FORMULATION AND EVALUATION OF NANOSUSPENSION OF ROSUVASTATIN CALCIUM

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RESEARCH ARTICLE

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ABSTRACT:

Poor water solubility and slow dissolution rate are issues for majority of upcoming and existing biologically active compounds. The aim of present work was to increase the dissolution rate of Rosuvastatin Calcium, a poorly water soluble drug and hence improve its oral bioavailability by Nanosuspension technology. Nanosuspension is new carrier free colloidal drug delivery system with nano sized particles below 1000 nm, and considered as a great drug delivery technique to enhance the drug dissolution and solubility. In the present work Nanosuspension is made by nanoprecipitation technique in the presence of sodium lauryl sulfate as surfactant and PVPK-30 as stabilizer. Prepared Nanosuspension was evaluated for its particle size study, in vitro dissolution study and characterized by Screening Electron microscopy (SEM).

Different concentrations of sodium lauryl sulphate (SLS) and PVPK-30 were evaluated. All formulations were in the nano size and showed marked improvement in dissolution and solubility compared to pure drug of micron size. Finally it was concluded that formulating poorly soluble drugs in the form of Nanosuspension would be a promising approach in delivery of poor water soluble drugs by oral route in a simple and effective way.

Key words: PVPK-30, HMG-CoA, Rosuvastatin calcium, Nanosuspension.

Introduction:

The design and formulation of a dosage form require consideration of the physical, chemical, and biological characteristics of all the drug substances and pharmaceutical ingredients to be used in its preparation. An important property of a drug substance is solubility, especially aqueous system solubility. (1) One of the critical problems associated with poorly soluble drugs is too low bioavailability and erratic absorption because of their low dissolution rates. (2) The solubility–dissolution behavior of a drug is a key factor to its oral bioavailability. Nanotechnology can be used to solve the problems associated with these conventional approaches for solubility dissolution and bioavailability enhancement. In Nanosuspension technology, the drug is maintained in the required crystalline state with reduced particle size (i.e. increase in the surface area) leading to an increased dissolution rate and therefore improved bioavailability.(3) Reduction of drug particles to nanometer range leads to an enhanced dissolution rate not only because of increased surface area but also because of saturation solubility.

Rosuvastatin Calcium is a synthetic, enantiomerically pure antilipemic agent that competitively inhibits hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase. HMG-CoA reductase catalyzes the conversion of HMG-CoA to mevalonic acid, the rate-limiting step in cholesterol biosynthesis. Rosuvastatin belongs to a class of medications called statins and is used to reduce plasma cholesterol levels and prevent cardiovascular disease. RVS is a white, crystalline, poorly soluble in water. It is generally considered that compounds with very low aqueous solubility will show dissolution rate-limited absorption. Improvement of aqueous solubility in such case is a valuable goal to improve therapeutic efficacy. The dissolution rate is a function of the solubility and the surface area of the drug, thus, dissolution rate will increase if the solubility of the drug is increased, and it will also increase with an increase in the surface area of the drug. (4, 5)

In this present study, nanoprecipitation technique is used where a drug solution in a water miscible organic solvent is mixed with an aqueous solution containing a surfactant(s). Upon mixing, the supersaturated solution leads to nucleation and growth of drug particles, which may be stabilized by surfactants. (6)

The aim of this work is to formulate the SMS Nanosuspension by nanoprecipitation method and enhance the dissolution rate .The optimize formulation was further characterize by Scanning Electron Microscopy (SEM).Dissolution study of Nanosuspension formulations was performed in distilled water. (7)

Materials and methods:

Rosuvastatin Calcium was obtained from Ranbaxy laboratories, Poanta Sahib, H.P (IND). Polyvinyl pyrrolidine k-30, Sodium Lauryl Sulphate, Acetonitrile were received from Central Drug House Pvt. Ltd., New Delhi (IND). All the materials used in this research study comply with the pharmaceutical and analytical standards, respectively.

Method of preparation:

Eight formulation were prepared by Nanoprecipitation method. The drug is dissolved in suitable organic solvent acetonitrile in which the drug is soluble. This was poured into different amount of water containing different amount of PVPK-30 and SLS at maintained at room temperature and subsequently stirred on homogenizer to allow volatile solvents to evaporate. Addition of organic solvents by means of a syringe positioned with the needle directly into stabilizer containing water. Organic solvents were left to evaporate off under continuous stirring of the Nanosuspension at room temperature for 5 hours.

