PREPARATION AND CHARACTERIZATION OF POLYOXYETHYLATED TERT-BUTHYLCALIX[4]ARENE NANOPARTICLES AS PLATFORMS FOR DELIVERY OF CURCUMIN

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INTRODUCTION

Curcumin, the constituent of Curcuma longa, is considered a very promising anticancer agent due to its potent and pleiotropic antineoplastic activity and low nonspecific toxicity to normal cells. A major hurdle towards clinical realization of curcumin's potential has been limited due to its poor aqueous solubility (11ng/ml) and very low systemic bioavailability. A possible aproach to overcome these limitations is the design of nanosized drug delivery systems. In this study we report the preparation, characterization and evaluation of drug release profiles of curcumin loaded polyoxyethylated tert-buthylcalix[4]arenes nanoparticles (CX[4]PEG)

EXPERIMENTAL

Preparation of curcumin loaded calix[4]arenes nanoparticles

Curcumin - CX[4]PEG inclusion complexes were prepared using two methods: heating method and solvent-evaporation method.

Phase – solubility studies

Phase – solubility profiles of curcumin - CX[4]PEG inclusion complexes prepared by two methods were obtained by plotting the solubility of curcumin determined by validated spectrophotometric method at 427 nm, versus the excipient concentration.

Dynamic light scattering

The size and size distribution patterns of curcumin loaded polyoxyethylated tert-buthylcalix[4]arenes nanoparticles were investigated by ZetaSizer NanoZS (Malvern Instruments)The parameters were evaluated from measurements in the scattering angle of 173°, at 25°C.

In vitro drug release studies

The in vitro drug release profiles were studied under simulated physiological conditions for different incubation periods from 2, 4, 6, 8, 10 and 24 hours.

RESULTS

The hydrophobic properties of curcumin allow it to be incorporated into CX[4]PEG. due to its amphiphilic nature. At concentration of 0.375 µmol/ml by far exceeding the critical micellar concentration, CX[4]PEG proved to drastically increased the solubility of curcumin -568 fold due to concomitant formation of inclusion complexes and supramolecular aggregates. The basic physicochemical characteristics of empty and curcumin loaded supramolcular aggregates are given in *Table 1*

Formulation	Size (nm)	PDI	Zeta-potential (mV)
Non- loaded aggregates	180 ± 1.2	**0.120** ± 0.021	**- 20.8 ± 2.2**
Curcumin-loaded aggregates	**178.8 ± 2.4**	**0.117± 0.013**	**- 15.5± 1.4**

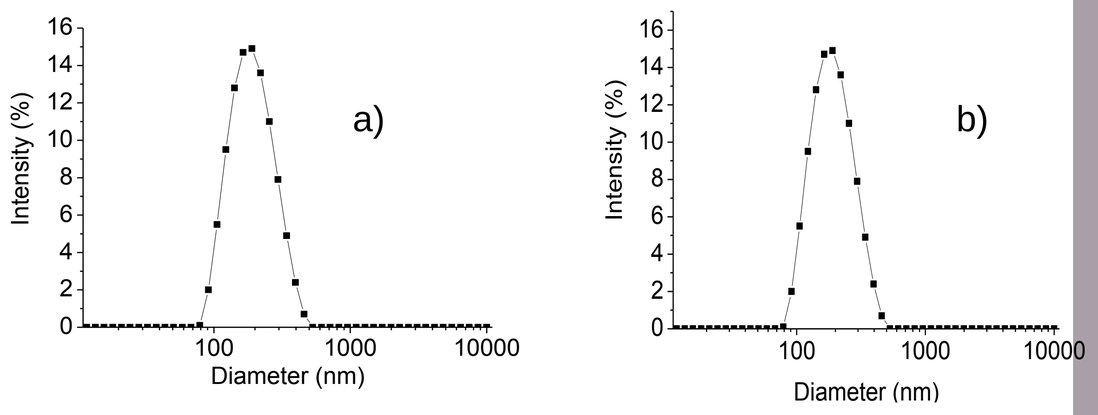

Figure 1 *Size distribution of a) CX[4]PEG free and b)* CX[4]PEG *curcumin loaded supramolecular aggregates*

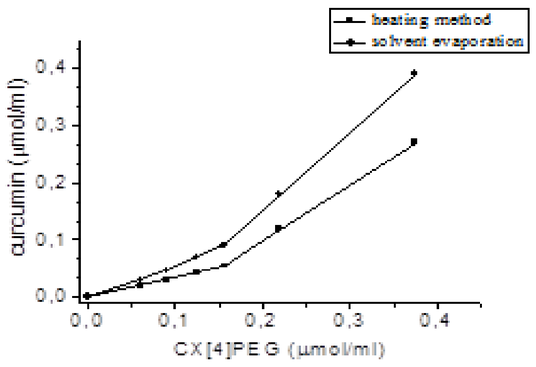

Figure 2. *Phase – solubility diagrams of curcumin in aqeous complexation media containing different concentrations of* CX[4]PEG

In vitro drug release profiles, studied under simulated physiological conditions for different incubation periods showed initial burst release of curcumin, folowed by slower drug release from both formulations prepared by solvent evaporation method and the heating method. (Figure 3).

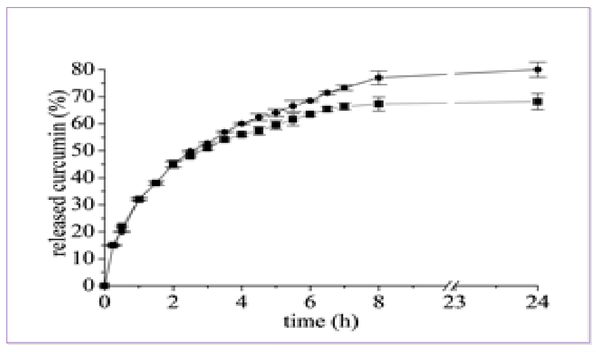

Figure 3. In vitro drug release profile of curcumin loaded CX[4]PEG *supramolecular aggregates*

Conclusion

Taken together all these findings give us reason to consider CX[4]PEG NPs as promissing drug delivery platform for curcumin

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