INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND NOVEL SCIENCES

IJPRNS

FORMULATION AND EVALUATION OF POLYMERIC NANOPARTICLES OF ANTIVIRAL DRUG ACYCLOVIR

G. Nirosha*, A. Anil kumar, N.Srinivas Rao

Department of Pharmaceutics, Vikas College of pharmacy, Putrela rode, Vissannapeta-521215, Andhra Pradesh, India.

ABSTRACT

Nanotechnology refers to the creation and utilization of materials whose constituents exist at the nanoscale; and, by convention, be up to 100 nm in size. Nanotechnology explores electrical, optical, and magnetic activity as well as structural behavior at the molecular and sub molecular level. It has the potential to revolutionize a series of medical and biotechnology tools and procedures so that they are portable, cheaper, safer, and easier to administer. Nanoparticles are being used for diverse purposes, from medical treatments, using in various branches of industry production such as solar and oxide fuel batteries for energy storage, to wide incorporation into diverse materials of everyday use such as cosmetics or clothes, optical devices, catalytic, bactericidal, electronic, sensor technology, biological labelling and treatment of some cancers. Due to their exceptional properties including antibacterial activity, high resistance to oxidation and high thermal conductivity, nanoparticles have attracted considerable attention in recent years. Nanoparticles can be synthesized chemically or biologically. Metallic nanoparticles that have immense applications in industries are of different types, namely, Gold, Silver, Alloy, magnetic etc. This study aims to develop polymeric nanoparticles of acyclovir using PLGA, TPGS. The prepared formulations were evaluated for compatibility and invitro drug release studies and the results were found to be positive.

Key Words: Nanoparticles, silver, bactericidal, thermal conductivity

Author for correspondence
G. Nirosha,
Department of Pharmaceutics,
Vikas college of pharmacy, Putrela rode,
Vissannapeta-521215, Andhra Pradesh, India.
Email: nirosha123ghantasala@gamil.com

INTRODUCTION

Comparing current practice of medicine to that of the last century, one cannot help but to notice innumerable advancements to address previously incurable diseases.

Numerous new medications have been developed to effectively treat complicated conditions, but at the same time some of them produce severe side effects that the benefit does not always outweigh the risk. On the other hand, some drugs have been proven to be very effective *in vitro* but cannot withstand the endogenous enzymes found within the gastrointestinal (GI) tract (if taken orally), deeming them nearly worthless in vivo.

While incredible progress has been made in identifying drug targets, designing and making better drug molecules; there is still room to improve the drug delivery systems and targeting. Within past few decades, nanotechnology, in particular manufacturing of nanoparticles has found an unprecedented attention in broad areas of science. A PubMed search ("nanoparticles") reveals, last year alone (2016), there were "19,338" articles published related to various aspects of nanoparticle technology. The clever use of nanoparticles has revolutionized how drugs are formulated and delivered. Nanotechnology is a multi-disciplinary scientific field applying engineering and manufacturing principles at the molecular level. By applying nanotechnology to medicine, nanoparticles have been created to mimic or alter biological processes. Nanoparticles are solid, colloidal particles with size range from 10 nm to <1000 nm; however, for nanomedical application, the preferential size is less than 200 nm. One of the most significant areas of study has been in the creation of nanoparticle drug delivery systems. This succinct review will focus on the desirable characteristics for successful nanoparticle based drug delivery systems as well as the various disease states in which these nanoparticle systems have shown promise.

