INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Research Article

PREFORMULATION STUDIES OF SIMVASTATIN FOR TRANSDERMAL DRUG DELIVERY SYSTEM

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Article Received on: 08/07/12 Revised on: 12/08/12 Approved for publication: 01/09/12

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ABSTRACT
The aim of the present work to study the preformulation parameters for Transdermal drug delivery system. The objective of Preformulation study is to generic information useful to the formulater in developing stable and bioavailable dosage form. The use of Preformulation parameter maximizes the chances in formulation an acceptable, safe, efficacious and stable product and at the same time provide the basis for optimization of the drug product quality. Administration of conventional tablets of simvastatin has been reported to exhibit fluctuations in plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor sites also, the maintenance of a constant plasma concentration of a cardiovascular drug is important in ensuring the desired therapeutic response, again since the half life of simvastatin is 3 hours hence multiple doses of the drug are needed to maintain a constant plasma concentration for a good therapeutic response, and improve patient compliance, hence the objective of the study was made to develop controlled release TDDS of simvastatin using polymer like HPMC and Carbopol, which will controlled the release of drug, increasing the bioavailability of the drug and thus decreasing the dosing frequency of the drug. The Preformulation studies were carried out in terms of testa for identification (physical appearance, melting point, and uv spectrophotometer), solubility profile, determination of partition coefficient and quantitative estimation of drug. All the observation and results showed that the simvastatin could serve as suitable candidate for Transdermal drug delivery system that may improve the bioavailability.
KEYWORDS: cardiovascular, Preformulation, controlled, optimization

INTRODUCTION

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied creams and ointments for dermatological disorders. The occurrence of systemic side-effects with some of these formulations is indicative of absorption through the skin. A number of drugs have been applied to the skin for systemic treatment. In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation. Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation. Moreover, it over comes various side effects like painful delivery of the drugs and the first pass metabolism of the drug occurred by other means of drug delivery systems. So, this Transdermal Drug Delivery System has been a great field of interest in the recent time. Many drugs which can be injected directly into the blood stream via skin have been formulated. The main advantages of this system are that there is controlled release of the drug and the medication is painless. Drug that are easily absorbed from the gastrointestinal tract (GIT) and have a short half-life are eliminated quickly from the blood circulation, so they require frequent dosing[1,2,3,4,5,6]. To avoid this drawback, the oral sustained-controlled release formulations have been developed in an attempt to release the drug slowly into the GIT and maintain an effective drug concentration in the serum for longer period of time. Simvastatin, an effective drug in the treatment of hyperlipidimic patients. Simvastatin is a methylated derivative of lovastatin that acts by competitively inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the enzyme that catalyzes the rate-limiting step in cholesterol biosynthesis. Administration of conventional tablets of simvastatin has been reported to exhibit fluctuations in plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor sites also, the maintenance of a constant plasma concentration of a cardiovascular drug is important in ensuring the desired therapeutic response, again since the half life of simvastatin is 3 hours hence multiple doses of the drug are needed to maintain a constant plasma concentration for a good therapeutic response, and improve patient compliance, hence the objective of the study was made to develop controlled release TDDS of simvastatin using polymer like HPMC and Carbopol, which will controlled the release of drug, increasing the bioavailability of the drug and thus decreasing the dosing frequency of the drug. In the present study TDDS formulation was preferred over conventional tablet or capsule formulations, as it has several advantages like it controlled the release pattern thus decreasing the dosing frequency[7,8,9,10,11].

PREFORMULATION STUDIES:

The objective of Preformulation study is to generic information useful to the formulater in developing stable and bioavailable dosage form. The use of Preformulation parameter maximizes the chances in formulation an acceptable, safe, efficacious and stable product and at the same time provides the basis for optimization of the drug product quality. The Preformulation studies were carried out in terms of testa for identification (physical appearance, melting point, and uv spectrophotometer), solubility profile, determination of partition coefficient and quantitative estimation of drug[12].

TEST FOR IDENTIFICATIN

.**Solubility profile of drugs** (as per USP) The solubility of simvastatin was tested in various solvents. A definite quantity (10mg) of drug was dissolved in 10 ml of each investigated solvent at room temperature. The solubility was observed only by the visual inspection[13].

Analytical method for for estimation of the drug (UV method)

The ultraviolet spectrophotometric method was selected in the present study for estimation of simvastatin the drug solution was scanned the wavelength between of 200-400nm[14].

Preparation of phosephate buffer,pH 7.4 (Indian Pharmacopoeia, 1996)

Dissolve 2.38 gm of disodium hydrogen phosphate, 0.19 gm of potassium dihydrogen phosphate and 8.0 gm of sodium

chloride in sufficient water to produce 1000 ml.adjust the pH if necessary.

Differential scanning calorimetery

Differential scanning calorimetery (DSC) of drug, simvastatin, HPMC, Carbopol, and mixture of all ingredients in simvastatin transdermal formulation were carried out by heating the sample from 30 ^{0}c to 400 ^{0}c at heating rate of 10 ^{0}C/min. in a nitrogen environment Thermograms obtained are shown in figure it was observed that no interaction has occurred between drug and the polymer.spectrophotometer and obtained[14].

