Asian Journal of Pharmaceutical Technology & Innovation
ISSN: 2347-8810

Research Article

Received on: 02-06-2016
Accepted on: 11-06-2016
Published on: 15-06-2016

Corresponding Author:

***Arpan Kumar Tripathi,**
Apollo College of Pharmacy,
Anjora, Durg,
Chhattisgarh 491001,
India.

*Email Id-
arpan260387@gmail.com

Development And *In vitro* Evaluation of PLGA Microsphere of Docetaxel

Arpan Kumar Tripathi*[1], Ashwani Patel[2], Rakesh Sahu[1], Pankaj Kashyap[1], Dusmanta Kumar Pradhan[1]

ABSTRACT
Breast-targeting docetaxel loaded (polylactic-co-glycolic) acid microsphere were prepared by a solvent evaporation method. The uniform design was used to optimize the technology of preparation, the appreance and size distribution were examined by scanning electron microscope, and the aspect such as in vitro release characteristics, stability drug loading efficiency. The experimental result show that the microspheres were globular in appearance and disperse well the average particle size decrease form is 24.49±0.38.49 micro-meter to 4.99± 0.11micrometer. The drug loading efficiency decrease75.01±1.2% to81.2±1.9% respectively. The in vitro release behaviour could be expressed by the drug release rate decrese from 90% to 84% with increasing amount of PLGA during preparation. The drug release rate increase from 81% to 98% with the increase in stirring rate from 200to800 RPM. Stability studies were carried out with selected formulation period of 45-Daysmicrospheres was found to increase slightly.

Key-words: Docetaxel; poly (latic-co-glycolic) acid;microsphere; breast-cancer

Cite this article as:
Arpan Kumar Tripathi, Ashwani Patel, Rakesh Sahu, Pankaj Kashyap, Dushmanta Kumar Pradhan, Development And Invitro Evaluation of PLGA Microsphere of Docetaxel, Asian Journal of Pharmaceutical Technology & Innovation, 04 (18); 2016, 134-138. www.asianpharmtech.com

1 Apollo College of Pharmacy, Anjora, Durg
2 Shri Ram Institute of Pharmacy, Jabalpur

INTRODUCTION:-

In recent year, several approaches have been carried out to control release drug delivery system due to their potential advantages over the conventional drug therapy. These delivery system can be localized at specific region in the body and make it possible to achieve prolonged pharmacological effect while lowering the systemic. Concentration of drug. Drug have been incorporated in bio-stable polymer as well as in biodegradable system. (Kreuter;Damge et al 1988;Quong et al 1998;Hyon,2000).nature or synthetic polymer,such as poly(lactic acid)(PLA),poly(DL-lactic-co-giycolic)acid(PLGA),ACRYLIC POLYMER OR COPOLYMER,PLURIC POLYS, ALGINAT AND SO ON.The most widely used polymer are PLGA because of their quite long history of biodegradable studies. PLGA provide a wide range of degradation rate, months to year ,depending opentheir composition and molecular weight(Sha and chien,1995;sha et al;1994;Luan and bodmereier,2006).The biodegradable microspheres can be prepared by different techniques recently (Jiang and scwendeman,2001) such as solvent evaporation or solvent extraction, spray drying ,using under superficial conditions without toxic residual solvent.

Docetaxel is one of the most potent anticancer agent know .however ,administration of the drug can lead to a number of side effect including renal distribution, nausea, vomiting ,and auditorytoxity.A promising way of optimizing its is to target its action is to tissue sites via selaectiveorgan with controlled release system. In present work we report the microspheres of docetaxel using biodegradable polymer (PLGA).

MATERIALS:-

Docetaxel was obtained as a gift sample from Dabur India Ltd, PLGA (Type A, Bloom) was purchased form Hi-media, India. Tween-80(25% w/v), ethanol,acetone was purchased from SD Fine chemical. All the other reagents used during Experiment were of analytical grade. Double distilled deionised water was used during the whole experiment.

METHOD:

PLGA microspheres were prepared following a described solvent deposition method.(Boisdron-cells et al,1995) Docetaxel (25 mg) and polymer (100 mg) was dissolved in acetone (20 ml). The organic phase was poured into 40 ml of a water/ethanol mixture (1:1 v/v), containing 0.5% (w/v) of Tween 80, under magnetic stirring, thus forming a milky colloidal suspension. The organic solvent was then evaporated off under vacuum by a rotavapor (). The PLA or PLGA colloidal formulations were purified from entrapped Docetaxel and unabsorbed surfactant by centrifugation (15,000×g) for 1 h. The obtained supernatants were collected and the pellets re-suspended in water (50 ml), then centrifuged again under the same conditions.

