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Formulation and Evaluation of Lamivudine Microspheres

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ABSTRACT

Objective: *Using lamivudine as a model Drug, the present research investigation focuses on the development and evaluation of microspheres using naturally occurring xanthan gum and guar gum in terms of their efficacy, biodegradability, affordability, and ability to regulate drug release rate.*
Methods: *Lamuvidine microspheres were prepared by the solvent evaporation method with the aid of guar and xanthan gum as rate-controlling agents. The developed tablets were subjected to various pharmacopoeial tests. Using a USP type-II tablet dissolution test apparatus, the in-vitro drug release rate was performed, and the data was fitted to kinetic modeling.*
Results: *The resulting microspheres were found to be freely flowing and had a soft yellow tint. For all nine formulations, the spherical shape and size range of 100µm to 200µm were deduced from the Scanning Electron Microscopy (SEM) examinations. When the concentration of xanthan gum increases, there is a decrease in the in-vitro drug release. The release rate is zero order and Fickian diffusion controlled. Studies on stability were conducted, and the results show that the chosen formulation was stable.*
Conclusion: *Our analysis of the data leads us to the conclusion that microspheres provide a workable and appropriate method for preparing controlled release of Lamuvidine, with naturally occurring xanthan gum acting as a rate-controlling agent to improve bioavailability and lower dosage frequency.*

Keywords: *Lamivudine, rate controlling polymers, Guar Gum, Xanthan Gum, Solvent evaporation.*

INTRODUCTION

The human immunodeficiency virus (HIV) is the cause of acquired immune deficiency syndrome (AIDS), an immune system illness. The AIDS Education and Research Trust, or AVERT, projected in 2009 that 33.3 million individuals worldwide were living with HIV/AIDS, that there were 2.6 million new HIV infections year, and that there were 1.8 million AIDS-related fatalities. Reverse transcriptase, a viral enzyme, copies the single-stranded viral RNA genome into double-stranded viral DNA when HIV infects a cell. After being integrated into the host's chromosomal DNA, the virus can then replicate within the host cell through activities including transcription and translation. Reverse transcriptase inhibitors inhibit the enzymatic activity of reverse transcriptase and stop the double-stranded RNA from being fully synthesised.[1]

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Lamivudine belongs to the group known as nucleoside reverse transcriptase inhibitors (NRTIs). It is an analogue of nucleoside that was first approved for the treatment of HIV. It can now be used to treat chronic hepatitis B in patients who show signs of viral replication. Conventional oral formulations of Lamivudine for the treatment of AIDS prescribe a daily dosage of 300 mg (i.e., 150 mg twice daily, many times a day). having a mean elimination half-life (t½) of 4 to 6 hours, a peak serum concentration of lamivudine (Cmax) of 1.5 ± 0.5 mcg/mL, and an absolute bioavailability of 86% ± 16%. Hence, in order to maintain consistent therapeutic drug levels, regular administration must be given for an extended length of time (lifelong in AIDS patients and one year in hepatitis patients).

The term "microsphere" refers to solid, roughly spherical particles with sizes between 1 and 1000µm.They are composed of modified natural goods such starches, gums, proteins, lipids, and waxes, as well as biodegradable synthetic polymers, polymeric, and other protective components. Microspheres have a large surface-to-volume ratio and are tiny. They have colloidal properties at the smaller end of their size range. Microspheres' interfacial characteristics, which frequently include their activity, are crucial.[2]

The method used to prepare microspheres improves the therapeutic efficacy of the drug being administered and provides a number of options for controlling its administration. There exist various methods for administering a medicinal material to the intended location in a controlled, continuous release manner. Using microspheres, commonly referred to as micro particles, as medication carriers is one of the main strategies. A well-thought-out controlled drug delivery system can improve a given medicine's therapeutic efficacy and solve some of the issues with traditional therapy. [3]

Natural polymers can be used orally as food additives or medication carriers because they are biodegradable in the environment. Natural gums have several benefits over synthetic ones, including being more widely available, less expensive, less poisonous, and biocompatible. Because colonic bacteria and enzymes found in the distal part of the gastrointestinal tract break down gums, biodegradability also has the benefit of granting the ability for full medication release from the dosage form. [4]

The main reason biodegradable natural polymers are still popular is that they are naturally occurring byproducts of living things that can undergo a wide range of chemical changes. Agar, Guar gum, Chitosan, Gelatin, Carboxy methyl cellulose, Xanthan gum, Sodium alginate, and lotus bean gum are a few examples of natural gums that may be used in pharmaceutical and biomedical applications. [5]

MATERIALS AND METHODS

Materials

A free sample of Lamivudine was acquired from PM Pharmaceutical Pvt. Ltd, Hyderabad Xanthan gum, obtained from Techno Scientific Products, Bangalore, as an encapsulating polymer, petroleum ether, glutaraldehyde as a crosslinking agent obtained from ML Chemicals, Coimbatore. Analytical grade solvents and chemicals were utilized only.

