International Journal of Research and Development in Pharmacy and Life Sciences
Available online at http//www.ijrdpl.com
February - March, 2014, Vol. 3, No.2, pp 925-934
ISSN: 2278-0238

Research Article

FORMULATION AND EVALUATION OF NANOPARTICLES CONTAINING ARTEMISININ HCL

Gupta Dilip Kumar*, Razdan B.K., Bajpai Meenakshi

Faculty of pharmacy, Uttarakhand Technical University, Sudhhowala, P.O. Chandanwari, Premnagar, Dehradun-248007, India

***Corresponding Author: Email kumarjai24sep@gmail.com**

(Received: November 01, 2013; **Accepted:** December 23, 2013**)**

ABSTRACT

The present study deals with the formulation and evaluation of Artemisinin HCl nanoparticles. Artemisinin is a sesquiterpene lactone chemical extract from Artemisia annua (sweet wormwood), is poorly soluble in water and a fast-acting blood schizonticide effective in treating the acute attack of malaria (including chloroquine – resistant and celebral malaria). Artemisinin are effective against multi-resistant strains of P. falciparum. The purpose of the present work is to minimize the dosing frequency, taste masking and toxicity and to improve the therapeutic efficacy by formulating Artemisinin HCl nanoparticles. Artemisinin HCl nanoparticles were formulated by solvent evaporation method using polymer poly(ε-caprolactone) with five different formulations. Nanoparticles were characterized by determining its particle size, polydispersity index, drug entrapment efficiency, particle morphological character and drug release. The particle size ranged between 100nm to 240nm. Drug entrapment efficacy was > 99%. The in-vitro release of nanoparticles were carried out which exhibited a sustained release of Artemisinin HCl from nanoparticles up to 24hrs. The results showed that nanoparticles can be a promising drug delivery system for sustained release of Artemisinin HCl.

Keywords: *Artemisinin HCl, Nanoparticles, Poly(ε-caprolactone), Solvent evaporation, Zeta potential, entrapment efficiency.*

INTRODUCTION

Despite the fact that we live in an era of advanced technology and innovation, infectious diseases, like malaria, continue to be one of the greatest health challenges worldwide [1]. The main drawbacks of conventional malaria chemotherapy are the development of multiple drug resistance and the non-specific targeting to intracellular parasites, resulting in high dose requirements and subsequent intolerable toxicity [2, 3]. Nanosized carriers have been receiving special attention with the aim of minimizing the side effects of drug therapy, such as poor bioavailability and the selectivity of drugs[4]. The most promising of these is Artemisinin HCl (sesquiterpene lactone) chemical extract from Artemisia annua (sweet wormwood), is poorly soluble in water and a fast-acting blood schizonticide effective in treating the acute attack of malaria (including chloroquine – resistant and celebral malaria). Artemisinin are effective against multi-resistant strains of P. falciparum [5, 6, 7].

Many drug candidates face problems like poor absorption, rapid metabolism and elimination, toxicity due to drug distribution to other tissues, poor drug solubility, unpredictable bioavailability, etc. These problems need to be resolved so as to make the existing drugs successful for therapy [8]. One of the promising strategies to overcome these problems is use of nanotechnology. 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 nanoparticles as compared to micro or macro particles [9]. Nanoparticles are solid colloidal particles with diameters ranging from 1 - 1000 nm [10]. They consist of macromolecular materials in

which the active ingredient is dissolved, entrapped, encapsulated, and adsorbed or chemically attached [10]. They may be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of materials is dependent on many factors including: (a) size of nanoparticles required; (b) inherent properties of the drug, e.g., solubility and stability; (c) surface characteristics such as charge and permeability; (d) degree of biodegradability, biocompatibility and toxicity; and (e) drug release profile desired [11]. By contrast [12] classified Artemisinin hydrochloride as BCS Class II/IV (borderline), because of the low solubility in the gastrointestinal pH range and the lack of reliable permeability data. Although the Artemisinin free base has been conjugated with acids other than hydrochloride, in this text Artemisinin will mean Artemisinin hydrochloride for the sake of brevity [13]. The purpose of this research is to minimize the frequency of doses, taste masking and toxicity and to improve the therapeutic efficacy by formulating Artemisinin HCl nanoparticles.

MATERIALS AND METHODS

Chemical and Drugs

Artemisinin HCl was obtained as a gift sample from Ipca Pharmaceutical Pvt. Ltd (Ratlam, India). PVA (Cold) M.W Approx 1, 25,000 CDH Laboratory reagent, Labrafac cc oil (Iot no.:450601008 for R&D purposes only) was obtained as gift sample from Gattefosse (France), Polyε-caprolactone diol (MW 09063, mp 36-48oc, d 1.073, batch no.:04216DH) was purchased from Sigma–Aldrich (St Louis, MO63103) USA, Ethyl cellulose (batch no. 01096, product no. 028330) CDH Laboratory reagent and All other reagents and chemicals used were of analytical grade.

