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Formulation and Evaluation of Polymeric Nanoparticle by Nano-Precipitation Method

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ABSTRACT

Acyclovir is also known as Acyclovir, this drug is used for treatment of viral infection, particularly for treatment of herpes simplex viral infection. These are taken for month during treatment of herpes simplex viral infection. These are showing the action against all herps virus family. The acyclovir is poorly water-soluble drug. Due to that main aim is to increase the solubility of acyclovir in other solvent. The bioavailability of acyclovir is very less about (15-35%) because it has less oral route absorption. Due to that the acyclovir are given in intravenous route. When acyclovir is taken in oral route, the peak plasma concentration occurs after 1-2 h. The acyclovir having 9-33% of plasma protein binding. The BCS class of acyclovir are Class third (high solubility and Low permeability). Due to that acyclo vir are formulate in the form of nanoparticle. Chitosan are the polymers which are used for the formulation of nanoparticle. The chitosan is found to be compatible with acyclovir. Formulation of acyclovir nanoparticle was done by Nano-precipitation method. Many evaluation tests performed during the formulation of Acyclovir nanoparticle mainly zeta sizer is use for the determination of particle size, zeta potential and PDI (poly disperse index) also performed evaluation of loading efficiency and % Drug entrapment.

Keywords: Acyclovir, Chitosan, Zeta sizer and Nanoparticle.

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INTRODUCTION

Nano is a metric measure of one billion of a meters[6]. The nanoparticle is the simplest forms of structure are having in nm range[9]. The nano-precipitation method is used for the formulation of nano particle. There are several methods are available for the precipitation of nano particle. For the preparation of acyclovir nanoparticle, the nano-precipitation method is used. There are several polymers which are used for the preparation of nanoparticle such as bovine serum albumin, chitosan and gelatine. For the preparation of acyclovir nanoparticle chitosan was used. The chitosan is clinically use for treatment of herpes simplex viral infection. The acyclovir present in BCS class third which are having low permeability and high solubility. The elimination half-life of acyclovir is about 3 hr. The acyclovir is generally absorbed from upper part of small intestine and stomach. It is need to formulate the nano particle of acyclovir. When Attia et. At, prepared noisome of acyclovir then the bioavailability of acyclovir was increased[1].

At presently Acyclovir are present in market in the form of capsule (200 mg) and also tablet in (200,400,800 mg) and also in the form of suspension, topical ointment and intravenous injection. The absorption rate of oral tablet of acyclovir as very slow about 5 times was taken a day. Acyclovir are having narrow absorption window. Th main aim of present study was to increase the bioavailability of acyclovir drug by formulating nano particle. The nano particle of acyclovir is easily entering inside the cell and

shoes the proper effect. The one and most important advantage of nano particle is that are made of polymer and polymer are having the ability to penetrate easily inside the cell and also having control release of encapsulated drug. The storage capacity of nanoparticle for drug are also high. The nanoparticle is having Diameter about range 10-1000nm, due to their size called as nanoparticle. They are used for target drug delivery system by changing their size, pharmacokinetic and pharmacodynamic property. The nanoparticle is the process in which active ingredient dissolved, encapsulation in matrix material such as polymer. They had been prepared from different polymer which are having therapeutic activity and may be reduces toxic effect. [2,3] Both synthetic and non-synthetic polymer is used for preparation of nanoparticle. The nanoparticle is having two main subtypes such as 1) nanosphere and 2) nano capsules. The nanospheres are complex structure of polymer in which drug molecule are cross link. In case of nano capsule, the drug is present in centre hallow space of polymeric layer[4,5]. The most important polymer during formulation of nanoparticle are chitosan and having main advantage are it including biocompatibility, biodegradability and low immunogenicity. Chitosan also has a very low toxicity[7].