Standard plot of simvastatin in phosphate buffer, pH 7.4

Weighed quantity of simvastatin 10 mg each was dissolved in phosphate buffer, pH 7.4 and volume made up to 100 ml with phosphate buffer, pH 7.4 to give a concentration of 100 µg/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 upto 5 ml with the phosphate buffer,pH 7.4 to gate the different concentration of 5,10,15,20 and 25 µg/ml. the absorbances were measured at 238 nm for simvastatin against a blank using uv spectroscopy[15,16].

RESULT

Table 1.Description/ Appearance of drug (as per USP)

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

Table 2. Solubility of simvastatin in different media

S No.	Solvent	Remarks
1.	Methanol	++++
2.	Ethanol	++++
3.	Aceton	+++
4.	Chloroform	+
5.	Water	-

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

Table : 3 standared plot of simvastatine in phosphate buffer 7.4 ph.

S.No	Concentration (µg/ml)	Absorbance (nm)
1	5	0.2308
2	10	0.493
3	15	0.765
4	20	1.013
5	25	1.198

Table 4. Statistical parameters related to calibration curve of simvastatin

S.No.	Absorption media parameters values	Parameters	Values
1.	Calibration curve of simvastatin in phosphate buffer pH 7.4	Beer's law range Regression coefficient (r^2) Egressed line equation.	10-15µg/ml 0.9946 Y=0.497-0.017

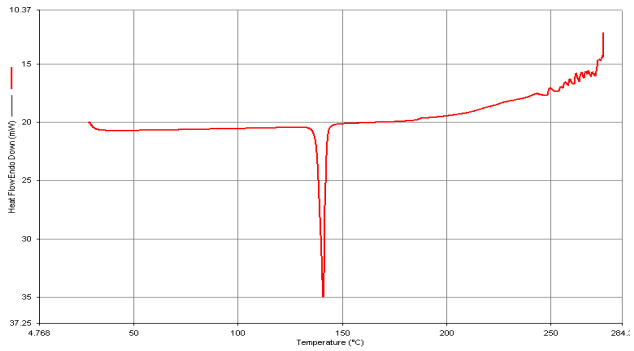

Fig. 1 DSC of Simvastatine

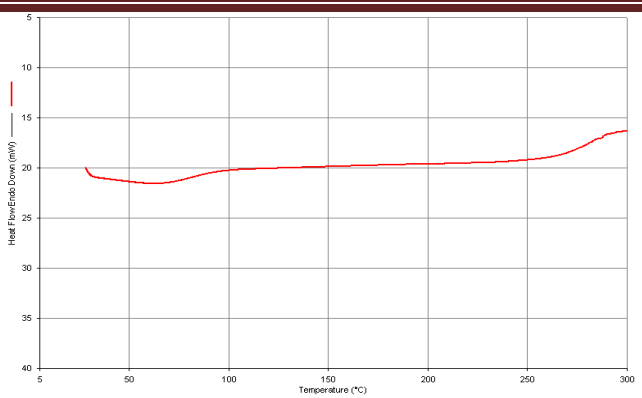

Fig.2 DSC of HPMC

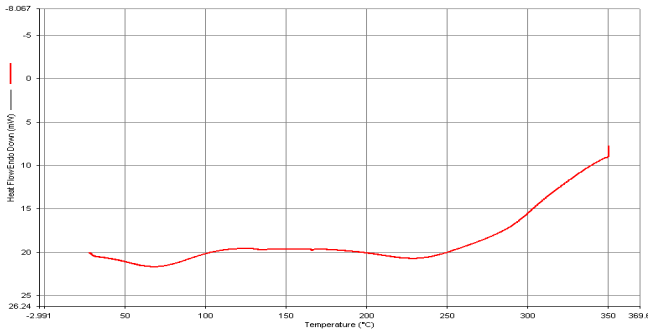

Fig.3 DSC of Carbopol

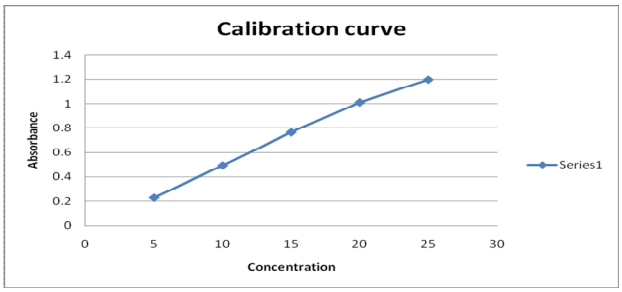

Fig4:- Standard curve of simvastatin

CONCLUSION & DISCUSSION

Transdermal drug delivery system promises many advantages over oral and/or inravenous administration,such as better control of blood levels,a reduced incidenc of systemic toxicity and absence of hepatic first pass metabolism.An ideal drug to be formulated as transdermal drug delivery should posses several physico-chemical prerequisites,such as short half life,small molecular size,low dose etc.

The present investigation was aimed to evaluate the possibility of using different parameters for the development of transdermal delivery of simvastatin, an antilipedamic drug Preformulation studies were done using various parameters such as identification test of ramipril. The description and appearance, melting point and solubility were also performed for further characterization & it was found that all results are satisfactory.

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Source of support: Nil, Conflict of interest: None Declared