Preparation of Lamivudine microspheres (Solvent Evaporation)

Microspheres were prepared by using different ratios of drug: natural gum (1:1.15, 1:1.20, 1:1.25). Gums were allowed to hydrate in 20 ml water for 3 hrs. Weighed quantity of drug (100mg) was dispersed in 10 ml of methylene chloride and adds the aqueous solution of gum.

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The above drug-gum dispersion was acidulated with 0.5 ml of concentrated sulphuric acid to give a clear viscous solution. The resultant solution was emulsified into the oily phase by poured into 200 ml of paraffin liquid containing 0.5 % w/w span 80 as an emulsifying agent. Stirred mechanically at 1800 rpm for 210 min using a stirrer and heated by a hot plate at 500C. 1.2 % w/v dichloromethane was added as encapsulating agent and 0.15 % w/v of gluteraldehyde as crosslinking agent, stirring and heating were maintained for 2.5 hrs until the aqueous phase was completely removed by evaporation. The oil was decanted and collected microspheres were washed with water to remove surfactant residue and three times with 100 ml aliquots of n-hexane, filtered through whatman filter paper, dried in an oven at 800C for 2 hr to collect discrete, solid, free flowing microspheres and stored in a desiccator at room temperature. The formulations are shown in Table 1. [6]

Table 1: Formulae for the Preparation of Lamivudine Microspheres

Name of Ingredients	Quantity of Ingredients								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lamivudine (mg)	100	100	100	100	100	100	100	100	100
Xanthan Gum (mg)	15	20	25	30	-	-	-	-	-
Guar Gum (mg)	-	-	-	-	15	20	25	30	35
Liquid Paraffin (mL)	200	200	200	200	200	200	200	200	200
Span 80 (v/v)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Evaluation Tests for prepared Formulations

Particle Size

The particle size of the microspheres was determined by using optical microscopy method. Approximately 100 microspheres were counted for particle size using a calibrated optical microscope. [7]

Morphological Study using Scanning Electron Microscopy

The morphological study was carried out by Scanning Electron Microscope (SEM). Microspheres were scanned and examined under Electron Microscope HITACHI SU 1500, Japan connected with Fine coat, JEOL JFC-1100E Ion sputter. The sample was loaded on copper sample holder and sputter coated with carbon followed by Gold. [8]

In-vitro Dissolution Study

Three distinct appropriate dissolving fluids were used to successively release drugs into the produced microspheres in vitro. The dissolving apparatus was USP type II. For the first two hours, 900 ml of 0.1 N HCl (pH 1.2) was used as the dissolution medium. For the following seven hours, phosphate buffer pH 6.8 was used. The dissolving media was kept at 37 ±0.5°C while the basket revolved at 50 revolutions per minute. To keep sink conditions constant, a 5-milliliter aliquot was removed at prearranged intervals and replaced with an equivalent volume of new dissolving medium. Using a UV-visible spectrophotometer, samples' absorbance was measured at 272 nm and the data was subjected to kinetic modeling. [9-10]

RESULTS AND DISCUSSION

Using polymers like Xanthan Gum and Guar Gum for the Lamivudine microspheres using solvent evaporation technique as per formulae presented in Table 1.

Table 2 displays the average particle size of the microspheres as assessed by optical microscopy using stage and ocular micrometers. The formulations F1 through F4 that contained Xanthan gum were found to have mean particle sizes ranging from 275±10.39 µm

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to 910±9.5 µm. The mean particle size ranged from 569±13.41 µm to 997±4.54 µm for formulations F4 to F9 that contained guar gum, respectively. The microspheres' particle sizes grow in proportion to the rise in polymer concentration from F1 to F9. This is due to the fact that when the concentration of the polymer increases, the viscosity of the polymer solution also rises, reducing the efficiency of stirring.

Table 2: Average Particle Size of Lamivudine Microspheres

Formulation code	Average particle size (µm)±SD
F1	910±9.5
F2	838±13.3
F3	453±15.24
F4	275±10.39
F5	997±4.54
F6	741±10.35
F7	648±9.03
F8	587±12.92
F9	569±13.41

The form and surface morphology were determined using a Japanese HITACHI SU 1500 scanning electron microscope. All of the prepared microspheres had a spherical shape, according to SEM analysis of the samples. In contrast to the porous, rough, substantially discrete spherical microspheres of xanthan gum, the lamivudine with guar gum microspheres were smooth, spherical, and somewhat aggregated particles. Figure 1 displays scanning electron photomicrographs of formulations F1 and F5.

