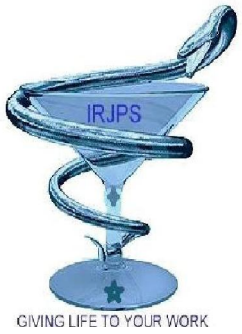
REVIEW



ISONIAZID LOADED DENDRIMER BASED NANO CARRIERS FOR THE DELIVERY OF ANTI TUBERCULOSIS

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ABSTRACT

The current study was designed todeveloping and discovering the usage of PPI dendrimers for delivery of anti-tuberculosis drug Isoniazid. INH was designated for assimilation into dendrimers established on hisant tubercular activity, solubility characteristics and short biological half-life. For this study, poly (propylene mine) dendritic design was loaded throughIsoniazid. Manyphysiological and physicochemical factors like UV, FT-IR, and drug release of formulations remained determined. The study was initiate to have rises their drug-loading capacity, reduced their drug release rate. Consequently the system has establish to be proper for extended delivery of Isoniazid.

KEY WORDS: PPI dendrimers, drug delivery system, Isoniazid, Prolonged release.

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INTRODUCTION

Tuberculosis is an extremely infectious determined infection caused by *Mycobacterium bovis* and *Mycobacterium tuberculosis* has maximum impermanence rate than any other communicable disease. There are numerous difficulties in treatment. It essentially get rears to the fashionable construction of the Tuberculosis that might source drug.[1] Acute tuberculosis is normally preserved with a multidrug therapy methodology, including pyrazinamide or rifampicin but Isoniazid mono therapy is typically used in the administration of dormant tuberculosis.Dendrimers are a curious class of synthetic macromolecules taking extremely branched, Nano scale, three dimensional design through very low poly disparity or high functionality. The word "dendrimer" initiated from two words the Greek word "Dendron", significance tree, and "meros", significance as part. Dendrimers are unlike after customary polymers in that they take a three dimensional architecture, multi-branched with very low poly disparity and high functionality.[2, 3]

Synthesis of dendrimer

i. Divergent growth method
ii. Convergent Dendrimer Growth
iii. Hyper cores and 'Branched Monomers'
iv. Double Exponential' or mixed

Dendrimer as drug delivery agent is reliable or safe and selective drug delivery method. Its vital property is selectively targeting the wanted tissue. It is taking talented prospect for the management of numerous disorders. Extra properties similar very small in size, poly valiancy, good stability makes it a good carrier for delivering drugs with precision and selectivity. Dendrimers are normally used to growth bioavailability especially sustained or controlled and targeted release of drug could be attained. The current study was proposed at evolving and sightseeing the use of PPI dendrimers for delivery of anti-tuberculosis drug. Isoniazid was designated for integration into PPI dendrimers established on its ant tubercular activity or short biological half-life.[4, 5]

MATERIALS

The following materials were used: Isoniazid obtained from Balaji Drugs, dialysis bag (MWCO 12-14 Kda, HI media, India), Methyl acrylate form Loba Chemical Pvt.Ltd., Methanol or Ethylenediamine form Loba Chemical Pvt.Ltd. All reagents used were of analytical grade.

Preparation of 1.5 G Pamam Dendrimers

2 gm. of 1 generation Methyl Acrylate were dissolved in suitable amount of methanol in amber colored round bottom flask which was corked tightly and then kept for 94 hours. After the Evaporate the methanol on water bath and observed under UV and FTIR Spectra.

Evaluation of 1.5 G Pamam Dendrimers

1. Colour test

PAMAM dendrimers were treated with aqueous solution of copper sulphate (1%w/v)[6]

2. Ultraviolet Spectroscopy

0.01% w/v concentration of PAMAM dendrimers was scanned in the range of 200 nm to 400 nm against distilled water. The changes in λ_{max} values were analyzed [7-8]

3. FT-IR Spectroscopy

The 1.5 G PAMAM dendrimer were subjected to FT-IR spectroscopy analysis.[9]

Drug loading in formulation

Drug loading was carried out by dialysis method .The amount of1.5 G PPI dendrimers and Isoniazidwere dissolved in methanolic solution. The solution werewith slow magnetic stirring (50 rpm) using Teflon beads for 30 Mins and kept for 24 Hours.These solution were dialyzed twice in cellulose dialysis bag (MWCO 12-14Kda, HI media, India).Which were then estimated spectrophotometrically at under (UV-VISIBLE spectrophotometer) to determine indirectly the amount of drug loaded within the system.

UV Spectroscopy

Compatibility study of drug with the excipients was determined by using by using Double Beam UV-Visible Spectrophotometer (UV-1800) manufacturer

was (200-400) nm by Shimadzu Corporation .The λ max of Isoniazid, Dendrimers + Isoniazid complex was found to be 262 nm and Dendrimers found to be 280 nm.