METHODOLOGY

Drug - excipient compatibility study

The DSC analysis was carried out to identify the compatibility between the drug and excipients. The DSC analysis of pure drug, 1:1 physical mixture of drug excipient was carried out using DSC 60, Shimadzu, Japan. Samples (2-8 mg) were accurately weighed into an aluminum pan, which was crimped non-hermetically and heated in sealed aluminum pans at a rate of 10oc/min between 0-300 OC temp ranges under nitrogen atmosphere.

Solubility study for oil selection

The solubility of Artemisinin HCl in various oils (Fig: 1) was determined by adding an excess amount of drug to 2 mL of selected oils in 5-mL stopper vials, and mixing using a vortex mixer. The vials were then kept at 25 ± 1.0-C in an isothermal shaker (Nirmal International, Delhi, India) for 72 hours to reach equilibrium. The equilibrated samples were removed from the shaker and centrifuged at 4000 rpm for 15 minutes. The supernatant was taken and filtered through a 0.45-µm (Rendisk) membrane filter. The concentration of Artemisinin HCl was determined in the oils using HPLC (Adept CECIL, CE4201) at 216 nm [14].

Method for Preparation

Artemisinin HCl nanocapsules were prepared by solvent evaporation method described in fig.1. First mutually saturated aqueous and organic phase were prepared [15]. The saturated water contained 8.3% of ethyl acetate and the saturated solvent contained 3% of water. PVA was dissolved in saturated water at 50oc for 2hr. Polyεcaprolactone was dissolved in saturated ethyl acetate at 50oc and Caprol micro-express oil was added when the solution has come back to room temperature. The resulting organic solution was poured into the aqueous phase and emulsified with lab stirrer devise (Remi Motor Ltd, India) for 45 min at 4000 rpm and sonicated (Bandelin Sonoplus, Germany 2006) for 15 min at 9 cycle/min. After sonications the emulsion under gentle stirring with magnetic bar allowed the ethyl acetate to leave the droplets. The organic solvent and part of the water were evaporated under reduced pressure to afford a purified and concentrated suspension. The prepared formulations were stored in cool and dry place. Five different batches were prepared and labeled as ATM-1 to ATM-5 with the following composition as shown in Table 1. The turbidity studied of all nanosuspensions is depended on ratio of drugs and excipients.

Evaluation of formulations

Percentage yield

Percentage practical yield is calculated to know about the efficiency of any method, thus it helps in selection of appropriate method of production. Practical yield was calculated as the weight of nanoparticles recovered from each batch in relation to the sum of starting material. The

percentage yield of prepared nanoparticles was determined by using the formula.

$$\text{Percentage Yield} = \frac{\text{Practical Yield} \times 100}{\text{Theoretical Yield}}$$

Table 1: Formulation of Artemisinin HCl Nanoparticles

S. No.	Ingredient	ATM-1	ATM-2	ATM-3	ATM-4	ATM-5
1	Artemisinin HCl (%)	1	1	1	1	1
2	PVA (%)	0.25	0.5	0.75	1	1.25
3	Polyεcapro lactone (%)	0.5	1	1.5	1	2
4	Water (ml)	40	40	40	40	40
5	Ethyl Acetate (ml)	10	10	10	10	10

Drug Entrapment Efficiency

The entrapment efficiencies of prepared systems were determined by measuring the concentration of free drug in the dispersion medium. The obtained suspension was centrifuged for 60 min at 10,000 rpm. The supernatant was separated and then filtered through 0.45 µm Millipore (Millipore Filter). The filtrate was diluted using 75% ethanol and measured specrophotometrically (Shimadzu, UV 1700, Japan) at 292 nm. The amount of free drug was detected in the filtrate and the amount of incorporated drug was determined as a result of the initial drug minus the free drug. The entrapment efficiency was calculated using the following equation.

$$\text{Entrapment Efficiency} = \frac{\text{W initial drug} - \text{W free drug} \times 100}{\text{W initial drug}}$$

Where "W initial drug" is the mass of initial drug used and the "W free drug" is the mass of free drug detected in the supernatant after centrifugation of the aqueous dispersion.

Particle size characterization

Particle size analysis

In order to analyze particle size drug loaded nanoparticles were dispersed in deionized water, vortexed for 10 min before sampling. Particle size was determined by laser scattering light using Malvern Laser Analyzer Instruments [16].

Zeta potential

Zeta potential is an abbreviation for electrokinetic potential in colloidal systems. Zeta potential is electric potential in the interfacial Double Layer (DL) at the location of the slipping plane versus a point in the bulk fluid away from the interface [17]. Zeta potential is not measurable directly but it can be calculated using theoretical models and an experimentally-determined electrophoretic mobility or dynamic electrophoretic mobility. Mobility is defined as the velocity of a particle per electric field unit and is measured by applying an electric field to the dispersion of particles and measuring their average velocity. This velocity can be determined by measuring the dropper shift of laser light scattered off the moving particles [18]. The surface charge (Zeta potential) was determined by measuring the electrophoretic mobility of the nanoparticles using a Malvern zeta sizer (Malvern instrument, UK). Samples were prepared by diluting with distilled water [19].

Polydispersity index

Polydispersity index is a parameter to define the particle size distribution of nanoparticles obtained from photon correlation spectroscopic analysis. It is a dimensionless number extrapolated from the autocorrelation function and range from a value of 0.01 for mono dispersed particles and up to value of 0.5 – 0.7. Sample with very broad size distribution have polydispersity index value >0.7 [20]. The obtained results are shown in Figure 5.

