Anti-Cancer Cyclodextrin Nanocapsules Based Formulation Development for Lung Chemotherapy

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Author’s contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

ABSTRACT

Lung carcinoma is one of the highly malignant carcinoma. Oncologists also face a difficulty in handling lung carcinoma. A novel therapeutically strategy in patients with pulmonary cancer may be the immediate injection of chemical-therapeutic agents within lungs. Many drugs are available for in market for treatment of lung cancer but face difficulty due to poor solubility. The paper discusses about development of cyclodextrin modified cationic polymer complex i.e. polyethylene glycol (PEG), wherein the complex is used for providing drug delivery of poorly soluble drugs, more specifically ellipticine. The complex was made by coating PEG over cyclodextrin nanocapsules wherein the core of the capsule is filled with PEG-7 Glyceryl Cocoate oil for enhancing the delivery of the anti-cancer agent. The complex was then evaluated under characterization studies which includes particle size analysis, zeta potential, morphological analysis, cytotoxicity analysis and anti-cancer effect of the complex. It was found that the complex was more potent in delivering the drug within cancerous cells and was potent to treat lung carcinoma.

Keywords: Anti-cancer; cyclodextin complex; polyethylene glycol; lung carcinoma.

1. INTRODUCTION

A worldwide development of melanoma records that are hazardous to malignant-cell physiologies but do not damage normal cells [1]. Recently utilized anti-cancer medicines demonstrated fairly strong potency not just for tumor cells as...
well as in human body cells that formed tumor. The hunt is presently being pursued for new anti-cancer agents among both terrestrial and marine species. Over decades, plants were utilized for disease control. Many plants are used in different areas of world as well of conventional herbal remedies for their beneficial effects [2,3]. Increasing the occurrence of multiple diseases provides a desire for novel anti-cancer treatments. In United States, for instance, 2,688,780 naive tumor cases and even minimum of 700,920 cancer kills are expected. Several herbal-isolated anticancer medicines are studied and eventually submitted to research studies, including multiple tumor cell lines [2].

A main reason of cancer-centered demise both in males and females is lung tumor that is responsible for just over 2 million deaths worldwide annually [4]. About 90 percent of lung carcinoma identified are large cells, and also linked with elevated rates of development and necrosis and low protection relative to other carcinomas in early stages. Most natural derived anti-cancer medicines are studied and eventually submitted to human trials by cells (including different carcinoma cell lines) and laboratory animals [5]. The amount of recently found chemical products has rising rapidly in current years [5]. In 2007 about 60,000 such compounds were identified, while in 2015 there were nearly 336,000 newly found molecules. For the substances in toxicity range, there were about 180,000 [6]. Moreover, the reactions are classified in quantitative terms as 196,000 pharmacologically agile substances [5]. Medicinal plants from certain biologically active substances are often referred to as effective inducers for lung cancer cell apoptosis. The acacetine flavonoid polynphenol compounds (5,7-dihydroxy-4'-methoxy-flavonoids) can suppress cell proliferation (IC50 = 9.46 μm) from Robinia pseudoacacia (legumes) A549. A version of artemisinin annua Altai Michael (Asteraceae), Dihydroartemisin (DHA) is utilized to cure disease, and it can also cause cell death in human cancers of the lung. Tripterygium wilfordii diterpenes (Celastraceae) were greatly sensitised to Apo2L/TRAIl-induced apoptosis, but did not cause cells to die significantly from PG490 (tripolide) [1].

Whilst intravenous treatment is more popular than many cancers, oral medication is considered to be next phase toward potential treatment with latest advancements. The oral path requires pain free self-medicament from perception of individual and is deemed to be most realistic method [1]. This also reduces repayment pressure in health system, as counseling in medical centers is not needed. Plants utilized as type of products of strong biological processes were utilized in mainstream healthcare for several decades. Another solution is to separate certain compounds from plant products. Another solution is utilization of biotechnological instruments to develop substances of plants anticancer [2]. The initial quick raise and eventual decline of drugs in bloodstream via the intravenous passage may be avoided through oral administration.

