Fabrication and characterization of sterically stabilized liposomes of bortezomib in effective therapy of multiple myeloma

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Introduction: Bortezomib is an anti-cancer medication used to treat multiple myeloma and mantle cell lymphoma. It works by inhibiting proteasomes, cellular complexes that break down proteins.

Objectives: To develop stable bortezomib liposome injection for intravenous infusion, 1.0 mg/mL (3.5 mL fill), with equivalent physicochemical parameters of Reference Product, which is indicated for multiple myeloma – heterogeneous disease.

Methodology: QbD approach used to ensure the quality, safety, and efficacy of liposome injection. A 2(5-1) fractional factorial design adopted to evaluate the effect of lipids concentration in ethanol, hydration temperature, hydration time, high pressure homogenization temperature and its pressure on Particle size. Based on design space, optimized process parameters were defined for maintaining the required particle size and percentage free drug. Based on patent and literature, HSPC and MPEG DSPE 2000 Lipid are selected for feasibility trials.

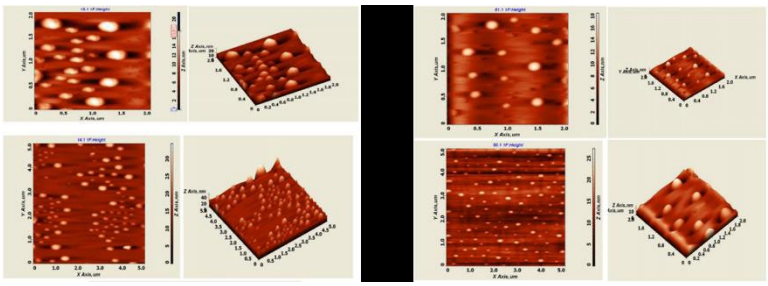
Results: Screening trials for drug (API) loading suggest that active loading process with HPH process at pressure 15000 psi and above using Meglumine with Acetic acid shows better drug entrapment with less free drug HEPES and Nacl solution as buffering agent. Simlilarly, Active loading process selected based on highest entrapment and stability of drug. The DOE formulations indicate

a) HPH temperature and lipid concentration in Ethanol have impact on D90 after hydration,

b) Hydration time and hydration temperature does not have major impact on D90 after HPH as Hydration will not control major particle size during HPH (table 1).

The Cryo transmission electron microscopic reveals that liposome have good uniformity and in terms of size, shape and, lamellarity. The stability study of final formulation suggests no degradation of impurity and no % free drug is increasing with respect to stability time.

Conclusion: Developed formulation showed less free drug and high entrapped drug with new remote loading agent and active drug loading process.



The AFM study of Bortezomib Liposome Injection reveals that, Test product have particle size around 110 nm which is same as zeta sizer and Cryo TEM.

Biography

Bhupendra Prajapati is a Professor in Department of Pharmaceutics, Shree S.K.Patel College of Pharmaceutical Education and Research, Ganpat University, Gujarat, India. He has 20 years of academic and research experience and published more than 250 research and review works in international and national Journals. He authored 150 book chapters in the field of novel drug delivery. He edited 20 books with publishers like Elsevier, AAP CRC, Wiley, Springer and Jenny Stanford. He published three Indian patent and three applications under evaluation. He is a reviewer in many high impact journals and is on the editorial board member.

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