Fourier Transform Infrared Spectrophotometer (FTIR)

Compatibility study of drug with the excipients was determined by using opus 5.0 - FTIR. In this study individual samples of pure drug (Isoniazid), i.e. Isoniazid and dendrimers complex prepared formulation i.e. Isoniazid loaded PPI dendrimers were analyzed by IR spectroscopy using FT–IR module.

Results and Discussion

UV Spectroscopy

The Standard Solution of Isoniazid deionized water and pH 7.4 Phosphate buffer (10µg/ml), PPI dendrimers, and Isoniazid Loaded PPI dendrimers, was Scanned (200-400) nm by using Double Beam UV-Visible Spectrophotometer (UV-1800) manufacturer by Shimadzu Corporation.

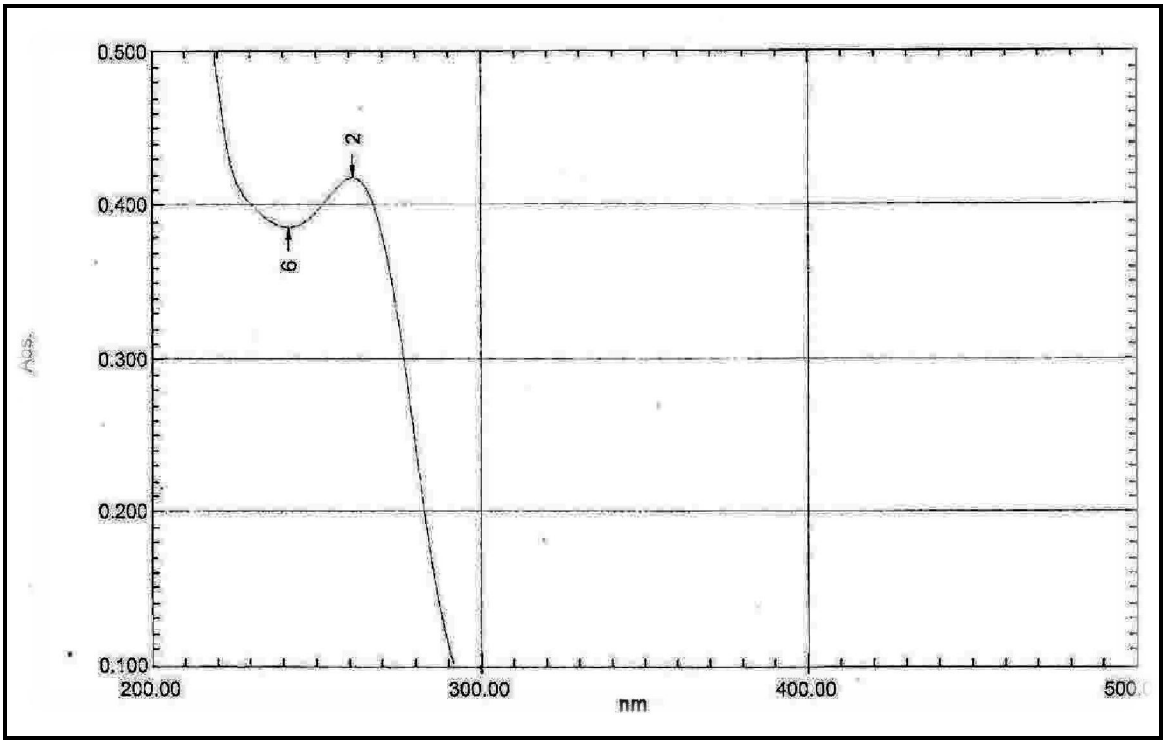

Figure 1: UV spectrum of Isoniazid in pH 7.4 Phosphate buffer

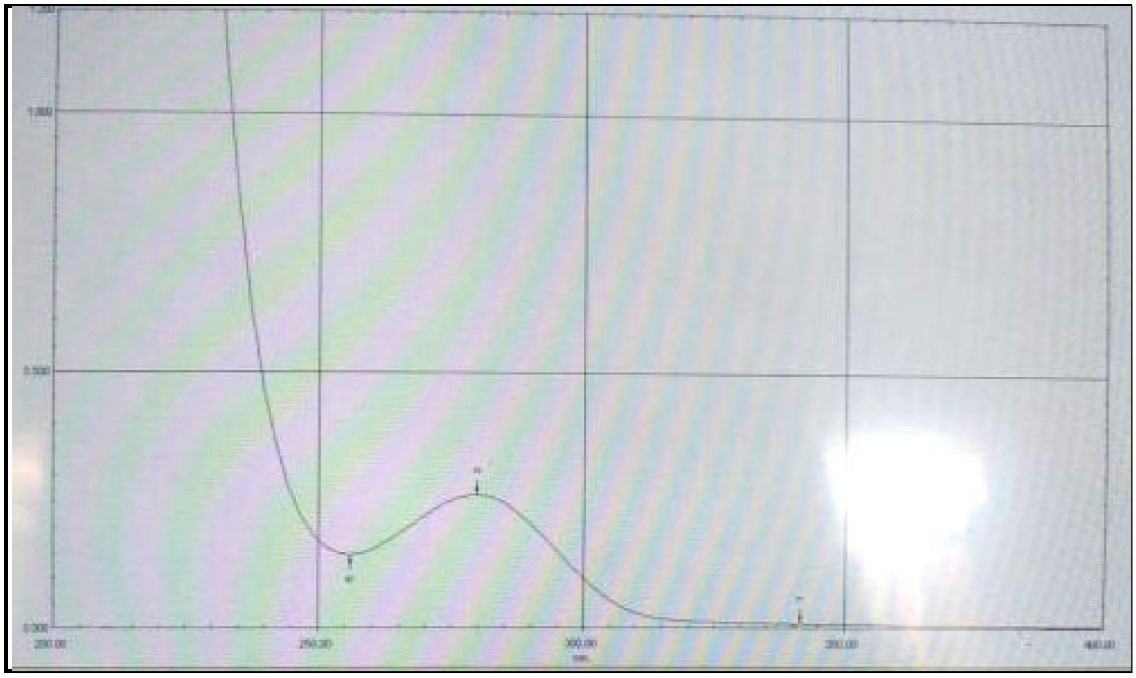

Figure 2: UV spectrum of Dendrimer

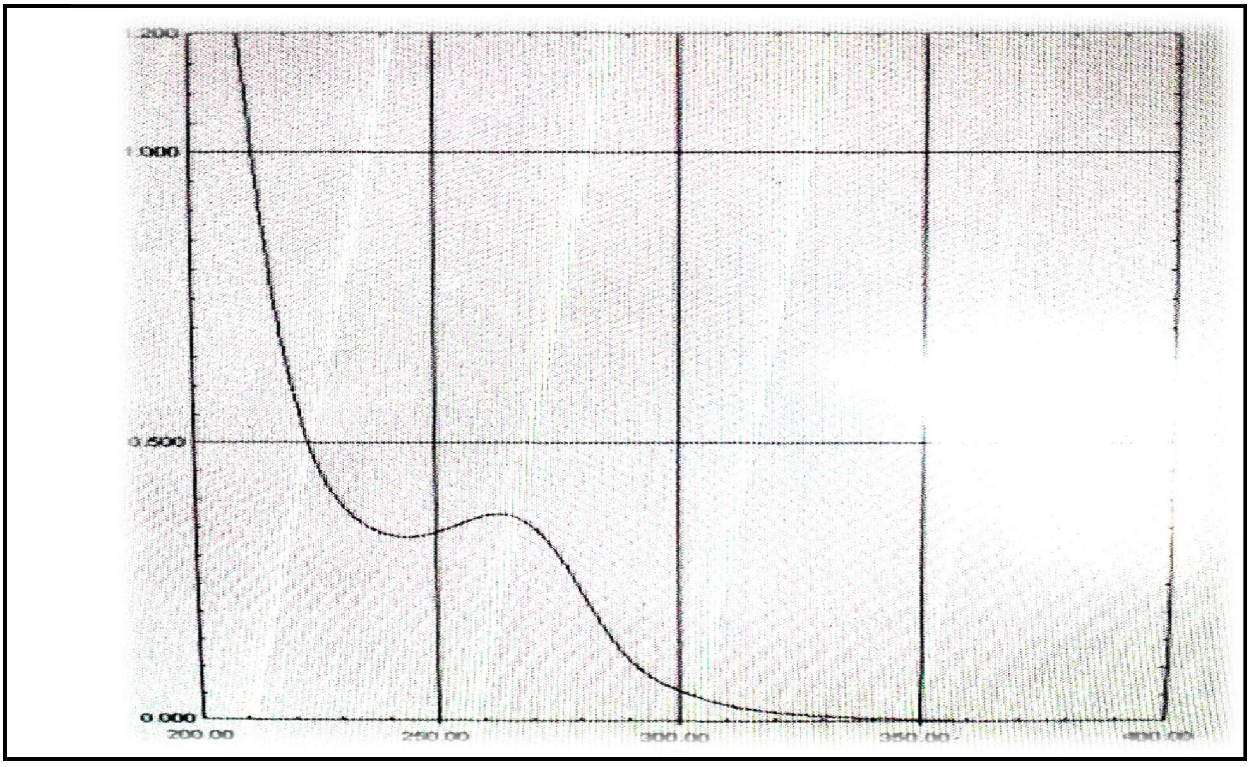

Figure 3: UV spectrum of Dendrimer + Isoniazid Complex

Color Test of dendrimer:10 drops of 10% Copper sulphate [$CuSO_4$] reagent was taken in a small test tube and 2 drops of dendrimers was added to it

