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RESEARCH ARTICLE

ABACAVIR LOADED NANOPARTICLES: PREPARATION, PHYSICO-CHEMICAL CHARACTERIZATION AND *IN VITRO* EVALUATION

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ABSTRACT

Objectives: Abacavir is a nucleoside analog reverse transcriptase inhibitor (NRTI), antiretroviral drug; it is used in treatment of AIDS. The present study deals with the formulation and evaluation of Abacavir nanoparticles.

Methods: Abacavir nanoparticles were formulated by solvent displacement method using Eudragit RL-100, chitosan and Poloxamer-188. Nanoparticles were characterized by determining its particle size, drug entrapment efficiency, particle morphological character and *in-vitro* drug release.

Results: Particle size range of nanoparticles was in the range of 121.4-140.6 nm. Zeta potential of formulations was determined, and it was found in range of 16.5-20.45 mv. The *in-vitro* release of nanoparticles were carried out which exhibited a sustained release of Abacavir from nanoparticles up to 10 hrs.

Conclusion: The study concludes that nanoparticles can be a promising drug delivery system for sustained release of Abacavir in terms of increased bioavailability.

Keywords: Abacavir, entrapment efficiency, nanoparticles, solvent displacement method, Zeta potential.

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INTRODUCTION

Nanoparticles are promising drug delivery systems of controlled and targeted drug release. Nanoparticles are solid colloidal particles with diameters ranging from 1-1000 nm. They possess unique properties like small size, high surface area, and ease of suspending in liquids, deep access to cells and organelles, variable optical and magnetic properties are offered by nanoparticles¹. Their advantages includes increased bioavailability, site specific drug delivery, sustained release of drug over longer period of time, retention of dosage form and reduction in dosing frequency². Abacavir is a nucleoside analog reverse transcriptase inhibitor (NRTI), antiretroviral drug; it is used in treatment of AIDS. It is used together with other HIV medications, and is not recommended by itself³. It has *in-vitro* activity against a range of HIV-1 and HIV-2 strains. It has been well tolerated, the main side effect is hypersensitivity, this can be severe, and in rare cases, possibility for fatal. It has short half life and frequent administration of it is necessary to maintain its effective plasma concentration⁴. In anti-retroviral therapy, a sustained release drug delivery system is

required for reduction of side effects and improving the bioavailability⁵. So, Abacavir is a suitable candidate to develop and evaluate as nanoparticles formulations⁵.

MATERIALS AND METHODS

Abacavir was a gift sample from Green life Pharmaceuticals Ltd. Eudragit RL-100 was obtained from Neimeth, and chitosan from Emzor Pharmaceuticals. All other chemicals used were of analytical grade.

Preparation of Abacavir nanoparticles

Abacavir nanoparticles were prepared by the solvent displacement method. Drug and various proportions of polymers i.e. Eudragit RL-100, and chitosan were dissolved in acetone. This solution was poured drop wise into solution of poloxamer 188 with magnetic stirring at room temperature. Nanoparticles were spontaneously formed and turned the solution slightly turbid then; acetone was removed by continuous stirring at 35-40°C. The prepared suspension was centrifuged, supernatant was removed and the sediment was freeze dried for further analysis⁶.

Particle size, surface morphology and zeta potential

The surface morphology (roundness, smoothness, and formation of aggregates) and particle size were studied by scanning electron microscopy. Zeta potential is an

abbreviation for electrokinetic potential in colloidal systems⁷. Zeta potential of the formulations was determined by zeta potential probe model DT- 300.

Table 1: Composition of different Abacavir nanoparticles

| Formulation code | Eudragit RL-100 (mg) | Chitosan (mg) | Water (ml) | Acetone (ml) | Poloxamer-188 (mg) |
|------------------|----------------------|---------------|------------|--------------|--------------------|
| NP1 | 100 | - | 40 | 10 | 10 |
| NP2 | 200 | - | 40 | 10 | 20 |
| NP3 | - | 100 | 40 | 10 | 30 |
| NP4 | - | 200 | 40 | 10 | 40 |

