Research Article

PREFORMULATION STUDIES OF STAVUDINE FOR TARGETED DRUG DELIVERY SYSTEM

Girjesh Vishwakarma *, Sharad P.Pandey, H.S.Chandel

Truba Institute of Pharmacy, Bhopal, Madhya Pradesh, India

*Corresponding Author Email: gv1448@gmail.com

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ABSTRACT

The aim of the present study was the pre-formulation parameters of Stavudine for targeted drug delivery system. Data generated from the pre-formulation study may be helpful to initiate the formulation development. The aim of the utilization of pre-formulation data is to maximize the possibilities in formulation for an appropriate, safe, efficacious and stable product and at the equivalent time offer the idea for optimization of the product quality. Stavudine is the nucleoside reverse transcriptase inhibitor used for the acquired immune deficiency syndrome with its oral bioavailability over 80%. The pre-formulation studies were conducted on physiochemical property for the determination of physical appearance, melting point, solubility profile, partition coefficient and ultra-visible spectrophotometer, infrared spectroscopy, differential scanning calorimetry, determination of quantitative estimation of drug. All the physiochemical data and results showed that the Stavudine could serve as an appropriate candidate drug for targeted drug delivery system.

Keywords: Pre-formulation, targeted drug delivery system, optimization

INTRODUCTION

The Targeted drug delivery system (TDDS) is a type of sensible drug delivery system which is phenomenal in delivering the drug to a specific site (cell or tissue). TDDS is a drug delivery system involving the retention of the drug across biological membrane, while the targeted release system is that the drug is released on the site of action.^{1,2}

The targeted drug delivery system relies on a way that delivers a definite quantity of a therapeutic agent for an extended period of time to a targeted site inside the body. This helps maintain the desired concentration of the drug in plasma and tissue within the body; thus avoiding any risk to the healthy tissue passing through the drug. The drug delivery system is very integrated and needs numerous disciplines, like chemists, life scientist to affix forces to optimize this technique. When implementing a targeted release system, the subsequent standard for the system require to get into account: the drug properties, facet effects of the drugs, the targeted to the site of action, and therefore the malady.^{3,5}

Products supported such a delivery system square measure being ready by considering the particular properties of target site, nature of carriers or vehicle transport carriers that convey drug to particular receptors and ligands and physically modulated parts. Ideally focused on targeted drug delivery systems ought to be biochemically latent, ought to be non-immunogenic, should be physically and with chemicals stable in vitro and in vivo conditions, and will have restricted drug distribution to focus on site specific areas such as cells, tissues or organs and should have a uniform capillary distribution. It ought to have governable and certain rate of drug release and conjointly drug release must not have an effect on the

drug action. It ought to have a therapeutic quantity of drug release and will have stripped drug run throughout transit.^{6,8}

Vehicle used ought to be bio-degradable or pronto eliminated from the body with none drawback. The preparation of the delivery system ought to be straight forward or moderately straight forward, fruitful and value effective. A Targeted drug delivery system (TDDS) is more popular over typical drug delivery systems owing to three main reasons. The primary being pharmaceutical reason. Typical drug has low solubility and additional drug instability compared to targeted drug delivery systems. Typical drug have poor absorption, shorter half-life and need giant volume of distribution. These represent its pharmacokinetic properties. The third reason constitutes the pharmacodynamic properties of drugs. The standard drug has low therapeutic index and low specificity as compared to site specific drug delivery system. Owing to these reasons targeted drug delivery system is more popular over typical drug delivery systems.^{9,11}

Site specific delivery of a drug molecule to particular organ sites is one of the stands out amongst the most difficult exploration zones in pharmaceutical sciences. By developing colloidal conveyance frameworks, nanoparticles, micelles, liposomes, and new boondocks have opened for enhancing drug delivery.¹²

PREFORMULATION STUDIES

Preformulation studies were developed in 1950 & mid 1960 and it is characterized as an examination of physical & synthetic properties of drug substance alone and when combined with an excipient. Preformulation includes the utilization of bio-pharmaceutical ethics

to the physicochemical characters of drug molecule are characterized with the target of wilyworst drug delivery system.¹³

The intention of preformulation study is to nonexclusive data valuable to the formulator in creating steady and bioavailable measurement structure. The utilization of preformulation factor maximizes the probability in formulation an safe, acceptable, efficacious and stable product and meantime gives the promises to improve the of the drug product quality. The preformulation studies have regarded tests for distinguishing proof (Physical appearance, Solubility profile, Melting point, determination of partition coefficient, ultraviolet spectroscopy, quantitative estimation of drug, infrared spectroscopy and Differential scanning calorimetry).¹⁴

TEST FOR IDENTIFICATIN

Solubility profile of drugs (as per USP)

The solubility of stavudine was tested in various solvents. A distinct amount 10 milligram of the drug was dissolved in 10 milliliter of each investigated solvent at room temperature. The solubility was watched just by the visual inspection.¹⁵

Melting Point

Capillary Method Determination

Capillary melting point tubes are square measure want to hold melting point samples. This tube needs to be sealed at one end. To pack the tube, the open end is pressed gently in a little quantity of the sample the crystalline material with a watch glass or deliberation paper. To transfer the crystals from the open end to the bottom of the tube, tap the bottle gently on the bench highest fringe of the tube on a little file. A densely packed column of crystals about 3 mm high on the tube is all that is required.

