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Formulation and invitro evaluation of albendazole nanosuspensions

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ABSTRACT

Albendazole is an BCS class II drug is a broad-spectrum anthelmintic structurally related to mebendazole that is effective against many diseases. It is successfully used in experimental and clinical chemotherapy of different intestinal and systemic parasitosis. Its efficacy is often limited by poor intestinal absorption due mainly to its low aqueous solubility. Efficacy of albendazole can be enhanced by improving its dissolution. Reduction in particle size to Nano scale can help in dissolution improvement by increase in surface area. Due to its high half-life it can be formulated as a Nano suspension. Nano suspension is a novel technique used to increase the solubility of the drug prepared by solvent evaporation method. The Nano suspensions are novel promising target and controlled released dosage form which is gaining importance because of ease of manufacturing and diversified applications. The present trend of pharmaceutical research lies in the usage of biodegradable polymer because of its availability and low toxicity. Nanosuspension containing drug was prepared by solvent evaporation method by using combinations of Tween 80, Polaxomer, PVP-K90, PVA, and Acetone and quantity sufficient water). Estimation of Albendazole was carried out spectrophotometrically at 246nm. The Nano suspension were evaluated for parameters such as drug content uniformity, scanning electron microscopy, particle size analysis, zeta potential, in-vitro release, short-term stability, drug excipient interactions (FTIR). The stability data was also subjected to statistical analysis. The drug release from the Nanosuspension was explained by the using mathematical model equations such as zero order, first order, and equation methods. Based on the regression values it was concluded that the optimized formulation F9 follows Zero order kinetics.

Keywords: Albendazole, Tween 80, PVA, Acetone, FTIR, In Vitro Dissolution Studies, Nanosuspensions.

INTRODUCTION

Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biological parameters pertinent to their performance. Despite tremendous

advantages in drug delivery, the oral route remains the most preferred route for the administration of therapeutic agents because of the low cost of therapy and ease of administration leads to high-level of patient compliance. On the other hand, this high-throughput screening process has done little to

address the issue of poor bioavailability of orally administered drug candidates [1-5].

Nanotechnology opens up new vistas of research in the development of novel drug delivery systems. "Nano" word comes from the Greek word 'nanos' which means dwarf. Nano means it is the factor of 10^{-9} or one billionth. Nanosuspension is submicron colloidal dispersion of drug particles. A pharmaceutical nanosuspension is defined as very finely colloid, biphasic, dispersed solid drug particles in an aqueous vehicle, size below 1 μm stabilized by surfactants and polymers prepared by suitable methods for drug delivery applications. Nanosuspension has revealed their potential to solve the problem associated with the delivery of poorly water soluble and poorly water and lipid soluble drugs. It enhances the absorption and bioavailability and help to reduce the dose of conventional oral dosage forms [6-10].

In the present research work an attempt was made to improve the solubility and dissolution rate of Albendazole. Albendazole is an BCS class II drug is a broad-spectrum anthelmintic structurally related to mebendazole that is effective against many diseases. Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies [11-15].

MATERIALS AND METHODS

Albendazole obtained as a gift sample from Regent chemicals, Mumbai. Tween 80, PVA, PVP K90, Acetone, Polaxomer, and all other chemicals and solvents used are from Rankem, Mumbai.

Preparation of Albendazole Nanosuspension by solvent evaporation method

Nanosuspension was prepared by the solvent evaporation technique. Albendazole was dissolved in acetone at room temperature (organic phase). This was poured into water containing different stabilizers of PVP K90, PVA, POLAXOMER, 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.

EVALUATION PARAMETERS OF ALBENDAZOLE NANOSUSPENSIONS

Drug content uniformity

10 ml of each formulation was taken and dissolved in 10 ml isotonic solution and kept overnight. 10 mg (similar as in formulation) of drug was taken and dilution was made to 10 $\mu\text{g/ml}$. 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 246 nm. The drug content in each formulation was calculated based on the absorbance values of known standard solutions.

Entrapment efficacy

The freshly prepared nanosuspension was centrifuged at 20,000 rpm for 20 min at 5°C temperature using cool ultracentrifuge. The amount of un incorporated drug was measured by taking the absorbance of the appropriately diluted 25 ml of supernatant solution at 246 nm using UV spectrophotometer against blank/control nanosuspensions. DEE was calculated by subtracting the amount of free drug in the supernatant from the initial amount of drug taken.