Drug content

The drug content in each formulation was determined by weighing nanoparticles equivalent to 30 mg of Abacavir and dissolving in 100 ml of 6.8 pH phosphate buffer, followed by stirring. The solution was filtered through a 0.45 μ m membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometrically at 271 nm using 6.8 pH phosphate buffer as blank⁸. The drug content of the prepared nanoparticles was determined by the formula:

$$\% \text{ Drug content} = \frac{\text{Weight of drug in nanoparticles}}{\text{Weight of nanoparticles}} \times 100$$

Nanoparticles recovery

The recovery of nanoparticles suspension was analyzed by centrifugation method, where 10 ml suspension was centrifuged at 15000 rpm at 4°C. The sediment nanoparticles were collected, freeze dried and calculated for % yield⁹.

$$\% \text{ Yield} = \frac{\text{Weight of recovered particles}}{\text{Weight of drug and polymer used}} \times 100$$

Drug entrapment efficiency

15 mg of freeze dried nanoparticles were taken in a volumetric flask filled with distilled water for extraction of drug and kept for 24 hours. The mixture was sonicated for 20 min. Then filtered by using

vacuum filter to obtain complete clear solution and sample will be assayed by UV-spectrophotometer at 271 nm¹⁰.

$$\% \text{ DEE} = \frac{\text{Weight of drug in nanoparticles}}{\text{Weight of drug used}} \times 100$$

In vitro release studies

In vitro release studies were carried out by using dialysis tubes with an artificial membrane. The prepared Abacavir nanoparticles and 10 ml of phosphate buffer pH 7.4 was added to the dialysis tube and subjected to dialysis by immersing the dialysis tube to the receptor compartment containing 250 ml of phosphate buffer pH 6.8. The medium in the receptor was agitated continuously using a magnetic stirrer a temperature was maintained at 37 \pm 1°C. 5ml of sample of receptor compartment were taken at various intervals of time over a period of 24h and each time fresh buffer was replaced. The amount of drug released was determined spectrometrically at 271 nm¹¹.

Kinetic modeling

In order to understand the kinetic and mechanism of drug release, the result of *in vitro* drug release study of nanoparticles were fitted with various kinetic equation like zero order, first order and Higuchi's model¹².

Table 2: Physicochemical characterization of Abacavir nanoparticles.

| Formulation code | Particle size (nm) | % Drug content | % Yield | Zeta potential (mv) | % Entrapment efficiency |
|------------------|--------------------|------------------|---------|---------------------|-------------------------|
| NP1 | 121.4 \pm 0.37 | 70.44 \pm 0.26 | 59.46 | 16.5 \pm 0.52 | 99.22 |
| NP2 | 125.5 \pm 0.25 | 78.32 \pm 0.41 | 64.38 | 18.31 \pm 0.37 | 99.45 |
| NP3 | 130.4 \pm 0.71 | 80.35 \pm 0.82 | 69.57 | 20.45 \pm 0.41 | 99.92 |
| NP4 | 140.6 \pm 0.43 | 84.22 \pm 0.31 | 70.65 | 19.72 \pm 0.73 | 99.85 |

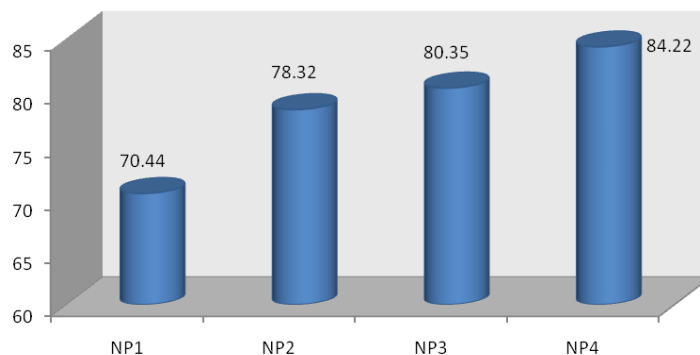


Figure 1: % Drug content of Abacavir nanoparticles

RESULTS AND DISCUSSION

Four different Abacavir nanoparticles formulations were prepared by the solvent displacement method with varying proportions of Eudragit RL-100, and chitosan. The scanning electron microphotograph

indicate that Abacavir nanoparticles have a discrete spherical structure without aggregation. The particle size of nanoparticles varied somewhat among the formulation due to variation in the composition of formulations. Particle size of nanoparticles was in the

range of 121.4-140.6 nm. Zeta potential of best formulation was determined and it was found in range of 16.5-20.45 MV. Since there was a decrease of

surface potential, it could be concluded that a part of drug was absorbed on the polymeric particles. The drug content was maximum in formulation NP4.

