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Research Article

FORMULATION AND EVALUATION OF TELMISARTAN NANOSUSPENSIONS

M. Sreenivasulu Reddy, J. Sreeramulu*,

Y. Narendra Reddy and G. Rammohan

Department of Chemistry, Sri Krishnadevaraya University,
Ananthapuram, Andhra Pradesh, India.

ABSTRACT

Oral Nanosuspension of Telmisartan was prepared by Solvent evaporation method using various polymers such as SLS, tween80, PVP-K30, PVA, and methanol. All the prepared formulations were found to be having drug content within acceptable limits in the range of 86.28±0.02 to 97.72±0.12% respectively. As the polymer concentration increases, the drug release rate decreases, whereas Nanosuspension strength increases. Optimized formulations of Nanosuspension displayed first order release kinetics. IR spectroscopic studies indicated that there are no drug-excepient interactions. When compared to other all the formulations F8 is the best formulation which showed 99.54% of drug released respectively with in 20 min and follows Zero order release kinetics.

Keywords: Telmisartan, PVP K30, PVA and tween 80.

1 INTRODUCTION[1-5]

One of the main problems responsible for the low turnout in the development of new molecular entities as drug formulations is poor solubility and poor permeability of the lead compounds. The increasing frequency of poorly water soluble new chemical entities exhibiting therapeutic activity is of major concern to the pharmaceutical industry. Various formulation parameters that play a crucial role for successful formulation are aqueous solubility, stability at ambient temperature and humidity, photostability, compatibility with solvents and excipients, etc. Of these, solubility is the most important property for developing formulations. A major hurdle that has prevented the commercialization of many promising poorly soluble drugs is dissolution rate-limited bioavailability.

Nanosuspensions are colloidal dispersions of nanosized drug particles stabilized by surfactants. They can also be defined as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle in which the diameter of the suspended particle is less than 1 µm in size. Nanosuspensions can be used to enhance the solubility of drugs that are poorly soluble in aqueous as well as lipid media. As a result, the rate of flooding of the active compound increases and the maximum plasma level is reached faster (e.g., oral or intravenous [IV] administration of the nanosuspension). This is one of the unique advantages that it has over other approaches for enhancing solubility. It is useful for molecules with poor solubility, poor permeability or both, which poses a significant challenge for the formulators. The reduced particle size renders the possibility of intravenous administration of poorly soluble drugs without blockade of the blood capillaries.

2 MATERIALS AND METHODS

Telmisartan obtained as a gift sample from Glenmarck pharmaceuticals, Tween 80, PVA,PVP K30, Methanol, PVA, and all other chemicals and solvents used are from Rankem, Mumbai.

2.1 Preparation of Telmisartan Nanosuspension by solvent evaporation method

Nanosuspension was prepared by the solvent evaporation technique. Telmisartan was dissolved in acetone at room temperature (organic phase). This was poured into water containing different stabilizers of PVP K30,

PVA, SLS, and Tween 80 maintained at room temperature and subsequently stirred on magnetic stirrer which is stirred at rpm 800-1000 for 30 min to allow the volatile solvent 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 a slow magnetic stirring of the nanosuspension at room temperature for 1 hour followed by sonication for 1 hour.

2.2 Evaluation parameters of Telmisartan Nanosuspensions[7-12]

A. Drug content uniformity

10 mL of each formulation was taken and dissolved in 10 ml isotonic solution and kept overnight. 40 mg (similar as in formulation) of drug was taken and dilution was made to 10 µg/ml. The drug content in each formulation was calculated based on the absorbance values of known standard solutions.

B. Scanning electron microscopy

The morphological features of Telmisartan nanosuspension are observed by scanning electron microscopy at different magnifications.

