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FORMULATION, DEVELOPMENT AND EVALUATION OF LIPOSPHERE OF AN ANTI HIV DRUG ZIDOVUDINE

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Abstract

HIV (interferes with body's immune system. As a result of this body is more likely prone to other infections and cancer which further prove fatal. In a standard antiretroviral therapy commonly called as ART is combination of at least 3 antiretroviral (ARV) drugs which is intended for maximal suppression of HIV virus in the body. There are unpleasant side effects of anti-HIV drugs. Therefore, there is a pressing call for improved drugs and more effective drug targeting systems that would address various challenges, improve the efficacy, and be cost-effective liposome based therapy represent convenient approach to improve the delivery of anti -HIV agents into the infected cells improving efficacy of drugs and reducing adverse effect. Thus aim of this study is formulation development & evaluation of lipospher of Zidovudine. Results showed that the maximum percentage yield and entrapment efficiency was found formulation F3 (78.85±0.14). The mean particle size of optimized formulation F3 lipospheres was 236.2 nm. The zeta potential of F3 lipospheres was found -29.4 Mv. The r^2 values for first order was found to be 0.994 suggesting release kinetics follow First order release kinetics. So, it can be concluded that Zidovudine Lipospheres may be a promising drug delivery system for HIV-1 treatment.

Keywords: HIV, Liposphere, Zidovudine, Antiretroviral Therapy (ART),

Introduction

HIV (Human Immunodeficiency virus) is the causative agent for AIDS (Acquired immuno deficiency syndrome). This virus interferes with body's immune system. The immune system helps body to fight off infections. But this virus if left untreated, infects and kills the CD4 cells, which are a type of immune cell called T cells. Due to weakened immune system the other bacteria and viruses take advantage and worsen the situation. As a result of this body is more likely prone to other infections and cancer which further prove fatal (Moss,2013; Yoshimura,2017).

In a standard antiretroviral therapy commonly called as ART is combination of at least 3 antiretroviral (ARV) drugs which is intended for maximal suppression of HIV virus in the body. It is also used to stop progression of HIV infection. This therapy has proven to be beneficial in reduction of large amount of death rates and sufferings when used effectively in early stages stage of infection. Drug like Zidovudine forces HIV virus to use faulty versions of building blocks by NRTIs so that more HIV are not made by infected cells hence known as Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs) (Sturt *et al*., 2010).

There are unpleasant side effects of anti-HIV drugs like diarrhea, fatigue, headache, nausea, kidney stones, abdominal pain, tingling, or numbness in the hand and feet and anemia etc. The greatest drawback in the treatment of AIDS is the high cost of treatment. Therefore, there is a pressing call for improved drugs and more effective drug targeting systems that would address various challenges, improve the efficacy, and be cost-effective (Ford *et al*., 2013; Chopra *et al*., 2013).

The development of an effective drug delivery system such as liposomes presents an opportunity to circumvent the many challenges associated with antiretroviral drug therapy. As liposomes are naturally taken up by the cells of mononuclear phagocytic system (MPS), liposome based therapy represent convenient approach to improve the delivery of anti -HIV agents into the infected cells improving efficacy of drugs and reducing adverse effect associated with their administration. (Ramana *et al*., 2010). Thus, this study deals with the formulation, development & evaluation of liposphere of anti HIV drug Zidovudine.

Material and Methods

Materials

Zidovudine Gift sample obtained from bioplus life sciences pvt. ltd. Bangalore. Other chemicals used were of laboratory grade.

Methods

Formulation Development of Liposphere

Drug encapsulated Liposphere were developed by melt dispersion technique. The formulation of different batches is depicted in Table 7.5. Briefly, the lipid core was melted on a water bath maintained at 70-72°C. Finely powdered drug was dispersed into the molten lipidic phase. The aqueous phase was prepared by heating a blend of water and surfactant to 70-72°C with a stabilizer. The molten lipidic phase was slowly transferred to the hot aqueous phase (o/w emulsion) and the emulsification was assisted by stirring the content on a sonicator continuously. The milky dispersion was then rapidly cooled to 20°C by immersing the formulation in an ice bath without stopping the agitation to yield a uniform dispersion of lipospheres. The obtained lipospheres were then washed with water and isolated by filtration (Elgart *et al*., 2012).

Table 1: Preparation of Liposphere of Zidovudine

F. Code	Drug (mg)	Lipid core (mg)		Tween 80 as Surfactant (ml)	Gelatin or pectin as Stabilizer (mg)	Water (ml)
		Stearic acid (mg)	Cetyl alcohol (mg)			
F1	150	100	100	1.5ml	2	98
F2	150	150	200	1.5ml	2	98
F3	150	200	300	1.5ml	2	98
F4	150	100	100	1.5ml	2	98
F5	150	150	200	1.5ml	2	98
F6	150	200	300	1.5ml	2	98

Characterization of Zidovudine encapsulated lipospheres

Percentage Yield of Lipospheres

Yield of Lipospheres percent w/w was calculated by dividing weight of liposphere by sum of Weight of drug and weight of excipients.

