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# FORMULATION AND EVALUATION OF CATIONIC NIOSOMES OF 5-FLUORO URACIL

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**Abstract:**

*Cancer is the second leading disease associated with combinations of chemotherapy, radiation treatment. The conventional treatment is limited due to its side effects. 5-fluorouracil encapsulated cationic vesicles form complexes with negatively charged cell or endoplasmic membrane and facilitate in drug release after endocytosis. multi lamellar and large uni lamellar vesicles without aggregation are obtained. The encapsulation efficiency and drug release increased with increase in stearyl amine. Cationic vesicles showed steryl amine dependent drug release.*

***Key Words:*** *5-fluorouracil, encapsulation, cationic vesicles, stearyl amine*

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## INTRODUCTION

Cancer is a leading cause of disease worldwide. In 2012, there were an estimated 14.1 million new cases of cancer in the world: The use of combination chemotherapy along with surgery or radiotherapy has been conventionally fallowed to treat cancer [1, 2]. However, the toxic side effects of the conventional therapy remained which sometimes reduced the chances of remission. The therapeutic regimen mainly involves the surgical removal of the diseased area followed by adjuvant chemotherapy involving either cisplatin or 5-fluorouracil (5-FU) or both in combination with docetaxel or cetuximab along with radiation therapy [3, 4]. The side effects involve bone marrow depression, cyto toxicity even breathing problems, in addition to chemotherapy related side effects such as nausea, fatigue, alopecia, anemia, neutropenia, and mucositis [5, 6]. Hence an efficient therapeutic modality that can act as a substitute for surgery and minimize the chemo- and radiotherapy related side effects

Niosomes are the uni or multi lamellar vesicles made up of non-ionic surfactants capable of entrapping both hydrophilic and hydrophilic drug (6, 7). The use of biodegradable drug delivery vehicles such as liposomes, niosomes would not only enhance the bioavailability of the drug and lower the concentration of the drug to be administered but also provide targeting options to the tumor cells thereby decreasing the extent of cytotoxicity [7, 8].

In the present study 5-fluorouracil was encapsulated in internal aqueous phase by preparing the miceller solubilized solution using Lauryl glucoside and Tween 80 as solubilizing agents. Cationic vesicles form complexes with negatively charged cell or endoplasmic membrane and facilitate in drug release after endocytosis. The presence of charge increases the encapsulation of drug and decreases aggregation of vesicles by electrostatic stabilization. (7, 8).

The objective of the present work is to develop a novel formulation of cationic niosomes encapsulated with micellar solubilized solution of 5-fluorouracil. The obtained niosomes were evaluated for entrapment efficiency, charge, and drug release studies.

## MATERIALS AND METHODS

5-fluorouracil was obtained from MSN pharmaceutical Pvt. Ltd; Hyderabad. Cholesterol from Qualigen fine chem. Ltd, Mumbai, Span from Koch light lab. Ltd; England, Stearyl amine from sigma chemicals, St.Louis U.S.A. and the lauryl glucoside were obtained from Henkel KGA, Germany. All the solvents used were of good analytical grade.

**Preparation of 5-Fluorouracil Cationic Vesicles**

5-fluorouracil cationic vesicles were obtained by encapsulating micellar solubilized solution in internal aqueous compartment of vesicular system.

**Preparation of Micellar Solubilized 5-fluorouracil:**

Tween 80 and lauryl glucoside in 1:1 proportion were dissolved in 5ml of methanol to which 5-fluorouracil is added to give a concentration of 500 µg\ml the total volume was adjusted to 10ml and the obtained solution was subjected to evaporation under reduced pressure in a vaccume evaporator at a temperature of 45-50˚c.After the complete evaporation 10ml of distilled water was added and rotated for 10 minutes to obtain a micellar solubilised 5-fluorouracil (6,9). Encapsulation of solubilized 5-fluorouracil in noisome: The cationic vesicles of 5-fluorouracil were prepared as per Rilm et.al. Span 60 and cholesterol in 1:1 ratio with different concentrations (15%-25%) of stealyl amine giving a total lipid content of 200umoles are dissolved in 14 ml of chloroform in a round bottom flask to which 1ml methanol was added. The resultant clear solution was subjected to evaporation under reduced pressure in a rotary vaccume evaporator at a temperature of 60ºc and the obtained thin dry film was hydrated by incorporating 10ml of micellar solubilized 5-fluorouracil solution.