C. In vitro drug release study

In –vitro dissolution studies were performed in USP apparatus-II (LAB INDIA DS 8000), employing paddle stirrer at rotation speed of 50 rpm and 200 ml of pH 6.8 phosphate buffer as dissolution medium. The samples were filtered through 0.22 µm membrane filter disc (Millipore Corporation) and analyzed for Telmisartan after appropriate dilution by measuring the absorbance at 238 nm.[13-15]

The results of in vitro release profiles obtained for the NDDS formulations were fitted into two models of data treatment as follows

1. Cumulative percent drug released versus time (zero order kinetic model).
2. Log cumulative percent drug remaining versus time (first- order kinetic model).

3 RESULTS AND DISCUSSION

Telmisartan is a BCS class-II drug having low solubility and high permeability. Thus, it is challenging to enhance the solubility of Telmisartan particles in an aqueous solution. Solvent evaporation with precipitation has been employed to produce nanosuspension of Telmisartan. The different formulative variables (1) amount of PVA or PVP K30 (2) amount of Tween 80 or sodium lauryl sulphate and organic to aqueous solvent ratio were contributed much towards the change in particle size in nanosuspension preparation. Determination of Telmisartan λ-max was done in pH 6.8 phosphate buffer buffer medium for accurate quantitative assessment of drug dissolution rate. The λ-max was found to be 238 nm, i.e., at its absorption maxima. Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and excipients were studied. The drug content of the formulated Nanosuspension was found in the range of 82.65 to 96.12 % respectively. The entrapment efficacy of the formulated Nanosuspension was found to be in the range of 83.16-98.52% respectively.

The optimized batch (F8) had an average particle size of 83.1 nm. The in vitro drug release studies were compared for F1 to F8 formulations. PVA, PVP K30 used as carriers and tween 80, sodium lauryl sulphte used as surfactants in these formulations. When compared to the SLS and PVP K30, the tween 80 and PVA drug release was more 98.64% drug was released within 20 minutes. On comparing the best optimized formula i.e., F3 with conventional formulation, it was clearly observed that the %drug release was more i.e 98.64% within 20 mins by best formulation, whereas it is 96.28% for the conventional formulation. So, the % of drug release was more in F8 Nanosuspension than the conventional tablet.

4 CONCLUSION

Oral Nanosuspension of Telmisartan was prepared by Solvent evaporation method using various polymers such as SLS, tween80, PVP-K30, PVA, and methanol. All the prepared formulations were found to be having drug content within acceptable limits in the range of 86.28±0.02 to 97.72±0.12% respectively. As the polymer concentration increases, the drug release rate decreases, whereas Nanosuspension strength increases. Optimized formulations of Nanosuspension displayed first order release kinetics. IR spectroscopic studies indicated that there are no drug-excepient interactions. When compared to other all the formulations F8 is the best formulation which showed 99.54% of drug released respectively with in 20 min and follows Zero order release kinetics.

Table 1: Composition of Nanosuspension of Telmisartan

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8
Telmisartan	320	320	320	320	320	320	320	320
SLS	2.5	2.5	5	5	2.5	2.5	5	5
PVP-K30	15	30	15	30	-	-	-	-
TWEEN-80	-	-	-	-	15	30	15	30
PVA	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Methanol	5	5	5	5	5	5	5	5
Water	40	40	40	40	40	40	40	40

Table 2: Drug content of Telmisartan Nanosuspensions

FORMULATION CODE	DRUG CONTENT (%)
F1	86.28±0.02
F2	92.62±0.14
F3	94.62±0.22
F4	92.96±0.06
F5	96.82±0.28
F6	98.83±0.42
F7	90.16±0.06
F8	97.72±0.12

