No	Time (hours)	Weight loss percentage	
		PMSC	PSSC
1.	0	0	0
2.	9	4.4	3.3
3.	24	9.9	6.9
4.	48	27.7	20.5
5.	72	39.9	30.7
6.	90	49.6	43.7

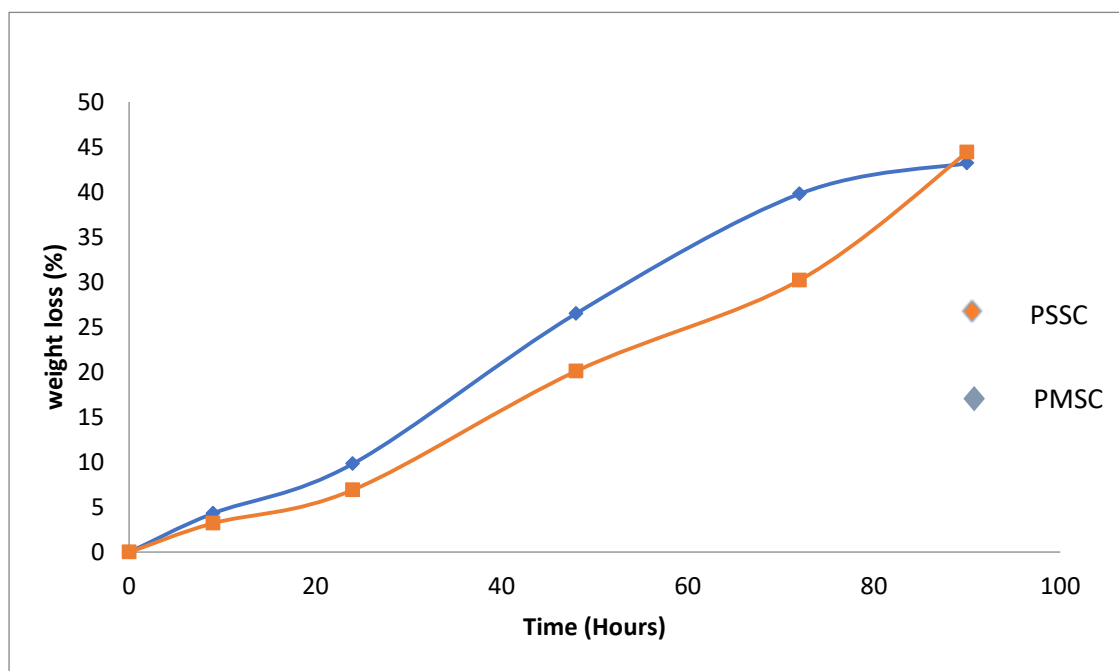


Fig 4.6.1 BIODEGRADATION GRAPH OF SEBACIC AND CITRIC ACID SERIES USING PHOSPHATE BUFFER

4.7.CONCLUSION

Synthesized polyesters PMSC, PSSC and HAp combined with write manner with using sonication method and converted into its Nanocomposites. Nanocomposites were loaded with commercially available antibiotic drug ciprofloxacin predetermined amount by using ultra sonication method.

The structure of the repeating unit of the synthesized polyesters (PMSC, PSSC), HAp, NCs and drug loaded NCs have been predicted by IR, and UV-Visible spectral studies. The IR spectra of polyester PMSC, PSSC and PMSC-HAp, PSSC-HAp nano composite shows characteristic absorption frequencies because of the ester carbonyl extending vibrations.

These polyesters are dissolvable in like manner natural solvents, for example, chloroform, 1, 4 Dioxane, methanol and sulphuric corrosive which help the simple handling of the polymers. The inherent viscosities η_{inh} of polyesters PMSC, PSSC and their Nanocomposites and Drug loaded nanocomposites have been calculated using 1,4 Dioxane solvent. From the viscosity values are explained based on the molecular weight.

