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Synthesis and Characterization of Nanocomposites for Drug Delivery Applications

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Abstract: *The use of nanotechnology for biomedical applications, has potential to change the landscape of the diagnosis and therapy of many diseases. Several therapeutic nanocarriers have been approved for clinical use. In this research paper polymeric biodegradable nanocomposites have been synthesized as a drug carrier for anticancer drug. Chitosan (CS) and sodium alginate (ALG) with different ratios were blended with different wt% of hydroxyl apatite by solvent evaporation method. Morphology and structure characterization of nanocomposites were investigated by X-Ray Diffraction (XRD), Scanning Electron Microscope (SEM) and Fourier Transmission Infra Red Spectroscopy (FTIR) respectively. Thermal property of nanocomposite was investigated by Thermo Gravimetric Analysis (TGA). The swelling behavior of the composites has been investigated I different pH medium of 1, 4 & 7.4. which revealed that out of the total possible swelling of polymer, 8 % is swelled in the 2 h period at pH 1.0 while 36 % was swelled in the next 2 h at pH 4.0. Finally, when the it was transferred into phosphate buffer of pH 7.4, it swelled 91 % in the next 6 h. This study gives a somewhat more realistic picture of release of drug from polymeric matrix also & probable in vivo behavior of the device in the gastrointestinal tract.*

Keywords: *Chitosan, Sodium alginate, Hydroxy apatite, Drug delivery*

I. Introduction

Nanotechnology is defined as the science and technology involved in the design, synthesis, characterization and application of materials and devices whose smallest unit in at least one dimension is of the nanometer size (one-billionth of a meter) [1]. In last few years nanotechnology has grown by leaps and bounds, and this multidisciplinary field is undergoing development at a tremendous rate [2]. Nanoscience and nanotechnologies have applications in areas as diverse as drug development, water decontamination, information and communication technologies, energy storage devices, production of strong yet materials etc.

At present, 95% of all new potential therapeutics have poor pharmacokinetics and biopharmaceutical properties [3]. Therefore, there is a need to develop suitable drug delivery systems. Nano medicines, based on nano technology play an important role in delivering the drugs to the site of action, without affecting healthy organs and tissues. Due to small size and higher efficacy, the drug doses are reduced, though the therapeutic indices are increased and also the safety profiles of new therapeutics.

Recently, biodegradable polymers have found importance for their uses as biomaterials in fields like tissue engineering, gene therapy, wound healing and controlled drug delivery systems. The most important advantage of biodegradable polymers is that they degrade within the body leaving behind no residue or foreign particles.

Alginate (ALG) is not only a biodegradable polymer, but also mucoadhesive, and biocompatible. It is water soluble linear polysaccharide extracted from brown sea weed and is composed of alternating blocks of 1-4 linked α-L-guluronic and β-d mannuronic acid residues. Alignate has a potential for applications in pharmaceutical and biomedical industry such as drug delivery system and cell encapsulation.

Chitosan is another biodegradable, marine –based polymer obtained by the deacetylation of chitin, which is present in shells of insects and marine crustacean. Chitosan, besides being biodegradable is also non-toxic as well as has good adhesion and sorption. This contributes to its multiple applications. Chitosan is also a valuable component of polymer blends and composites. It can be obtained in the form of films, gels , fibers, foams and beads of different sizes and morphology. A number of in vitro studies have been carried out to find the response of smooth muscle cells, macrophages, osteoblasts, chondrocytes, erythrocytes and whole blood, to chitosan.

Hydroxyapatite is mimics the mineral component of bones and hard tissues in mammals. For its bioactive nature, it is used in bone implants, where it integrates in bone structures and supports bone. Hence hydroxyapatite coatings are often applied to metallic implants to alter their surface properties. This makes it easier for the body to accept them. Nanosized hydroxyapatite can be used in drug delivery systems like intestinal delivery of insulin or other drugs such as antibiotics [4].