Necessity for nanoparticle-based drug formulations

There are various reasons why using nanoparticles for therapeutic and diagnostic agents, as well as advancement of drug delivery, is important and much needed. One of them is that, traditional drugs available now for oral or injectable administration are not always manufactured as the optimal formulation for each product. Products containing proteins or nucleic acids require a more innovative type of carrier system to enhance their efficacy and protect them from unwanted degradation. It is notable that the efficiency of most drug delivery systems is directly related to particle size (excluding intravenous and solution). Due to their small size and large surface area, drug nanoparticles show increase solubility and thus enhanced bioavailability, additional ability to cross the blood brain barrier (BBB), enter the pulmonary system and be absorbed through the tight junctions of endothelial cells of the skin. Specifically, nanoparticles made from natural and synthetic polymers (biodegradable and non-biodegradable) have received more attention because they can be customized for targeted delivery of drugs, improve bioavailability, and provide a controlled release of medication from a single dose; through adaptation the system can prevent endogenous enzymes from degrading the drug. Secondly, the development of new drug delivery systems is providing another advantage for pharmaceutical sales to branch out. Innovative drug delivery is driving the pharmaceutical companies to develop new formulations of existing drugs. While these new formulations will be beneficial to the patients, it will also create a powerful market force, driving the development of even more effective delivery methods. Furthermore, not only will the companies thrive to develop new formulations for their own "intellectual property," but will have motivation due to patent expirations. The benefit of pharmaceutical companies taking advantage of this new technology is that nanotechnology gives new life to those drugs those were previously considered unmarketable due to low solubility and bioavailability, and high toxicity and marked side effects. Finally, we would like to highlight a very recent article from Prof. Robert Langer's group, at the Massachusetts Institute of Technology, with an up-to-date survey of the types of polymeric systems used in the drug delivery (1-6).

MATERIALS AND METHODS

IR spectroscopic study of Acyclovir

Compatibility study (IR spectroscopy)

The drug-polymer compatibility was ascertained by subjecting the drug and homogenates of drug and polymer to Infrared spectrophotometric study.

Method of preparation of acyclovir loaded nanoparticles (7-9)

Solvent dispersion (Nanoprecipitation)

The nanoparticles are prepared by dissolving the drug in organic phase along with the polymer (PLGA) and added to the aqueous solution containing TPGS which acts as an emulsifier (Table-1). The solution of organic phase was added in drop wise into aqueous phase under homogenization at 11,000 rpm. The dispersion was kept under magnetic stirring for 4hrs at room temperature. The solution is kept under reduced pressure for about 2-3min. This process forms nanoparticles loaded with drug (fig-1).

Fig-1 Homogenizer used for preparation of Nano particles

Table-1 Composition of the Nanoparticles

Ingredients	Batch no							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
PLGA (50:50)(mg)	1300	1300	1300	2500	5000	7500	10000	12500
TPGS(%g/ml)	3	4	5	6	7	8	9	10
Acyclovir (mg)	200	200	200	200	200	200	200	200
Acetone (ml)	30	30	30	30	30	30	30	30
Water (ml)	100	100	100	100	100	100	100	100

***In Vitro* Acyclovir Release**

10 mg drug equivalent freeze dried Acyclovir loaded nanoparticles were dispersed in 3 ml pH 7.4 phosphate buffer solution which is transferred in dialysis bag and suspended in 100 ml of isotonic pH 7.4 Phosphate buffer solution (PBS). The bag was placed under magnetic stirring in a water bath maintained at 37 ± 0.5° C. At fixed time intervals 5ml of samples were taken out and fresh buffer was replaced. The obtained solution was analyzed by UV to determine the drug content.

RESULTS AND DISCUSSION

The present study was aimed to developing Nano particles of Acyclovir using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

The nanoparticles prepared were evaluated as per the following parameters- Drug Loading, Entrapment efficiency, Particle size, Zeta Potential and *In vitro* release diffusion study