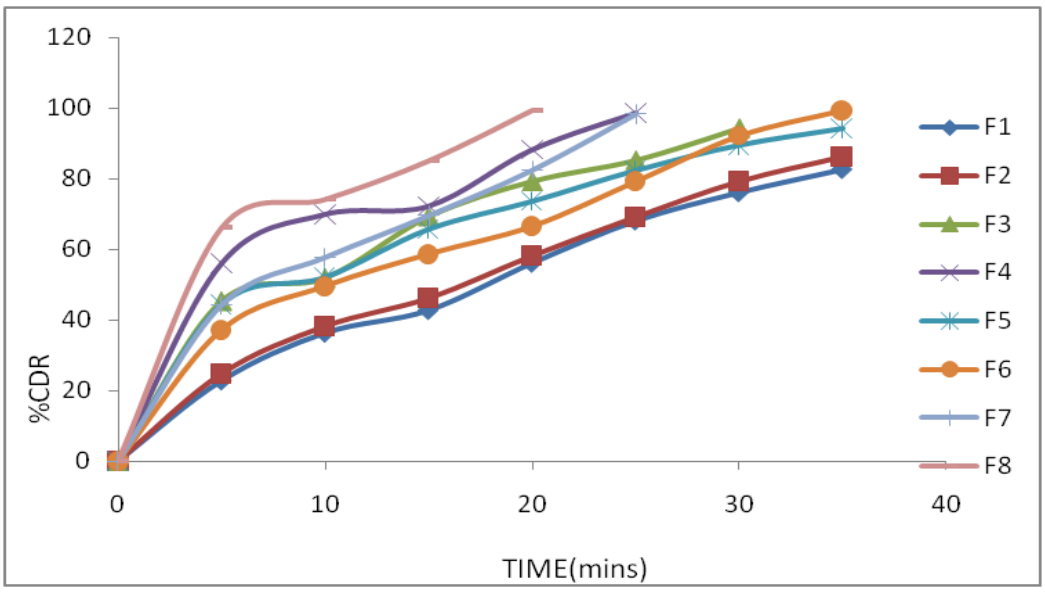

Fig. 1: In vitro dissolution profiles of Telmisartan Nanosuspensions

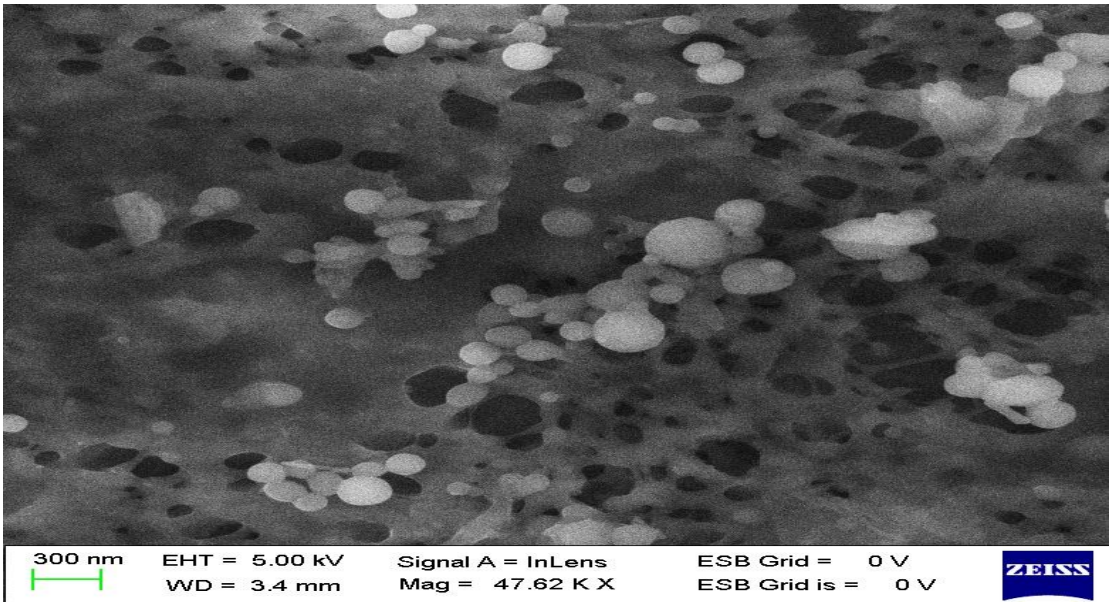

Fig. 2: Scanning electron microscopy of best formulation

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