Cancer remains one of the world's most devastating diseases, with more than 10 million new cases every year [5]. However, mortality has decreased in the past two years [6] owing to better understanding of tumors biology and improved diagnostic devices and treatments. Current cancer treatments include surgical intervention, radiation and chemotherapeutic drugs. These often kill healthy cells besides the cancerous ones and cause toxicity in the patient. It is therefore desirable to develop chemotherapeutics that can either passively or actively target only cancerous cells.

Engineering polymeric nanostructures such as hyperbranched polymers, dendrimers and polymeric micelles [7] are a growing area of contemporary biomaterials science, due to their unique properties and large potential in drug delivery [8]. For using polymers in drug delivery, a polymer must be biocompatible. Biocompatibility was defined as the ability of a material to act with an appropriate host response in a specific application [9].

Efficient use of drugs requires their selective delivery at the site of action at a controlled rate, especially in the case of potent drugs with strong side effects. Cisplatin is one of the most potent anticancer agents known [10]. However, its use is associated with serious side effects, including renal and auditory toxicity, nausea and vomiting. The selective delivery (targeting) of cisplatin to tumor cells would significantly reduce drug toxicity by improving its therapeutic index.

II. Methods And Materials

A. MATERIALS

Sodium Alginate, Chitosan and hydroxyl apetite were purchased from Sigma- Aldrich, Mumbai, India. The crosslinker CaCl2 was obtained from Qualigens, Mumbai, India. Drug Cisplatin was purchased from Medico Point, Pune. The double distilled water was used throughout the investigations.

B. PREPARATION OF CHITOSAN-ALGINATE NANOCOMPOSITE

Both the sodium alginate and chitosan solutions were prepared by dissolving the chemicals in distilled water and 1% acetic acid respectively. Blend solution of different compositions (i.e. the weight ratios between chitosan and alginate of 70/30, 50/50, 30/70 (w/w) respectively) were then prepared by casting a mixture of the solutions in a respective weight ratio on a petri dish. To this blend solution of CS-ALG (30:70) hydroxyl apatite (HA) of compositions 1wt% was added with constant stirring for 3 hours at room temperature to get a homogenous solution. It should be noted that stirring was used to homogenize the mixture prior to pouring onto the dish. The casting was let dry at room temperature for 3 days.

C. SWELLING STUDIES

The completely dried pre-weighed hydrogel sample was placed in 250 mL of buffer solution of desired pH at 30°C. The swollen gel was taken out at regular time intervals, samples were wiped superficially with filter paper to remove surface-water, weighed and then placed in the same bath. The mass measurements were continued till the attainment of the equilibrium. The percentage of mass swelling (SM) was determined using the following expression:

$$Sw\ (\%) = (mt\text{-}mo) / mo \times 100$$

where, mo and mt are the initial mass and mass at different time intervals & Sw % is percent swelling respectively. For pH 4.0, citric acid-trisodium citrate buffer was used while for pH 7.4 phosphate buffer was used and for 2 pH HCl solution was used.

III. Characterization

A. FOURIER TRANSMISSION INFRA-RED SPECTROSCOPY (FTIR)

The FTIR spectrum of the chitosan, alginate, and chitosan-alginate blend was obtained using a spectrophotometer from Central Instrumentation Facility of Pune University.

B. X-RAY DIFFRACTION (XRD)

The change in gallery height of the blend was investigated by XRD analysis, which were carried out using an X-ray diffractometer with Cu Kα radiation at a generator voltage of 40 kV and a generator current of 100 mA. Samples were scanned from 2θ = 1-100o at a scanning rate of 2 o/min.

C. SCANNING ELECTRON MICROSCOPY (SEM)

Morphological study was done by SEM analysis from Central Instrumentation Facility of Pune University.

D. ENERGY DISPERSIVE X-RAY SPECTROSCOPY (EDS)

EDS makes use of the X-ray spectrum emitted by a solid sample bombarded with focused beam of electrons to obtain a localized chemical analysis. All elements from atomic number 4 (Be) to 92 (U) can be detected by EDS analysis.