The first part of the plan of work was to optimize the concentration of surfactant to be used in the formulation of nanoparticles. To achieve this, the first three formulations were planned with TPGS concentrations 3, 4 and 5% respectively. The optimization of surfactant concentration was done on the basis of particle size and entrapment efficiency of nanoparticles obtained (Table-2). As the least particle size and best entrapment efficiency was obtained for F2 formulation when compared to F1 and F3, it was decided that the 3%(with concentration increased according to the total weight) of TPGS was the optimum concentration to be used in further formulations. The next part of the plan of work was to optimize the drug polymer ratio. For this, 5 batches were planned (F4 to F8) using the drug polymer ratios of 1:5, 1:10, 1:15, 1:20 and 1:25 respectively. The optimum drug polymer ratio was selected on the basis of entrapment efficiency of the polymer. The entrapment efficiency was found to be very low for 1:5 (49.88%) and 1:10 (75.816%) drug polymer ratio. In case of F6, F7 and F8 formulations the entrapment efficiencies were found to be 88%, 94% and 96% respectively.

Therefore, it was decided to perform *in vitro* diffusion studies for all these three (F6, F7 and F8) batches. Based on the entrapment efficiency, a set of formulations (F6, F7 and F8) were considered as optimized compositions which can be taken up further studies and evaluated for the diffusion studies (Table-3).

Table-2 Evaluation Studies of Prepared Nanoparticles: Entrapment Efficiency, Particle size, Zeta Potential and Drug Loading

Batch No	Particle size (nm)	Zeta potential (mV)	Drug Loaded (mg)	Entrapment Efficiency (%)
F1	152.3	-25.34	724.2	90.52
F2	164.21	-24.16	753.4	94.17
F3	174.25	-23.41	702.14	87.76
F4	253.1	-22.18	722.1	90.27
F5	100.3	-21.34	789.54	98.69
F6	124.8	-12.14	793.48	99.18
F7	121.5	-6.47	736.47	92.05
F8	152.4	-16.48	741.1	92.63

N=6, average values are represented

Table-3 Selected formulations used for *in vitro* diffusion study

Ingredients (mg)	F6	F7	F8
PLGA (50:50)	7500	10000	12500
TPGS%(g/ml)	8	9	10
Acyclovir (mg)	200	200	200
Acetone (ml)	30	30	30
Water (ml)	100	100	100

SEM studies

SEM image of formulation F6 Optimised formulations (Fig-2)