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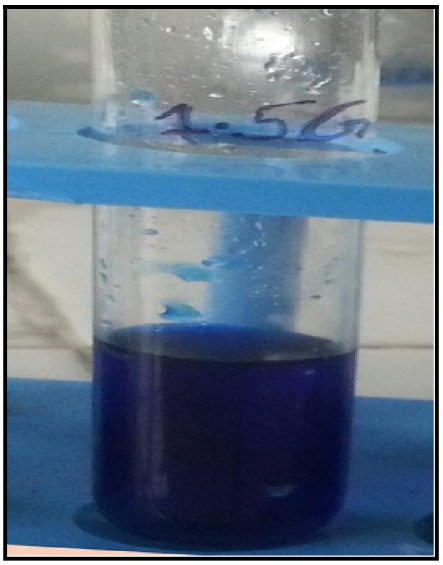

Figure 4: Copper Sulphate Test of Dendrimer

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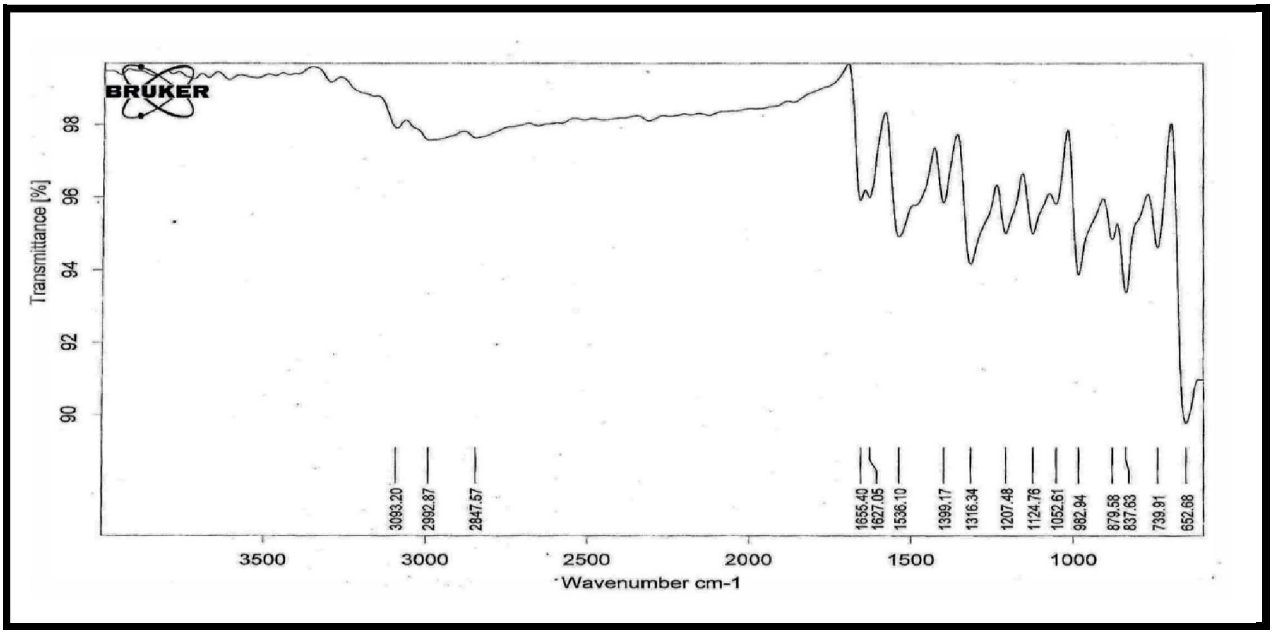

Figure 5: FTIR Spectrum of Isoniazid

Table No 1: FTIR Spectrum of Isoniazid showing different wave number with Assignment

Sr.No	IR Absorption Band (cm-1) (Experimental)	IR Absorption Band (cm -1) (Literature)	Functional Groups
1.	3093.2	3100-3000	N-H Asymmetric Stretching
2.	2992.8	2990-2900	C-H Symmetric Stretching
3.	1655.4	1689-1471	C=O stretching
4.	1627.0	1635	C=N Asymmetric Stretching
5.	1536.1	1540	Pyridine Nitrogen
6.	1399.1	1342	C-N Stretching
7.	1207.4	1210	Ring C-C-H Asymmetric Bending
8.	1124.7	1140	N-X Stretching (X = NH_2)
9.	1052.6	1020	Ring C-C-N Asymmetric Bending
10.	982.9	924	Ring C-C-N Symmetric Bending
11.	879.5	888	Ring C-N-C Bending
12.	739.9	745	Ring C-C-N Asymmetric Bending

FTIR spectrum of 1.5 G Pamam Dendrimers:

FTIR spectrum of 1.5 G Pamam Dendrimers was performed using wave 4000 to 600 Cm^{-1}.Observed wave number are shown in figure 6 along with assessment of some specific groups enlisted in table No 2 confirmed the presence of 1.5 G Pamam Dendrimers

