Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Suppl 3, 2012

Research Article

FORMULATION AND EVALUATION OF VINPOCETINE LOADED LIPOSPHERES

KHULBE PREETI*, MUNJAL PRIYANKA

Department of Pharmaceutical Science, Bhimtal Campus, Kumaon University Nainital, India. Email: khulbe.preeti@yahoo.in

Received: 27 Jan 2012, Revised and Accepted: 04 Mar 2012

ABSTRACT

The aim of this study was to prepare and evaluate vinpocetine loaded lipospheres by emulsion method. The lipospheres carrier system has several advantages over other delivery systems in term of physical stability and low cost of ingredients. Vinpocetine is selected because it is best known for its neuroprotective effects and age-related memory impairment. Lipospheres were prepared by using bees wax, cetyl alcohol, paraffin wax and stearic acid. In this study prepared lipospheres were evaluated on the bases of particle size distribution, drug loading , entrapment efficiency and drug release. To determined surface morphology of prepared lipospheres scanning electron microscopy (SEM) was used. For this study seven formulations were made. Formulation F4 shows the best results. By this study it came to know that best lipospheres were prepared by combination of bees wax- stearic acid and paraffin wax was unable to produce lipospheres. liposphere prepared by bees wax and stearic acid shows 23.72% drug loading, 89.67% entrapment efficiency and 78.54% drug release upto 12 hrs. lipospheres offers a new approach to improve the oral bioavailability of poorly soluble drug.

Keywords: Lipospheres, Vinpocetine, Emulsion method, SEM, Drug loading, Entrapment efficiency.

INTRODUCTION

The liposphere drug delivery system is an aqueous micro dispersion of solid water insoluble spherical micro particles of a particle size between 0.2 and 100 μm. The lipospheres are made of solid hydrophobic triglycerides having a monolayer of phospholipids embedded on the surface of the particle.[1,2] The solid core contains the bioactive compound dissolved or dispersed in a solid fat matrix. These are generally used as carrier vehicle for hydrophobic drugs. These exhibit low entrapment of hydrophilic drugs which could be improved by using polar lipids like cetyl alcohol, stearyl alcohol and cetostearyl alcohol etc.[3] The lipospheres carrier system has several advantages over other delivery systems in term of physical stability, low cost of ingredients, ease of preparation and scale-up, high dispersability in an aqueous medium, high entrapment of hydrophobic drugs, controlled particle size and extended release of entrapped drug.[4,5]

The selected drug is vinpocetine. Vinpocetine is a semi-synthetic derivative of vincamine. Vincamine is an alkaloid extracted from the Periwinkle plant, *Vinca minor L.*. Vinpocetine is an herbal supplement used to treat thinking and memory problems, such as Alzheimer's disease.[6] It is best known for its neuroprotective effects (cerebral infarction and cerebral haemorrhage) and age-related memory impairment. It is widely marketed as a supplement for vasodilation and as a nootropic.[7] It is mainly used as cerebral enhancer and neuroprotector. It is also very effective in the treatment of short term memory loss. It is reported to have short half life of about 2.54 ± 0.48 hours & usually absorbed to a larger extent in the region of small intestine.[8] Vinpocetine is a poor aqueous soluble drug and due to its poor aqueous solubility and extensively metabolized during first pass, its clinical use is greatly restricted by the low bioavailability after oral administration and so there is a need to improve its poor aqueous solubility to increase its oral bioavailability.[9] An oral formulation with a high degree of oral absorption would, therefore, be highly desirable.

MATERIAL AND METHOD

Vinpocetine is a gift sample from Sinochem Jiangsu Co. Ltd. Other ingredients like cetyl alcohol, stearic acid, bees wax, paraffin wax, tween 80 and butanol used are of analytical gread.