Characterization of PLGA microspheres

Particle size analysis:

Particle size and size distribution of gelatin microspheres were determined using laser light diffractometry equipment (Mastersizer X, Malvern Instrument, UK). The average particle size was expressed as the volume mean diameter in micrometers.

Surface Morphology

The surface morphology of microspheres was observed scanning electron microscopy (SEM). The samples for SEM were prepared by lightly sprinkling the microspheres powder on a double adhesive tape which stuck to an aluminum stub. The stubs were then coated with gold to a thickness of about 300^0A using a sputter coater. These samples were than randomly scanned and photomicrographs were taken.

Drug Entrapment Efficiency

About 50 mg of microspheres was taken and triturated with small quantity of ethanol and distilled water and transferred to a 50 ml standard flask. The volume was made up to 50 ml and mixed well. The solution was then kept aside for 12 hrs. It was then filtered and estimated for drug content by measuring the absorbance at 230 nm. The drug entrapment efficiency was calculated using the following formula.

$$\% \text{ Entrapment Efficiency} = \frac{\text{Estimated \% Drug Content}}{\text{Theoretical \% Drug Content}} \times 100$$

Differential Scanning Calorimetery

Differential scanning calorimetery (DSC) of Docetaxel, gelatin and drug loaded gelatin microspheres were carried out by heating the sample from 0 to 300°C at the heating rate of 10°C/min. in a nitrogen environment. The DSC studies were conducted on Jade DSC Instrument, Type Pyris 6 DSC with Software Version: 9.0.1.0174.

In Vitro Drug Release Studies

The in vitro release studies of drug loaded microspheres were carried out at 37± 0.5 and 100 rpm using phosphate buffer pH 7.4 (900 ml) in a USP dissolution apparatus under sink condition. Accurately weighed sample of microspheres 100 mg of drug loaded microspheres placed in a dissolution medium at preset time intervals aliquots were withdrawn and replaced by an equal volume of fresh dissolution medium. After suitable dilution, the samples were analyzed spectrophotometrically at 230 nm

STABILITY OF DOCETAXEL LOADED PLGA MICROSPHERES

Docetaxel microspheres stored in amber colored bottles were subjected to accelerated stability studies for 45 days at 4^0C, 25^0C and 45^0C. Samples were withdrawn after 15, 30 and 45 days and analyzed to determine percent residual drug content, the initial drug content of all the formulations was taken to be 100%.

RESULT AND DISCUSSIN

PLGA microspheres were prepared by solvent deposition method. The effect of various process variables viz. amount of PLGA, concentration of emulsifier and stirring speed were studied. The results suggested that these variables influence the shape, size, size distribution, drug entrapment efficiency and in vitro drug release of the final preparation. Hence these parameters were optimized to prepare microspheres of small size with narrow size distribution, good drug entrapment efficiency and good drug release.

The increase in the particle size with increasing amount of PLGA from 50 mg to 200 mg. This was probably caused by the increasing viscosity of the dispersed phase (polymer solution), resulting in poor dispersibility of the PLGA solution into the aqueous phase. There is likely to be higher viscous resistance against the shear forces during the emulsification. Coarse emulsions are obtained at higher polymer concentrations and viscosities, which led to the buildup of bigger particles during the diffusion process. This fact is explained by the greater probability that the desolvated macromolecules (or small aggregates formed from these molecules) coalesce in a more concentrated solution, thereby forming larger particles.

The SEM photomicrograph of the PLGA microspheres displayed a spherical shape with a smooth surface and no aggregation was observed.

The particle size of PLGA microspheres decreased from 24.49±0.38 μm to 4.99±0.11 μm with increasing concentration of emulsifier from 0.5 to 2% w/v. The presence of an anionic surfactant is important to reduce the dynamic interfacial tension and to stabilize the micro-suspension. The surfactant is adsorbed on the microsphere surface, increasing the stearic repulsion between particles. In this study, Tween 80 was used at 1.5% (w/v)

concentration, because this concentration being sufficient to obtain small PLGA microspheres and higher entrapment efficiency and permits to remove the excess of surfactant by centrifugation and washing. The particle size of PLGA microspheres decreased from 24.6± 0.21 μm to 6.30±0.32 μm with increasing stirring rate from 200 rpm to 800 rpm.

