Abstract Title: Development and *in-vitro* evaluation of Lapatinib-Loaded binary micelles for Breast Cancer Treatment

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Abstract

Statement of the Problem: Breast cancer is second cause of death among women women constituting 6.53 % of total 9.6 million cancer deaths in 2018. USFDA approved Lapatinib (LP) for HER2-positive breast cancer treatment; however, its clinical application is limited due to its poor aqueous solubility, large daily oral dose (1250 mg/day) and associated toxicities.

It is, indeed, to mention that no commercial dosage form other than oral tablet of Lapatinib is available till date in market. A search through literature indicated that micelles have been proven as an excellent nanocarrier for intravenous administration. Therefore, we hypothesized that micelles, owing to their core-shell structure, can enhance the aqueous solubility of Lapatinib and can deliver the drug by passive targeting to tumors by enhanced permeation and retention effect. Thus, we fabricated Lapatinib-loaded nanocolloidal Binary Polymeric micelles (LP-BMs) using Soluplus® and Solutol® HS15 by a thin-film dispersion method. LP-BMs evaluated for solid state characterization that confirmed amorphization of drug and no typical incompatibility other than hydrogen bonding within formulation components, while DSC and XRPD showed successful encapsulation of LP. They were of spherical shape and uniform size of 71.41±6.23 nm diameter, confirmed by HR-SEM and they also showed high drug encapsulation (approx 93 %). Further, BMs exhibited sustained release showing 33% and 54% of LP release from LP-BMs in 48 h in pH 7.4 and pH 5.0 release media, respectively. Moreover, LP-BMs induced no platelet aggregation with significantly less hemolysis than pure LP; indicating their appreciable hemocompatibility and suitability for intravenous administration. On the other hand, MTT assay against breast cancer cell lines (SKBr3) showed significantly lower IC_{50} values of LP-BMs than pure drug, confirming their anti-cancer efficacy. Conclusively, these results indicated that the LP-BMs can serve as a promising intravenous alternative that can open the new route for breast cancer treatment.

Keywords—*Soluplus, Solutol HS15, nanocolloids, enhanced permeation and retention.*

Professional Biography

Gunjan Vasant Bonde is pursuing his PhD (Pharmaceutics) from Department of Pharmaceutical Engineering & Technology, Indian Institute of Technology (Banaras Hindu University), Varanasi (India). His research areas include Pluronics and Soluplus based drug delivery systems e.g. in situ gel, nanoparticles, polymeric micelle etc. for sustained delivery of anticancer agents especially delivery to solid tumors. His previous research dealt with development of intra-articular injectable in-situ gel for prosthetic joint related infections. He is affiliated to 'Teaching Assistanceship' in the above said institute. He pursued his B. Pharm. from Mumbai University and M. Pharm. (Pharmaceutics) from Pune University. He is a recipient of prestigious "Sir Ratan Tata Scholarship" (2006-07), "Maharashtra State Scholarship" (1998-2003), "Maharashtra Talent Search Scholarship" (2001-2003).



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