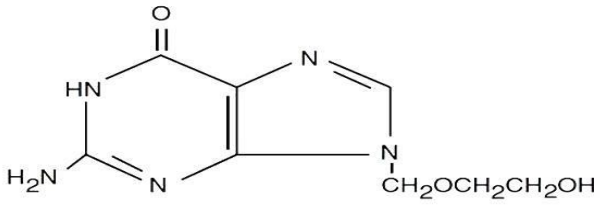
Nanoparticles are sub-nano sized colloidal structure composed of synthetic and semisynthetic polymer[4]. The atomic force microscope (AFM) is ideally suited for characterizing nanoparticle[8]. Near about this solid matter on the earth can be found in size range of colloids and nanoparticle[10]. There are different ideal methods that are used for synthesis of nanoparticle[11]. Nanoparticle synthesis by chemically or biologically, many adverse effects occur due to chemical synthesis because toxic chemical is adhering on surface[12].

MATERIAL AND METHOD

Table-1: List of material used for the study

S.N.	Ingredients	Supplier
1	Acyclovir	Modern Laboratories (Indore, India)
2	Chitosan	Indian sea food (Cochin India)
3	Dimethyl sulfoxide	Laboratory
4	Rotary flash evaporator	KNF
5	Ultra-centrifugation	Beckman Coulter
6	Zeta sizer	Malvern
7	Magnetic stirrer	REMI
8	Weighing Balance	Jepson's

Drug Profile



Structure of Acyclovir

Acyclovir is a guanosine derivative and it has 100 times potent than other antiviral drugs. It has antiviral activity against the herpes virus, particularly against herpes simplex. It is 10 time more active than idoxuridine. Acyclovir selectively inhibits the herpes virus DNA Replication. Acyclovir triphosphate is the active antiviral agent that inhibits the host cell DNA Polymerase. Headact, nausia, vomating, skin rash, fever, increase hair loss, and depression are the adverse reaction of acyclovir.

Preparation of Nanoparticle

Nanoparticles were prepared according to the Nano-precipitation method. 200mg of polymer such as chitosan dissolved in 25ml of acetone separately. Then 100mg Acyclovir dissolved in 2ml of Dimethyl sulphoxide (DMSO) separately. After both solutions was mixed together and add 50ml of water and stirred the solution for 30min. Then this solution was added to rotary flash evaporator for evaporation of Acetone under reduced pressure. Finally, volume of suspension was adjusted to 10ml. Then this final 10ml volume of suspension was centrifuge at 15000 rpm at 4°C for 30 min. After centrifugation the supernatant was discard and precipitate was wash with water for 3 times. Then finally nanoparticle was dried in hot air oven at 60°C for 1 to 2 hr [1].

Table 2: Composition of Acyclovir nanoparticle.

Sr. No.	Batch Code	Amount of Drug (mg)	Chitosan (mg)
1.	F1	50	100
2.	F2	100	200
3.	F3	150	250
4.	F4	200	200

Characterization of Acyclovir Nanoparticle: -

Particle Size:

Particle size mainly determine by zeta sizer instrument. The instrument equipped with Malvern PCS software. Before taking result of sample, the sample solution was diluted with water (mainly take distilled water) and then takes a reading. In Result average particle size obtained. The particle sizes for nanoparticle are must be required in nano range. The particle size of sample solution was determined using light scattering technique and by Transmission electron microscope. Increased in particle size then decreased in uptake and bioavailability.

Analysis was carried out for 60s at 165^{0}c scattering angle of detection.[15] Particle size are more important because micro particle has been less effective drug delivery as compared to nanoparticle. The large particle having more care area and which fill more drugs in it. But release pattern is very slow. Large particle resists the fast drug release and polymer degradation. [3,16] The particle size and its distribution pattern are most important characterization of nanoparticle.[18] The particle size of nanoparticle also influences the drug loading, drug release and stability.[17] Particle size distribution is also called as PDI. Different technique used for determination of size of nanoparticle such as SEM, TEM, XRD, AFM and dynamic light scattering (DLS) [19,1,7,13,14].