IV. Results And Discussion

A. Fourier Transmission Infra Red Spectroscopy (FTIR):

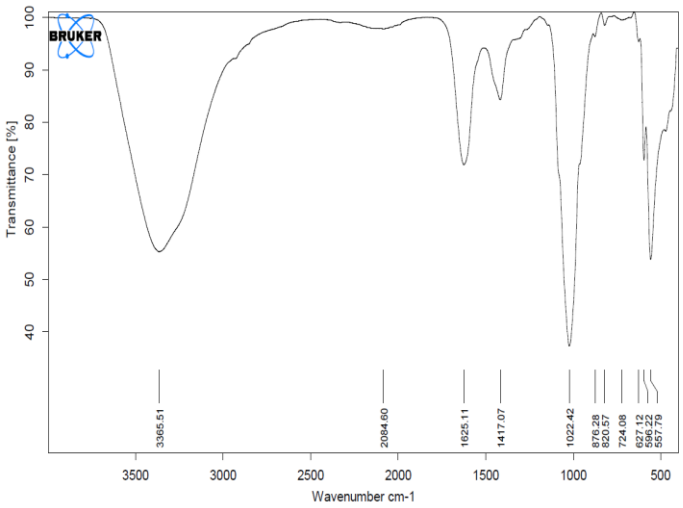


Figure 1. FTIR-Spectra of chitosan Alginate hydroxyl apatite nanocomposite.

FT-IR spectra of chitosan (CS), alginate and CS/alginate nanocomposites are shown in Figure 1.In the spectra of CS, the broad band at 3365.51 cm-1 corresponded to the amine and hydroxyl groups; the absorption band of the carbonyl (C=O) stretching of the secondary amide (amide I band) at 1625 cm-1, and the bending vibrations of the N–H (N-acetylated residues, amide II band) at 1599 cm-1. The peaks at 1417 belongs to the N–H stretching of the amide and ether bonds. The peaks observed at 1022 cm-1 is the primary hydroxyl group (characteristic peak of -CH2- OH in primary alcohols, C-O stretch). The bands around 1030 cm-1(C-O-C stretching) presenting in the IR spectrum of sodium alginate are attributed to its saccharide structure. In addition, the bands at 1625 and 1417 cm-1 are assigned to asymmetric and symmetric stretching peaks of carboxylate salt groups.

B. X-RAY DIFFRACTION (XRD)

Wide-angle X-ray diffraction (WAXD) is a classical method for determining the gallery height (*d*-spacing distance) in particles. **Scherrer equation** was used to determine particle size of nanocomposite which is as follows.

$$D_p = \frac{0.94\lambda}{\beta_{1/2}\cos\theta}$$

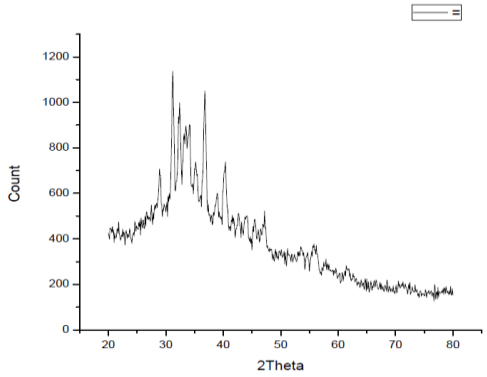
Where - Dp=AverageCrystallitesize,

B =Line broadening in radians.

θ =Braggangle.