**Characterization of 5-fluorouracil Cationic Vesicles:**

**Morphological Characterization:**

Freshly prepared niosomal dispersion was scanned and imaged using on optical microscope attached to video camera. Particle size distribution of vesicular dispersion was observed for aggregation and appearance.

**Entrapment Efficiency:**

Encapsulation efficiency of vesicular system was determined using Centrisart tubes (solitorius, Germany) with a molecular weight cut off of 20kDa. The prepared cationic niosomes were separated from unencapsulated 5-fluorouracil by ultra filtration. The niosomal dispersion is taken in centrisort tubes and rotated at 10,000 r.p.m for 15 min from the obtained supernatant 0.5 ml was taken and made up to 10 ml with solvent mixture (20:80) of chloroform and methanol. The absorbance of resultant solution was determined at 280 nm using UV spectrophotometer (10).

**Drug Release Studies:**

The release pattern of 5-fluorouracil from niosomal dispersion was carried out in dialysis bag method.

Accurately measured 2 ml of cationic niosomal dispersion was taken in dialysis bag and the bag was suspended in 100 ml of 7.4 phosphate butter. The aliquots of dialysis medium were removed at predetermined intervals of 0.5,1, 2, 4, 6, 8,10,12,24 hrs. Every withdrawal was followed by replacement with fresh medium to maintain the sink conditions. The drug content in dialysis medium was estimated by diluting the aliquot with phosphate buffer and measuring the absorbance at 280 nm using UV spectrophotometer (Shimadzu, Japan) (11).

**RESULTS & DISCUSSION**

**Morphological Characterization:**

The optimized dispersions of cationic noisome were examined for vesicle formation under optical microscope attached with video camera. Fig. 1 revealed that vesicles are multi lamellar and large uni lamellar in nature. Incorporation of cholesterol and stearyl amine assumed to be responsible for the formation large vesicular structure.

