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Preparation and Evaluation of Chitosan Loaded Nanoparticles Containing Lamivudine

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Abstract: *The goal of this study was to make and test chitosan nanoparticles that were loaded with Lamivudine to improve drug delivery and effectiveness. We used the ionic gelation method to make nanoparticles out of chitosan, which is a biocompatible and biodegradable polysaccharide. Lamivudine, an antiviral drug that is often used to treat HIV, was added to the chitosan nanoparticles to make them more soluble, stable, and available to the body. We looked at the size, surface charge (zeta potential), shape, drug encapsulation efficiency, and drug release kinetics of the nanoparticles. We used scanning electron microscopy (SEM) and dynamic light scattering (DLS) to confirm that spherical nanoparticles with an average size range of 100–200 nm had formed. It was found that the drug encapsulation efficiency was .more than 80%, which means that Lamivudine was loaded successfully. In vitro release studies showed that Lamivudine was released in a controlled and steady way over a period of 48 hours. This suggests that these nanoparticles could have long-lasting therapeutic effects. Cytotoxicity tests also showed that the nanoparticles were not harmful to human cell lines, which means they are safe for use in possible clinical settings. This study shows that chitosan nanoparticles could be a good way to deliver Lamivudine, which could improve the way the drug works and the results of treatment for HIV infection.*

Keywords: Lamivudine, Drug delivery system, Nanotechnology, Nanocarriers, Nanotechnology, Drug delivery system, Chitosan nanoparticles

I. INTRODUCTION

To make antiviral drugs more effective, easier to take, and more available to patients, the way they are delivered must keep getting better. This is especially important for treating chronic diseases like HIV. Lamivudine (LMV) is a nucleoside reverse transcriptase inhibitor (NRTI) that is commonly used to treat HIV. Even though Lamivudine works well in the clinic, it has some problems, such as low bioavailability, quick clearance, and side effects from high systemic concentrations. To get the most out of its therapeutic potential, these problems need new ways to deliver drugs. Nanoparticles are a promising way to get around the problems with traditional drug delivery. Chitosan-based nanoparticles have gotten a lot of attention in the pharmaceutical field as one of the many types of nanocarriers.

A naturally occurring polymer made from chitin, chitosan has exceptional qualities like non-toxicity, biocompatibility, biodegradability, and the capacity to alter drug release profiles. Because of these qualities, chitosan is a perfect fit for the creation of drug delivery systems that enhance the stability, solubility, and controlled release of medications that are encapsulated. Typically, ionic gelation, coacervation, or solvent evaporation are used to prepare chitosan nanoparticles; the ionic gelation method is the most popular for hydrophilic drug encapsulation. This method creates a stable colloidal dispersion by combining chitosan with anionic agents such as tripolyphosphate to form nanoparticles.

By allowing controlled and sustained release of the medication at the target site, chitosan nanoparticles for Lamivudine delivery seek to overcome the drawbacks of traditional oral formulations, lowering the frequency of administration and minimizing side effects.The purpose of this work is to use the ionic gelation technique to create chitosan nanoparticles

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loaded with lamivudine. The size, surface charge, morphology, encapsulation effectiveness, and in vitro drug release profile of the produced nanoparticles will all be evaluated. The cytotoxicity and stability of chitosan nanoparticles will also be assessed in order to determine whether they can improve the therapeutic efficacy of lamivudine through regulated drug delivery.

The ultimate objective of this study is to demonstrate that chitosan nanoparticles are a feasible means of delivering lamivudine, which could provide a novel strategy for the long-term management of HIV infections with better patient outcomes.Antiviral medication delivery systems must be continuously improved for the treatment of chronic illnesses like HIV in order to increase patient compliance, bioavailability, and efficacy. One common nucleoside reverse transcriptase inhibitor (NRTI) used to treat HIV infections is lamivudine (LMV). Lamivudine has drawbacks, including poor bioavailability, quick clearance, and adverse effects from high systemic concentrations, despite its clinical success. To maximize its therapeutic potential, these problems call for the creation of novel drug delivery systems.

One promising way to get around the drawbacks of traditional drug delivery is through nanoparticles. Chitosan-based nanoparticles are one type of nanocarrier that has attracted a lot of interest for use in pharmaceutical applications. A naturally occurring polymer made from chitin, chitosan has exceptional qualities like non-toxicity, biocompatibility, biodegradability, and the capacity to alter drug release profiles. Because of these qualities, chitosan is a perfect fit for creating drug delivery systems that enhance the stability, solubility, and controlled release of medications that are encapsulated.