λ = X-ray wavelength

Figure 2 shows XRD pattern of nanocomposite



C. SCANNING ELECTRON MICROSCOPE(SEM):

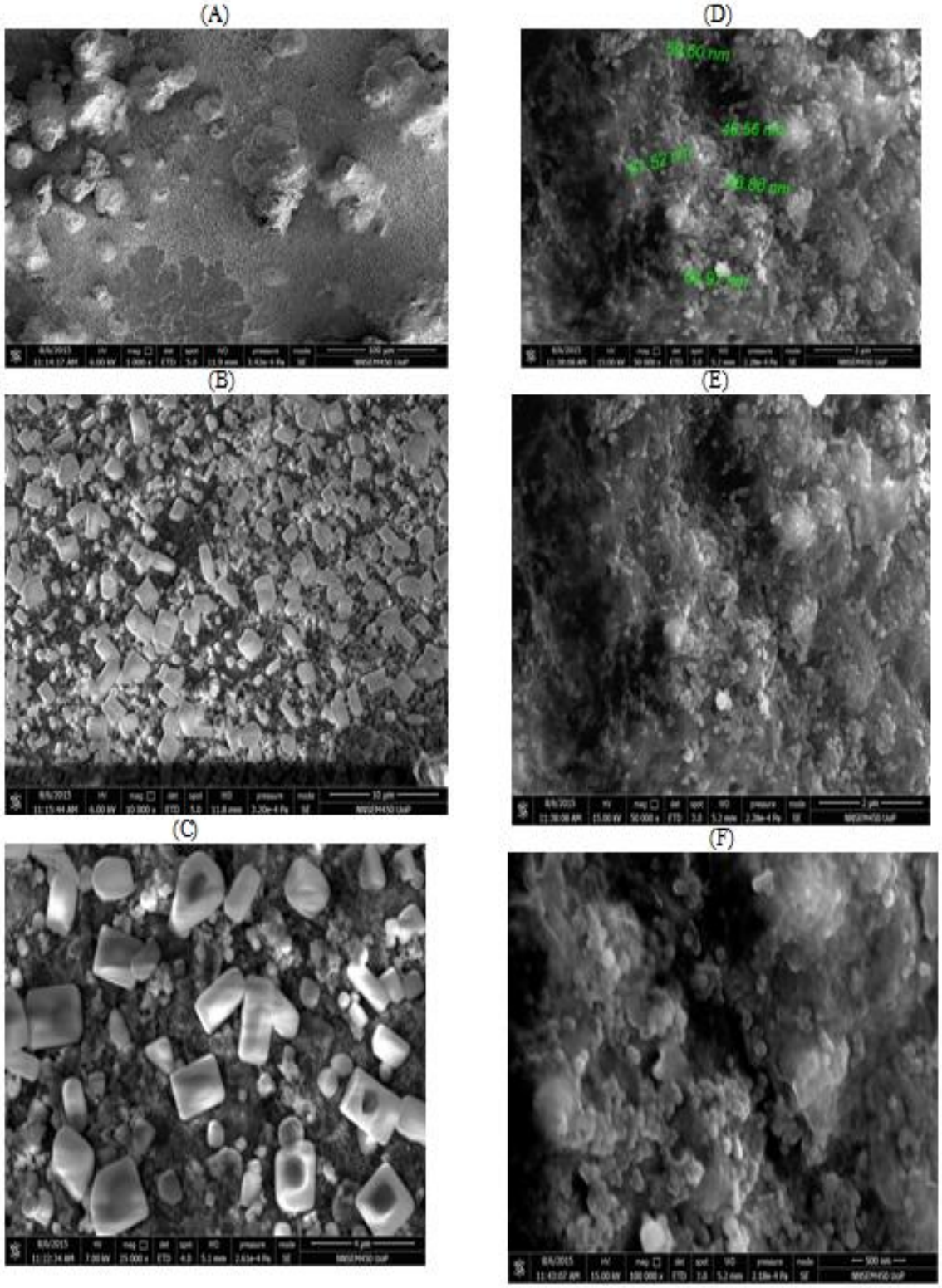


Figure 3. *Scanning Electron Micrograph of Chitosan-alginate-hydroxy apatite Nanocomposites (A-F).*