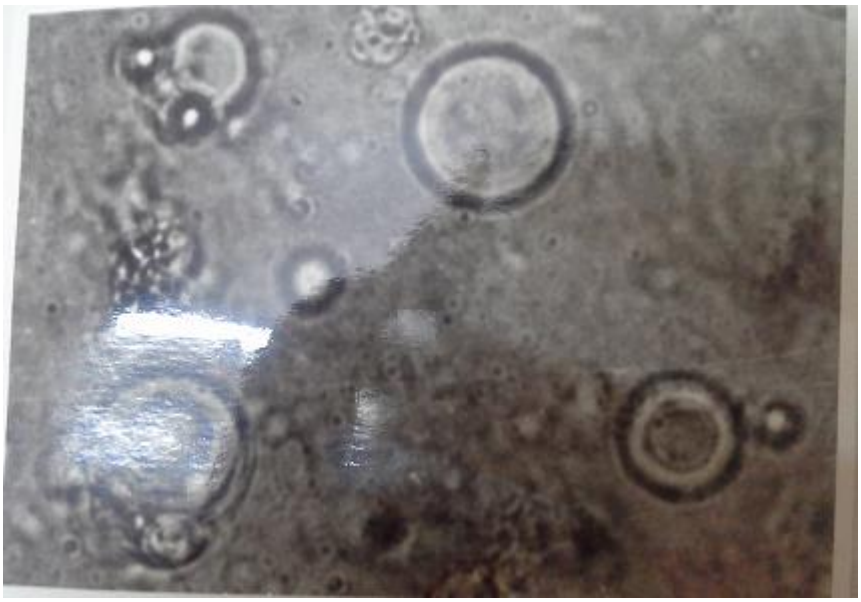

**Fig 1: Optical Microscopy of the Cationic Vesicles of 5-Fluorouracil**

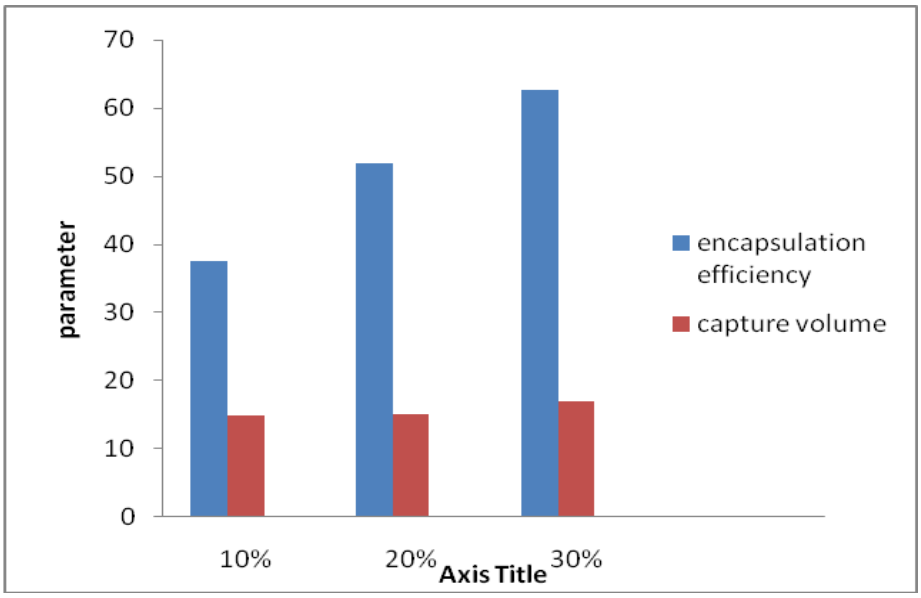


**Fig 2: Encapsulation Efficiency and Capture Volume of Different Niosomal Formulation**

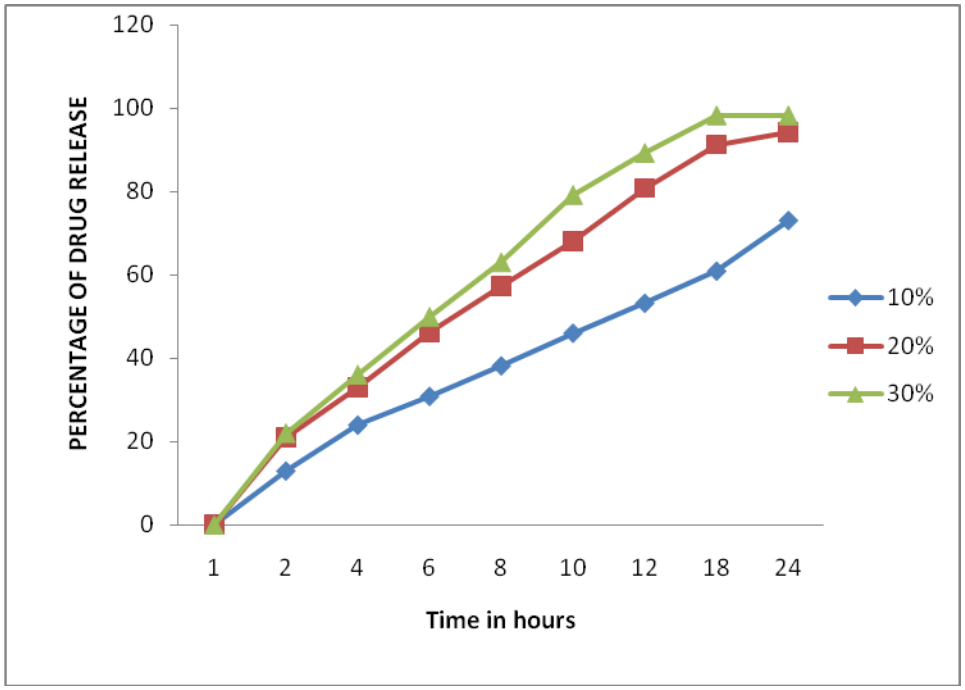


**Fig 3: Drug Release Profile of Cationic Niosomal Formulation of Fluorouracil**

The obtained vesicles were spherical, discrete, abundant and uniformly distributed. Vesicles are observed wish out any aggregation tendency.