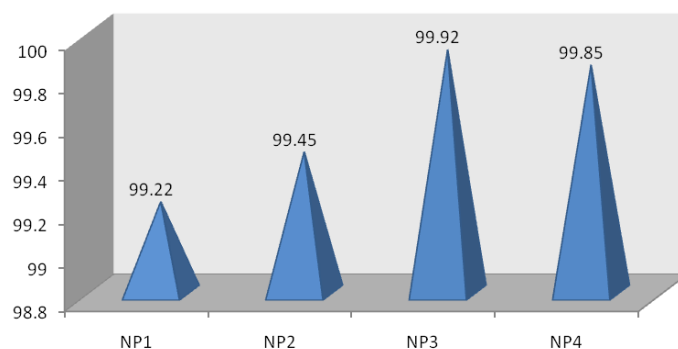


Figure 2: % Drug entrapment efficiency of Abacavir nanoparticles

In general nanoparticles exhibited an increase in drug content with an increased in the polymer ratio, up to particular concentration. A decrease in drug content was observed after that point due to the saturation capacity of polymer. The percent entrapment efficiency was found to be more than 99 % in all formulations.

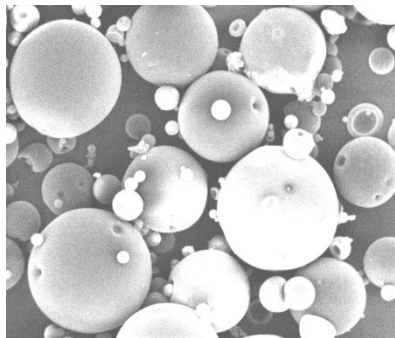


Figure 3: SEM of Abacavir nanoparticles of batch NP4

The *in-vitro* release study was conducted for 10 hrs. The release of Abacavir mainly depends upon the polymer concentration. The burst release of Abacavir from nanoparticles at initial stage resulted from the dissolution of drug crystals on the surface of nanoparticles. Nanoparticles of batch NP3 shows maximum release 82.11 % in 10 hrs. The *in vitro* release data was applied to various kinetic models to predict the drug release kinetic mechanism. Nanoparticles were fitted with various kinetic equations like zero order, first order and Higuchi's model. The release constant was calculated from the slope of appropriate plots, and the regression

coefficient (r^2) was determined by the means of PCP Disso software version 3.0.

Table 3: Correlation coefficient of different nanoparticles formulations.

| Formulation code | Correlation Coefficient (r^2) | | |
|------------------|-----------------------------------|----------------------|---------------------|
| | Higuchi kinetics | First order kinetics | Zero order kinetics |
| NP1 | 0.993 | 0.882 | 0.956 |
| NP2 | 0.992 | 0.884 | 0.950 |
| NP3 | 0.982 | 0.917 | 0.893 |
| NP4 | 0.976 | 0.925 | 0.900 |

CONCLUSION

The method used for preparation of nanoparticles of Abacavir was found to be simple and reproducible. The slow and constant release of Abacavir from nanoparticles maintain constant drug plasma concentration thereby increasing therapeutic efficacy. The developed formulation overcome and alleviates the drawbacks and limitations of Abacavir sustained release formulations. The development of effective nano delivery systems capable of carrying a drug specifically and safely to a desired site of action is one of the most challenging tasks of pharmaceutical formulation investigators. On the basis of different parameters i.e. physicochemical and *in-vitro* release study, nanoparticles of batch NP4 are concluded as optimum formulations. Further, it can be concluded that the nanoparticulate formulation can be an innovative and promising approach for the delivery of Abacavir.