Shape and Surface morphology

Shape and surface morphology of nanoparticles was done by Scanning Electron Microscopy (JSMT6360A, JEOL). SEM has been used to determine surface topography, texture and to examine the morphology of fractured surface. Small volume of nanoparticulate suspension was placed on an electron microscope brass stub. The stubs were placed briefly in a drier and then coated with gold in an ion sputter. Pictures of nanoparticles were taken by random scanning of the stub. The shape and surface morphology of the nano-particles was determined from the photomicrographs of

Table 2: % Yield of Artemisinin HCl

S. No.	Formulation	weight of empty bottle (gm)	Practical Yield (gm)	Theoretical Yield (gm)	% Yield = Practical yield/ theoretical yield X 100
1	ATM-1	16.4330	0.2232	0.25	89.280
2	ATM-2	16.2672	0.3953	0.4	98.825
3	ATM-3	16.4621	0.5411	0.55	98.382
4	ATM-4	16.4947	0.5653	0.6	94.217
5	ATM-5	17.1540	0.7423	0.8	92.7875

Table 3: Characterization Reports of Prepared Nanoparticles

S. No.	Formulation	% Yield	% Entrapment Efficiency	Z-Average Particle Size(nm)	Polydispersity Index	Zeta Potential (mV)
1	ATM-1	89.280	99.12	230.7	0.192	-27.2
2	ATM-2	98.825	99.69	270.8	0.214	-17.7
3	ATM-3	98.382	99.82	233.7	0.231	-18.3
4	ATM-4	94.217	99.93	499.0	0.196	-22.2
5	ATM-5	92.7875	99.68	229.2	0.217	-16.3

Table 4: Comparative Cumulative % Drug Release

S. No.	Time (hr)	CUMULATIVE % DRUG RELEASE				
		ATM-1	ATM-2	ATM-3	ATM-4	ATM-5
1	0	0	0	0	0	0
2	1	15.7	10.2	13.4	12.4	29
3	2	14.9	17.3	15.2	13.2	38.6
4	3	17.99	18.9	21.4	12.7	46.1
5	4	25.51	21.2	24.7	15.8	48.9
6	5	29.49	25.5	26.3	23.9	51.2
7	6	33.89	28.3	31.3	33.1	56.6
8	12	39.59	43.7	49.8	52.5	81.8
9	24	46.32	51.2	57.7	66.5	89.1

Table 5: Model Fitting on *In-Vitro* Data

S. No.	Formulation	Zero order	First order	Higuchi Matrix	Korsmeyer Peppas	Hixson Crowel	Best Fit
1	ATM-1	0.715	0.649	0.924	0.897	0.043	Higuchi Matrix
2	ATM-2	0.837	0.741	0.978	0.982	0.087	Korsmeyer Peppas
3	ATM-3	0.847	0.756	0.974	0.969	0.121	Higuchi Matrix
4	ATM-4	0.903	0.811	0.937	0.893	0.188	Higuchi Matrix
5	ATM-5	0.726	0.498	0.943	0.753	0.27	Higuchi Matrix

each batch. Artemisinin HCl nanoparticles have shown smooth and spherical shape with different sizes depending on the ratios of the surfactant and polymer used.

In-vitro drug release studies

The in vitro drug release of the formulation was studied by using dialysis membrane and modified apparatus. The dissolution medium was freshly prepared phosphate buffer of pH 7.4. Dialysis membrane (molecular weight cut off - >12, 000, Hi- media, Mumbai, India), previously soaked overnight in the dissolution medium and was tied to one end. 1ml of formulation was placed and another end was also tied. The dialysis bag containing formulation was placed in beaker containing 200 ml of phosphate buffer pH 7.4, maintained at 37oc ± 2oc. The dissolution medium was stirred at low speed (100 rpm) using USP/IP/BP-II apparatus. Aliquots, each of 5 ml volume were withdrawn at various intervals of time over a period of 24h. The aliquots were suitably diluted with dissolution medium and analyzed by UV-Vis Spectrophotometer at 292 nm. The quantity of drug equivalent to 10 mg of Artemisinin HCl was taken for dissolution study.

Release Kinetics

There are number of kinetic models, which described the overall release of drug [21] from the dosage forms. Because qualitative and quantitative changes in a formulation may alter drug release and the use of in-vitro drug dissolution data (Table.5) of the Artemisinin HCl release from poly-ε-caprolectone nanocapsules were analyzed to investigate [22] the release kinetics.

Zero order kinetics:

Zero order kinetics model follows the equation as

(Q / Q0) = k0t

Where k0 = Zero order rate constant, hour-1, Q = the amount of Artemisinin HCl released, mg, Q0 = the amount of Artemisinin HCl initially, mg. To study the release kinetics, data obtained from in vitro drug release studies were plotted as cumulative amount of drug released versus time.

