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β-CASEIN MICELLES AS NANODELIVERY VEHICLES FOR CHEMOTHERAPEUTIC DRUGS

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Beta-casein (β-CN), one of the four main caseins in bovine milk, has a pronounced amphiphilic structure, which enables it to self-associate under appropriate conditions thereby forming stable micelle-like structures in aqueous solutions. Few studies have investigated the binding of lipophilic molecules (e.g. vitamins D3 and A) to β-CN. In this respect, many of the antitumor agents are lipid-soluble. Most of the current chemotherapeutic drugs for cancer treatment are given intravenously (IV). Studies suggest it is a major source of cost, discomfort and stress to patients, and multiple hospitalizations are required in order to complete the relatively long I.V. combination chemotherapeutic regimen. The availability of oral therapeutic agents would make a significant contribution to patients' quality of life, and may significantly reduce cost.

The major goal of this study was to develop a rationally designed drug delivery system comprising hydrophobic anticancer drugs encapsulated within β-CN based nanoparticles. This drug delivery system will allow the lipid-soluble drugs to be thermodynamically stable in aqueous solutions and to be readily delivered into the gastrointestinal tract. Moreover, by entrapping a drug-combination within these nanoparticles, we may increase the therapeutic index of the treatment.

Mitoxantrone (MX) is a fluorescent chemotherapeutic drug. Its encapsulation in β-CN micelles was performed by dissolving it in a proper solvent, and adding into a phosphate buffered solution containing β-CN micelles. The encapsulation was characterized by dynamic light scattering (DLS), and by the decrease in fluorescent emission of MX and of Trp 143 of β-CN following association of β-CN and MX. We confirmed that MX is encapsulated within β-CN micelles. The maximal MX loading was apparently 6:1 (mol:mol, MX:β-CN). Assuming that one β-CN micelle contains approximately 15-60 molecules of β-CN (as has been reported for pure β-CN micelles), then the maximal MX loading per micelle would be ~90-360 molecules. We conclude that β-CN displays a very good binding and encapsulation capacity for this model hydrophobic anticancer drug, and thus may serve as a useful nanoscopic vehicle for the solubilization and delivery in aqueous drug preparations.