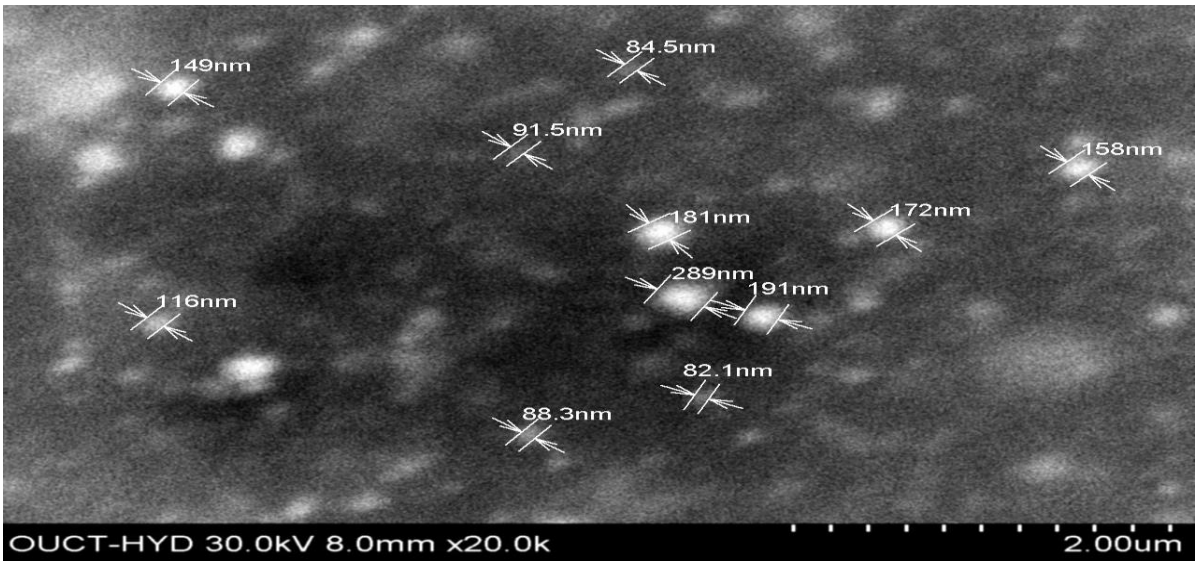

Fig-2 SEM image of formulation F6 Optimised formulations

DSC studies

Following the above DSC spectrums it is observed that there was no incompatibility observed between the polymers selected and the pure drug hence considered the formulations to be compatible (Fig-3, 4).