Drug loading and Entrapment efficiency

The amount of Zidovudine present in lipospheres was determined by taking the known amount of lipospheres in which 10mg of drug should be present theoretically [60]. Then the lipospheres were crushed and the powdered microspheres was taken and dissolved in 10 ml of methanol and stirred for 15 minutes with an interval of 5 minutes and allowed to keep for 24 hours. Then the solution was filtered through whatmann filter paper. Then the absorbance after appropriate dilution was measured spectrophotometrically at 264nm by UV-visible spectrophotometer (Brown *et al*., 2013).

Microscopic Evaluation

An optical microscope (Cippon-Japan) with a camera attachment (Minolta) was used to observe the shape of the prepared microspheres for each drug: lipid ratio.

Measurement of mean particle size

The mean size of the lipospheres was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the lipospheres suspended in 5 ml of distilled water was used for the measurement (Khulbe and Manjal, 2012).

Determination of zeta potential

The zeta potential of the drug-loaded lipospheres was measured on a zeta sizer (Malvern zetasizer instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water.

Surface morphology (Scanning electron microscopy)

Morphology and surface topography of the lipospheres were examined by scanning electron microscopy (Shivakumar *et al*., 2007).

***In-vitro* drug release studies**

The dissolution of Zidovudine from the prepared lipospheres was monitored using USP XXV paddle II apparatus. The Amount of the lipospheres equivalent to 10mg of Zidovudine was dispersed into the dissolution medium. The dissolution media was 900 ml of pH 1.2 buffers maintained at 37 ±0.5ºC and rotating at 50 ±1 rpm. The 5ml

aliquots were withdrawn at pre-determined time intervals and the withdrawn samples were replaced with fresh dissolution medium. The samples were then analyzed spectrophotometrically at 264 nm for Zidovudine content (Wagner,1969).

Results & Discussion

The percentage yield of different formulation was in range of 74.23±0.45–83.35±0.95%. The drug entrapment of different formulations was in range of 68.98±0.14±68.98±0.14%w/w. The maximum percentage yield and entrapment efficiency was found formulation F3 (78.85±0.14). The mean particle size of optimized formulation F3 lipospheres were found 236.2 nm. Results of zeta potential of optimized formulation F3 lipospheres was found -29.4 Mv. When the regression coefficient values of were compared, it was observed that 'r^2' values of First order was maximum i.e 0.994 hence indicating drug release from formulations was found to follow First order release kinetics. The results of this study suggest that Zidovudine Lipospheres may be a promising drug delivery system for HIV-1 treatment. Further research is needed to explore the efficacy and safety of this system for HIV-1 management.

Results of percentage yield

Table 1: Percentage yields of lipospheres

S. No.	Formulation Code	% Yield*
1	F1	78.35±0.45
2	F2	80.23±0.89
3	F3	83.35±0.95
4	F4	75.65±0.63
5	F5	74.23±0.45
6	F6	76.65±0.25

Table 2: % Drug entrapment efficiency

S. No.	Formulation Code	% Drug entrapment efficiency
1.	F1	73.25±0.25
2.	F2	74.05±0.32
3.	F3	78.85±0.14
4.	F4	74.65±0.25
5.	F5	72.23±0.31
6.	F6	68.98±0.14