First order kinetics

First order kinetics model follows the equation as; log (Q / Q0) = -k1t / 2.303 Where k1 = first order rate constant, hour-1, Q = the amount of Artemisinin HCl released, mg; Q0 = the amount of Artemisinin HCl initially, mg. The data obtained were plotted as cumulative percentage drug release versus square root of time.

Higuchi model

The values of R2 indicated that the Higuchi model was best fitted with the release kinetic data of Artemisinin HCl. Higuchi equation: Q / Q0 = kht1/ 2 Where, Q = the amount of Artemisinin HCl released, mg; Q0 = the amount of Artemisinin HCl initially, mg; kh = Higuchi matrix release kinetics, hour-1/2.The data obtained were plotted as cumulative percentage drug release versus square root of time.

Korsmeyer-Peppas model

Korsmeyer et al. (1983) derived a simple relationship which described drug release from a polymeric system equation Mt / M∞ = Ktn where Mt / M∞ is a fraction of drug released at time t, k is the release rate constant and n is the release exponent[23]. To study the release kinetics, data obtained from in vitro drug release studies were plotted as log cumulative percentage drug release versus log time.

Hixson-Crowell model

Hixson and Crowell (1931) recognized that the particles' regular area is proportional to the cube root of its volume. They derived the equation: W0 1/3 -Wt 1/3 = κ t where W0 is the initial amount of drug in the pharmaceutical dosage form, Wt is the remaining amount of drug in the pharmaceutical dosage form at time t and κ (kappa) is a constant incorporating the surface volume relation. To study the release kinetics, data obtained from in vitro drug release studies were plotted as cube root of drug percentage remaining in matrix versus time [24].

Results and Discussions

Solubility study for oil selection

The solubility of the drug in oils is most important, therefore, the components used in the system should have high solubilization capacity for the drug, ensuring the solubilization of the drug in the resultant dispersion. Results from solubility studies are reported in Figure 1. As seen from the figure, Lebrafac CC and Transcutol showed the highest solubilization capacity for Artemisinin HCl, followed by Capryol 90 and Caprol micro-express. Thus, for our study we selected Lebrafac CC for the development of the formulation.

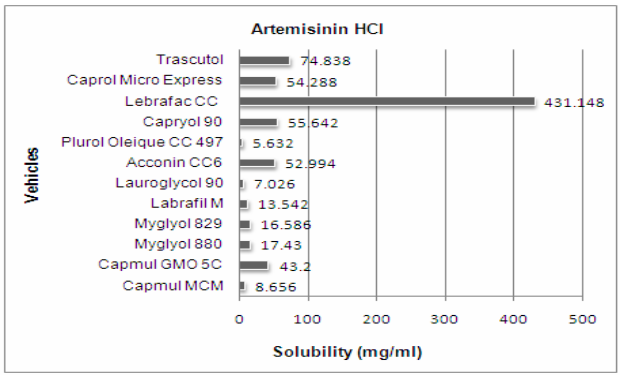


Figure 1: Solubility of Artemisinin HCl in different Vehicles

Drug - excipient compatibility study

The pure drug Artemisinin HCl and physical mixture of excipients with drug were studied. The thermo gram of pure drug showed endothermic peak at – 153.86OC and 205.14 OC either physical mixture of drug and excipient shows peak at 153.41OC. The obtained DSC thermo-grams are shown in Figure 2(a) and 2(b).

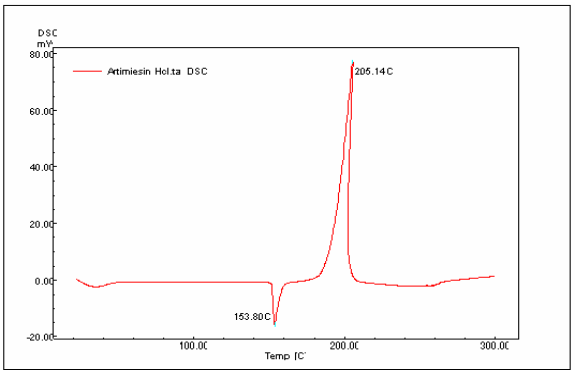


Figure 2: (a) DSC spectrum of pure Artemisinin HCl drug

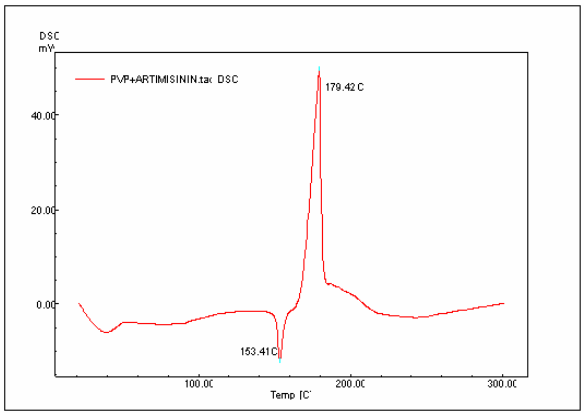


Figure 2: (b) DSC spectrum of physical mixture of Artemisinin HCl drug + PVA

Percentage yield

The results of the percentage practical yield are shown in Table 2. Percentage practical yield depends on the concentration of polymer added. It increases with increase in concentration of polymer added to the formulation. Maximum percentage practical yield was found to be 98.825 ATM-2 for formulation.

