pharmaceutics

MDPI

PREPARATION AND CHARACTERISATION OF DIETHYLDITHIOCARBAMATE ZINC CYCLODEXTRIN INCLUSION COMPLEXES FOR POTENTIAL LUNG CANCER TREATMENT

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1. Intrinsic solubility prediction of $Zn(DDC)_2$ in water

1.1 Methods

DMSO was used as co-solvent to determine the intrinsic aqueous solubility of $Zn(DDC)_2$. Following the same method for solubility determination of Zn $(DDC)_2$ with cyclodextrin but with the absence of cyclodextrin. Zn $(DDC)_2$ was added to DMSO/water mixture using different ratios (70, 75, 80, 85 and 95 % v/v) of DMSO. The resulting solutions were sonicated for two hours then agitated for 3 days using Stuart shaker, 150 rpm at room temperature to reach equilibrium. Afterwards, the solutions were centrifuged for 10 min at 13,000 rpm. The supernatants were transferred into Spin X centrifuge tube with 0.45um filter and centrifuged again under the same conditions. Drug concentrations were determined using the reported HPLC method.

1.2 Results

The solubility of Zn $(DDC)_2$ in DMSO/water mixtures is exponential with DMSO concentration figure (S1). Similar findings were reported for the intrinsic solubility of Cu $(DDC)_2$ in DMSO (Suliman et al., 2021). The intrinsic solubility can be determined from the value of the intercept in the exponential equation below. Therefore, the intrinsic solubility of Zn $(DDC)_2$ in water is 0.0006 mg/L.

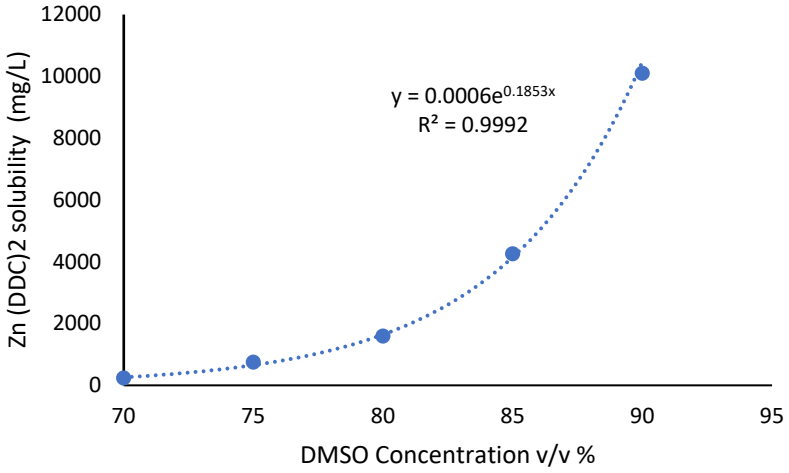

Figure S1. Zn $(DDC)_2$ solubility in DMSO/water mixtures against DMSO concentrations v/v%

2.Drug Precipitation Study

2.1 Method

The drug content of freshly prepared formulations was assessed over three months. Samples were stored at room temperature and at intervals of a week, drug concentrations were tested by HPLC method explained earlier.

2.2 Results

One of the challenges for the preparation of any formulation encapsulating Zn $(DDC)_2$ is its rapid precipitation in the form of crystals. The stability of freshly prepared formulations for both HP-CD and SBE-CD was performed for six months, to confirm that there was no crystallisation, precipitation, or degradation of Zn $(DDC)_2$. Figure (S2) illustrates that both solutions were stable with no significant change in Zn $(DDC)_2$ concentration ($p > 0.05$). These findings correlate with cyclodextrins properties of enhancing the chemical stability of the drugs and improving its shelf-life (Popielec and Loftsson, 2017).

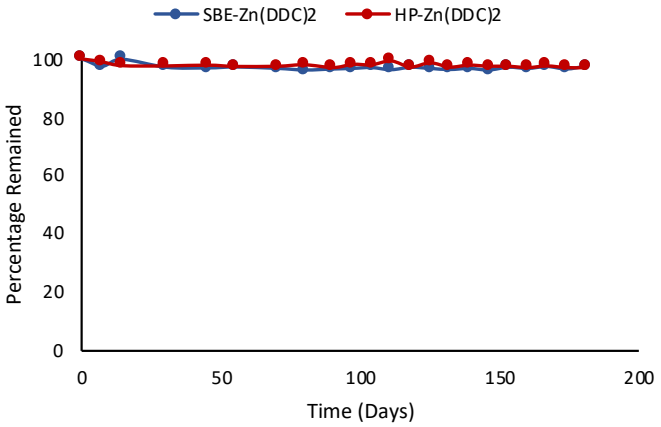

Figure S2. Stability study for freshly prepared SBE and HP Inclusion complexes with Zn $(DDC)_2$

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