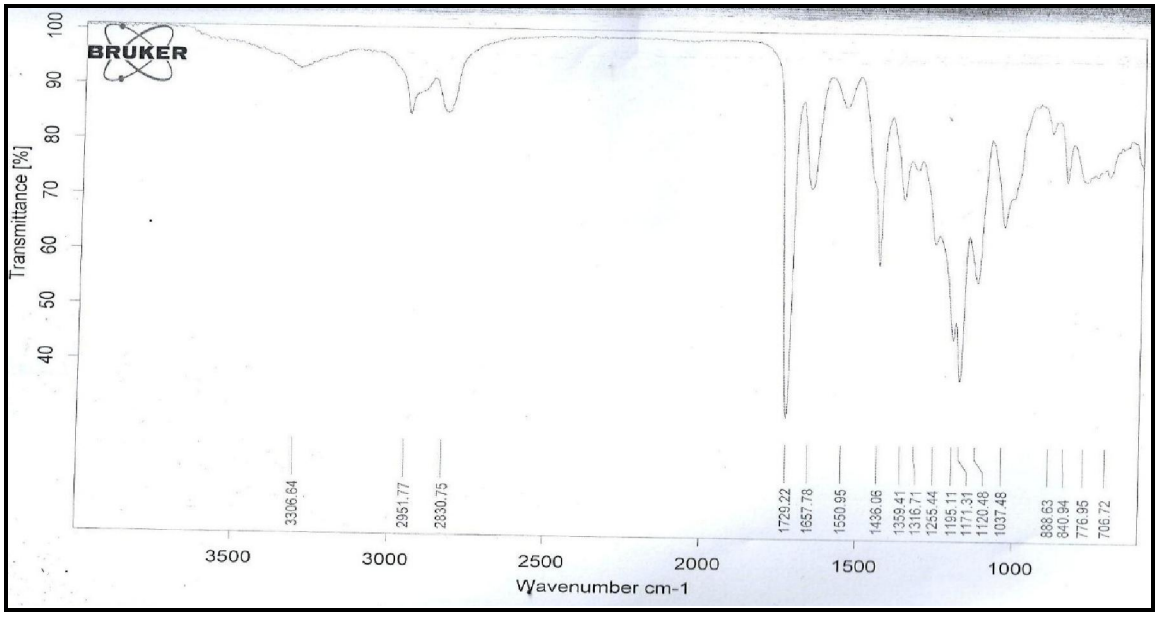

Figure 6: FTIR Spectrum 1.5 G Pamam Dendrimers

Table No 2: FTIR Spectrum of 1.5 G Pamam Dendrimers showing different wave number with Assignment

Sr.No	IR Absorption Band (cm-1) (Experimental)	IR Absorption Band (cm -1) (Literature)	Functional Groups
1.	3306	3220	Secondary N-H stretching
2.	2830	2888, 2850	Aliphatic C-H stretching
3.	1729,1657	1710, 1605	Aromatic C=N stretching),
4.	1037	1052	C-O stretching
5.	776	786	C-Cl stretching

FTIR spectrum of 1.5 G Pamam Dendrimers + Isoniazid Complex:

FTIR spectrum of 1.5 G Pamam Dendrimers + Isoniazid Complex was performed using wave 4000 to 600 Cm^{-1}.Observed wave number are shown in figure 7 along with assessment of some specific groups enlisted in table No 3 confirmed the presence of 1.5 G Pamam Dendrimers + Isoniazid Complex.