**Entrapment Efficiency:**

Enacapsulation efficiency and capture volume of different niosomal formulation of 5-Fluoro uracil is shown in figure-2.Encapsulation of 5-fluorouracil in cationic vesicular dispersion was determined by ultra filtration using centrisort tubes was found we be 37.63 to 62.58% with a capture volume of 14.92µl/mol to16.90 µl/mol. Formulation of large uni lamellar vesicles are most appropriate type to achieve higher capture volume, This is because large internal core is available for the efficient entrapment of 5-fluorouracil solution.

**Drug Release Studies:**

The drug release profile of cationic niosomes containing different concentrations of stearyl amine showed aried dissolution profile shown in figure-3.As the cholesterol molar ratio increases in niosomes particle size, entrapment increases. The stearyl amine may affect the entrapment efficiency of the drug molecule in the vesicle. The incorporation of stearyl amine in bi layers of niosomes enhances the vesicle size which could be due to electrostatic stabilization, resulting in increase in size and entrapment efficiency. The incorporation of different molar concentrations of cholesterol and stearyl amine showed entrapment efficiency from 37.63 to 62.58%.

The cumulative drug release profile of different formulations is graphically illustrated shows that the percentage drug released increases with increase in cholesterol and stearyl amine. The optimized niosomal dispersion when stored for one month does not showed any leakage and aggregation, which may be due to the incorporation of 5-fluorouracil in internal aqueous compartment and steryl amine.

**CONCLUSION**

The niosomes are the well preferred drug delivery system as they have greater drug delivery potential for targeted and controlled delivery of anti cancerdrugs. Thus these areas need further exploration and research so as to bring out commercially available niosomal preparation.

**REFERENCES:**

1.Thomas A .M, Kapanen A. I, Hare J. I, Ramsay E, Edwards K, Karlsson G, Bally M. B. Development of a liposomal nanoparticle formulation of 5-fluorouracil for parenteral administration: formulation design, pharmacokinetics and efficacy. J Control Release. 2011 Mar 10; 150(2):212-9.

2. Gyanendra singh, Hemant K Raghuvanshi, Anubhav Anand, Rakesh pundir, Harinath Dwivedi., Targeted delivery of 5-fluorouracil by niosomal drug delivery system. J of pharmacy research, 2010; 3(5), 1152-1154.

3. Tianmeng Sun Younan Xia. Engineered Nanoparticles for Drug Delivery in Cancer Therapy. Nanotechnology & Nanomaterials, Nanotoxicology & Nanomedicine.2014; 53, 46, 12320–12364.
4. Namdeo. A, Jain. N. k, Niosomes as drug carries, Indian J. Pharm. sci.1996; 58, 2, 41-46.
5. Alladi Saritha, D. Rambhau, S. Srinivasan , K. Mahalingan. Preparation and evaluation of cation in niosomes encapsulated with micellar solubililised rifampicin. Journal of Global Trends in Pharmaceutical Sciences:2010; 1( 1): 7-14.
6. S. S. Biju, SushamaTalegaonkar, PRMishra,RKKhar., Vesicular systems :an over view,Ind j of pharm sci.2006,68(2),141-152.
7. Wafa Mossa Ramadan, Ajay pal Singh. Preparation of Acyclovir loaded non – ionic surfactant vesicles (niosome) using Reverse phase evaporation technique. Research J pharm and tech.2009; 2(4): 193-198. .
8. Yoshida. H, Lehr. C. M, Kok.w, Juginger H.E, Verhoef. J.C,Bouwstra. J.A, Niosomes for oral delivery of peptide drugs, J controlled rel. 1992; 21, 145-154.
9. D'silva. J.B, Notary.R.E, Drug Stability in liposome suspension, hydrolysis of indomethacin,cyclocytidine& p–nitro phenyl acetate, Journal of pharm sci.,1982;71,1394-1398.
10. Andrew S.Janoff, Liposomes Rational Design, Marcel decker, Inc. 1999; 79-81
11. Rambhau, Devraj, Saritha, A, Raju, J, Gopinath, D, Apte, S S. A Novel Method To Determine The Encapsulation Efficiency Of Cationic Vesicles By Heparin Induced Aggregation.AAPS;2002:W-14151.