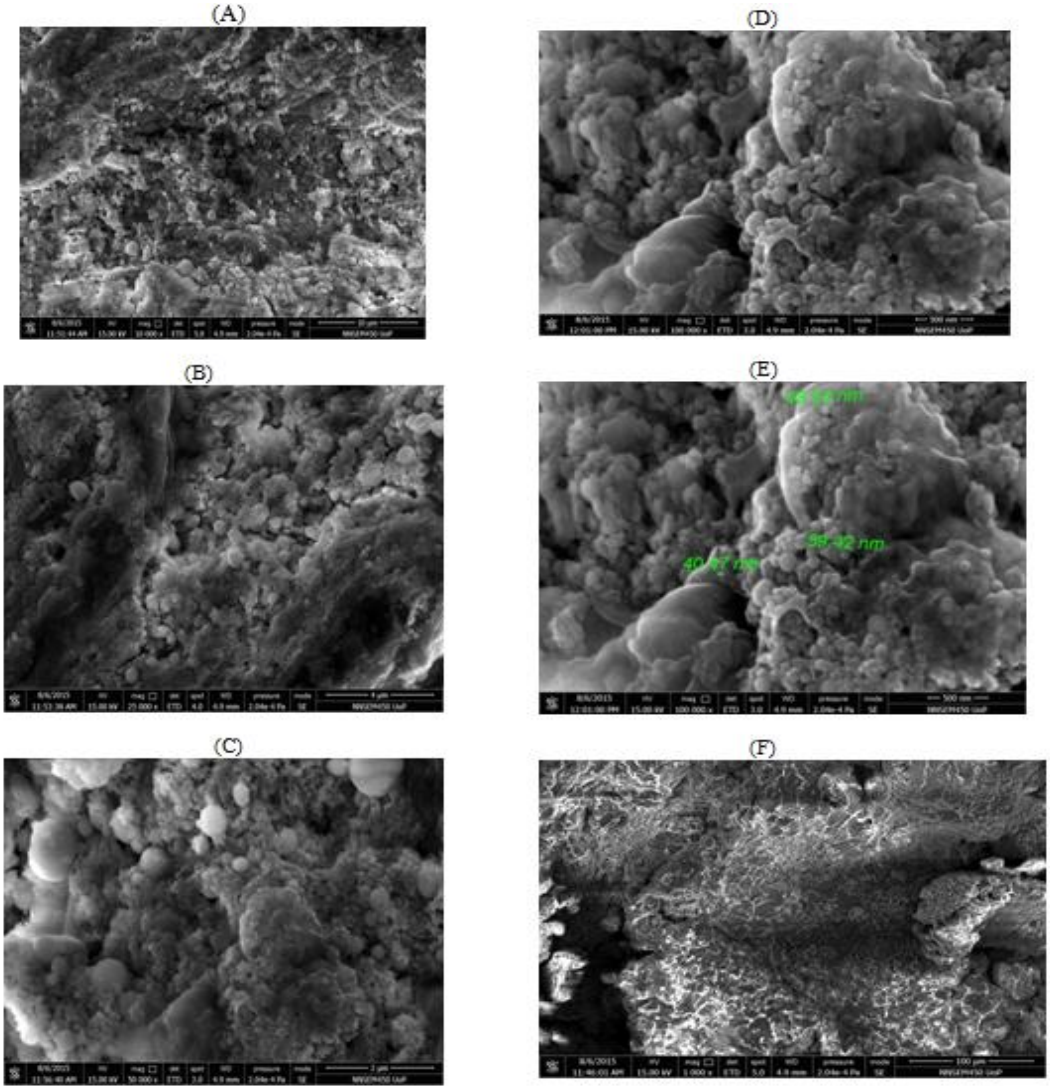


Figure 4. Scanning Electron Micrograph of drug loaded Chitosan-alginate- hydroxy apatite Nanocomposites (A-F).