Determination of Partition coefficients

Get a 25 ml of n-octanol and 25 ml of distilled water and 100mg of stavudine drug. Shake the over solution mixture through using an incubator shaker for 30 minutes. Permit this solution to face for

twenty-four hours for separating the liquid and organic layers when twenty four hours, liquid and organic layers separated, move into totally different beakers with the assistance of UV photometer, the absorption of liquid and organic layer determined at totally different wavelengths.¹⁷

Analytical method for estimation of the drug (UV method)

The ultraviolet spectrophotometric was chosen in the present study for estimation of stavudine the drug solution was scanned the wavelength between of 200-400nm.¹⁸

Preparation of phosphate buffer, pH 6.8 (Indian Pharmacopoeia, 2007)

Dissolve 28.80 grams of di-sodium hydrogen phosphate and 11.45 grams of potassium di-hydrogen phosphate in adequate water to produce 1000 milliliter. Alter the pH if important.

Differential scanning calorimetry

Differential scanning calorimetry (DSC) of drug, stavudine, and lipid blend of all fixings in stavudine targeted formulation were completed by warming the specimen from 300-400°C at warming rate of 10°C/min. In a nitrogen environment thermograms obtained are shown in figure.¹⁹

Standard curve of Stavudine in phosphate buffer, pH 6.8

Measured amount of stavudine 10 milligram each was disintegrated in phosphate buffer, pH 6.8 and volume made up to 100 millilitre with phosphate buffer, pH 6.8 to give a concentration of 100µg/ml from this stock solution, different volume 1,2,3,4 and 5ml were transferred into 100 ml volumetric flask and the volume were made up to 5 ml with the phosphate buffer, pH 6.8 to gate the different concentration of 5,10,15,20 and 25µg/ml. The absorbance was measured at 265nm for stavudine against a blank using UV spectroscopy.^{20,21}

RESULT

Table 1. Appearance of drug (as per USP)

S.No.	Description/ Appearance	Result
1.	Stavudine is a white crystalline powder	Complies

Table 2. Solubility of stavudine in different media

S.No.	Solvent	Solubility behavior
1	Water	+++
2	Ethanol	++
3	Dichloromethane	+
4	Methanol	++
5	Chloroform	+
6	Acetone	--

++++: Freely soluble, +++: Soluble, ++: Sparingly soluble, +: Slightly soluble, --: Insoluble

Table 3. Determination of melting point

S.No.	Drug Name	Melting Point	Melting point on perform
1	Stavudine	159-160°C	157-159°C

Table 4. Determination of partition coefficients

Partition coefficients value of stavudine	0.93
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Table 5. Standard plot of Stavudine in phosphate buffer 6.8 pH

S. No.	Concentration ($\mu\text{g/ml}$)	Absorbance (nm)
1	5	0.201
2	10	0.390
3	15	0.596
4	20	0.809
5	25	0.991

Table 6. Statistical parameters related to the calibration curve of Stavudine

S.No.	Absorption media parameters values	Parameters	Values
1.	The calibration curve of stavudine in Phosphate buffer pH6.8	Beer's law range	10-50 $\mu\text{g/ml}$
		Regression coefficient (r^2)	0.999
		Regression line equation.	$Y=0.497X-0.017$

Figure 1: Standard curve of Stavudine

Figure 2: IR of Stavudine

Figure 3: IR of Drug + Lipid

Figure 4. DSC of Stavudine

DISCUSSION & CONCLUSION

Delivery of drug particle to achieve its particular site it a difficult task in the complex cells network of an individual. At long last, focused on medication conveyance is approached as one of the brightest progressed technique in the therapeutic sciences in the finding and treatment of couple of deadly illnesses. It has crossed the early stages period and now touching stature of developments in innovative work in clinical and pharmaceutical fields. By and large, it might be finished up with the immeasurable database of

distinctive studies, the exploration of site particular or focused on conveyance of these medications has got to be more shrewd and keen to them and the headway of exploratory innovation.

The present analysis was meant to assess the likelihood of utilizing physiochemical parameters for the development of targeted delivery of stavudine a nucleotide analog reverse transcriptase inhibitor (NRTI) drug preformulation studies were done utilizing different parameters, for example, recognizable proof test of simvastatin. The description and physical identification, melting point, solubility and

partition coefficients were also performed or further characterization & it was found that all results are satisfactory.

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