Preparation of Lipospheres

In this study Liposphere was prepared by emulsion method (Manju Rawat Singh et al, 2009) with some modification. At first Lipid phase was taken in a beaker and was melted at 70⁰C-80⁰C.then the drug was disperse into it while stirring. Then aqueous phase was taken in another beaker and was heated at 70⁰C-80⁰C. Aqueous phase was added into lipid phase at same temperature with stirring to form emulsion. Then continues stirring was done upto 1 hrs with maintained temperature using mechanical stirrer 2000 rpm. Then 1000 ml ice cold water was taken into a beaker and prepared emulsion was added dropwise into it, with continuous stirring upto 2 hrs.and was stored overnight at room temperature. After this it was filtered by using wattman filter paper and was collect and dried from filter paper.[10,11]

Table 1: Formulation table

Ingredients	F1	F2	F3	F4	F5	F6	F7
Lipid phase							
Drug	500mg	500mg	500mg	500mg	500mg	500mg	500mg
Stearic Acid	2 gm	2 gm	3 gm	2gm	-	-	1 gm
Bees wax	-	-	-	1 gm	-	3 gm	1 gm
Cetyl alcohol	-	1 gm	-	-	-	-	1 gm
Paraffin wax	2 gm	-	-	-	3gm	-	1 gm
Aqueous Phase							
Tween 80	2 ml	1 ml	1 ml	2 ml	2 ml	1 ml	1 ml
Butanol	5 ml	4 ml	4 ml	5 ml	5 ml	4 ml	4 ml
Water	43 ml	95 ml	95 ml	43 ml	43 ml	95 ml	95 ml

Characterization[12,13,14,15,16,17]

Particle size determination

Particle size analysis of vinpocetine-loaded lipospheres was performed by optical microscopy using a compound microscope. A small amount of dry lipospheres was suspended in purified water (10mL). The suspension was ultrasonicated for 5 seconds. A small drop of suspension thus obtained was placed on a clean glass slide.

The slide containing lipospheres was mounted on the stage of the microscope and 100 particles were measured using a calibrated ocular micrometer.

Drug loading and entrapment efficiency

The amount of vinpocetine present in lipospheres was determined by taking the known amount of lipospheres in which 200 mg of drug should be present theoretically. Then the lipospheres were crushed and the powdered microspheres was taken and dissolved in 100 ml of phosphate buffer (pH 7.4) solution and stirred for 15 minutes with an interval of 5 minutes and allowed to keep for 24 hours. Then the solution was filtered through whatman no. 1 filter paper. Then the absorbance was measured spectrophotometrically at 269 nm against phosphate buffer(ph 7.4) solution as blank and concentration were determined by employing simultaneous equation y=mx+c.

Drug Entrapment Efficiency (%) = (Experimental drug content / Initial drug content into the formulation) × 100

Drug Loading (%) = (Quantity of the drug present in microspheres / Weight of the microspheres) ×100

In vitro Drug release

In vitro drug release of vinpocetine from lipospheres was evaluated in both acidic buffer (pH-1.2) and phosphate buffer (pH-7.4). Amount of lipospheres equivalent to 30mg of vinpocetine were transferred to the prewarmed dissolution media and maintained at 37±0.5°C under stirring at 50rpm. Samples were withdrawn every hour up to 12hrs and the volume was replaced immediately by fresh phosphate buffer. The sample solution was filtered and analyzed for vinpocetine content by measuring absorbance in UV-spectrophotometer (Shimadzu UV-1700) at 269 nm.

Surface Morphology

The surface morphology and shape of the lipospheres were analyzed by scanning electron microscopy for selected formulations.

RESULT AND DISCUSSION

Table 2: Particle size and Polydispersity Index

S. No.	Average particle size (μm)	Polydispersity Index
F1	30	0.437
F2	25	0.433
F3	20	0.675
F4	21	0.532
F5	-	-
F6	22	0.322
F7	20	0.376

According to table the particle size of all the formulations are in micron range it ranges to min. 20 (F7) and max.30 (F1) micrometer. Polydispersity index was found to be min. 0.322 (F6) and max. 0.675 (F3).

