CURCUMIN LOADED HYBRID pH-SENSITIVE LIPOSOMES- PREPARATION AND CHARACTERIZATION

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INTRODUCTION

Curcumin, the yellow powder derived from the plant Curcuma Longa, exhibited numerous therapeutic applications against wide range of chronic diseases such as diabetes, pancreatitis, arthritis, neurodegenerative diseases and various types of cancer without toxicity to normal cells. Despite the numerous advantages, clinical realization of curcumin's potential has been limited due to its poor aqueous solubility (11ng/ml) and very low systemic bioavailability. An intriguing strategy to overcome these limitations is the design of nanosized drug delivery systems. Present study reports the preparation and characterization of hybrid pH-sensitive liposomal nanoparticles as platforms for delivery of curcumin.

EXPERIMENTAL

Preparation of curcumin:BEC-X inclusion complexes:
Curcumin:BEC-X inclusion complexes were prepared by a solvent evaporation method.

Preparation of conventional and pH-sensitive hybrid liposomes
Liposomes were prepared by modified thin film hydration method and extrusion trough polycarbonate membrane filters with pore size of 100nm.

Dynamic light scattering
The size and size distribution patterns of curcumin loaded liposomes were investigated by ZetaSizer NanoZS (Malvern Instruments)The parameters were evaluated from measurements in the scattering angle of 173°, at 25°C.

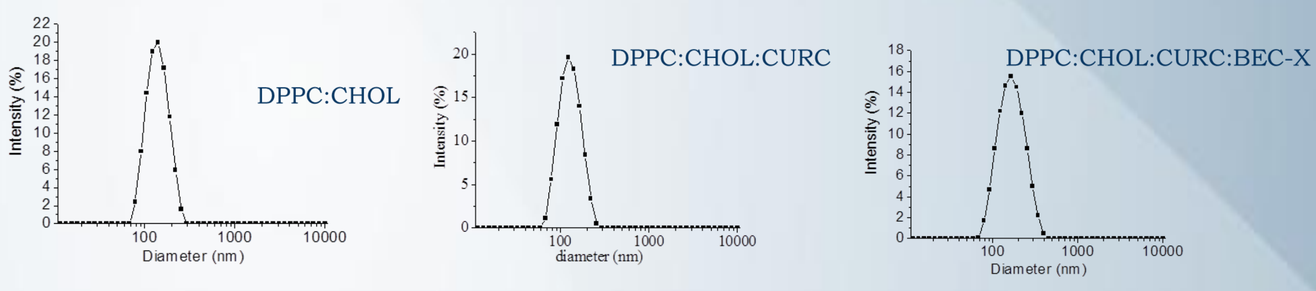
In vitro drug release
Curcumin release from hybrid pH-sensitive liposomes was tested as a function the pH of the medium, at 37 C over 1 h.

Cytotoxicity assay
The cytotoxicity of free and loaded curcumin was evaluated by using the MTT-dye reduction assay in panel of human cancer cell lines. The tested compounds were applied in concentration range 6.5 to 25μM for 72 h.

RESULTS

The hydrophobic properties of curcumin allow it to be incorporated into the liposomal bilayer. We found that the optimal curcumin to phospholipids ration is 0,25:1 (mol:mol). In order to increase the entrapment capacity of curcumin into the liposomes we encapsulate calixarene-solubilized curcumin within the liposomes' aqueous cavity. The basic physic-chemical and technological characteristics of liposomes are given in table 1 and 2.

Composition	Size (nm)	IP	ζ-potential (mV)
DPPC: CHOL	124 ± 4.2	0.096 ± 0.002	-15
DPPC: CHOL:CURC	145 ± 3.6	0.14± 0.04	-14.5
DPPC: CHOL:CURC:BEC-X	147± 4.2	0.135± 0.08	-16



Composition	Size (nm)	IP	ζ-potential (mV)
DPPC: CHOL	124 ± 4.2	0.096 ± 0.002	-22
DPPC: CHOL: pI-pAA 2.5 mol%	127.4 ± 2.6	0.084± 0.002	-28,2±5.5
DPPC: CHOL: pI-pAA 5 mol%	137.2± 3.5	0.08± 0.08	-34±2.3
DPPC: CHOL: pI-pAA 7.5 mol%	137± 2.8	0.163	-40.8

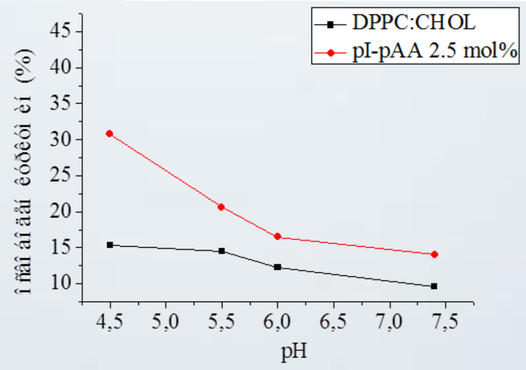


Figure 1. In vitro curcumin release from hybrid non pH sensitive (black) and hybrid pH-sensitive liposomes

Cytotoxic effect of free curcumin, curcumin loaded into BEC-X supramolecullar aggregates and pH-sensitive hybrid liposomes was investigated on two human cancer cell lines. IC_{50} values are presented on table 3.

Formulations	IC_{50} (μmol/L) (n=8)	
	KG-1[a]	RPMI-8226[b]
Curcumin (DMSO solution)	13,45 ± 2,31	2,89 ± 0,77
Hybrid pH sensitive liposomes: curcumin	2,19 ± 0,71	0,59 ± 0,21
BEC-X supramolecular aggregates	8,70 ± 1,44	2,22 ± 0,79

CONCLUSION: Thus on the grounds of the excellent in vitro biocompatibility profile and the favorable physicochemical and drug loading characteristics of the tested pH-sensitive hybrid liposomes, and their ability to retain the intrinsic pharmacological properties of encapsulated drug they could be considered promising drug delivery platforms for lipophilic curcumin.

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