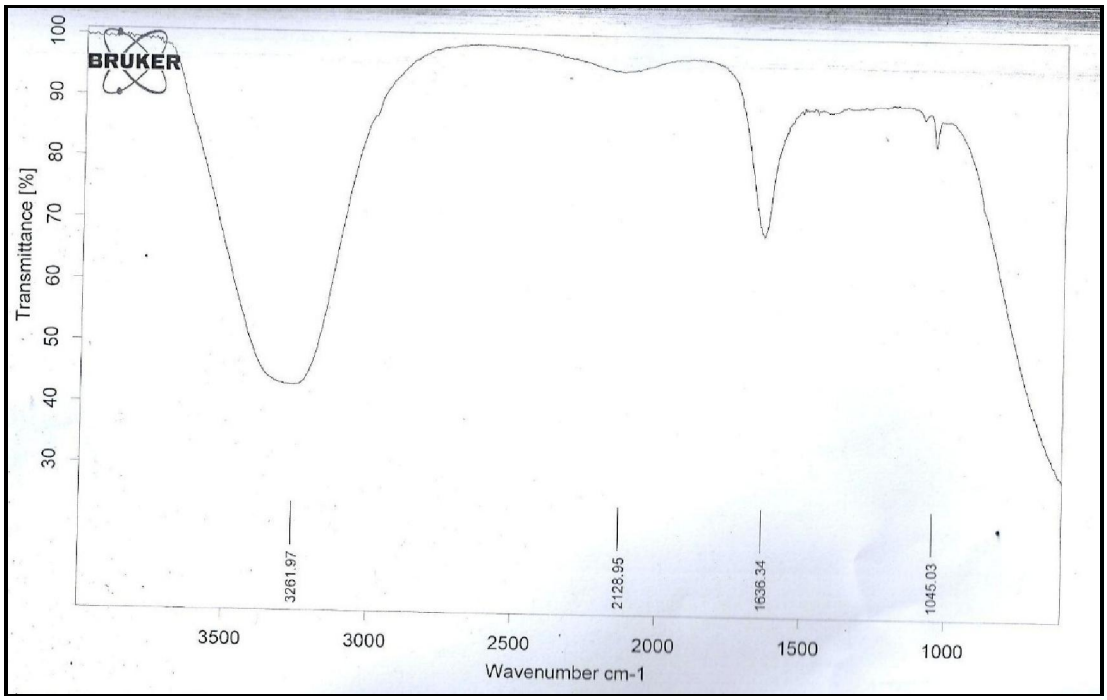

Figure 7: FTIRspectrum of 1.5 G Pamam Dendrimers + Isoniazid Complex

Table No 3: FTIR Spectrum of 1.5 G Pamam Dendrimers+ Isoniazid Complex showing different wave number with Assignment

Sr.No	IR Absorption Band (cm-1) (Experimental)	IR Absorption Band (cm -1) (Literature)	Functional Groups
1.	3261	3220	Secondary N-H stretching
2.	16.38	1635	C=N Asymmetric Stretching
3	1037	1052,1020	C-O stretching, Ring C-C-N Asymmetric Bending

Table 4. Cumulative percentage release of formulations in- vitro drug release profile

Sr.No	Formulation Code	Dendrimers (mg)	(Isoniazid mg)	Cumulative percentage release
1	F1	30	3	93.25 %

Table 5: *In-Vitro* Kinetic data of Isoniazid Loaded dendrimers.

Formula Code	Zero-order Plots	First-order Plots	Higuchi's Plots	Koresmeyer-peppa's plot	Possible Drug release Mechanism
	Regression Coefficients (R^2)	Regression Coefficients (R^2)	Regression Coefficients (R^2)	Regression Coefficients (R^2)	
F1	0.985	0.941	0.933	0.846	Zero order Non-Fickian release

The graph was plotted between time (hours) and percentage (%) cumulative release and the following graph was obtained

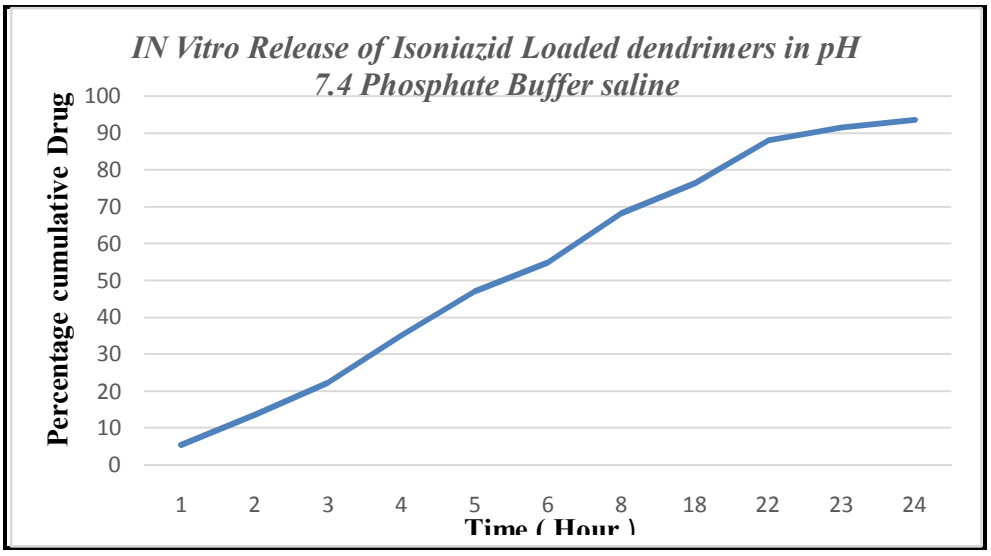

Figure 8: In Vitro release study of Isoniazid Loaded dendrimers.(Mean ±S.D. n=3).