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Our goal in this work is to use the ionic gelation technique to create chitosan nanoparticles loaded with lamivudine. The size, surface charge, shape, encapsulation effectiveness, and in vitro drug release profile of the produced nanoparticles will all be evaluated. Chitosan nanoparticles' capacity to improve Lamivudine's therapeutic effectiveness by means of regulated drug delivery will also be assessed in terms of stability and cytotoxicity.

The ultimate objective of this study is to demonstrate that chitosan nanoparticles are a feasible means of delivering lamivudine, which could provide a novel strategy for the long-term management of HIV infections with better patient outcomes.

II. MATERIALS AND METHODS

Lamivudine was obtained from Sigma, chitosan and tripoly phosphate was obtained from Otto biochemika, acetic acid, sodium hydroxide and potassium dihydrogen phosphate were purchased from SISCO research laboratories, India. All equipments for the synthesis and evaluation were carried out in the Vels University(old pallavaram,Chennai-117) and Malvern laboratories.

PREPARATION OF NANOPARTICLES CONTAINING LAMIVUDINE

A Chitosan nanoparticle was prepared by ionotropic gelation process. Chitosan solution (0.1% w/v) as prepared by dissolving 100 mg of chitosan in 100ml of 1% v/v acetic acid. TPP (tripolyphosphate) solution of 0.1% was prepared by dissolving 100mg of TPP in 100ml of deionized water. Lamivudine was added to the TPP solution. The chitosan solution was then stirred at1500rpm for 30min in an ultrasonicator (vibronics) and add TPP solution containing lamivudine drop by drop (10ml) and kept stirring for 1hr on magnetic stirring. Nanoparticles were obtained upon the addition of a TPP aqueous solution to a chitosan solution. [5] The NP suspension is then centrifuged at 15,000 rpm for 10 min using high-speed centrifuge (Sigma). Discard the sediment and the preserve the supernatant. The formation of nanoparticles results in interaction between the negative groups of TPP and the positively charged amino groups of chitosan.

Table1: Formulation of lamivudine nanoparticles

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S.NO	Ingredients	F1	F2	F3	F4	F5	F6
1	Lamivudine	40mg	40mg	40mg	40mg	40mg	40mg
2	Chitosan	0.2%	0.3%	0.35%	0.5%	0.15%	0.050%
3	Tripoly phosphate	40ml	40ml	40ml	40ml	40ml	40ml
4	0.1% Acetic acid solution	100ml	100ml	100ml	100ml	100ml	100ml

III. EVALUATION STUDIES

Organoleptic properties

Color, odor, taste, and appearance play an important role in the identification of the sample and hence they were recorded in a descriptive terminology.

Solubility studies

The solubility of drug and polymer was carried out in various solvents such as distilled water, buffer solutions and organic solvents. The resulting solutions were filtered and analyzed for dissolved drug by measuring absorbance at 271 nm.

Compatability studies*:* Fourier Transform InfraRed Spectroscopy(FTIR) studies.

The fourier transform infrared analysis was conducted for the structure characterization. FTIR spectra of lamivudine, pure polymer and formulated nanoparticles were recorded.

FTIR spectra were recorded on Bomem FTIR MB II Spectrophotometer. Test samples were mixed with KBr, pressed into a pellet and scanned from 400 to 4000 cm^{-1}.

Differential scanning colorimetry

DSC can be used to determine the nature and speciation of crystallinity within nanoparticles through the measurement of glass and melting point temperatures and their associated enthalpies. A complement to X-ray diffraction, this method is regularly used to determine the extent to which multiple phases exist in the interior or to which the various constituents, including the drug, interact.[6]

Characterization of nanoparticles

The optimized nanoparticles containing lamivudine were characterized by studying various physico-chemical properties.

Particle size[6]

Nanoparticle size was determined using Photon Correlation Spectroscopy (PCS). All samples were diluted with ultra-purified water and the analysis was performed at a scattering angle of 90° and at a temperature of 25°C. The mean diameter for each sample and mean hydrodynamic diameter was generated by cumulative analysis in triplicate.

Zeta potential and Surface morphology

Nanoparticles were characterized with Zeta potential using a Zeta Sizer. The measurements were performed using an aqueous dip cell in an automatic mode by placing diluted samples in the capillary measurement cell and cell position is adjusted.The surface morphology of the particles was studied using Scanning Electron Spectroscopy set at from260 nm-632 nm, 200kV by placing an air dried nanoparticle suspension on copper electron microscopy grids.

