The present research was designed to prepare polymeric micelles for DFO oral delivery system for increasing DFO oral absorption. It was shown that PMDDS with particle size less than 81 nm provided 80% EE that led to DFO protection against degradation in the gastrointestinal tract and supplied sufficient area for oral absorption. PMDDS increased DFO permeability through rat intestine more than 3-fold compared to aqueous solutions. We have to explain the correlation between PMDDS and physicochemical properties such as particle size, %EE%, D1%, and D24% with Papp was evaluated. Our results indicated a significant and direct correlation between %EE% and Papp. Therefore, Papp was controlled by %EE% in a way such that higher increased Papp was provided by resulted from higher increased %EE%. Therefore, it seems that PMDDS increased DFO permeability without any effect on intestinal structure. Likewise, similarly, higher increased %EE% was produced by resulted from higher increased PMDDS particle size, higher increased surfactant concentration, and/or using carbomer as the polymer. Micelles were formed by carbomer with higher concentration showing higher increased PMDDS particle size and %EE% in comparison with poloxamer. Finally, polymer type ascertains affected Papp by affecting altering PMDDS characteristics such as particle size and %EE%. As a result, Papp is controlled directly and indirectly by EE% and particle size, respectively. The effect of particle size on drug permeation through different membranes such as intestine and skin has been reported in several studies. Researchers reported that as the size of gold nanoparticles increased, the permeability coefficient and diffusion coefficient through rat skin and intestine membrane was found to be decreased [53]. In another study, vitamin B12 transport across the Caco-2 cell membranes was increased to 2-3-fold times after nanocapsulation that was directly dependent on particle size [54].