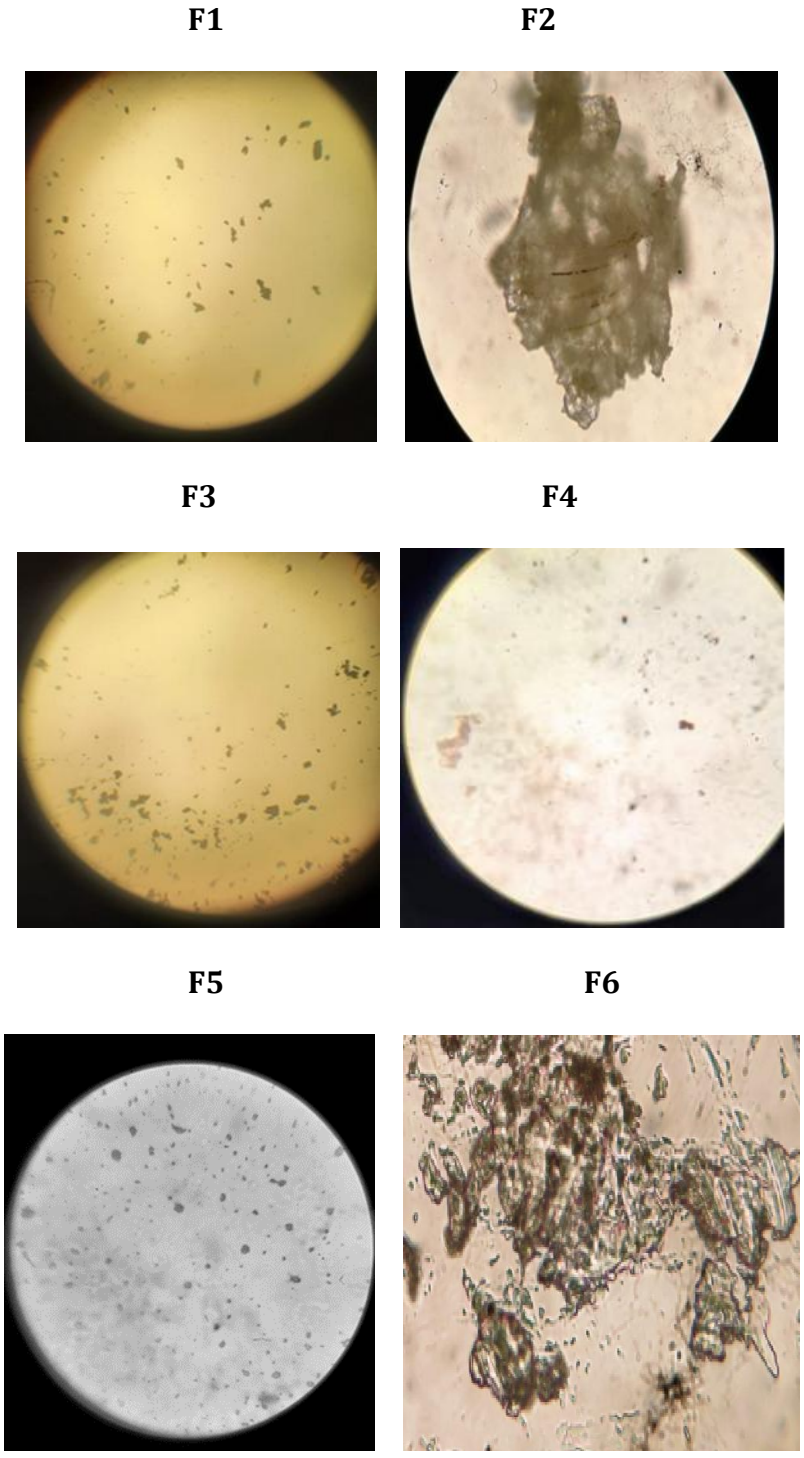

Figure 1: Microscopic observation of prepared liposphere formulation

Table 3: Result of Flow Properties of different liposphere formulation

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.565	0.678	16.667	1.200
F2	0.574	0.685	16.204	1.193
F3	0.535	0.641	16.537	1.198
F4	0.526	0.632	16.772	1.202
F5	0.557	0.665	16.241	1.194
F6	0.585	0.687	14.847	1.174

Table 4: Release study of Formulation F-3

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative *% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	13.32	1.125	86.68	1.938
1	1	0	26.65	1.426	73.35	1.865
1.5	1.225	0.176	38.85	1.589	61.15	1.786
2	1.414	0.301	46.65	1.669	53.35	1.727
3	1.732	0.477	63.32	1.802	36.68	1.564
4	2	0.602	71.14	1.852	28.86	1.460
6	2.449	0.778	86.65	1.938	13.35	1.125
8	2.828	0.903	94.74	1.977	5.26	0.721
12	3.464	1.079	99.05	1.996	0.95	-0.022

Table 5: Comparative study of regression coefficient for selection of optimized batch

	Zero order	First order	Higuchi	Peppas model
r^2	0.819	0.994	0.939	0.942

Conclusion

The results of the study showed that zidovudine lipospheres may be a useful tool for the treatment of HIV. The lipospheres were found to be more effective in the delivery of

zidovudine than other methods of delivery, such as tablets and capsules. Furthermore, the lipospheres were found to be stable and able to withstand harsh environmental conditions. The results suggest that zidovudine lipospheres may be a promising approach for the delivery of antiretroviral drugs, and further research is needed to evaluate their efficacy and safety. The results of this study suggest that Zidovudine Lipospheres may be a promising drug delivery system for HIV-1 treatment. Further research is needed to explore the efficacy and safety of this system for HIV-1 management.

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