Polydisperse Index (PDI):

PDI is also called as particles size distribution. The sample having very broad size distribution then polydisperse index value >0.7.[1] PDI of nanoparticle are obtained by photon correlation spectroscopic analysis. Polydisperse is composed of non-uniform molecular mass if its chain length very over a wide range of molecular mass[13]. During formulation of nanoparticle the effort of manufacturer is to achieve lowest polydisperse index[5].

Zeta Potential: -

During taking zeta potential two samples must be diluted with distilled water in ration 1:1000. Zeta sizer (Malvern instrument) was used. The analysis was carried out at 25^{0}c with the angle of detection of 90^0. The zeta potential in which we study the charge which are present on a surface of nanoparticle. In nanoparticle the drug molecule is covered with polymer, indirectly in zeta potential in which we study the charge present on surface of polymer. The ideal zeta potential value is must be required in range of above +30 to -30mV and this range prevent the aggregation of particle. The zeta potential of Acyclovir nanoparticle containing chitosan was observed -20mV [20,21,22].

Entrapment Efficiency:

For determination of drug entrapment, the amount of drug present in the clear supernatant after centrifugation was determined (w) by UV spectrophotometer at 254 nm. A standard calibration curve of drug was plotted for this purpose. The amount of drug in supernatant was then subtracted from the total amount of drug added during the preparation (W). Effectively, (W-w) will give the amount of drug entrapped in the particles [22].

$$\%\text{Drug Entrapment} = (W\text{-}w/W) \times 100$$

Loading Efficiency:

Drug content in the preparation was determined by extracting drug from the nanoparticle with 0.1M hydrochloric acid. In this method nanoparticle (50mg) were stirred in 50ml hydrochloric acid until dissolved. It was filtered by Millipore filter paper and drug content was determined, after suitable dilution. At 254nm by UV spectroscopy. The loading efficiency(L) of the nanoparticle was calculated according to following formula.

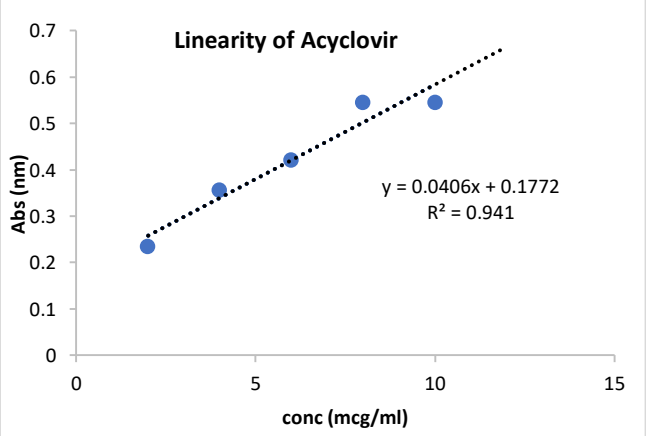
$$L\ (\%) = (Qn / Wn) \times 100$$

Were, Qn is the amount of drug present in nanoparticle and Wn is weight of nanoparticle[23,24,25].

In vitro drug release: -

The acyclovir chitosan nanoparticle was present in aqueous suspension they separated by using ultracentrifugation. Then 2mg of Acyclovir Nanoparticle was taken and dispersed in 10ml 7.4-phosphate buffer. After this 10ml solution place in dialysis membrane bag. Then make 900ml 7.4 phosphate buffer and add it in dissolution apparatus beaker. Make the temperature 37^{0}c. For the dissolution the USP paddle was used. At appropriate time intervals 1mL of the release medium was removed and 1mL fresh 7.4 phosphate buffer solution was added in to the system. The amount of acyclovir in the release medium was estimated by UV-Visible Spectrophotometer at 253 nm [15].