The UV spectrum of HAp, Nanocomposites and drug loaded nanocomposites explain about the drug adsorption capacity. The comparison of X-Ray Diffractograms of PMSC, PSSC and HAp, Nanocomposites, drug loaded PMSC-HAp and PSSC-HAp shows the difference in crystallinity. This characterization conforms the fact that Nanocomposites as drug loader. The synthesized polyesters PMSC, PSSC exhibit biodegradable behaviour. The biodegradability was studied by determined the weight loss percentage of the polymer thin films using phosphate buffer. Emerging the trends of the recent research is Nano drug carrier with biodegradable nature of polymers. PMSC exhibit higher weight loss than PSSC In this point of view the works have been started. Drug release and effect of nano composites interaction mechanism will be studied further.

REFERENCE

1. Ana Janković A., Eraković S, A. Dindune, D. Veljović, T. Stevanović, D. Janačković, V. Mišković-Stanković, Electrochemical impedance spectroscopy of a silver-doped hydroxyapatite coating in simulated body fluid used as a corrosive agent, Journal of the Serbian Chemical Society 2012 : 77, : 1609-1623

2. George Z., Papageorgiou, Dimitrios N, Bikiaris Synthesis, CocrySTALLization, and Enzymatic Degradation of Novel Poly(butylene-co-propylene succinate) Copolymers *Biomacromolecules* 2007, 8, 8, 2437–2449
3. Jaisankar V, Nanthini R, Ravi A and Karunanidhi M. J. Biodegradation of new series of aliphatic copolyesters by fungi *Oriental Journal of Chemistry*. 2010, 26(2), 547-554.
4. L Sowbagyalakshmi Prabha; R Nanthini; G Krishnaveni, Synthesis and characterization of novel biodegradable aliphatic copolyesters - poly(ethylene sebacate-co-propylene succinate) and poly(ethylene sebacate-co-propylene adipate) *Journal of chemical pharmaceutical research*. 4(5).2442-2457, 2012.
5. J Margaret Maric; R Puvanakrishnan; R Nanthini. Design, synthesis and characterization of elastomers based on itaconic acid *Journal of Chemical and Pharmaceutical Research*. 2012 4(1).175-179.
6. J. Gowsika; R Nanthini. Design, synthesis, characterization and cytotoxicity of certain itaconic acid based biodegradable aliphatic copolyesters *Journal of Chemical and Pharmaceutical Research*. 2014, 6(3).1152-1461.
7. Sushil P. Narkhede, Harsh V. Raval, Atul R. Bendale, Anil G. Jadhav and G. Vidyasagar. *J. Chem. Pharm. Res.*, 2011, 3(6):361-368.
8. Sundar Raj M., Arkin V.H., Adalarasu and Jagannath. Nanocomposites based on polymer and hydroxyapatite for drug delivery application. *Indian Journal of science and technology*. 2013, 4653-4658.
9. Raval J.P, D.R. Naik, K.A. Amin, P.S. Patel, J. Saudi. Controlled-release and antibacterial studies of doxycycline-loaded poly (ϵ -caprolactone) microspheres *Journal of Saudi Chemical Society*. 2014, 18: 566.
10. Kalpana Jayachandran., Ravichandrencingaram., Jaisankarviswanathan., Suresh Sagadevan and Venkatachalam jayaraman, investigations on preparation and characterization of certain copolyester. 2016, 19(2), 394-400.
11. Mirza, EH, Khan, AA, El-Sharawy, MA, et al. Physical, mechanical, thermal, and dynamic characterization of carbon nanotubes incorporated poly(methyl methacrylate)-based denture implant. *J Compos Mater*; 51: 3931–3940:2017.
12. Yamini B. and Nanthini R., synthesized biodegradable aliphatic copolyesters, poly(ethylene glycol octane diol sebacate) and poly(ethylene glycol dodecane diol adipate). 2018, 11(1), 413-425.

13. ZeyuFu, JinjieCui, BinZhao, Steve GF.Shen, KailiLin,An overview of polyester/hydroxyapatite composites for bone tissue repairing ,Journal of Orthopaedic Translation 2021, 118-130.
14. Kohei Okuda,KenHirota,TadashiMizutaniand Yusuke Numamoto,Enhanced toughness of hydroxyapatite–poly(ethylene terephthalate) composites by immersion in water, Mater. Adv., 2, 5691–5703 | 5691:2021.