Drug Entrapment Efficiency

The entrapment efficiency of six batches of Artemisinin HCl nanoparticles are recorded in Table 3.As the polymer concentration was increased from 100-500 mg the encapsulation efficiency was increased. The PVA concentration was varied as 0.25%, 0.5%, 0.75 %, 1 % and 1.25 % the encapsulation efficiency was slightly increased. The result indicates the polymer concentration plays a major role in drug entrapment efficiency rather than the PVA concentration. The maximum entrapment efficiency was found in ATM-4 with 99.93 % (Figure 3). The preparation parameters, such as PVA concentration and Artemisinin HCl/Polyεcaprolactone ratios were modified to obtain nanoparticles with higher entrapment efficiency.

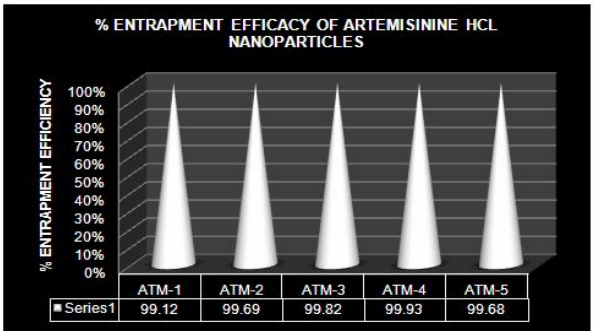


Figure 3: % Entrapment Efficiency of Artemisinin HCl Nanoparticles

Particle size analysis

The size distributions along the volume mean diameter of the nanoparticles were measured by laser scattering light using Malvern Laser Analyzer Instruments. The obtained results are shown in Figure 4. Particle sizes of all five batches are shown in Table 3.

Zeta potential

The stability study of the nanoparticles was evaluated by measuring the zeta potential of the nanoparticles by the zeta meter (Table 3). Zeta potential of all formulated

nanoparticles was in the range of 16.3 mV to 27.2 mV which indicates moderate stability with no agglomeration. The obtained results are shown in Figure 5.

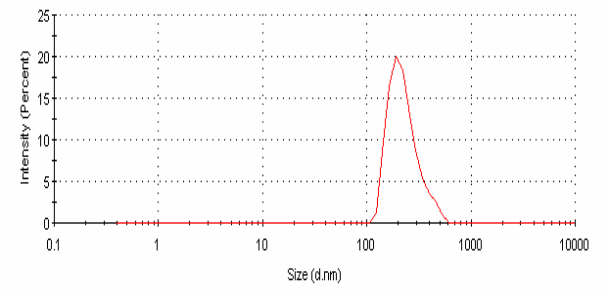


Figure 4: Average Particle Size Distribution Report

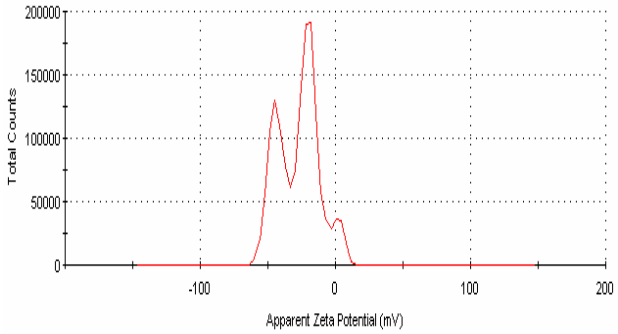


Figure 5: Zeta Potential Report

Characterization of Prepared Nanoparticles

Table 3 and Fig 6 shows that all data are summarized characterization reports of prepared nanoparticles such as percentage yield, percentage entrapment efficacy, average particles size, zeta potential and polydespersity index.

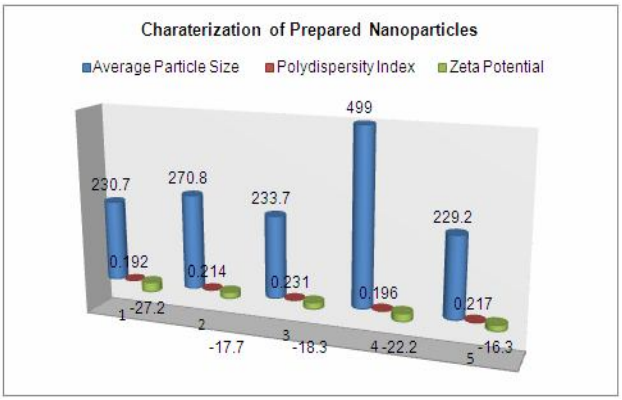
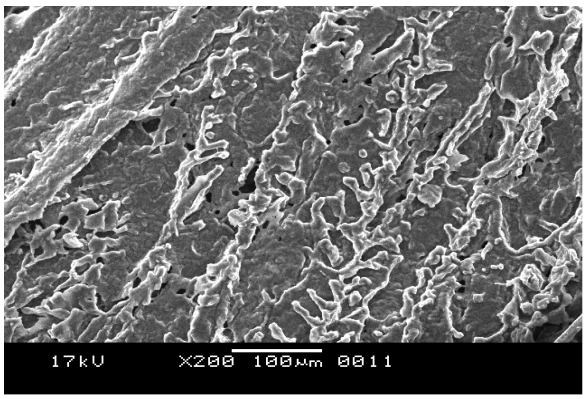