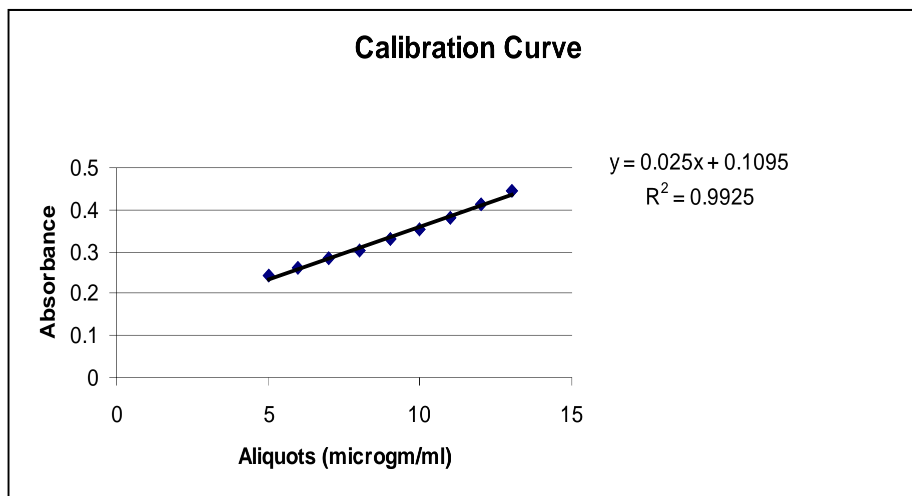

Fig. 1: Calibration curve

Table 3: Drug loading and entrapment efficiency

S. No.	Drug Loading (%)	Entrapment Efficiency (%)
F1	17.88	89.17
F2	20.13	73.12
F3	25.78	92.88
F4	23.72	89.67
F5	-	-
F6	18.22	64.29
F7	16.78	78.41

According to table drug loading was found to be 16.73 % (F7) min and 25.78% (F3) max and entrapment efficiency was 73.12% (F2) min and 92.88 % (F3) max. So as a result of this table formulation F3 and F4 shows maximum drug loading and entrapment efficiency.

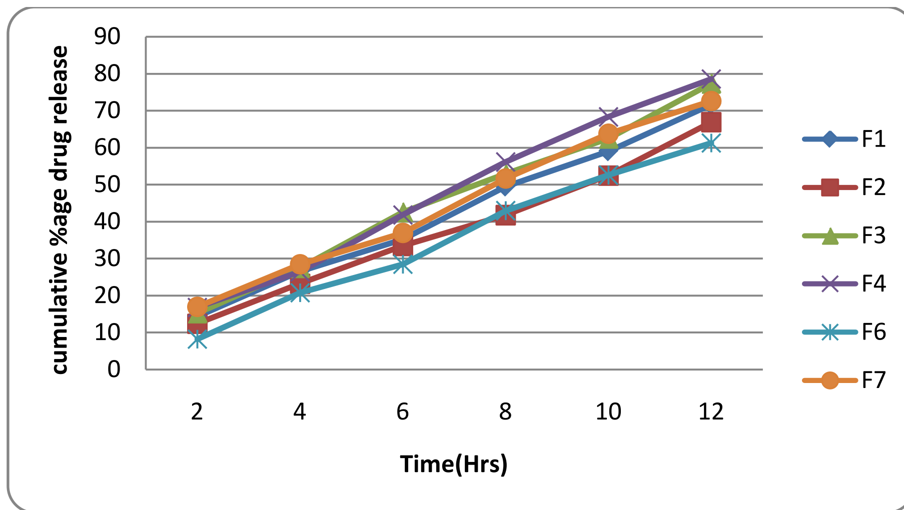

Fig. 2: Drug release

According to figure drug release was found to be 61.22 % (F6) min and 78.54% (F4) max. As a result of this figure formulation F3 and F4 shows maximum drug release 77.31% and 78.54% respectively.