The DSC thermograms of pure Docetaxel, PLGA, Docetaxel loaded gelatin and PLGA microspheres were obtained. Pure Docetaxel showed an endothermic melting peak at 183◦C. Docetaxel melting peak totally disappeared in the calorimetric curve of loaded micro particles, evidencing the absence of crystalline drug in the microsphere samples, at least at the particle surface level.

In vitro drug release study of PLGA microspheres was performed in PBS (pH 7.4). The drug release rate decreased from 90.23±1.45% to 84.12±2.13% with the increase in amount of PLGA during the preparation of microspheres. No significant effect was found on drug release rate of PLGA microspheres, when the concentration of emulsifier increased from 0.5 to 2% w/v. The drug release rate increased from 81.23±1.45 to 98.03±0.85 with the increase in stirring rate from 200 to 800 rpm.

In conclusion, the obtained results demonstrated that biodegradable polymeric colloidal systems made up of gelatin can entrap Docetaxel providing a sustained drug release.

Microspheres with optimum size for oral administration were always obtained.

Stability studies were carried out with selected formulations PM1 which were stored as a powder for a period of 45 days at 4±1ºC, 25±1ºCand at 45±1ºC. The particle size of formulations was determined by optical microscopy using a calibrated ocular micrometer. The particle size of the microspheres was found to increase slightly at 45±1ºC, which may be attributed to the melting out the polymer at higher temperature, which cause the aggregation of microspheres. No effect was found on surface morphology of microspheres at 4±1ºC, 25±1ºC, but slight change on surface morphology was at 45±1ºC.

The selected formulations were stored at 4±1ºC, 25±1ºC and at 45±1ºC and the residual drug content of the formulation was measured after 15, 30 and 45 days. The results showed that no mark able effect was found in the residual drug content.

The release rates of the selected formulations were examined after 45 days of storage at selected temperatures. There was no change in release rate of formulation stored at 4±1^{0}C and 25±1^{0}C in PLGA microspheres. The rate of drug release for formulation stored at 45±1^{0}Cwas increased as compared with the fresh formulation; it might be due to the formation of more pores in the microspheres due to evaporation of residual amount of solvent. It could be said that the storage conditions 4±1^{0}C do not have any drastic effect on the microspheres integrity. The formulations were found to be reasonably stable at 4±1^{0}C used in this study.

CONCLUSIONS

The PLGA microspheres were successfully prepared by solvent evaporation method respectively. In conclusion, the obtained results demonstrated that biodegradable polymeric microspheres made up of PLGA entrap Docetaxel providing a sustained drug release and reduce the side effect. We present a cost-effective drug delivery system for docetaxel that is easy to prepare and has potential for further development

REFERENCES

1.Bala,I.,Hariharan,S,kumar,M.N.,2004.PLGA nanoparticalin drug delivery; the state of rat .Rev.ther.drug carr.sys.21,387-482.

2.Boisdorn-cells,M,P.M.,Benei,J.P.,1995.prepration and characterization of 5-fluorouracil-loaded microparticles as biodegradable anticancer drug carriers.J.pharma.sci,86,891-895

3-damag, c ,Michel,c, aprahanmian,m., 1988.new approach for oral administration of insulin with polyalkyl cyanoacry nanocapcule as drug carrier dibatic 2,246-251.

4-hyon s.g. 2000. Biodegradable poly (lactic acid)microspheerses for drug delivery system.yonsei,med.j41,720-734.

5-keruter j,1994 .nanoparticals .in; kreuter,j.(Ed.),colloidal drug delivery system.marcel dekker , new yark ,pp.219-342.

6-quong ,d.neufeld,r.j.skjak-break,g,1988.externalversusinternalsource of calciumduring the gelation of alginate beads for DNA encoaculation .biotechnol.bioeng.57,438-446.

7-sha h.k. ,chien, y.w.,1995.degradability and antigen-release characteristics of polyester microspheres prepard from polymer blends.j.appl.polymer sci.58,197-206.

8-sha.h.k.., toddywala, r, chien, Y.M. 1994 .the influence of biodegradable microcapcule formulation on the controlled release of a protein. J.controlled relese 30,201-211.

9-luan,X., bodmeier,R .,2006 .influence of the poly(poly-lactide-co- glycolide)type on the leuprolied release from in situ forming microparticle system.j. controlled release 110,266-272.

10-schwendeman,S.P., tiobio, m .joworowicz,m,Alonso, m.j. langer, r., 1998 new stratergies for the microencapsulation of tetanus vaccine .j. microencopsul. 154, 299-318.