Drug content

The total drug amount in nanosuspension was determined spectrophotomertically. A 0.50-ml aliquot of nanosuspension was evaporated to dryness under reduced pressure at 35 ◦ c. the residue was dissolved in water and filtered with a 0.45µm filter, and lamivudine content was assayed spectrophotomertically at 271nm.

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$$Total\ Drug\ Conent = \frac{Volume\ total}{Volume\ aliquot} \times drug\ amount\ in\ aliquot$$

Drug entrapment efficiency

The entrapment efficiency is also known as Association Efficiency. The drug loaded nanoparticles are centrifuged at a high speed of 3500-4000 rpm for 30 min and the supernatant is assayed for non-bound drug concentration by UV spectrophotometer. Entrapment efficiency was calculated as follows.

$$DEE\% = \frac{\text{Amount of drug actually present}}{\text{Theoretical drug load expected}} \times 100$$

***In vitro* release studies**

In-vitro diffusion studies (drug release studies) were performed by using diffusion apparatus. A semipermeable membrane was supported on a ring of diffusion cell and the sample was kept on a membrane in such a way backing layer was phased towards donar compartment.[7] The glass beaker was filled with 100ml of phosphate buffer of (ph:6.8) at a temp 37 ◦ csample of 1ml was withdrawn at regular intervals from glass beaker for analysis.1ml of phosphate buffer was replaced immediately after sampling to maintain volume equal to 100ml.The absorbance of sampling was measured at 271nm by using UV spectrophotometer.

IV. RESULT AND DISCUSSION

All the organoleptic characters of lamivudine were studied and it was found that all the characters comply with USP standards.

Table 2: Organoleptic properties.

Properties	**Results**
Description	Crystalline
Taste	Slightly bitter
Odour	Odourless
Colour	White to off white crystalline solid

Solubility

The drug was found to be very soluble in water, pH6.8 phosphate buffer, 1M HCL and pH4.5 acetate buffer.

Compatibility studies (FTIR)

The FTIR spectrum of lamivudine, polymer, and the prepared nanoparticles were studied to detect the compatibility studies. The peaks in the IR spectrum of lamivudine were compared with that of the prepared nanoparticles.

The distinct peaks at 1722.67 shows a C=O stretching, and peaks at 1646, 1591 and 1502 shows at N-H bending. From the above observations we can conclude that, there is no incompatibility between the pure drug and polymer.

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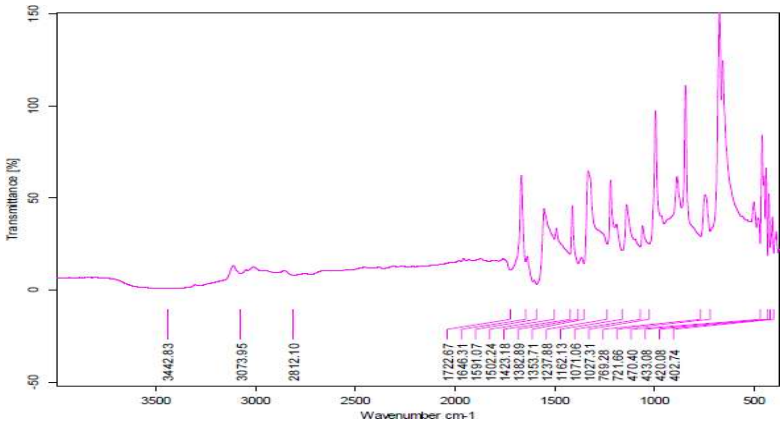

Fig 1: FTIR spectrum of Lamividine and chitosan Differential scanning calorimetry (DSC)

The DSC analysis was carried out for standard lamivudine, chitosan and lamivudine-chitosan mixture. The DSC studies performed in order to determine the compatibility studies. The peak that is obtained for lamivudine in nanoparticles was compared with standard lamivudineand its ensure there was no interaction between drug and drug with polymer.