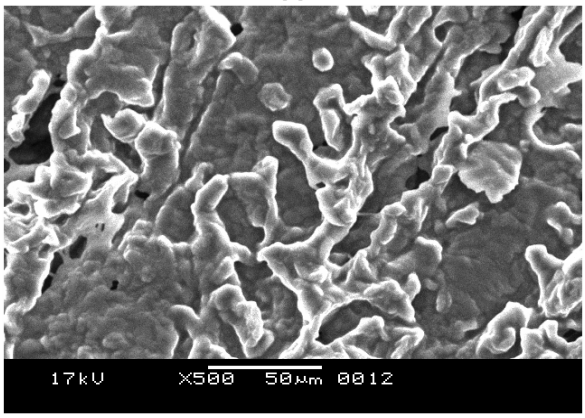
Figure 6: Shows summarized data of average particle size, zeta potential, & PDI

Shape and Surface morphology

Shape and surface morphology of nanoparticles was studied by Scanning Electron Microscopy (SEM) (JSM-T330A, JEOL). SEM photographs of all formulations were shown in Figure 7(a) and 7(b). Artemisinin HCl nanoparticles have shown smooth and spherical shape with different sizes depending on the ratios of the surfactant and polymer used.



(a)



(b)

Figure 7: (a) & (b) SEM Photomicrograph of Artemisinin HCl Nanoparticles Formulation

In-vitro drug release studies

The obtained release profile data of Artemisinin HCl from nanocapsules until 24 hr after dispersion are shown in Figure 8 and Table 4. As evident from the graph, the curve of dissolution release profile indicates that, with the increase in the polymer ratio release of Artemisinin HCl from the nanocapsules decreases. In the third hour i.e. in the alkaline medium, the concentration of the drug released from the nanocapsules increased and reached a maximum. The initial burst release could be related to the surface drug as well as small size of the nanocapsules with increased surface area.