Table 1. Formulation prepared

Ingredients	Formulation code							
	F1	F2	F3	F4	F5	F6	F7	F8
Rosuvastatin(mg)	10	10	10	10	10	10	10	10
PVPK-30(mg)	20	40	20	40	20	40	20	40
SLS	0.01	0.01	0.02	0.02	0.01	0.01	0.02	0.02
Acetonitrile(ml)	1	1	1	1	1	1	1	1
Water(ml)	40	40	40	40	10	10	10	10
Organic to Aqueous ratio	0.025	0.025	0.025	0.025	0.1	0.1	0.1	0.1

Evaluation parameters:

The Nanosuspension was evaluated for various parameters:-

1. Content uniformity
2. pH
3. Particles size and shape
4. In-vitro drug release studies

Drug content uniformity

10ml of each formulation was taken and dissolved in 10ml isotonic solution and kept

overnight. 10 mg (similar as in formulation) of drug was taken and dilution was made to 10µg/ml. The dilutions were filtered and analyzed using UV for their content uniformity. The absorbance of the formulations were read using one cm cell in a UV-Vis spectrophotometer. The instrument was set at 245 nm. The drug content in each formulation was calculated based on the absorbance values of known standard solutions.

pH

The pH values were measured at 25 °C using a pH digital meter at 20 ± 1 °C. The formulation was brought in contact with the electrode of pH meter and equilibrated for 1 min. This method was done in triplicate and mean was calculated along with standard deviation.

Particle size and shape

Particle size and shape of the formulated Nanosuspension was determined by using Scanning Electron Microscopy.

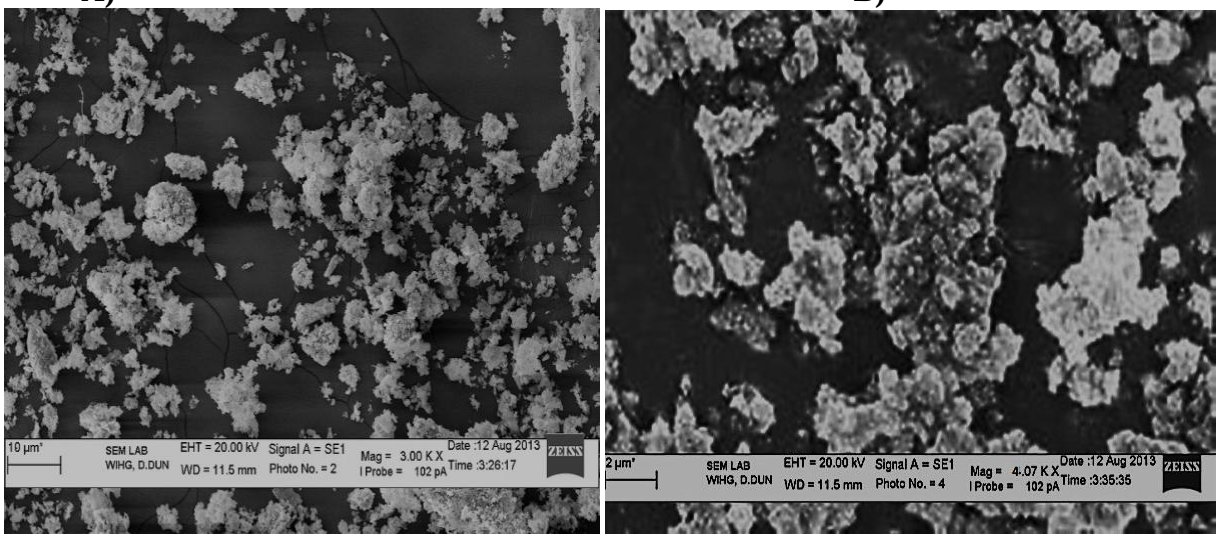
In-vitro drug release

In-vitro drug release studies were performed in a dissolution apparatus using paddle method at rotation speed of 50 rpm. The volume and temperature of the dissolution medium were 900 ml and 37.0±0.2 °C, respectively. Samples were withdrawn at fixed times and were filtered and assayed through ultraviolet absorbance determination at 245 nm using a Shimadzu UV-Visible spectrophotometer.