Nanoparticulate structures in this area of drug distribution are successful. The concept of nanoparticulate structures, both nanosphereal and nanocapsule, is submicron colloidal. Nanospheres are characterized as matrix frameworks, while nanocapsules are structural framework consisting of inner fluid layer, (which, based on component, may be soluble or oily) covering a polymer shell [1]. Nanospheres pose several advantages: enhances water solubility; defend the molecule against environment; and offers regulated environmental security. The oily core provides increased solubilities to hydrophobic products, taking into consideration the benefits of nanocapsules dependent on proteins, and also polymeric shell defends them from severe environmental conditions. The nanoparticles-based drug delivery system demonstrate increased effectiveness compared with conventional drug delivery system, with: 1) the half-life of susceptible pharmaceutical products and peptides; 2) enhances hydrophobic medication solubility; and 3) allow regulated and selective delivery of drugs in infected locations [1,7].

Many drawbacks confronting traditional drug delivery methods may be solved by managed drug delivery frameworks. For example, historically non-specific chemotherapy drugs utilized for carcinoma treatment are utilized that harms both normal tissue and cancerous cells which lead to low efficicy and great toxicity[8]. The regulated Drug delivery frameworks should be ideal carriers of chemotherapeutic agents and therefore improve the amount of chemotherapy within tumor site and prevent natural cell toxicity. Ellipticin is addressed as 4-ring comprising aromatic planar molecule and two heterocyclic nitrogen atoms along with dual methyl groups. The scale and structure of molecule is identical as comparable to base pair of purine-
pyrimidines and is desirable situation for interspersing nucleic acids [2].

Ellipticine is an established intercalator and can be used among nucleotides to join a DNA strands. Ellipticine attaches tightly from its intercalated condition and lies opposite to nucleotides, growing the supercoiled concentration of DNA. Intercalated ellipticine specifically binds to DNA replicating enzyme Topoisomerase II, which prevents the enzyme and induces significant anti-tumor action [2]. The ellipticine variants were found in laboratory experiments in order to promote tumor growth remediation, but were not approved for therapeutic purposes owing to their elevated toxicity, including stomach pain, vomiting, cramps, extreme weariness, sore throat, tongues and esophagus. Further DNA damaging is induced by development of DNA adducts followed by enzyme alleviation via cytochromes P450 and peroxidases ensuring that ellipticine are treated as prodrug [2].

Cyclodextrins are natural polymers formed by enzyme starch decay. Those are cyclic oligosaccharides which comprises of minimum of at least six divisions of α-(1,4) glucosides, which are connected by α-(1,4) [1]. Within the pharmaceutical industry, the most important benefits of cyclodextrins are improving flexibility, permeability and bio-availability of drugs molecules. Amphiphile cyclodextrins are variants of natural cyclodextrins produced and adjusted chemically over primary and/or secondary phase [1,7]. For improving water solubility, preserve durability, maximize permeability and eventually bioavailability, cyclodextrins are very widely used as dynamic agents. Cyclodextrins are natural polymers formed by enzyme starch decay. Those are cyclic oligosaccharides which comprises of minimum of at least six divisions of α-(1,4) glucosides, which are connected by α-(1,4) [1]. Within the pharmaceutical industry, the most important benefits of cyclodextrins are improving flexibility, permeability and bio-availability of drugs molecules. Amphiphile cyclodextrins are variants of natural cyclodextrins produced and adjusted chemically over primary and/or secondary phase. For improving water solubility, preserve durability, maximize permeability and eventually bioavailability, cyclodextrins are very widely used as dynamic agents. Despite the downside of minimizing oral chemotherapy and benefits of Nano particular methods of distribution, the present paper discusses about the drug delivery through nanocapsule wherein a cyclodextrin complexed with a cationic polymer is synthesized followed by drug loading to provide a sustainable release of anti-cancer agent to treat the lung cancer.

Roa et al. embedded Doxorubicin (DOX)-centered nanoparticles within effervescent and non-effervescent carriers by utilizing spray-freeze drying technology. The synthesized powders that can be inhaled were further analyzed in tumor in mouse model. It was hypothesized that, treatment with effervescence nanoparticles carrier are effective in restricting tumor growth in comparison to non-effervescent nanoparticles i.e. lungs of animals treated with inhalable effervescent DOX represented small tumors as compared to control sample. This suggested that effervescent DOX nanoparticles are found to be potent in treating lung carcinoma [9]. FDA has also approved some of the PEGlyated drugs such as Doxil®, Lipodox®).