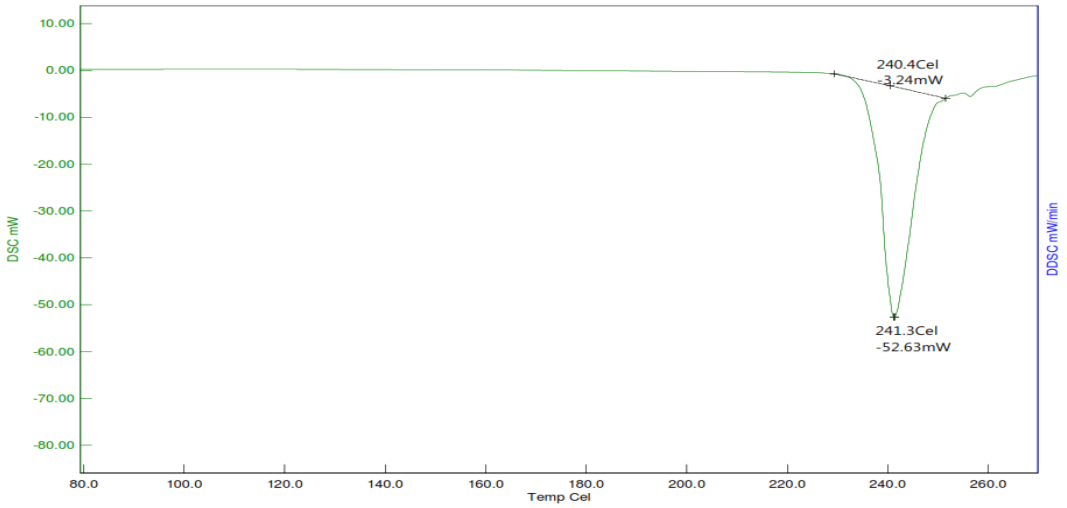

Fig-3 DSC spectrum of pure drug

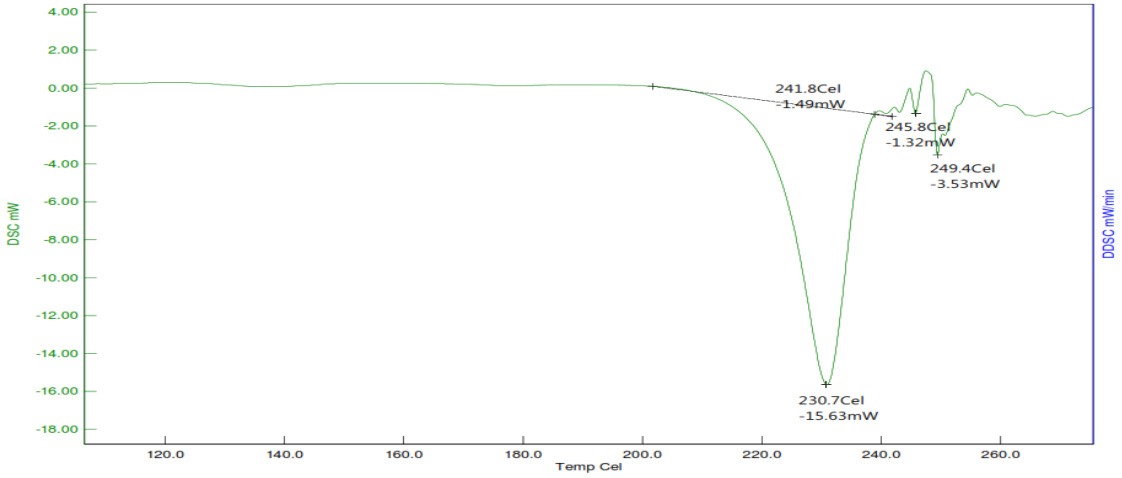

Fig-4 DSC spectrum of optimised formulation

Stability Studies

There were no significant changes in physical and chemical properties of capsule of formulation F-6 after 2 months (Table-4).

Table-4 Results of stability studies of optimised formulation F6

Formulation code	Parameters	Initial	1st Month	2nd Month
F6	%Drug release (%)	97.62	96.85	96.14
	particle size (nm)	124.8	128.6	131.8
	Entrapment efficiency (%)	99.18	98.26	98.19

CONCLUSION

The present research proposed a novel formulation by applying as an emulsifier to fabricate Nanoparticles by solvent dispersion/nanopresipitation for controlled release of Acyclovir. Investigation of the preparation, characterization and in-vitro release of the Nanoparticles was carried out. The different formulations of with various ratios of drug-polymer and surfactant were evaluated and optimised. Our results demonstrated that vitamin E TPGS could be an efficient emulsifier for fabrication of polymeric nanoparticles, which can achieve excellent effects in drug encapsulation efficiency, size and size distribution and *in vitro* release kinetics of the nanoparticles. In this research, a drug encapsulation efficiency as high as 97% has been achieved. The particle size and size distribution strongly depends on the amount of TPGS added in the fabrication. Drug release kinetics indicated that drug release was best explained by peppas equation, as these plots showed the highest linearity (r^2=0.907) but a close relationship was also noted with first order kinetics (r^2 =0.989)

REFERENCES

1) Remington: *The Science and Practice of Pharmacy*, 20th Edition, Vol. 1 Edited by Alfonso R Gennaro Published by Lippincot Williams and Wilkins, Philadelphia, 2000; Page No. 903.
2) *Controlled Drug Delivery Fundamentals and Applications*, 2nd Edition edited by Robonson JR, Lee VHL, and New York: Dekker, 1987; Page No. 3.
3) *Controlled and Novel Drug Delivery*", 1st Edition, Edited by Jain NK, Published by CBS Publishers & Distributors, New Delhi, 1997; Page No. 1.
4) *The Theory & Practice of Industrial Pharmacy*, 3rd Edition Edited by Leon Lachman, Herbert A. Liberman, Joseph L.Kanig Published by, Varghese Publishing House, Bombay, 1991; Page No. 430-439.
5) *Targeted and Controlled Drug Delivery Novel Carrier Systems*. 1st Edition, Edited by SP Vyas and Khar RK, CBS Publishers & Distributors, New Delhi, 2002; Page No. 39.
6) Subal C Basak, Novel Drug Delivery Systems. *The Indian Pharmacist*, April 2005: 7-10.
7) Yerikala Ramesh, Koorapati Balasaradhi, Kaki Rohan Abhilash. Formulation andevaluation of albendazole nanoparticles. *Journal of Drug Delivery &Therapeutics*. 2019; 9(1-s):16-22.
8) S. S. Shelake, S. V. Patil, S. S. Patil and Pallavi Sangave. Formulation and Evaluation of Fenofibrate-loaded Nanoparticles by Precipitation Method. *Indian J Pharm Sci* 2018; 80(3): 420-427.
9) S.Selvaraj, V. Niraimathi and M.Nappinnai, Formulation and evaluation of acyclovir loaded chitosan nanoparticles, *Int. J. of Pharmacy and Analytical Research* Vol-5(4) 2016 619-621.