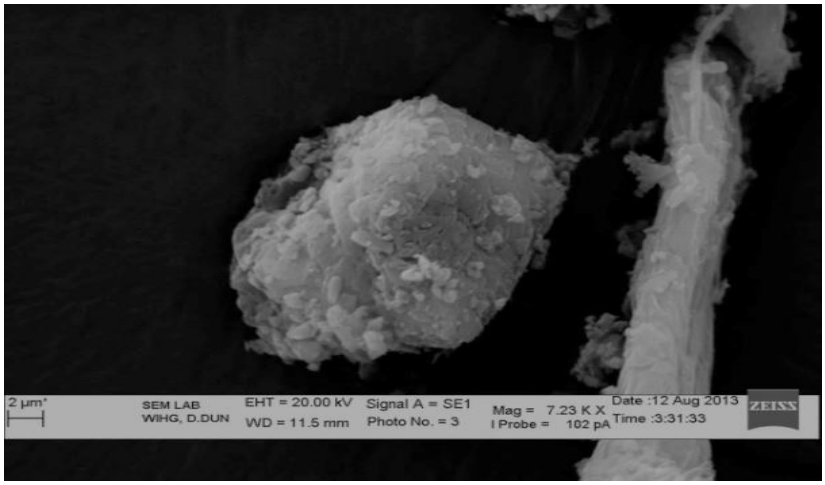
Result and Discussions:

- **Drug content: -** The drug content of the formulated Nanosuspension was found in the range of 67 to 78% respectively.
- **pH Measurement:-** The pH of the Nanosuspension was obtained in the range of 7.2 to 7.4 for all the formulations. Thus, the polymer is suitable for Nanosuspension formulation.
- **Particle size and Surface morphology:-** The particle size of all the formulation was found in range of 450-850nm.(fig. A, B, C). The optimized formulation F4 has average particle size of 450nm. It was observed that all samples of particles were smooth, sub-spherical in shape and aggregated to form small clusters.
- **In-Vitro drug release:-** In-vitro drug release data from the Nanosuspension were carried out for 60 min and graphically represented as % CDR v/s Time profile (Figure 19 and 20). The release of Erythromycin stearate Nanosuspension of pure drug, F1 to F8 was found to be respectively 42.12%, 77.21%, 82.99%, 70.37%, 87.87%,

A) **B)**



C)



SEM Images of Formulation F4

- 65.78%, 70%, 69.08%, 70.07% Thus from the above results it was found that as the particle size is decreased, drug release is increased. When the % CDR v/s Time profiles of all 8 formulations were compared the rate of drug released from the formulation with pure drug was significantly increased. (Fig.1,2,3)

