

Modulation of metformin hydrochloride water solubility via hydrophobic ion pairing approach to sustain its release from calcium alginate beads

Sara I. Abd-El Hafeez¹, Nermin E. Eleraky¹, Sara A. Abouelmagd^{1,2}, Ehsan Hafez¹

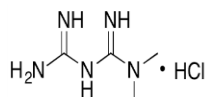
¹Department of Pharmaceutics, Faculty of Pharmacy, Assiut University, Assiut, Egypt; ²Drug Research Center, Assiut University, Assiut, Egypt.

Contact info: sabouelm@aun.edu.eg

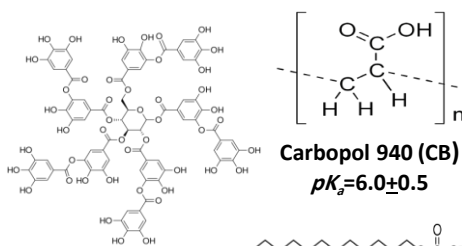
Objective

Metformin hydrochloride (MET) is an oral antidiabetic drug of high-water solubility. Modulation of MET solubility was done via hydrophobic ion pairing (HIP) approach to help overcome MET poor encapsulation efficiency into polymeric drug carriers (alginate beads) and prevent burst release. Three ligands: Carbopol (CB), sodium dodecyl sulphate (SDS) and tannic acid (TA) were screened to form MET hydrophobic ion pairs.

Materials

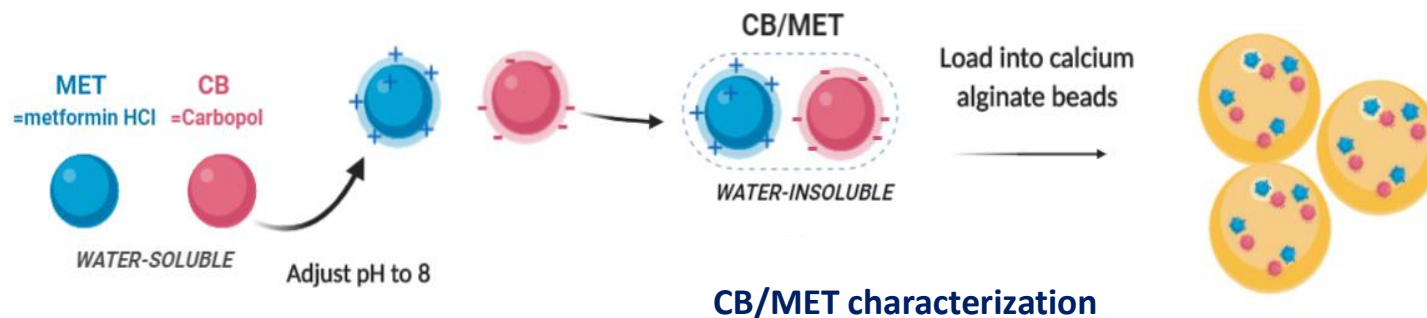
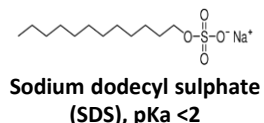


Metformin hydrochloride (MET), pKa= 2.8/ 11.6



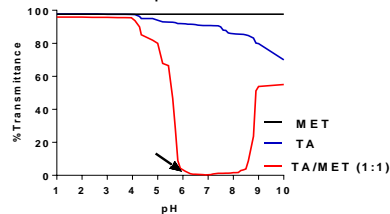
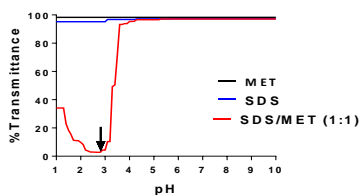
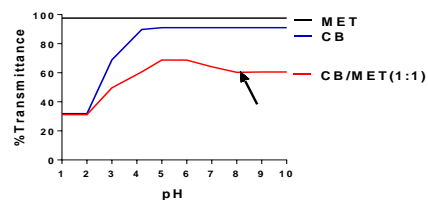
Carbopol 940 (CB)
pK_s=6.0±0.5

Tannic acid (TA)
pKa = 6



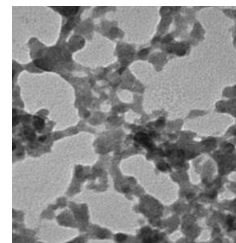
CB/MET characterization

Optimization of pH

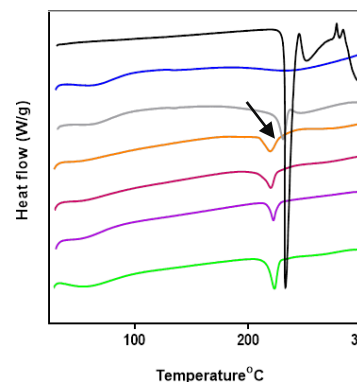
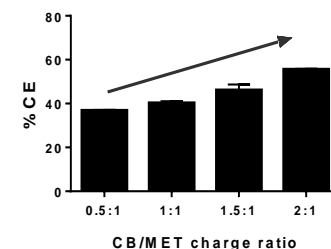


Change of % transmittance ligand/MET solution at 520 nm upon pH change (optimum pH indicated by arrow).

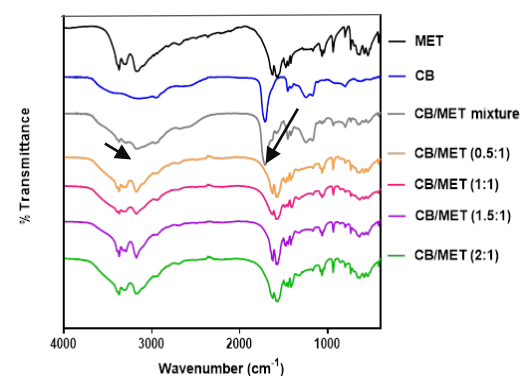
TEM (size: 1.67 μm, PDI : 1)



Complexation efficiency

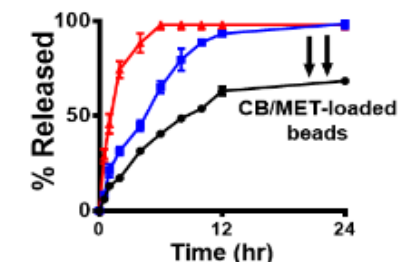


DSC thermogram shows interaction between MET and CB (MET endothermic peak shift) which is different from physical mixture.



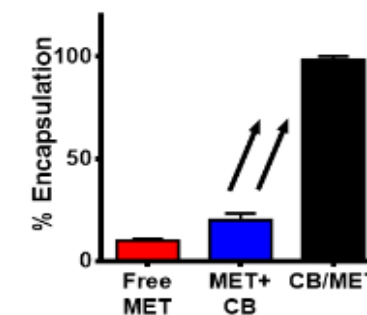
FTIR spectroscopy shows decreased intensity of CB and MET peaks confirming hydrophobic ion pairing which kept the native structure of MET.

In-vitro release



Free MET (▲), CB+ MET mixture (■) and CB/MET complex (●) loaded beads.

Encapsulation efficiency



Conclusions

HIP decreased MET water solubility. Thus, CB /MET complex-loaded beads achieved highest MET encapsulation and slowest *in vitro* MET release in comparison with MET + CB mixture –loaded beads (polymer blend effect) indicating additional effect of HIP step.