

The present research was designed to prepare polymeric micelles ~~as-for~~ DFO oral delivery system ~~for-to~~ increasing its DFO oral absorption. ~~It was shown~~ Here, we showed that PMDDSs with particle size less than 81 nm provided 80% EE ~~that leads~~ and led to DFO protection against degradation in the gastrointestinal tract and supplied sufficient area for oral absorption. PMDDSs increased DFO permeability through rat intestine more than 3-fold compared to aqueous solutions. ~~We have to explain~~ The correlation between PMDDSs and physicochemical properties such as particle size, %EE%,  $D_{1\mu}$  and  $D_{2\mu}$  with Papp was evaluated. Our results indicated demonstrated 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~~ It appears that PMDDSs increased DFO permeability without any effect on intestine structure. ~~Likewise~~ Similarly, higher increased %EE% was produced by resulted from higher increased PMDDSs 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 compared to poloxamer. Finally, polymer type ~~ascertains~~ affected Papp by affecting altering PMDDSs 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 B<sub>12</sub> transport across the Caco-2 cell membranes was increased to 2-3-fold times after nanocapsulation that was directly dependent on particle size [54].

Commented [WS1]: You might mean "at high concentrations of carbomer" here.