RESULT AND DISCUSSION



Graph 1: Linearity of Acyclovir

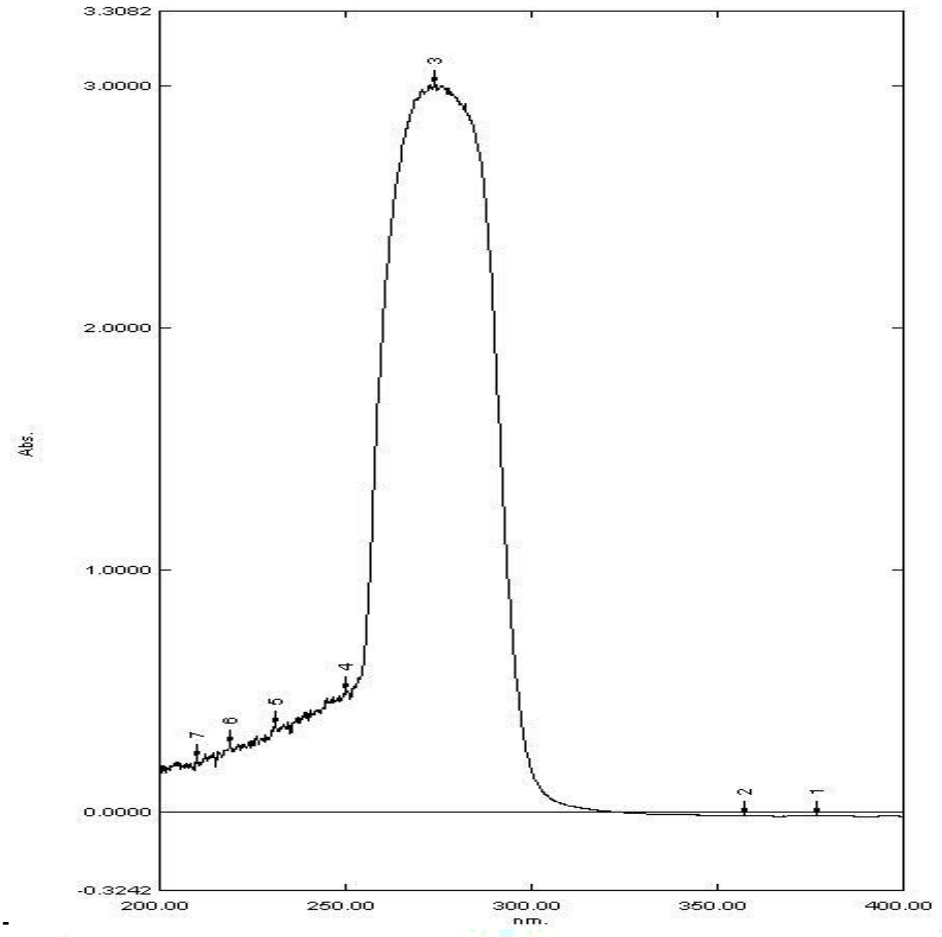
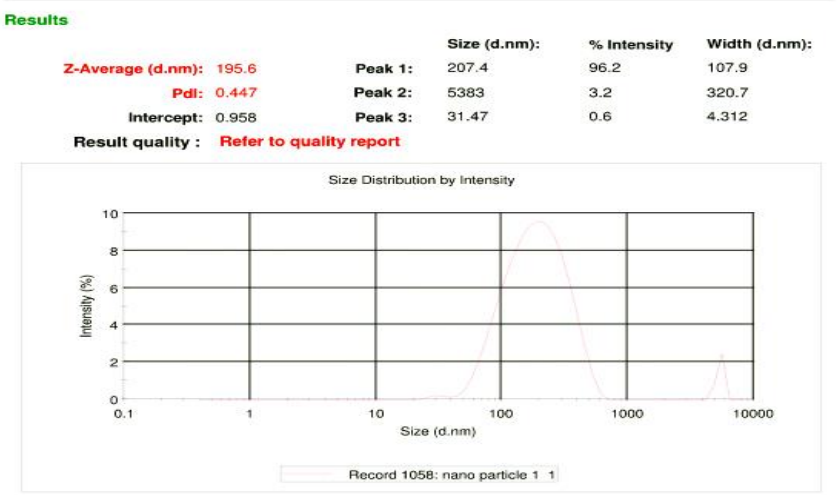


Figure 1: Spectrum of Acyclovir

Particle size

The particle size of liposome Increases by increasing the concentration of drug. In F2 batch the particle size occurs about 195.6 nm. Then final observation is as concentration of Acyclovir increase then particle size is also increase. Very slightly particle size change occurs in all batches.