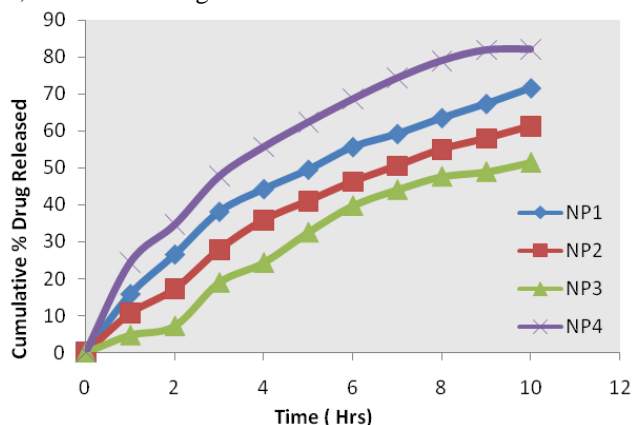


Figure 4: In-vitro drug release profile of Abacavir nanoparticles

AUTHOR'S CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

REFERENCES

1. Tamizhrasi S, Shukla A, Shivkumar T, Rathi V, Rath JC. Formulation and evaluation of lamivudine loaded polymethacrylic acid nanoparticles. *Int J Pharm Tech Res* 2009; 1(3): 411-415.
2. Yaowalak B, Ampol M, Bernd WM. Chitosan drug binding by ionic interaction. *Eur J Pharm Sci* 2006; 62, 267-74. <https://doi.org/10.1016/j.ejpb.2012.04.007>
3. Rauch A, Nolan D, Martin A. Prospective genetic screening decreases the incidence of abacavir hypersensitivity reactions in the Western Australian HIV cohort study. *Clin Infect Dis* 2006; 43(1): 99-102. <https://doi.org/10.1086/504874>
4. Heatherington. Genetic variations in HLA-B region and hypersensitivity reactions to abacavir. *Lancet* 2006; 359 (9312): 1121-1122. [https://doi.org/10.1016/s0140-6736\(02\)08158-8](https://doi.org/10.1016/s0140-6736(02)08158-8)
5. Mallal S, Phillips E, Carosi G. HLA-B5701 screening for hypersensitivity to abacavir. *New England J Med* 2008; 358 (6): 568-579. <https://doi.org/10.1056/NEJMoa0706135>
6. Kheradmandnia S, Vasheghani-Farahani E, Nosrati M, Atyabi F. Preparation and characterization of ketoprofen-loaded solid lipid nanoparticles made from beeswax and carnauba wax. *Nanomed Nanotechnol Biol Med* 2010; 6:753-9. <https://doi.org/10.1016/j.nano.2010.06.003>
7. Min-Soo K, Shun-Ji J, Jeong-Soo K, Hee Jun P, Ha-Seung S, Reinhard HH. Neubert Sung-Joo Hwang. Preparation, characterization and *in vivo* evaluation of amorphous atorvastatin calcium nanoparticles using supercritical anti-solvent (SAS) process. *Eur J Pharm Biopharm* 2008; 69, 454-465. <https://doi.org/10.1016/j.ejpb.2008.01.007>
8. Corsini A, Bellosta S, Baetta R, Fumagalli R, Paoletti R, Bernini F. New insights into the pharmacodynamic and pharmacokinetic properties of statins. *Pharmacol Ther* 1994; 84: 413-428. [https://doi.org/10.1016/s0163-7258\(99\)00045-5](https://doi.org/10.1016/s0163-7258(99)00045-5)
9. Schwarz C, Mehnert W. Freeze-drying of drug-free and drug-loaded solid lipid nanoparticles (SLN). *Int J Pharmaceutics* 1997; 157(2): 171-179. [https://doi.org/10.1016/S0378-5173\(97\)00222-6](https://doi.org/10.1016/S0378-5173(97)00222-6)
10. Shegokar R, Singh KK, Müller RH. Production and stability of stavudine solid lipid nanoparticles from lab to industrial scale. *Int J Pharm* 2011; 416: 461-470 <https://doi.org/10.1016/j.ijpharm.2010.08.014>
11. Mohanty C, Sahoo SK. The *in vitro* stability and *in vivo* pharmacokinetics of curcumin prepared as an aqueous nanoparticulate formulation. *Biomaterials* 2010; 31: 6597-6611. <https://doi.org/10.1016/j.biomaterials.2010.04.062>
12. Gourish C, Seth N, Sharma V. Nanoparticles and nanotechnology: clinical, toxicological, social, regulatory and other aspects of nanotechnology. *J Drug Deliv Therap* 2013; 3(4): 138-141. <https://doi.org/10.22270/jddt.v3i4.541>