SEM

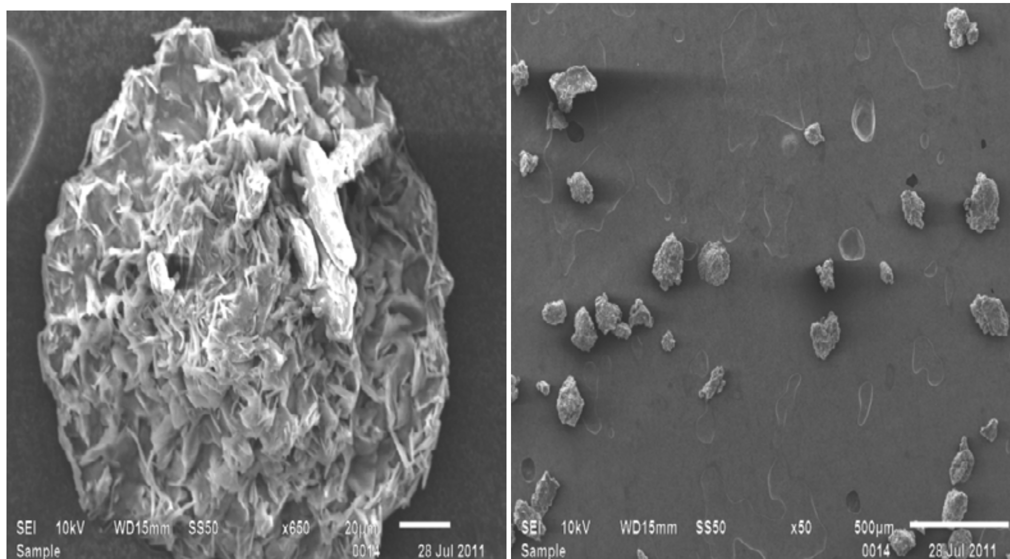

Fig. 3: Sem of formulation F3 (stearic acid)

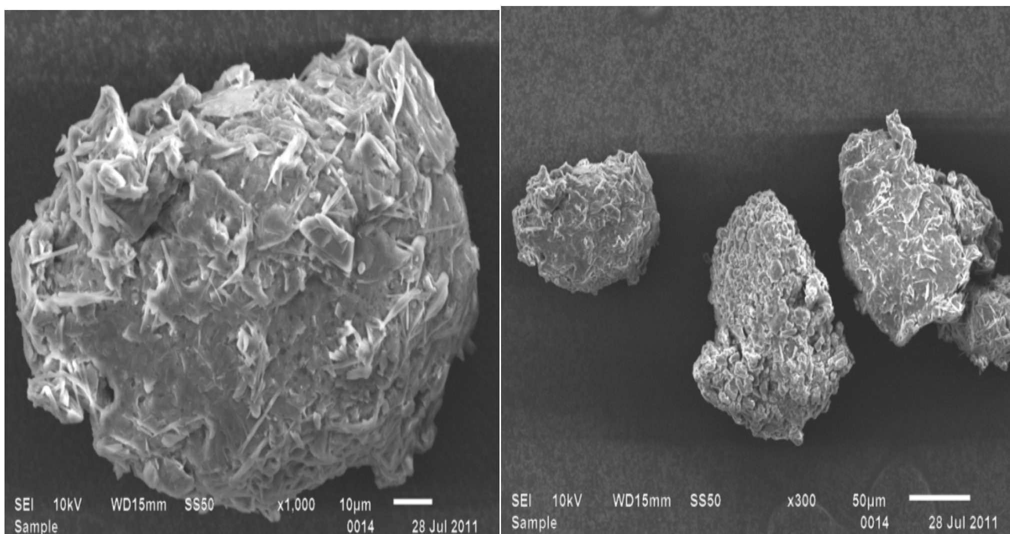

Fig. 4: SEM of Formulation F-5 (stearic acid and bees wax)

CONCLUSION

Lipospheres can be considered as a promising delivery system for oral delivery of lipophilic drugs. Lipospheres were able to entrap the lipophilic drugs at high levels and sustain its release over a prolonged time. By this study it is concluded that in prepared liposphere formulations (F1 to F7), formulation F3 and F4 shows good polydispersity index, maximum drug loading, maximum entrapment efficiency and maximum release upto 12 hrs. by this study it also seen that formulation F1 has waxy appearance and yield was not good, F2 has yield problem and poor release, by F5 lipospheres was not formed only hazy solution was appear, F6 shows poor release and F7 has also poor yield. So it is concluded that best lipospheres were prepared by bees wax- stearic acid and paraffin wax was unable to produce lipospheres it may be due to its less softening nature. Tween 80 was selected as a stabilizing agent and butanol acts as a cosurfectant. Cosurfactants can reduce the surfactant concentration in microemulsion preparation. It also increases the interaction in interface. These novel lipospheres were found to be promising for formulation of lipophilic drugs exhibiting better therapeutic effect. But, further studies in terms of pharmacokinetics, toxicology and animal studies are required for clinical utility of the formulation. The encouraging results obtained in this study could propose lipospheres for future in vivo studies.