Kinetic Mathematical Release Models:

1. Zero order release kinetics Model:

The graph was plotted between % cumulative drug releases vs. time

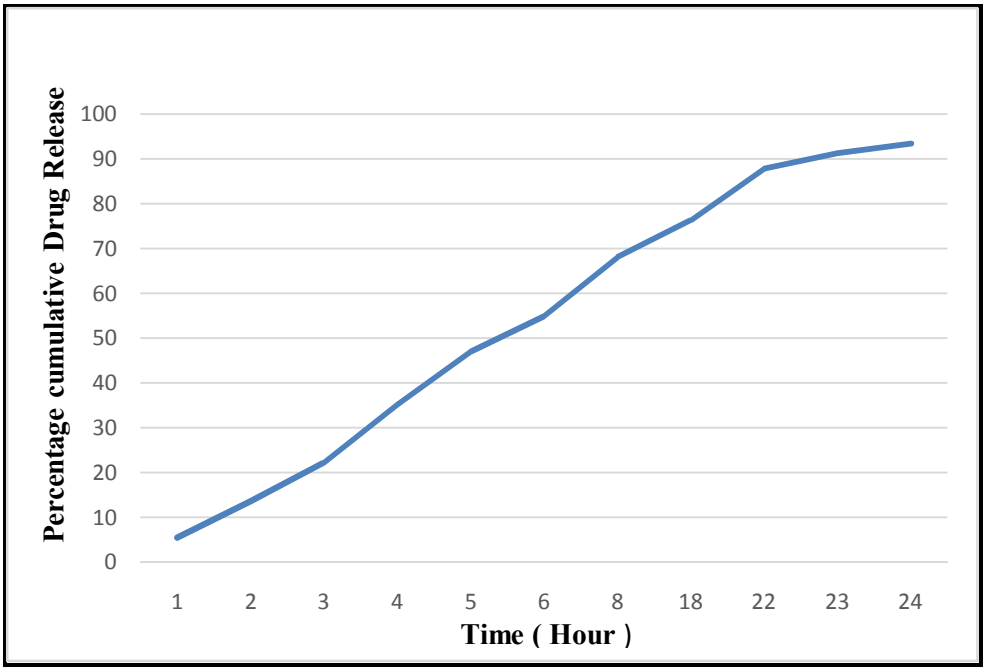

Figure 9:Zero order drug release from Isoniazid Loaded dendrimers. (Mean ±S.D. n=3).

2.First order release kinetics Model:

The graph was plotted between Log % cumulative drug releases vs. time

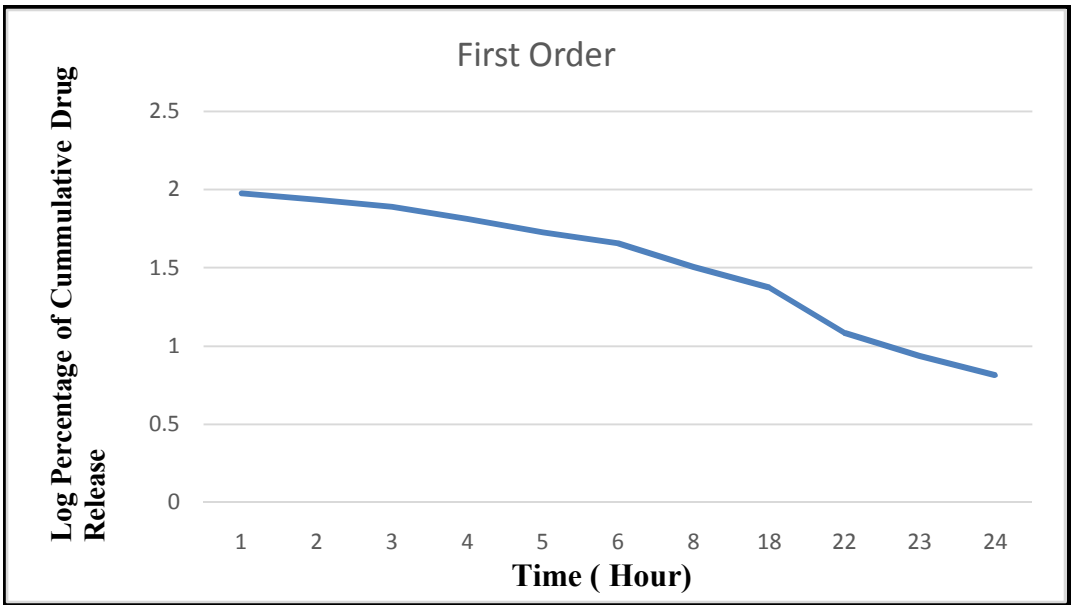

Figure 10:First order drug release from Isoniazid Loaded dendrimers. (Mean ±S.D. n=3).