Although the above cited research work had shown effective results to some extent, but still lacked in terms of enhanced drug delivery as it is not easily absorbed by the cells. Also PEGylation has some loop holes such as steric hindrance of PEG chain restricts uptake of liposomes by target cells. Therefore, there is a need to develop a formulation overcome the above mentioned problems and provide enhanced drug delivery to target side along with increased bioavailability. The ideal size of the nanocapsule obtained ranged from 10 nm -1000 nm [12].

1.1 Research Question

How to enhance drug delivery of inappropriate drugs in order to treat lung cancer at the time of chemotherapy?

2. MATERIALS AND METHODS

2.1 Design

For synthesis of cyclodextrin adapted polymer, PEG is overlaid on cyclodextrin via using various solvents for improving the cellular uptake and bioavailability. The end product is consequently then tested under different characterization methods.

2.2 Sample

Samples undertaken for the preparation of cyclodextrin adapted Polyethylene glycol (PEG) involvesPEG-7 Glyceryl C cocoate in the range of 0.2%w/v to 2% w/v in 5 ml of ethanol,
cyclodextrin solution, Ellipticine powder in the range of 95%w/w (MW: 348.34 g/mol, Sigma Aldrich) [13].

2.3 Instruments Used

Instruments used includes Dynamic light scattering tool, zeta potential analyzer (Shimadzu), vacuum evaporator, incubator.

The methodology involved in the synthesis of cyclodextrin adapted PEG is prepared in two steps: i) synthesis of Cyclodextrin altered polymer nanocapsule, ii) preparation of ellipticine loaded nanocapsules.

2.4 Synthesis of Cyclodextrin Altered Polymer Nanocapsule

Core-shell nanoparticles were formulated by an altered nanoprecipitation method followed by addition of cyclodextrin and PEG-7 Glyceryl Cocoate oil in 5 ml of ethyl alcohol in double distilled water in a drop wise manner to obtain a mixture [14]. The mixture is stirred continuously for 20-30 minutes at 150 rpm in order to obtain a solution. The organic solvent is further evaporated by subjecting the solution to vacuum at 35°C for 15 minutes to obtain an organic phase solution [1].

2.5 Synthesis of Preparation of Ellipticine Loaded Nanocapsule

Ellipticine encumbered nanocapsules were developed by dissolving 12% w/w of ellipticine in organic phase solution followed by addition of 0.03% w/v of portasan to obtain nanocapsules with a positive charge [1]. Finally, the obtained nanoparticles were subjected to characterization studies in order to determine the efficacy in regards to oral chemotherapy [15].

2.6 Physiochemical Characterization of Ellipticine Loaded Nanocapsule

2.6.1 Particle size analysis and zeta potential

Particle size and polydispersity index of ellipticine loaded nanocapsule were calculated via dynamic light scattering (DLS) (Shimadzu) with scattering angle of around 173 °C. Zeta potential was also measured by setting an angle around 10°C and 25°C. Measurements were conducted in triplicate [1].

2.7 Morphological Analysis

Morphological analysis of nanocapsules were performed by utilizing Scanning electron microscopy (SEM), wherein sample was placed on metal stubs coated with Ag-Pd alloy followed by imaging 5-25 kV. The content of nanocapsule was determined by HPLC device, which had subsequently been validated, fitted with fluorescence sensor at 436 nm wavelengths (μm) and 380 nm excitation wavelength (±). (Germany, Agilent 1100). Briefly, the precipitate is isolated and completely frozen to achieve a drug-laden nanomaterials powder shape with a segregation of unbound drugs by centrifugation for 20 min at 3600 rpm. The Nanocapsules filled with ellipticine (1.5 mg) are soluble in 3 ml of DCM-DMSA-mixture. The clinical loading of ellipticine is calculated utilizing every sample formulation’s peak area.