The scanning electron micrograph of a without drug sample is shown in Fig. 3 & drug-loaded sample is shown in Figure 4. The nanocomposite showed surface cracks probably caused by partial collapsing of the polymer network during drying.

D. ENERGY DISPERSIVE X-RAY SPECTROSCOPY (EDS)

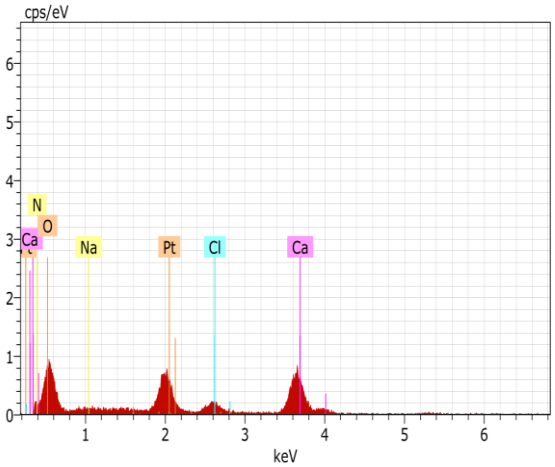


Fig 5: EDS of drug loaded sample

In our nanocomposite we have added chitosan, sodium alginate, hydroxyl apatite nanopowder and cisplatin drug(containingg Pt). Above fig.5 shows the presence of element Ca & Cl (from crosslinker CaCl2), Na from sodium alginate, Pt from drug cisplatin which confirms their existence to nanocomposite of chitosan, sodium alginate, hydroxyl apatite and cisplatin.

E. THERMOGRAVIMETRIC ANALYSIS

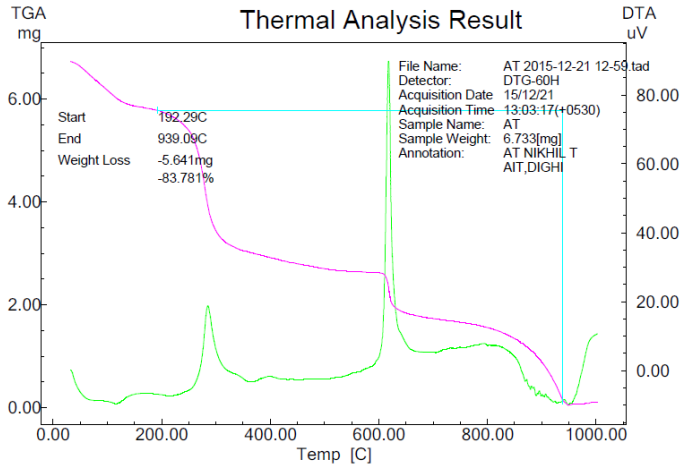


Fig. 6: Thermogravimetric analysis of nanocomposite.

The graph depicts the thermogram of nanocomposite. The value Tid(initial decomposition temperature), Tdf(final decomposition temperature) and Tmax(temperature of maximum rate of weight loss). They are found to be 192,900 and 610 ^{o}C respectively for this sample. Since the proposed system is intended to be used for the release of drug at physiological temperature 37^{o}C.

F. SWELLING STUDIES

The swelling behavior of the composites has been investigated. It is generally known that the swelling behavior of the polymer network depends upon the nature of the polymer, polymer solvent compatibility and degree of cross-linking. However, in the case of ionic networks, swelling behavior depends upon mass transfer limitations, ion exchange and ionic interaction. The swelling behavior of the composites is depicted in Figure 7.