3. Higuchirelease kinetics Model

The graph was plotted between% cumulative drug releases vs. Square root of time

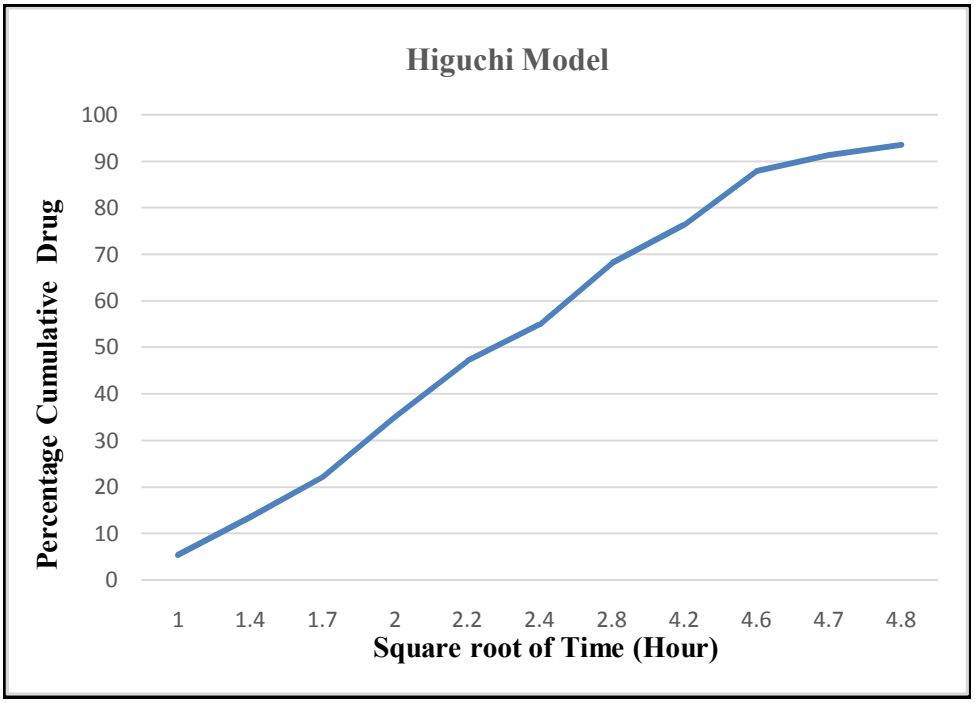

Figure 11:Higuchirelease from Isoniazid Loaded dendrimers. (Mean ±S.D. n=3).

4 Korsmeyer-Peppasrelease kinetics Model :

The graph was plotted betweenLog % cumulative drug release vs. Log time

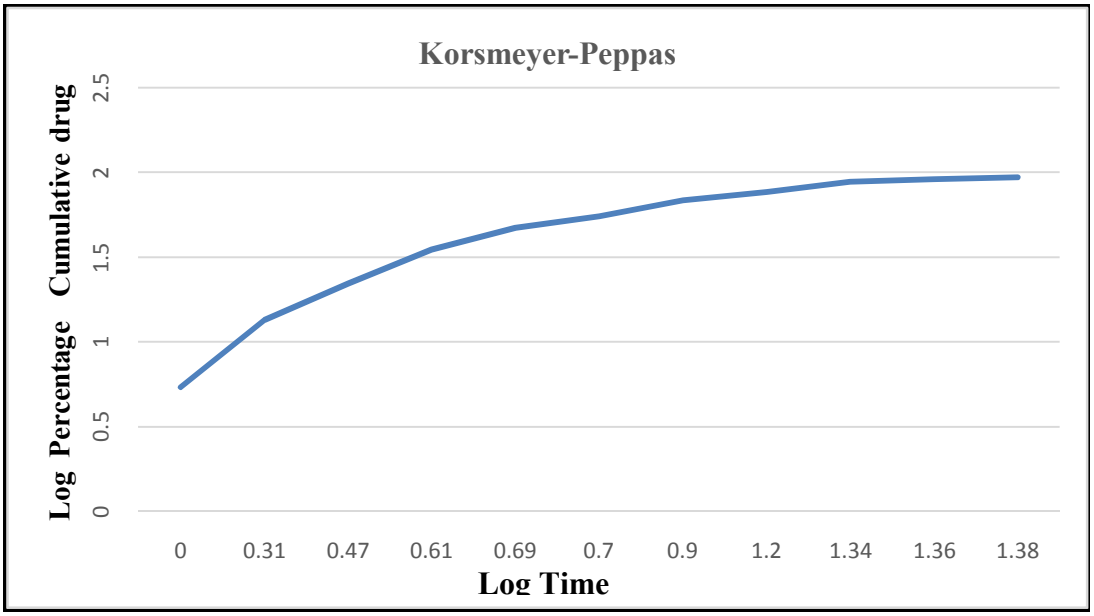

Figure 12:Korsmeyer-Peppasrelease from Isoniazid Loaded dendrimers. (Mean ±S.D. n=3).

DISCUSSION

The Current study concluded the dendrimers as drug delivery system for Isoniazid Because of its particle size, it can be administered safely through i.v route. The formulations showed constant release of drug from dendrimeric system throughout the study period, around 93.25 % of drug was released up to 24hrs. From the drug release kinetics, dendrimers showed controlled release of Isoniazid Zero order non-fickian diffusion. The drug therapy in tubercular patient by delivering the drug at a controlled rate for prolonged period of time.

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