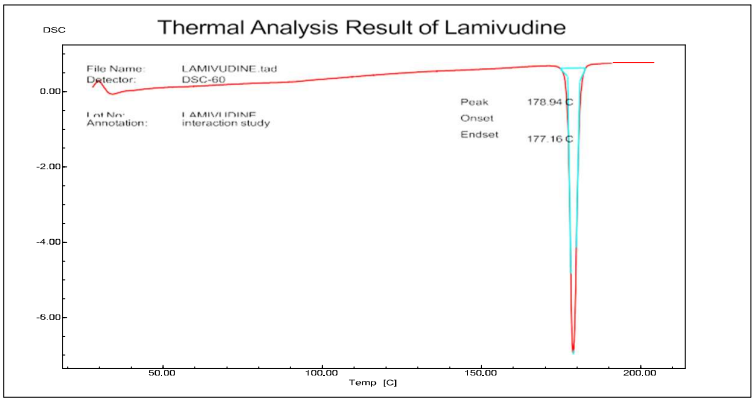

Fig 2: DSC curve of Lamividine

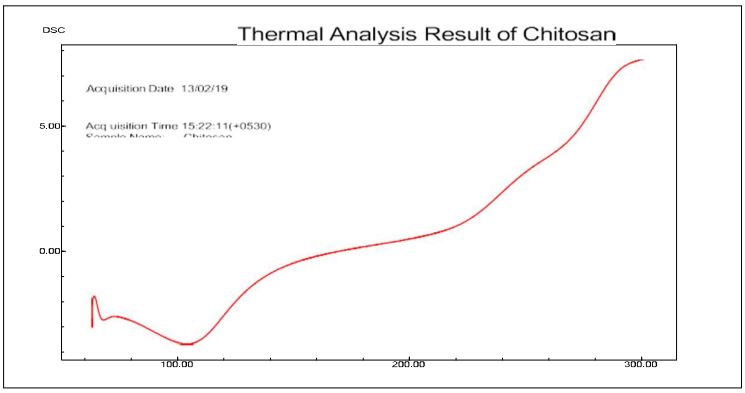

Fig 3: DSC curve of chitosan

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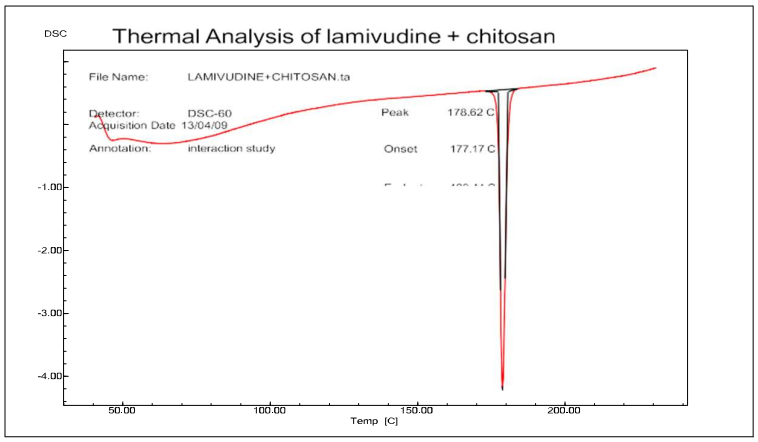

Fig 4: DSC curve of lamivudine and chitosan

Measurement of particle size of Nanoparticles and surface morphology

The particle sizes of prepared nanoparticles were measured from the microphotograph of 100 particles. The particle size ranged from 260 to 632 nm for various batches.