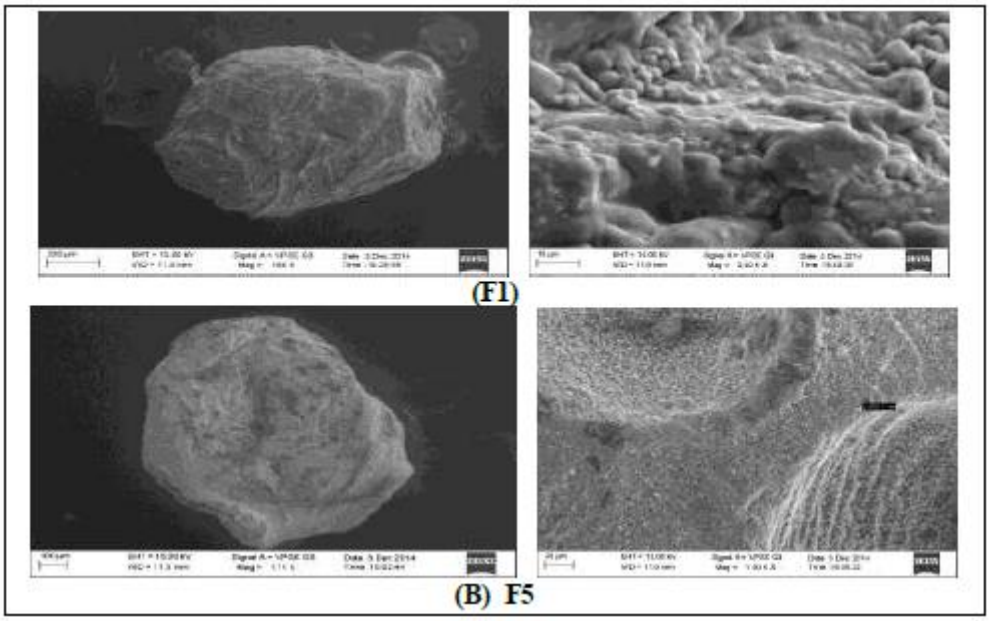

Figure 1: Scanning Electron Microscopic Images of Formulation F1 and F5.

With a USP dissolving equipment Type II, dissolution studies were conducted on all nine formulations of Lamivudine microspheres. As the dissolution medium, 0.1 N HCl (pH 1.2) and pH 6.8 were utilized. For formulations F1, F2, F3, and F4, the cumulative percent drug release after 12 hours was found to be 81.73, 79.04, 76.39, and 71.56%, respectively; for

formulations F5 to F9, the cumulative percent drug release after 12 hours was 82.14, 80.57, 74.48, 69.11, and 63.57%. The Dissolution profiles for all formulations presented as Figure 2.

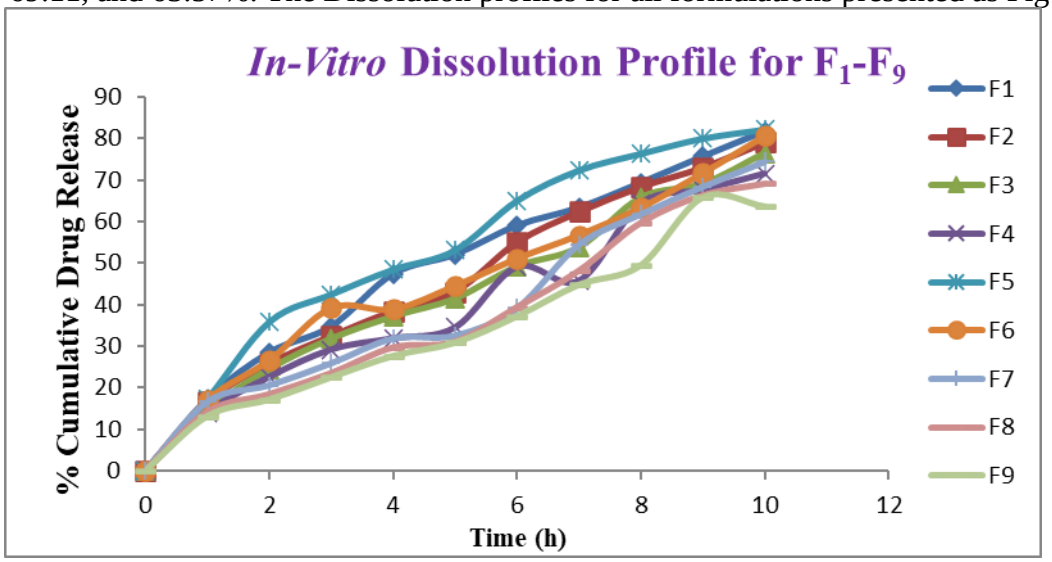

Figure 2: Comparative In-vitro Dissolution Profiles for Lamivudine Microspheres

An increase in polymer concentration resulted in a considerable decrease in cumulative medication release. Diffusional path length increases with increasing concentrations due to the polymer matrix's increased density. This might lessen the drug's overall release from the matrix of polymers. Moreover, smaller microspheres with a larger surface area exposed to the dissolving liquid and a lower polymer content result in faster drug release. The results presented in Table 3.