The entrapment efficiency (EE %) could be achieved by the following equation

$$\% \text{Entrapment efficiency} = \frac{\text{Drug content}}{\text{Drug added in each formulation}} \times 100$$

Scanning electron microscopy

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

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. Accurately weighed bulk drug and nanosuspensions were dispersed in dissolution medium. The release study is performed at $37 \pm 0.5^\circ\text{C}$. Samples of 5 ml are withdrawn at predetermined time intervals and replaced with fresh medium to maintain sink condition. The

samples were filtered through 0.22 μm membrane filter disc (Millipore Corporation) and analyzed for Albendazole after appropriate dilution by measuring the absorbance at 246 nm.

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

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

Table-1: Composition of Nanosuspension of Albendazole

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Albendazole	400	400	400	400	400	400	400	400	400
PVP K-90	5	--	--	7.5	--	--	10	--	--
Polaxomer	--	5	--	--	7.5	--	--	10	--
PVA	--	--	5	--	--	7.5	--	--	10
SLS (mg)	10	10	10	10	10	10	10	10	10
Acetone (ml)	5	5	5	5	5	5	5	5	5
Water (ml)	40	40	40	40	40	40	40	40	40

RESULTS AND DISCUSSION

Solubility data of Albendazole

From the conducted solubility studies in various buffers we can say that pH 6.8 phosphate buffer has more solubility when compared to other buffer

solutions. Hence the solubility of Albendazole was pH dependent. Determination of Albendazole λ -max was done in pH 6.8 phosphate buffer medium for accurate quantitative assessment of drug dissolution rate.

Standard curve of Albendazole

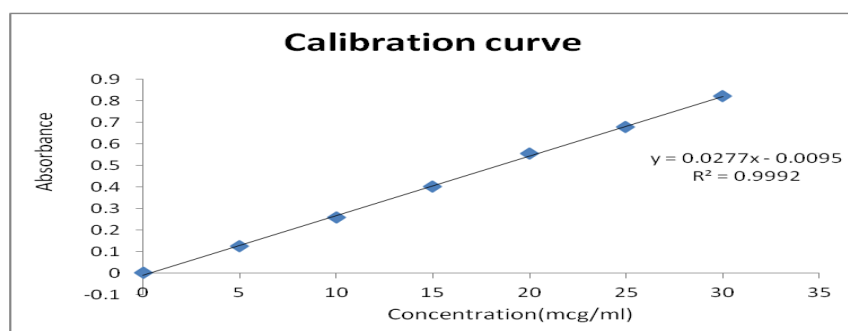


Fig-1: Standard calibration curve of Albendazole in pH 6.8

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and excipients were studied. From the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Albendazole) and optimized

formulation (Albendazole+ excipients) which indicates there are no physical changes. By this studies it was confirmed that there is no variation and shift in the position of characteristic absorption bands it can be justified, there is no interaction between drug and polymer. The drug content of

the formulated Nano suspension was found in the range of 80.14to 96.45% respectively. The

entrapment efficacy of formulations F1-F9 was found to be 81.16-97.52% respectively.