Associated Drug (%) = (Experimental Drug loading)/ (theoretical drug loading) ×100

Entrapment Drug quantity = (CPT quantity (μg))/ (Formulation volume (ml))

Drug release activity of ellipticine loaded nanocapsule was conducted at 37 °C under sink environment. 3 ml of nanocapsule was kept in dialysis bag, wherein the bag comprising nanocapsule suspension was further kept in 45 ml of phosphate buffer solution (PBS) comprising 0.2% v/v tween 20 at physiological pH and acidic pH for mimicking physiological situations [16]. The system was further kept in water bath. At certain durations, 550 μL of sample was taken from medium and further replaced with fresh medium and finally cumulative percentage drug release was calculated for every duration [10].

2.8 Cytotoxicity Analysis

In vitro toxicity studies have been conducted on fibroblast cells have strong absorption of intestinal medicines and can also be conducted with MTT Assay for mimicking gastrointestinal impediments [17]. In this case MCF cells were developed on seed regulators with seed density of 7 x 10^3 at seeding with circulatory quantity. In cultivation medium, Apical (456 μL) and Basilicate (2 ml) filter inserts were inserted to replace incubator with humidity levels of 97 percent at ambient temperature per second day after conservation of cells underneath 97 percent air and 6 percent CO2 [10].
2.9 Anti-cancer Efficacy of Ellipticine Loaded Nanocapsule

In contrast to ellipticine solution with MTT check, the anti-carcinoma potency of nanocapsules filled with ellipticine as assessed against MCF-7 cell lines. The cells were developed in Dulbecco’s modified eagle Medium (DMEM) with 7 percent fetal bovine serum (FBS), penicillin (55 units / mL) and amoxicillin (49 μg / mL) augmented by lines of the human breast adenocarcinoma cells of the American Form of Culture Series. The communities have been protected at 37°C in a 5 percent incubator with humidified CO₂[1].

Developed nanoparticles are advantageous over emulsomes in terms of their efficacy and percentage drug release. The biggest downside is that the medication is subjected to organic solvents and mechanical treatment. Phospholipids in organic solvents like chloroform, isopropyl ether, or freon are dissolved in this process. In order to facilitate good emulsification conditions, two organic solvents can often be required to blend to change the density in unity closer to aqueous phase densities. Biologically active molecules such as enzymes, protein medicinal and RNA molecules can be exposed, due to harsh conditions of organic solvent penetration and mechanical agitation, to conformational changes, protein denaturation or splitting of DNA strands [3].

3. RESULTS AND DISCUSSIONS

The small size of nanoparticles is advantageous with regards to pharmacodynamics and pharmacokinetics profile like release profiles, bio-availability, absorption and cellular uptake. This indicates that, particle size would lie in optimum range that allows particles for diffusion and permeate via biological membranes and in addition encapsulation and long term release capacity. To maximize the formulation of nanocapsules, the effect of cyclodextrin quantity, oil phase composition and organic-aqueous state volume ratio were examined. The impact of cyclodextrin on particle size and polydispersity index. Particle size analyzer is analytical tool for measuring, visualizing and reporting the allocation of particle sizes to a particular population of particles. During the framework development and performance monitoring of particular systems, particle size analyzers serves significant role in developing effective processes and achieving great quality final end-product.

Impact of ellipticine loaded nanocapsules on particle size and polydispersity index is examined, wherein a linear surge in particle size was observed with increase in polymer concentration. This infers an increased viscous nature of the ellipticine loaded nanocapsule. Table 1 represents impact of modified nanocapsule concentration on particle size and polydispersity index.