Zeta Potential

The zeta potential is most important Evaluation parameter. There are many drugs which are affecting the zeta potential value of Nanoparticle. Due to some drug means those drugs incorporated in Nanoparticle which are causes the charge on the surface of Nanoparticle. Here in this work also observed that as amount of Acyclovir increases then zeta potential also increases. If zeta potential value is not in range of -30mV to +30mV then the aggregation of nanoparticle take place in formulation.

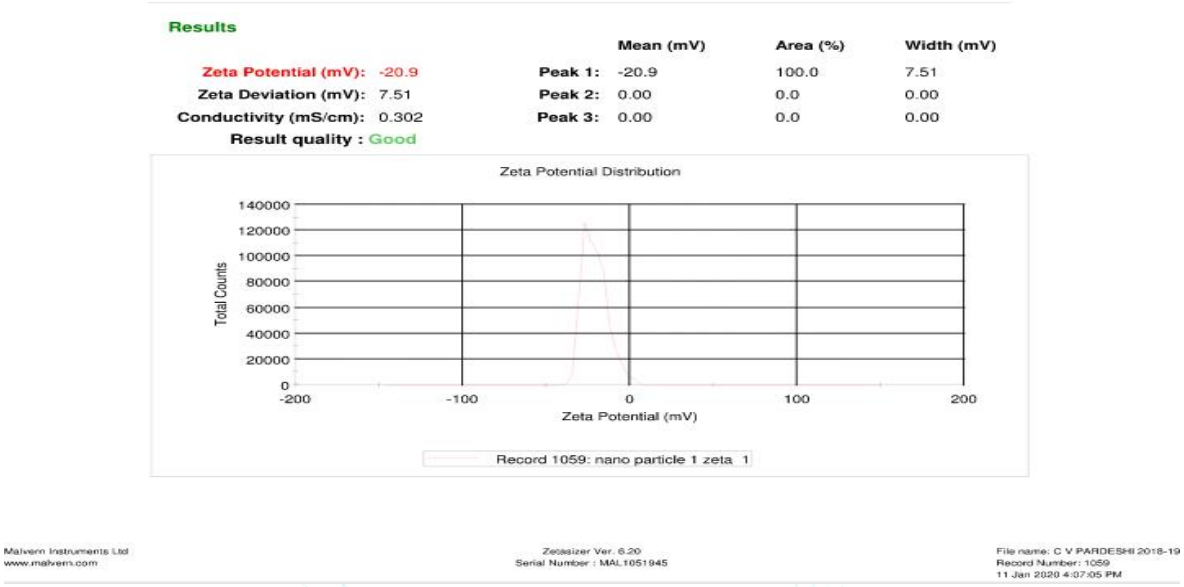


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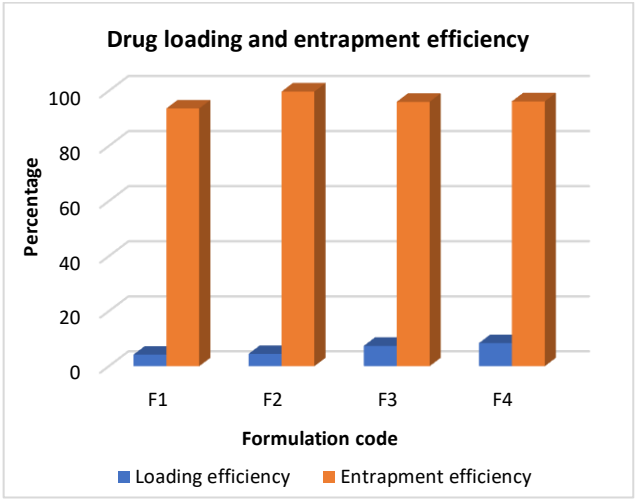
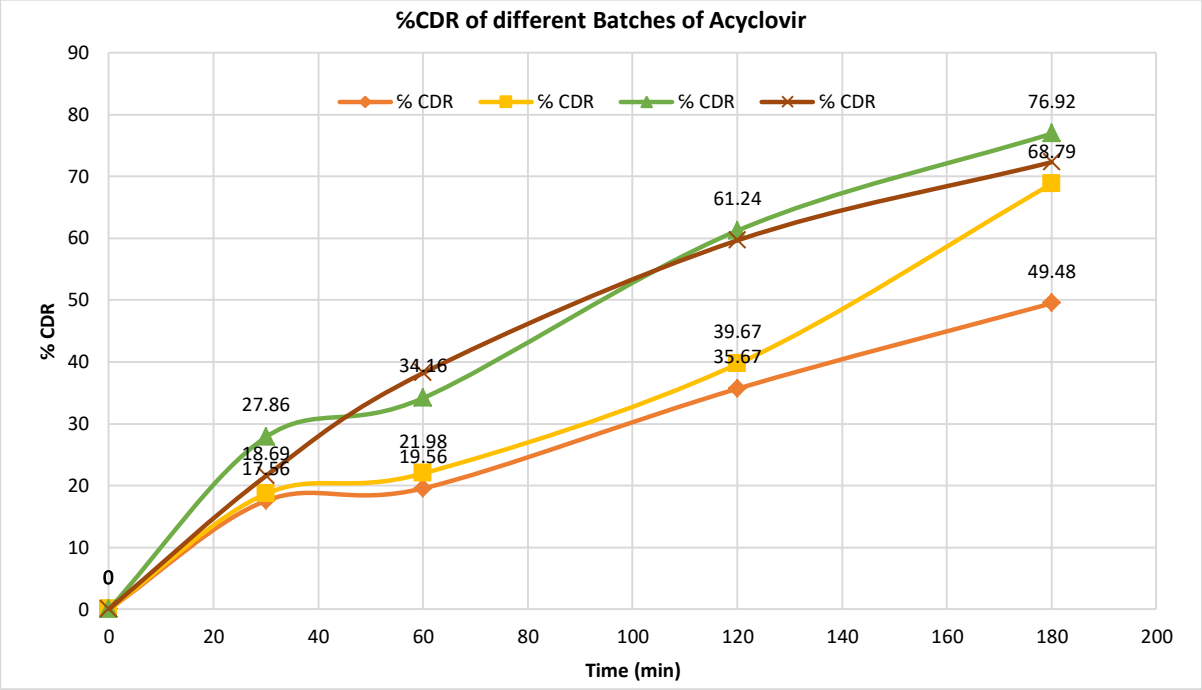
Table 3: Evaluation Parameter of Nanoparticle

Sr.no.	Evaluation Test	F1	F2	F3	F4
1.	Entrapment Efficiency (%)	93.64	99.76%	96.04	96.22
2.	Loading Efficiency (%)	4.2	4.48	7.41	8.41
3.	Particle Size (nm)	186.9	195.6	200.4	254.8
4.	Polydisperse Index (PDI)	0.245	0.447	0.569	0.698
5.	Zeta Potential (mV)	-15.4	-20.9	-22.3	-27.6



Graph 2: Effect of drug and polymer on Loading efficiency and Entrapment efficiency



Graph 3: % CDR of Different batches of Acyclovir.

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CONFLICT OF INTEREST

No conflict of interest.

CONCLUSION

During formulation of polymeric nanoparticle thus the polymer is most important. By using Chitosan as polymers for formulation of nanoparticle the result are obtains in well manner. The entrapment efficiency was 99.76 %. Loading efficiency was 4.48, Particle size-195.6nm, Polydisperse index was 0.447 and zeta potential was obtained in between -30 to +30 mV and that was -20.9mV.

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