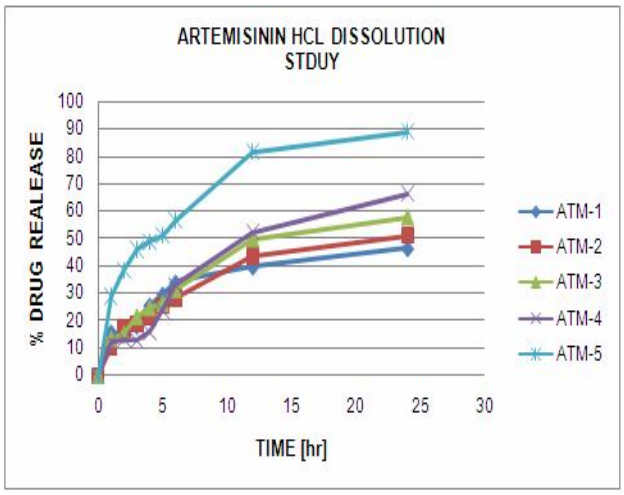


Figure 8: Comparative Dissolution Study

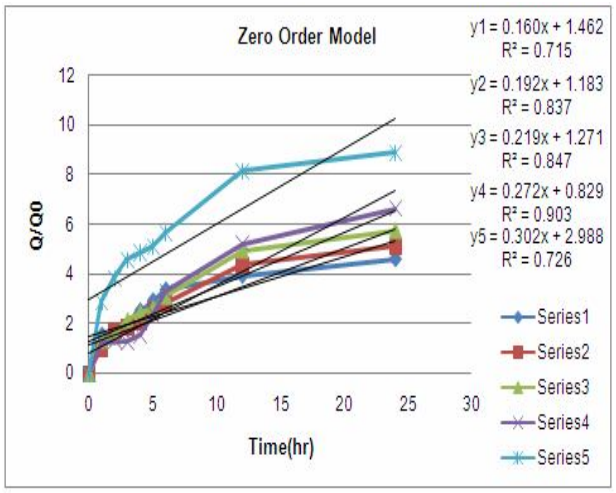


Figure 9: Zero–order kinetics

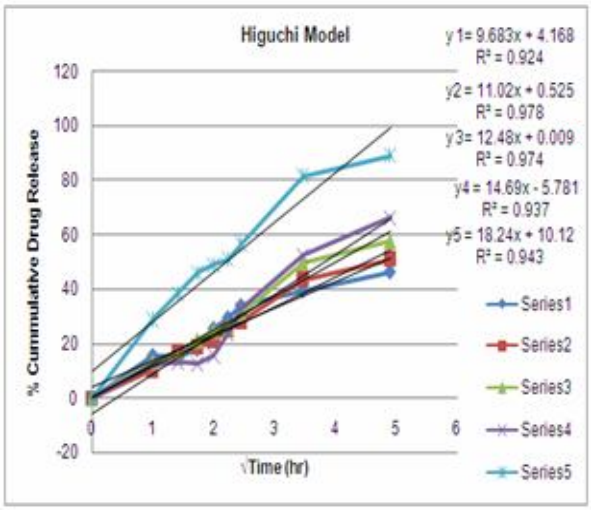


Figure 10: First order kinetics

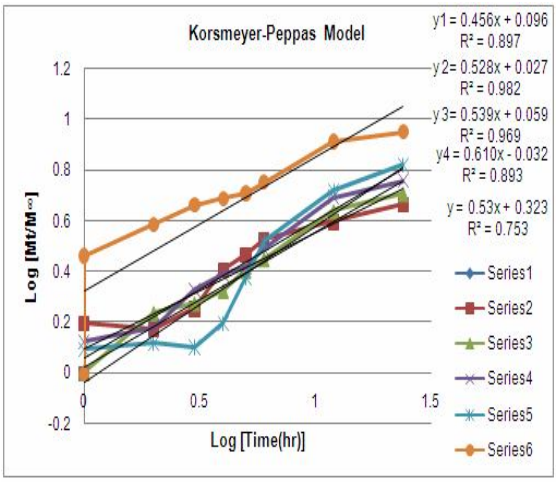


Figure 11: Higuchi Model

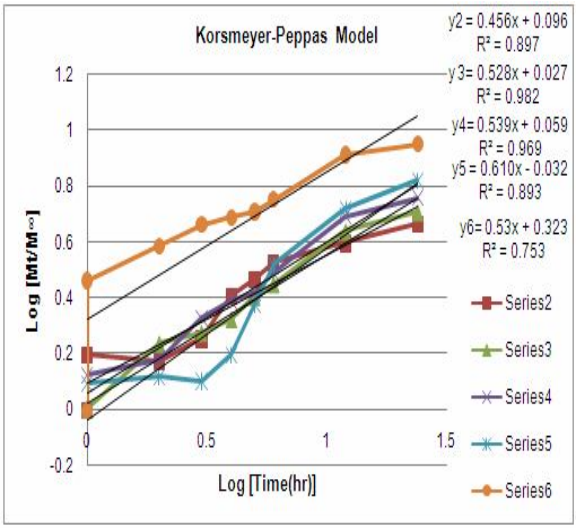


Figure 12: Korsmeyer-Peppas model

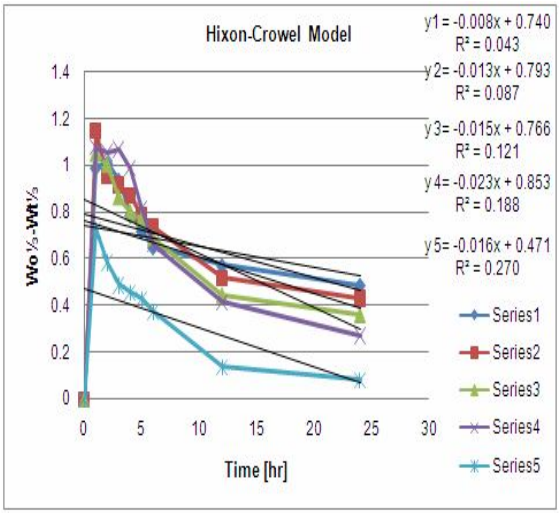


Figure 13: Hixson Crowell model

Kinetics of drug release

In order to understand the mechanism and kinetic of drug release, the drug release data of the in-vitro dissolution study were analyzed with various kinetic model like Drug release kinetics from nanocapsules was analyzed by using Zero – order kinetics (Fig.9), first order kinetics (Fig.10), Higuchi (Fig.11), Korsmeyer-Peppas model (Fig.12) and Hixson Crowell model (Fig.13) and Coefficient of correlation (r) values were calculated for the liner curves by regression analysis of the above plots. It was difficult to predict exact fit model for the nanocapsules but as the R2 value for Higuchi model and Korsemeyer-Peppas models was highest it can be proposed that the prepared Artemisinin HCl nanocapsules followed the release kinetics for diffusion model. The obtained best fit model results shown in Table 5.

CONCLUSION

The result of the present investigation proposes a novel formulation of Artemisinin HCl nanoparticles by solvent diffusion method. It was found that nanoparticles with desirable particle size and high entrapment efficiency can be produced by adjusting the process parameters. The particle size and drug entrapment as well as the drug release kinetics can be optimally controlled.

Acknowledgements

The authors would like to thank R.K.G.I.T College of Pharmacy, Ghaziabad (U.P.) for providing the facility for nanoparticles formulation and development. And also thank to Dr. D.C.Jain (Green Technology Department) Ipca Pharmaceutical Pvt. Ltd, Ratlam (M.P.) for providing gift sample of Artemisinin HCl and also thankful to Uttarakhand Technical University, Dehradun.