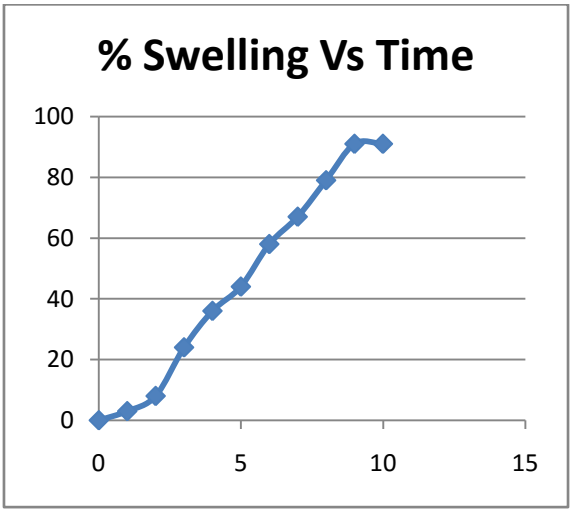


Figure 7. Water Absorption of the chitosan-sodium alginate nanocomposites

It is reported that a mean gastric emptying time of 1.08 ± 0.11 h and a mean colonic arrival time of 2.83 ± 0.33 h. This means that the small intestine transit time is likely to be 1.75 ± 0.25 h, thus suggesting that the formulation should enter the colon between 1.75 and 3.75 h after administration [11]. Relying on their data, we opted to expose a device for a period of 2 h at pH 1.0, for another 2h at pH 4.0, and then for the next 6 h at pH 7.4, thus mimicking the transition from stomach to colon. The results, as depicted in Fig 7, reveal that out of the total possible swelling of polymer, 8 % is swelled in the 2 h period at pH 1.0 while 36 % was swelled in the

next 2 h at pH 4.0. Finally, when the it was transferred into phosphate buffer of pH 7.4, it was swelled 91 % in the next 6 h. This study gives a somewhat more realistic picture of release of drug from polymeric matrix also & probable *in vivo* behavior of the device in the gastrointestinal tract.

V. Conclusion

Biodegradable Controlled delivery devices have a significant advantage over competing delivery systems because there is no need for surgical removal of the devices and if the polymer degrades only at the surface, the drug release process is simplified in water diffusion into the bulk is minimized and drug release rate is governed by polymer degradation rate.

Novel nanocomposites of chitosan and alginate blended with hydroxyl apatite were prepared and characterized by FTIR spectroscopy, X-ray diffractometry (XRD),Thermogravimetric Analysis (TGA),Scanning Electron Microscopy (SEM) & Energy Dispersive Spectrometry (EDS) analysis to determine their suitability as drug carrier. The results conclude that Novel nanocomposites of chitosan and alginate blended with hydroxyl apatite have a good potential for use as drug carrier.

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References

[1]. Emerich DF, Thanos CG. Nanotechnology and medicine. Expert Opin Biol Ther 3,2003,655 - 63.
[2]. Chan WC. Bionanotechnology progress and advances. Biol Blood Marrow Transplant;12,2006,87–91.
[3]. Brayden DJ. Controlled release technologies for drug delivery. Drug Discov Today;8,2003,976 - 8.
[4]. Ferraz MP, Monteiro FJ, Manuel CM. Hydroxyapatite nanoparticles: A review of preparation methodologies. J App Biomateria & Biomech.; 2,2004, 74-80.
[5]. Stewart, B. W. & Kleihues, P. World Cancer Report,World Health Organization Press, Geneva, 2003.
[6]. Cancer Facts & Figures (American Cancer Society, Atlanta), 2007.
[7]. Xu, Q., Liu, Y., Su, S., Li, W., Chen, C., Wu, Y., 2012. Biomaterials5, 2012, 1627–1639.
[8]. Kim, J.H., Li, Y., Kim, M.S., Kang, S.W., Jeong, J.H., Lee, D.S., Int. J. Pharm. 427, 2012,435– 442,.
[9]. Williams. D.F., The Williams Dictionary of Biomaterials Liverpool: Liverpool University Press. 1999.
[10]. B. Rosenberg, Fundamental studies with cisplatin, Cancer 55,1985 ,2303–2316,.
[11]. SK Bajpai and Seema Dubey. Modulation of dynamic release of vitamin B2 from a model pH-sensitive terpolymeric hydrogel system , , *Polymer International*, 0959(53), 2004, ,8103.