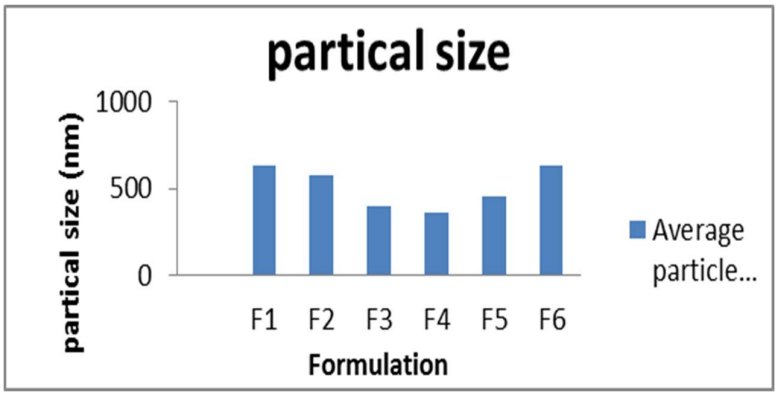

Fig 5: Particle size of lamivudine NP formulations

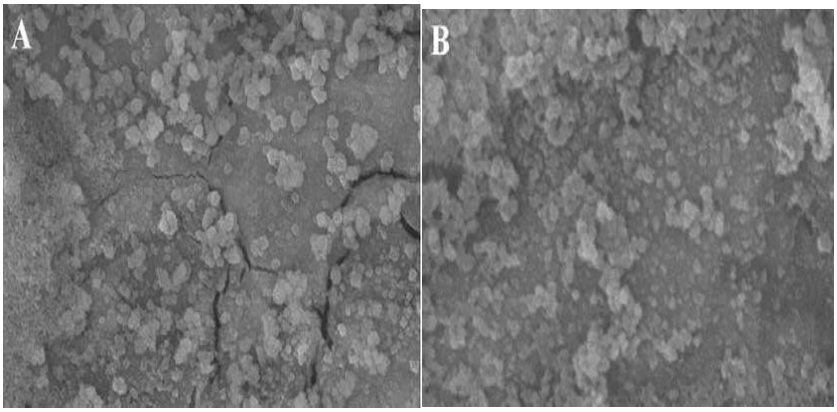

Fig 6: Lamivudine chitosan loaded nanoparticle

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Drug content and entrapment efficiency

The total drug amount in nanosuspension was determined spectrophotomertically. A 0.50-ml aliquot of nanosuspension was evaporated to dryness under reduced pressure at 35 ◦ c. the residue was dissolved in water and filtered with a 0.45µm filter, and lamivudine content was assayed spectrophotomertically at 271nm

Table 3: Drug content and entrapment efficiency of lamivudine nanoparticle formulations.

Formulation	Drug cont (%)	ge entrapmentefficiency
F1	65.4	57.1%
F2	58.8	65.26%
F3	80.2	68.14%
F4	86.7	70.87%
F5	72.4	62.41%
F6	81.7	59.28%

***In vitro* release studies**

In vitro diffusion studies (drug release studies) were performed by using diffusion apparatus

.A semi permeable membrane was supported on a ring of diffusion cell and the sample was kept on a membrane in such a way backing layer was placed towards donor compartment.

The formulation F1 shows 78.9% of drug release at the end of 24 hr The formulation F2 shows 80.42% of drug release at the end of 24 hrThe formulation F3 shows 84.06% of drug release at the end of 24 hr

The formulation F4 shows 97.9% of drug release at the end of 24 hr compared to other formulation. The rate of release was based on concentration of a polymer, if the concentrationof polymer increase the rate of release of a drug was slow. Based on the solubility nature ofan polymer the drug will get release slowly in a desire amount at the particular site of action there by fluctuation of drug was avoided and the plasma concentration of an drug was maintained there by the therapeutic action of an drug was more at the site of action there by the side effects were avoided.

The formulation F5 and F6 shows 90 % of drug release with in 10 hrs. there by the sustained action of an drug at the targeted site was not obtained.

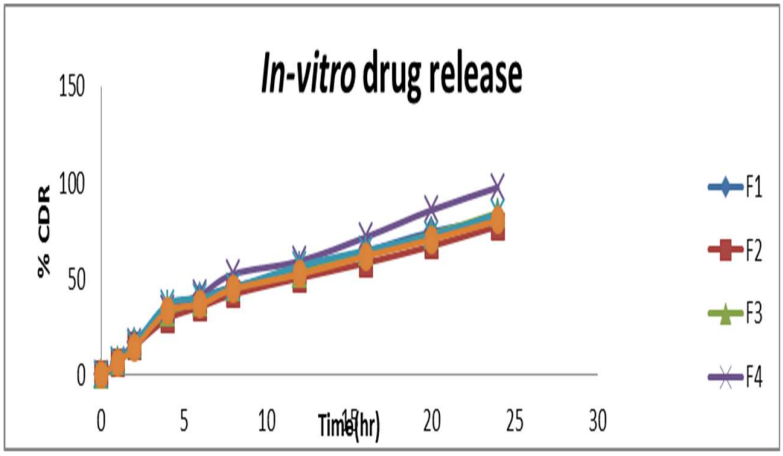

Fig 7: *In-vitro* release of lamivudine nanoparticals CONCLUSION

The F4 formulation with the lamivudine concentration of 40mg provided the highest entrapment efficiency of 70.87% when compared to that of other formulations and the highest extent of release (97.67%at 24thhr) suggesting the possibility to achieve a therapeutic doseand would be capable of reducing the frequency of administration and the dose-dependent side effects associated with the repeated administration of conventional lamivudine tablets. According to the data

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obtained, this chitosan-based nanotechnology opens new and interesting perspectives for anti HIV and antihepatitis B activity.

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