REFERENCES

1. N.S. Santos-Magalhães, (2010) V.C.F. Mosqueira / Advanced Drug Delivery Reviews 62 560–562.
2. G.M. Barratt, (2000) Therapeutic applications of colloidal drug carriers, Pharm. Sci. Technol. Today 3 163–171.
3. C. Vauthier, P. Couvreur, (2007) Nanomedicines: a new approach for the treatment of serious diseases, J. Biomed. Nanotechnol. 3 223–234.
4. M.L. Forrest, G.S. Kwon, (2008) Clinical developments in drug delivery nanotechnology, Adv. Drug Deliv. Rev. 60 861–862.
5. The merck index. "an encyclopedia of chemicals, drug and biological", Merck research laboratories,13thedition. 2001. pp 139.
6. Sweetman Sean C. Martindale "The Complete Drug Reference ", 33th Edition .pp 2002.431-432, 438-440, 436-437.
7. Global malaria control and elimination: report of a meeting on containment of artemisinin tolerance, 19January 2008. Geneva, World Health Organization, 2008.
8. http://www.who.int/malaria/docs/drugresistance/Malaria_Artemisinin.pdf
9. Jain NK (2010). Pharmaceutical technology: pharmaceutical nanotechnology. Available at: http://nsdl.niscair.res.in/bitstr /123456789/748/1/revised+Pharmaceuticall+Nanotech. pdf. Accessed on 23 November.
10. Gupta R B. "Fundamentals of drug nanoparticles", In: Gupta R B, Kompella U B. ed. Nanoparticles technology for drug delivery. Taylor & Francis Group, New York. (2006) 17.
11. Mohanraj V J, Chen Y (2006). Nanoparticles-a review. Trop J Pharm Res. 5: 561-573.
12. Thassu D, Pathak Y, Deleers M. "Nanoparticulate drugdelivery dystems: an overview", In: Thassu D, Deleers M, Pathak Y. eds. Volume 166. (2007) Informa healthcare USA, Inc.270 Madison avenue New York.
13. Lindenberg M, Kopp S, Dressman JB (2004). Classification of orally administered drugs on the World Health Organization Model List of Essential Medicines according to the biopharmaceutics classification system. Eur J Pharm Biopharm 58:265–278.
14. Florey Klaus. Analytical profiles of drug substances. Volume-14. Academic press. Pp159. [14]
15. Shafiq-un-Nabi Sheikh, Faiyaz Shakeel, Talegaonkar Sushma, Ali Javed, Baboota Sanjula, Ahuja Alka,. Khar Roop K, and Ali Mushir (2007). Formulation Development and Optimization Using Nanoemulsion Technique:A Technical Note. AAPS PharmSciTech 8 (2) Article 28.
16. Delphine Moinard-Checot,Chevalier Y,Riancon Stephanie,Benney Laurent, Hastem Fessi (2008) Mechanism of nanocapsules formulation by emulsion-diffusion process. Journal of Colloidal and Interface Science. 317:458-468.
17. Pandey H., Sharma U. K., Pandey A. C., A review on "Eudragit-based nanostructures: a potential approach for ocular drug Delivery", Int. J. Res. Dev. Pharm. L. Sci., 2012, 1(2), pp. 40-43.
18. Kreuter J (1994). Nanoparticles in Colloidal Drug Delivery Systems. New York, Marcel Dekker Inc: 9nd. 219-220.
19. Zeta potential of colloids in water and waste water" (1985). ASTM Standard D 4187-82. American Society for Testing and Materials
20. Jelvehgari M., Barar J., Valizadeh H., Delf Loveymi B. and Ziapour M, (2010). Preparation of Diclofenac Sodium Composite Microparticles with Improved Initial Release Property.Transaction F: Nanotechnology 17(2):79-89.

21. Pignatello R, Ricupero N, Bucolo, Maugeri F Maltese A and Puglisi G (2006). preparation and characterization of eudragit retard nanosuspensions for the ocular delivery of cloricromene.AAPS Pharma Sci tech 24:7:E27.
22. Nidhin M, Indumathy R, Sreeram KJ and Balachandran U (2008). synthesis of iron oxide nanoparticles of narrow size distribution on polysaccharide templates. Bull Mater Sci 31:93-96.
23. Dash Suvakanta, Murthy Padala Narasimha, Nath Lilakanta And Chowdhury Prasanta (2010). Kinetic Modeling on Drug Release from Controlled Drug Delivery Systems. Acta Poloniae Pharmaceutica-Drug Research, 67(3): 219-220.
24. Khan S., Tiwari T., Tyagi S., Mithun B, Joshi A., Dubey B., "Preformulation studies and preperation of dithranol loaded solid lipid nanoparticles", Int. J. Res. Dev. Pharm. L. Sci., 2012, 1(4), pp. 183-188.
25. K. Satish Kumar D. Gnanaprakash, K. Mayilvaganan, C. Arunraj And S. Mohankumar (2012). Chitosan-Gold Nanoparticles As Delivery Systems For Curcumin. IJPSR 3(11): 4537-4538.
26. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA (1983). Int. J. Pharm. 15:25.
27. Hixson AW, Crowell JH (1931). Ind. Eng. Chem.23:923.
28. Allemann E, Gurny R, Doelker E (1993). Drug-loaded nanoparticles- preparation methods and drug targeting tissues. Eur J Pharm Biopharm 39: 173-191.

How to cite your article:
Kumar G. D., Razdan B.K., Bajpai M., "Formulation and evaluation of nanoparticles containing artemisinin HCl", Int. J. Res. Dev. Pharm. L. Sci., 2014, 3(2), pp. 925-934.