ACKNOWLEDGEMENT

Authers wish to give thanks to department of pharmaceutical science bhimtal for laboratory and analytical grade chemicals. We would like to thanks Sinochem Jiangsu Co., Ltd. for providing us gift sample of vinpocetine drug. We also want to acknowledge my all the colleagues for their support.

REFERENCES

1. Rawat M, Singh S, Saraf S, Nanocarriers: Promising vehicle for bioactive drugs. BiolPharm Bull 2006; 29:1790-1798.
2. Reithmeier H, Hermann J, Gopferich A. Development and characterization of lipid microparticles as a drug carrier for somatostatin. Int J Pharm 2001; 218: 133-143.
3. Domb AJ, Bergelson L, Amselem S. lipospheres for controlled delivery of substances. In: Benita S. editor. Microencapsulation, method and industrial application, new York. NY: Marcel Dekker; 1996; 377-410.
4. Cortesi R, Espocito E, Luca G, Nastruzzi C . Production of lipospheres as carriers for bioactive compounds. Biomaterials 2002; 23: 2283-94.
5. Esposita E, Cortesi R, Nastruzzi C. Production of lipospheres for bioactive compound delivery. In: Claudio nastruzzi editor, lipospheres in Drug Targets and Delivery Approaches, methods and Applications. Boca Raton . Florida: CRC Press; p.23-40.
6. Szilágyi G, Nagy Z, Balkay L, et al. "Effects of vinpocetine on the redistribution of cerebral blood flow and glucose metabolism in chronic ischemic stroke patients: a PET study". Journal of the Neurological Sciences 2005; 229-230: 275–84.
7. Vinpocetine. Monograph". Alternative Medicine Review 7- 3: 240–3. June 2002.
8. Szatmari SZ, Whitehouse PJ. "Vinpocetine for cognitive impairment and dementia". Cochrane Database of Systematic Reviews 2003; 1: CD003119
9. Adám-Vizi V. "[Neuroprotective effect of sodium channel blockers in ischemia: the pathomechanism of early ischemic dysfunction]" (in Hungarian). Orvosi Hetilap 2000; 23: 1279–86.
10. Maheshwari M, Ketkar AR, Chauhan B, patil VB, Paradkar AR. Preparation and characterization of ibuprofen cetyl alcohol beads by melt solidification technique: effect of variables. IntJ Pharm 2003; 261: 57-67.
11. Iscan Y, Hekimoglu S, Sargon MF, Hincal AA. Deetloaded solid lipid particles for skin delivery: In vitro release and skin permeation Singh et al. Int J DD 2009; 1: 15-26.
12. Nasr M, Mansour S, Mortada ND, El Shamy AA. Lipospheres as carrier for Topical delivery of aceclofenac : Preparation, Characterization and In Vivo Evaluation. AAPS PharmSciTech 2008; 9: 154-162.
13. Gibalya El, Abdel-Ghaffar SK. Effect of hexacosanol on the charecterstics of novel stained – release allopurinol solid lipospheres SLS: factorial design application and product evaluation. Int J Pharm 2005; 294: 33-51.
14. Adeyeye CM, Price JC. Development and evaluation of sustained release ibuprofen- wax microspheres. II. In vitro dissolution studies. Pharm Res 1994; 11: 575-579.
15. Rawat M, Singh S, Saraf S, Development and In vitro evaluation of polar lipid based lipospheres for oral delivery of peptide drugs. Int J D D 2009; 15-26.
16. YiFan Luo, DaWei Chen, LiXiang Ren, XiuLi Zhao, Jing Qin, Solid lipid nanoparticles for enhancing vinpocetine's oral bioavailability. Journal of Controlled Release2006; 114: 53–59.
17. Gert Fricker & Torsten Kromp & Armin Wendel & Alfred Blume & Jürgen Zirkel & Herbert Rebmann & Constanze Setzer Ralf-Olaf Quinkert & Frank Martin & Christel Müller-Goymann. Phospholipids and Lipid-Based Formulations in Oral Drug Delivery. Pharm Res 2010; 27:1469–1486.