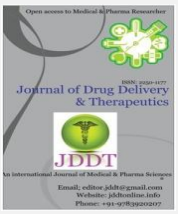
Available online on 25.12.2017 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research



Open Access Research Article

A NOVEL CLASS OF PHOTOTRIGGERABLE LIPOSOMES CONTAINING PACLITAXEL FOR THE TREATMENT OF SKIN CANCER

Neeraj Sharma[1], Vimal Kumar[2]

[1]IPS Academy College of Pharmacy, Indore, (M.P.), India

[2]ITM School of Pharmacy, ITM Universe, Vadodara, Gujarat, India

E-mail address: neerajsharma236@gmail.com

ABSTRACT

Success of nanocarriers-mediated drug delivery solely depends on delivery of therapeutics to a specified target. Secondly therapeutically active amount of drug should be released within defined space and time (triggered release). Recently, we formulated a novel class of photo-triggerable liposomes prepared from soy lecithin (SPC), cholesterol (CHOL) and photosensitive agent ketoprofen that can efficiently released entrapped paclitaxel upon UV light treatment. To explore these formulations for *in vivo* applications, we have examined the effect of released anticancer drugs on cellular toxicity. Liposomes were loaded with paclitaxel and biophysical properties (including liposome size and stability) and paclitaxel encapsulation efficiency of the liposomes were determined. Subsequently, the effect of UV light treatment on paclitaxel release, and cellular toxicity by released paclitaxel were examined. Since liposomes using the 5:1 molar ratio of SPC and CHOL, showed highest encapsulation of paclitaxel, these formulations were investigated further. UV light treatment of co-cultures containing paclitaxel loaded liposomes and cells (SK-MEL-2) resulted in improved cell killing as compared to untreated samples. These phototriggerable liposomes described here may provide a platform for future drug delivery applications.

Cite this article as: Sharma N, Kumar V, A novel class of phototriggerable liposomes containing paclitaxel for the treatment of skin cancer, Journal of Drug Delivery and Therapeutics. 2017; 7(7):1-3

INTRODUCTION

The development of a drug delivery system is one of the most important technological challenges in the present time. Liposomes are bilayered vesicles made from fatty materials, predominantly phospholipids and ranging from 50 nm to several micrometers in diameter. It is highly explored drug delivery system and can be safely and effectively used in various fields like protein /drug delivery, controlled delivery, antiviral therapy, tumour therapy, gene delivery, vaccine delivery, cosmetics and dermatology and others[1]. However, to achieve therapeutic efficacy of the liposomal dosage form the encapsulated associated drug should become available to the target cells. A main reason for this is that accumulation of liposomes in the tumor area does not guarantee that the encapsulated drug becomes bioavailable to the tumor cells[2,3]. Local administration of drugs has always been attractive because of the avoidance of systemic distribution of the drug and the need to use excessively high doses to enable effective concentrations at target sites. One of the crucial aspects of liposome use is to achieve the release of components at the target site. In local drug delivery, there are many methods to trigger the controlled release of drugs at the target site; such as the release of contents from liposomes in response to external stimuli of temperature, pH and light[4]. The use of light to stimulate the release of encapsulated compounds from liposomes is attractive, because spatial and temporal delivery of the radiation can be possible to control. The aim of present study was to achieve release of model drug encapsulated in SPC based liposomes upon photoactivation of ketoprofen in bilayer by UV light exposure. The objective of the present study is to develop safe and effective phototriggerable liposome carrier system for effective delivery of anticancer drugs[5].

MATERIALS AND METHODS

Materials

Soya phosphatidylcholine (SPC) were purchased from HiMedia, India. CHOL was purchased from Sisco Research Laboratories Mumbai, India. Ketoprofen was purchased from Msd Laboratories Ltd., Delhi. Paclitaxel was obtained as a gift sample from Dabur India. All other chemicals and solvents used were purchased from

local suppliers and were of analytical grade unless mentioned.

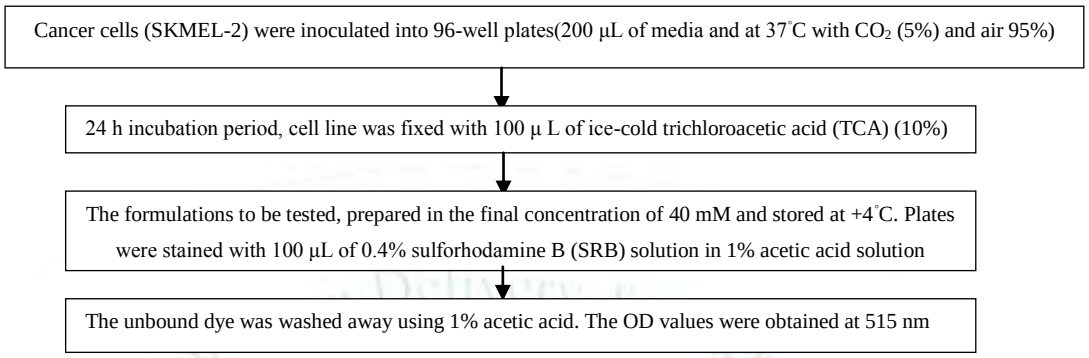
Formulation and optimization of novel phototriggerable liposomes

