Nanoparticle Formulation of Hydrophobic Solutes and Factors Governing the Stability

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Recent interests in hydrophobic drug molecules have resulted in a variety of drug carriers and formulation techniques. Traditional methods to formulate nanoparticles include solvent-non solvent exchange through dialysis, emulsification followed by solvent stripping etc., which are thermodynamically controlled and result in low drug-loading [1].

Thermodynamic model of drug loading is based on the molar free energy of the drug, which depends on the block copolymers size (entropic term), the interaction parameter between the drug and the hydrophobic core (enthalpic term), and the pressure-volume work to load the particle. To validate the model, calculations are compared with experimental results for organic solutes, including paclitaxel, loaded into poly(ethylene glycol)-*b*-poly(ε-caprolactone), PEG-*b*-PCL block copolymer micelles.

However, the precipitation technique is a kinetically driven formulation approach where anti-solvent is added to a solvent stream to yield a high degree of supersaturation resulting in nucleation of solutes. Nanoparticle formulation and its stability depend on various factors involved. The formulation of nanoparticles of antifungal drug, Itraconazole (ITZ) and its stability using stabilizers PS-*b*-PEO and Poloxamer P407 have been studied. The stability of drug nanoparticles in terms of its interfacial tension, solubility and particle size are analyzed. Stability of ITZ particles was also observed to depend on the type of stabilizers. Lyophilization approach was implemented for the long term stability of P407 stabilized particles.

[1] Kumar, V., Prud'homme, RK. *Journal of Pharmaceutical Sciences*. 97: 4904-4914.