Table 3: Kinetic parameters

Formulation code	Kinetic Parameters				
	Korsmeyer–Peppas		Higuchi	First order	Zero order
	R	n	R	R	R2
F1	0.9405	0.4596	0.9633	0.8892	0.9893
F2	0.9352	0.4480	0.9687	0.8979	0.9834
F3	0.9239	0.4408	0.9499	0.8678	0.9552
F4	0.943	0.4374	0.9748	0.9084	0.9914
F5	0.9466	0.4574	0.9748	0.9103	0.9868
F6	0.9349	0.4231	0.9618	0.8874	0.9636
F7	0.967	0.4460	0.9908	0.9304	0.9961
F8	0.972	0.4192	0.9885	0.9479	0.9942
F9	0.9676	0.4358	0.9855	0.9471	0.9896

CONCLUSION

In order to improve treatment for HIV and chronic hepatitis B, the current study describes a novel attempt to create lamivudine microspheres using natural gums like xanthan gum and guar gum as carriers. Lamivudine microspheres were made using the solvent evaporation technique. A range of assessment metrics were evaluated in order to achieve a controlled release of lamivudine.

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A considerable decrease in cumulative percentage of medication release was seen as the polymer concentration increased. It was discovered that the overall curve that fit into different mathematical models was average. The medication was released from the formulations F1 through F9 by a non-Fickian diffusion mechanism, and the formulations fitted well to the zero-order kinetic model.

In order to prolong the drug's retention in the gastrointestinal tract, the prepared microspheres appear to be a promising option for an oral controlled drug delivery system.

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REFERENCES

1) Vamshi Allam K, Dr Praveen Kumar G, Vishvasa Cheruku, Anand Jannu, Chaitanya Kumari Bairi.Controlled and sustained release approaches in developing suitable dosage forms for the Antiretroviral drug Lamivudine.2011;8(1):21-27.
2) Raghavendra Kumar Gunda, J.N. Suresh Kumar, KNVL Padmaja, Gajja Bhargavi, A. Bhavani Satya Prasad, Bodepudi Sandhya, Sriram Praveen. A short review on Microspheres. A.N.U Journal of Pharmaceutical Technology & Research.2022;14(1):40-6.
3) Sahil K, Akanksha M, Premjeet S, Bilandi A, Kapoor B. Microsphere: A Review. Int J Res Pharm Chem 2011;1(4):1184–98.
4) Patel PK, Pandya SS . Preparation and Characterization of Crosslinked Gum Acacia Microspheres by Single Step Emulsion In-Situ Polymer Crosslinking Method: A Potential Vehicle for Controlled Drug Delivery. J Pharm Pharm Sci. 2013;2(1):40–8.
5) T.S.Keerthi, S. K. Senthil Kumar: Formulation and Evaluation Of Microspheres Of Losartan Potassium Using Biodegradable Natural Polymers. International Bulletin of Drug Res. 2010; 1(2):120-131.
6) Anjana J, Hukuman Z, D.V.Gowda.Preparation,Evaluation and vioavailability studies of propafenonr hydrochloride loaded with gum microspheres for controlled study. Int J Pharm Bio Sci 2013; 4(2):1036-1049.
7) Liberman H, Lachman L. The Theory and Practice of Industrial Pharmacy. 3rd ed. Bombay: Verghese Publication House; 1991; 171-93.
8) Martin A, Micromeretics. In: Martin A, ed. Physical Pharmacy. Baltimores, MD: Lippincott Williams and Wilkins; 2001.423-54.
9) Chavda Y, Bhimani B, Patel G, Daslaniya D. IJPRBS Preparation and evaluation of Lamivudine Microspheres with eudragit ® polymers by solvent evaporation method for lymphatic system. International Journal of Pharmaceutical Research and Bio-Science. 2013;2(3):89–106.
10) Raghavendra Kumar Gunda, Suresh Kumar JN, Chandan Kumar Brahma, Satyanarayana V. Design, Formulation and Evaluation of Lamivudine Controlled ReleaseTablets. Pharmaceutical and Biological Evaluations.2015;2(4): 110-21.