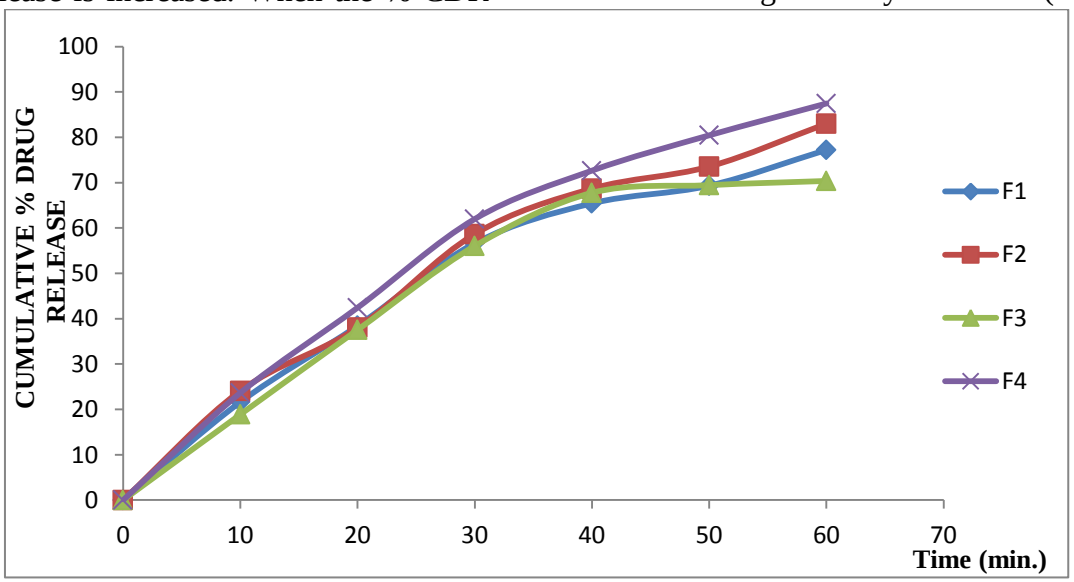


Fig.1: In Vitro release plot of formulation F1-F4

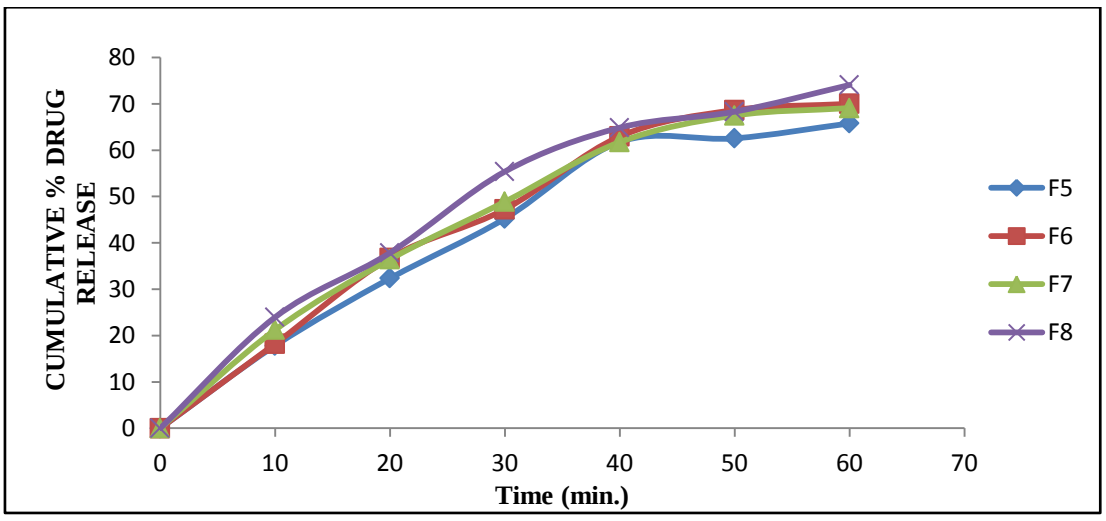


Fig.2: In-Vitro release plot of formulation F4-F8

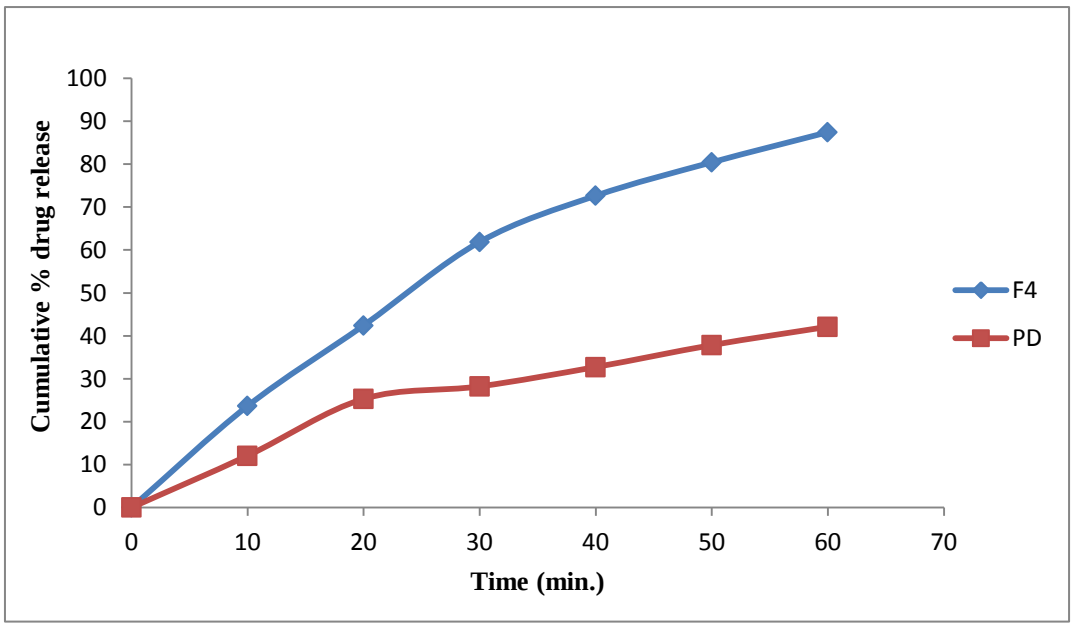


Fig 3.Comparative dissolution study of formulation F-4 with pure drug

Conclusion:

In the present study, an attempt was made to develop Nanosuspension of Rosuvastatin calcium to enhance its low dissolution rate.

In the current work, we had prepared Nanosuspension using nanoprecipitation method in the presence of PVP- K30 as a stabilizer and Sodium lauryl sulphate as a surfactant. All the formulation showed marked improvement as compared to pure drug. Different concentrations of stabilizers and surfactant were evaluated. It can be concluded that formulating poorly water soluble drugs in the form of Nanosuspension would be a promising approach in the delivery of poorly water soluble drug by oral route in a simple and effective way.

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