SCANNING ELECTRON MICROSCOPY

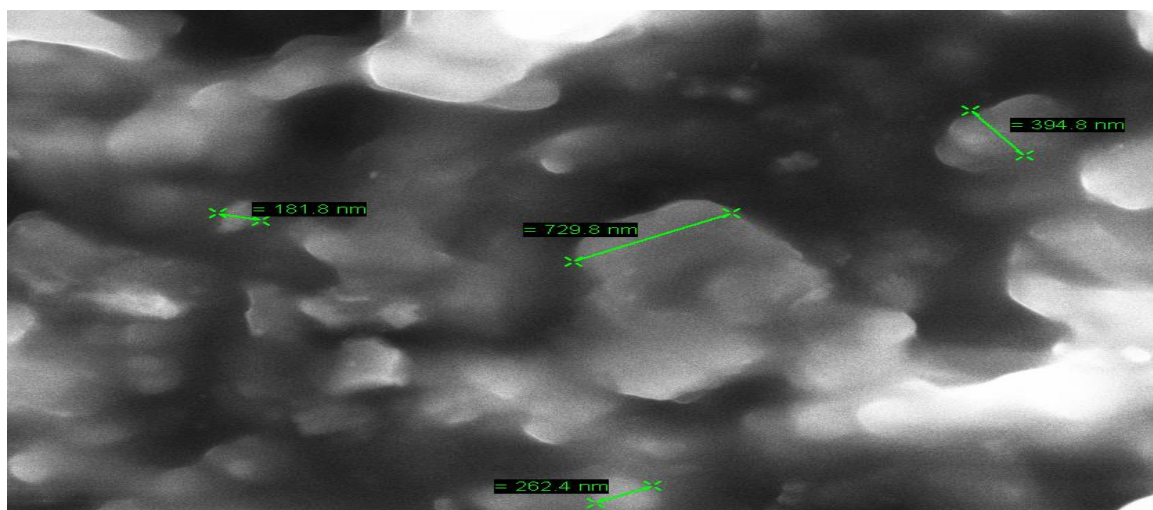


Fig: 2 SEM OF NANOSUSPENSION

The SEM analysis indicates that the formulated nanosuspension was in the range of 200nm. Average particle size of nanosuspension of optimized

formulations (F11) was found to be having maximum particles at a range of 118 nm.

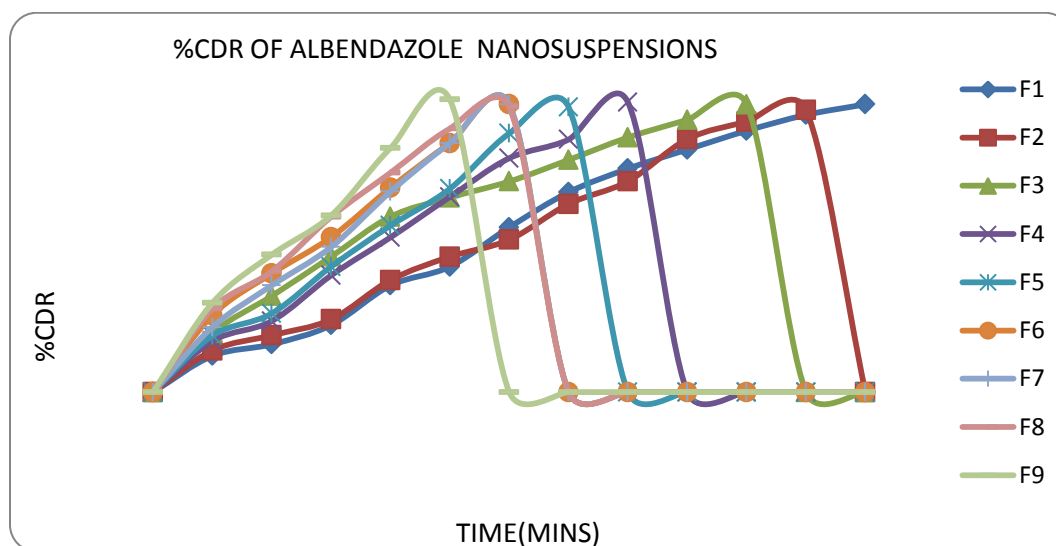


Fig-3: IN-VITRO DRUG RELEASE DATA OF FORMULATION F1 – F9

In vitro release studies were carried out in USP dissolution test apparatus-I employing paddle stirrer at 50 rpm and 900 ml of pH 6.8 buffer as dissolution medium. The in vitro dissolution data of all the designed formulations are shown and dissolution profiles depicted in figures. In vitro drug release data of all the Nanosuspension formulations of Albendazole was subjected to

goodness of fit test by linear regression analysis according to zero order, first order kinetics and according to equations of drug release. The results of linear regression analysis including regression coefficients from the above data it is evident that the optimized formulation (F9) follows zero-order release kinetics.

CONCLUSION

From the present study, the following conclusions can be drawn

Oral Nanosuspension of Albendazole was prepared by Solvent evaporation method using various polymers such as SLS, Polaxomer, PVP-K90, PVA, and Acetone. All the prepared formulations were found to be having drug content within acceptable limits in the range of 80.14 to 96.45% respectively. All the prepared formulations were found to be having entrapment efficiency within acceptable limits in the range of 81.16-97.52% respectively. As the polymer concentration

increases, the drug release rate decreases, whereas Nano suspension strength increases. Optimized formulations of Nano suspension displayed zero order release kinetics and drug release. IR spectroscopic studies indicated that there are no drug-excipient interactions. When compared to other all the formulations F9 is the best formulation which showed 99.52% of drug released respectively within 25 min and follows Zero order release kinetics as the formulation F9 contains higher concentration of SLS as well as PVA, the decreased drug release time was due to that PVA is an hydrophilic polymer.

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