Solubility Enhancement for Zinc Diethyldithiocarbamate for Lung Cancer Treatment

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Introduction

Diethyldithiocarbamate zinc $Zn(DDC)_2$ is a disulfiram (anti-alcoholism drug) metabolite, has shown strong anti-cancer activity in vitro (Wiggins et al., 2015). Disulfiram activity is dependent on the availability divalent cations as Cu^{++} and Zn^{++}. Few reports studied the combination of Zinc and disulfiram for cancer treatment. However, this application was limited by low aqueous solubility and rapid metabolism for disulfiram .

Cyclodextrins (CDs) are cyclic oligosaccharide pharmaceutical excipients used to increase the solubility of drugs. CDs have a truncated shape with an external hydrophilic surface and internal hydrophobic cavity, that enable complexation with hydrophobic drugs .

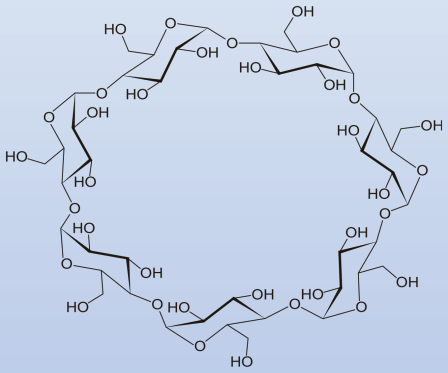


Figure 1. Beta Cyclodextrin structure

Therefore, development of stable solutions of $Zn(DDC)_2$ complex is required to permit further investigation exploring its anti-cancer activity. In this study complexes of CDs and $Zn(DDC)_2$ were prepared, characterised and in-vitro assessed for lung cancer treatment.

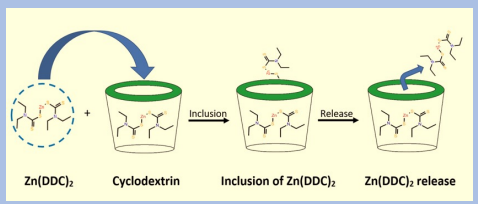
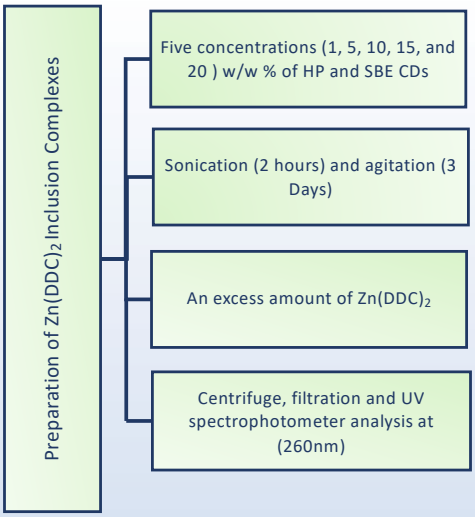


Figure 2. $Zn(DDC)_2$ inclusion with cyclodextrin cavity

Materials and Methods



Results

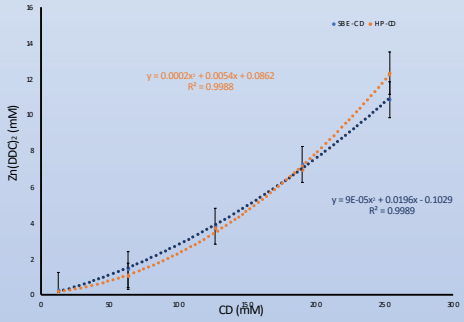


Figure 3. Phase solubility diagram of $Zn(DDC)_2$ in CDs (mean ± SD, n=3)

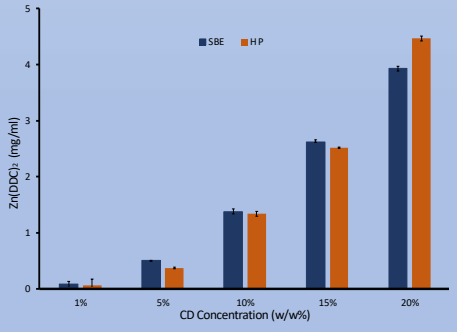


Figure 4. $Zn(DDC)_2$ solubility (mg/ml) in CDs solutions (W/W%) (mean ± SD, n=3)

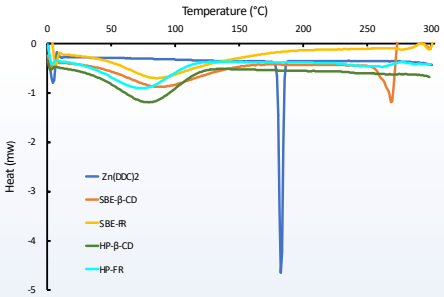


Figure 5. DSC Thermograph for CD-$Zn(DDC)_2$ complexes and freeze-dried formulations

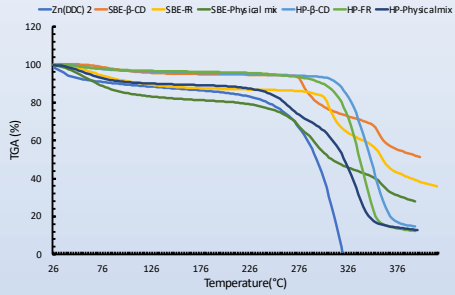


Figure 6. TGA Thermograph for CD-$Zn(DDC)_2$ complexes, freeze-dried formulations and physical mixture

Conclusion

The use of $Zn(DDC)_2$ as anticancer has always been challenged by its poor aqueous solubility. Inclusion complexes of $Zn(DDC)_2$ in CDs have overcome poor solubility issues to enable potential clinical application. The formulation of inclusion complexes was confirmed using thermal analysis. Results suggest that the developed formulations have a great potential for further studies for anticancer applications.

Reference

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