Liposomes were prepared by REV method. Both conventional and photosensitive liposomes were prepared (PC:CHOL 5:1 to 5:5 molar ratio) for study. Ketoprofen (drug-to-lipid ratio 0.25 wt/wt) was incorporated to membrane by dissolving in a mixture of chloroform and methanol (2:1v/v). Paclitaxel was incorporated in the liposomal bilayer. The shape and morphology of these liposomes were observed with the help of transmission electron microscope (Morgagni, 268, FEI, Electron microscope, Netherlands) after negative staining.

Light treatment

Effect of light-triggered release of entrapped contents from liposomes was evaluated after exposure to UV. Effect of exposure to UV was studied in a Kompakt UV cabinet, India fitted with a UV lamp.

Cellular toxicity assay



RESULTS AND DISCUSSION

Formulation of photosensitive liposomes: Several formulations of liposomes were prepared to study the effect of SPC: CHOL ratio. Five different batches of both conventional and photosensitive liposomes containing various SPC/CHOL molar ratios from 5:1 to 5:5 were prepared Table 1. Separation of liposomes was achieved by centrifugation at 16500 rpm for 90 min at –5 °C. The liposomal concentrate was washed twice with PBS pH 7.4. TEM micrograph was taken and clearly showed the formation of liposomes (Figures 1). Most of the liposomes formed appeared spherical and symmetrical in shape and were mainly unilamellar in nature. Sizes of formulated liposomes were found between 200-400 nm.

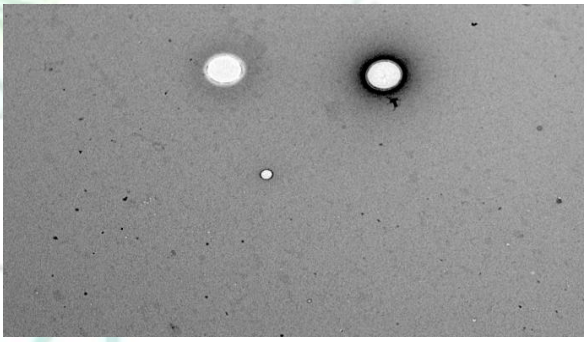


Figure 1: Transmission electron microscopic photograph of prepared liposomes

Table 1: % EE of formulations of photosensitive and conventional liposomes

S. No	Formulation Code	PC/CHOL ratio	Encapsulation efficiency (%)	
			With ketoprofen	Without ketoprofen
1.	LP-1	5:1	30.36 ± 1.49	26.55 ± 2.04
2.	LP-2	5:2	27.55 ± 0.50	17.40 ± 0.40
3.	LP-3	5:3	24.72 ± 0.78	14.62 ± 1.01
4.	LP-4	5:4	15.87 ± 0.56	11.75 ± 1.55
5.	LP-5	5:5	10.25 ± 0.55	07.82 ± 0.205

Light treatment

Shape was observed before and after exposure for photosentive liposomes using phase contrast microscope. It was observed visibly that size increased after exposure.

Table 2: GI_{50} values of different formulations

Samples	GI_{50} values
Free drug solution	55.6
Paclitaxel loaded liposomes	37.4
Paclitaxel loaded phototriggerable liposomes	24.0

SRB assay:

Co-cultures containing paclitaxel-loaded phototriggerable liposomes and cells (SK-MEL-2), resulted in improved cell-killing as compared to untreated samples Table 2.

CONCLUSION

UV light treatment of co-cultures containing paclitaxel-loaded liposomes and cells (SK-MEL-2) resulted in improved cell-killing as compared to untreated samples. These phototriggerable liposomes described here may provide a platform for future drug delivery applications.

REFERENCES

1. Thompson DH, Gerasimov OV, Wheeler JJ, Triggerableplasmlogen liposomes: Improvement of system efficiency, Biochim Biophys Acta, 1996. 1279, 25-34.
2. Bisby RH, Mead C, Morgan CG, Active uptake of drugs into photosensitive liposomes and rapid release on UV photolysis, FEBS Lett, 1999, 463, 165-168.
3. Kono K, Yoshino K, Takagishi T, Antiinflammatory effect of retrovirally transfected interleukin-10 on monosodium urate monohydrate crystal induced acute inflammation in murine air pouches, J Control Release, 2002, 80, 321-332.
4. Gerasimov OV, Boomer JA, Qualls MM, Synthesis and characterization of oligomaltose grafted lipids with application to liposomes, Adv Drug Deliv Rev, 1999, 38, 317-338.
5. Gerasimov OV, Schwan A, Thompson DH, Acid catalysedplasminylcholine hydrolysis and its effect on bilayer permeability: A quantitative study, Biochim Biophys Acta, 1997, 1324, 200-214.