Microfluidic Co-encapsulation of Curcumin with SN-38 in PCL-*b*-PEO PNPs

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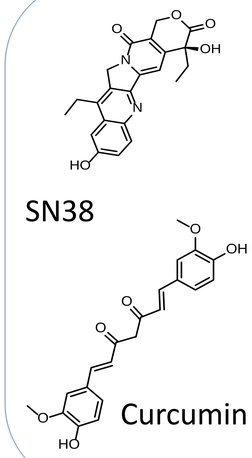
Introduction

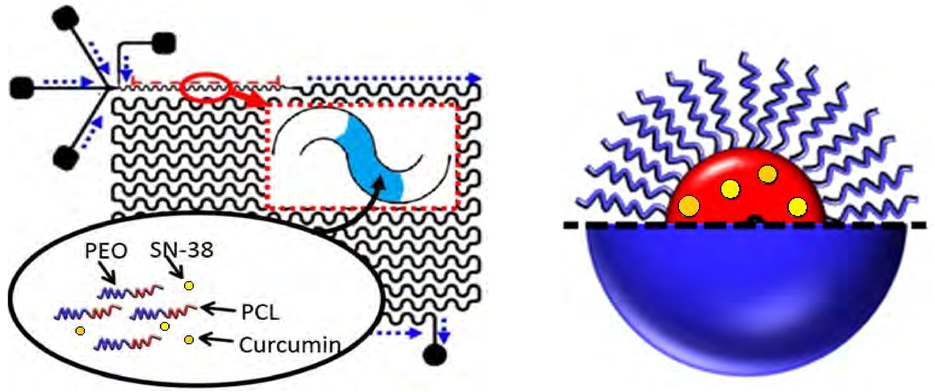


- SN-38 is a potent anti-cancer drug, but has limited clinical use due to low water solubility and inactivity above pH 6.
- Encapsulating SN-38 in polymer nanoparticles (PNPs) could address solubility and stability issues; however, SN-38 encapsulation efficiencies are commonly below 10%.
- Curcumin (CUR) has recently been shown to combat multi-drug resistance in cancer cells, increasing the efficacy of chemotherapy.[1]
- Research has shown that co-encapsulation of multiple drugs can increase the loading efficiencies of certain drugs.[2]
- We prepared PNP formulations of polycaprolactone(12k)-*block*-poly(ethylene oxide)(5k) (PCL-*b*-PEO) with different loading ratios (*r)* of SN-38 and CUR and monitored $EE_{SN\text{-}38}$, PNP size, and polydispersity.

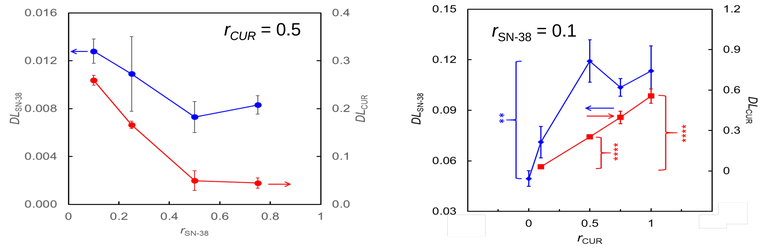
$$r_{SN\text{-}38} = \frac{mass\ SN{-}38\ added}{mass\ of\ polymer\ added} \qquad r_{CUR} = \frac{mass\ CUR\ added}{mass\ polymer\ added} \qquad EE_{SN\text{-}38} = \frac{mass\ SN{-}38\ encapsulated}{mass\ SN{-}38\ added}$$

PNP Preparation

Gas-liquid microfluidic reactor provides faster mixing than bulk nanoprecipitation methods, and allows for tunable shear processing of the PNPs [2, 3, 4] Flow rate *Q* = 200 µl/min for all preparations.

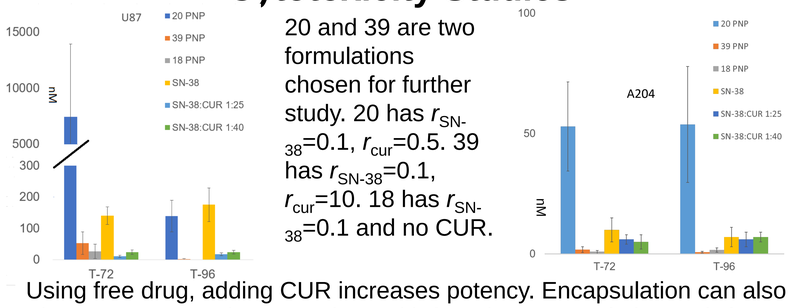


SN-38 Encapsulation Efficiency/ Drug Loading



Co-encapsulation of CUR enhances SN-38 encapsulation. Increased r_{CUR} increases CUR drug loading. Increased $r_{SN\text{-}38}$ decreases both SN-38 and CUR loading.

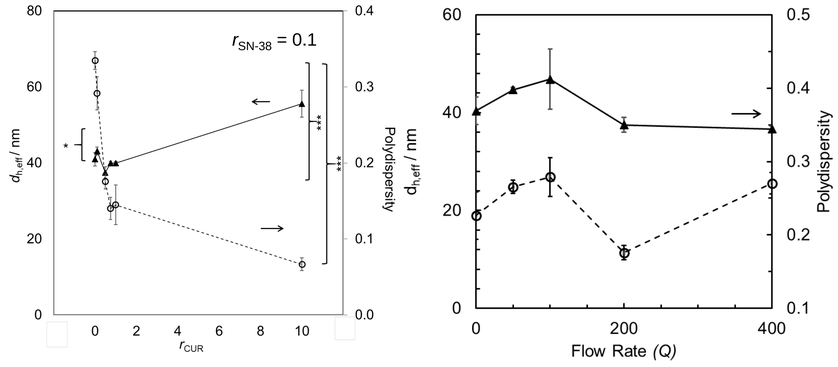
Cytotoxicity Studies



20 and 39 are two formulations chosen for further study. 20 has $r_{SN\text{-}38}$=0.1, r_{cur}=0.5. 39 has $r_{SN\text{-}38}$=0.1, r_{cur}=10. 18 has $r_{SN\text{-}38}$=0.1 and no CUR.

Using free drug, adding CUR increases potency. Encapsulation can also increase potency in comparison with free drug. Formulation 20 is less potent than either formulation 39 or formulation 18. Formulations 18 and 39 are roughly equivalent.

PNP Size and Polydispersity



Increased curcumin has little effect on size but greatly decreases PNP polydispersity. Flow rate of 200 gives lowest polydispersity, while flow rate appears to have little effect on particle size.

Conclusions

- Mean hydrodynamic sizes of PNPs are consistent (~40 nm) for different amounts of added CUR, up to r_{CUR} of 1.
- PNP polydispersity decreased with increased added CUR.
- SN-38 encapsulation efficiency increased and then plateaued with increased added CUR.
- SN-38 encapsulation efficiency increased by up to a factor of two with CUR co-encapsulation.
- Future experiments will investigate the effects of crosslinking on encapsulation and release rates.

Acknowledgements

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References

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