

Enhanced *in vitro* anti-tumor activity of 5-azacytidine by entrapment into solid lipid nanoparticles

Farhad Jahanfar^{1,2}, Akbar Hasani², Dariush Shanebandi³, Mohammad Rahmati-Yamchi², Hamed Hamishehkar^{4*}

¹ Biotechnology Research Center and Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

² Department of Biochemistry and Clinical Laboratories, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

³ Immunology Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

⁴ Drug Applied Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

*Correspondence author: Hamed Hamishehkar, Tel: +98 413 3355965, Fax: +98 413 3346977, Email: Hamishehkarh@tbzmed.ac.ir

Abstract

Purpose: In this study the effectiveness of encapsulating of 5-azacytidine into the lipid nanoparticles was investigated and *in vitro* effect of encapsulated 5-azacytidine studied on MCF-7 cell lines

Methods: 5-azacytidine -loaded solid lipid nanoparticles were produced by double emulsification (w/o/w) method by using stearic acid as lipid matrix, soy lecithin and poloxamer 407 as surfactant and co-surfactant respectively. Particle size, zeta potential, surface morphology, entrapment efficiency and kinetic of drug release were studied. *In vitro* effect of 5-azacytidine on MCF-7 cell line studied by MTT assay, DAPI staining, Rhodamine B relative uptake, and also Real time RT-PCR was performed for studying difference effect of free and encapsulated drug on expression of RAR β 2 gene.

Results: The formulation F5 with 55.84 \pm 0.46 % of entrapment efficiency shows zero order kinetic of drug release and selected for *in vitro* studies; the cytotoxicity of free drug and encapsulated drug in 48 h of incubation have significant difference. DAPI staining shows morphology of apoptotic nucleus in both free and encapsulated drug, Rhodamine B labeled SLNs show time dependency and accumulation of SLNs in cytoplasm. Real time qRT-PCR doesn't show any significant difference ($p > 0.05$) in expression of RAR β 2 gene in both cells treated with free or encapsulated drug.

Conclusion: The results of the present study indicated that the entrapment of 5-azacytidine into SLNs enhanced its cytotoxicity performance and may pave a way for the future design of a desired dosage form for 5-azacytidine.

Keywords: 5-azacytidine, solid lipid nanoparticles, SLN, cancer, Cytotoxicity