Table 1. The following table represents the physical characteristics (Particle size and Polydispersity index (PDI)) of the cyclodextrin modified nanocapsule at different concentration

<table>
<thead>
<tr>
<th>Polymer concentration (%)</th>
<th>Particle engrossment (%)</th>
<th>Particle size</th>
<th>PDI±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.06</td>
<td>150±1.4</td>
<td>0.13±0.02</td>
<td></td>
</tr>
<tr>
<td>0.09</td>
<td>157±1.7</td>
<td>0.15±0.33</td>
<td></td>
</tr>
<tr>
<td>0.2</td>
<td>245±3.5</td>
<td>0.21±0.19</td>
<td></td>
</tr>
<tr>
<td>0.4</td>
<td>396±2.5</td>
<td>0.42±0.24</td>
<td></td>
</tr>
</tbody>
</table>

*The table represents that polymer concentration of 0.06% was suitable for nanocapsule synthesis

It was observed that, at 0.06%w/v polymer concentration, particle size obtained was small indicating an increase in solubility of ellipticine loaded cyclodextrin nanocapsule. The consistency of polymer concentration may be a major factor in choosing it and applying here as polymer framework that has central role to preserve and sustain the stabilization of encapsulated substances. The polymer used herein is prepared without employing any kind of stabilizing agents. This indicated that drug stability was mainly due to highly stabilized polymeric wall. Estimation of polydispersity index indicates that, particles were monodispersally distributed and polydispersity was high. This was due to increased cyclodextrin concentration.

The oil used in synthesis of ellipticine loaded nanoparticles was mainly to increase the solubility of the drug, which was achieved by employing the oil within the core of nanocapsule. Table 2 indicates the impact of oil concentration on solubility of drugs. Surge in oil concentration has contributed to the surge in nanoparticles size. The change in viscosity of organic phases is responsible to this effect. Because greater the oil amount, more viscous is organic stage. From the findings conducted oil with concentration of 0.9% v/v is regarded most suitable for providing enhanced solubility to the drug.

Throughout the analysis of particle size nanocapsules, the impact of enhanced aq. phase
volume was calculated by organically aqueous 1:1, 1:4 and 1:6 scale. At organic to aq. stage ratio of 1:1 a large change in particle sizes was found probably due to insufficient phase separation for lower amount of water (4 mL). Nonetheless, O / A ratio declining, that to say growing the amount of aqueous process, contributes to a decline in percentage of product correlated with aqueous phase, as has been seen in Simoes et al. [33]. Thus, ratio of 1:1 between organic and aqueous volume was selected for further synthesis of ellipticine loaded nanocapsule. Table 3 shows the impact of organic to aqueous phase ratio on particles size and polydispersity index.

Table 2. The following table represents the physical characteristics (Particle size and Polydispersity index (PDI)) of the cyclodextrin-modified nanocapsule at different oil concentration

<table>
<thead>
<tr>
<th>Oil concentration (v/v)</th>
<th>Particle size</th>
<th>PDI±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>170±1.4</td>
<td>0.08±0.03</td>
</tr>
<tr>
<td>0.5</td>
<td>190±1.3</td>
<td>0.10±0.02</td>
</tr>
<tr>
<td>0.9</td>
<td>210±2.4</td>
<td>0.26±0.10</td>
</tr>
<tr>
<td>1.0</td>
<td>285±2.5</td>
<td>0.33±0.20</td>
</tr>
<tr>
<td>2.5</td>
<td>312±2.4</td>
<td>0.45±0.25</td>
</tr>
<tr>
<td>3.0</td>
<td>320±1.4</td>
<td>0.54±0.25</td>
</tr>
</tbody>
</table>

*particle size and PDI with oil concentration of 0.9%v/v was considered suitable for forming nanocapsule

Table 3. Effect of organic to aqueous phase (O/A) ratio on particles size and polydispersity index, wherein mean±SD values are represented for three different data

<table>
<thead>
<tr>
<th>O/A</th>
<th>Particle size</th>
<th>PDI±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1</td>
<td>171±1.4</td>
<td>0.33±0.05</td>
</tr>
<tr>
<td>1:4</td>
<td>130±1.2</td>
<td>0.09±0.41</td>
</tr>
<tr>
<td>1:6</td>
<td>120±1.1</td>
<td>0.07±0.21</td>
</tr>
</tbody>
</table>

Thus from the above analysis it can be concluded that 0.06% w/v of polymer concentration, 0.9% w/v of PEG-7 Glyceryl Cocoate oil concentration and 1:1 ratio of aqueous to organic phase particles were considered suitable for synthesis of ellipticine loaded nanocapsule. The Mean diameter, polydispersity index, zeta potential and morphology were further carried out for ellipticine loaded cyclodextrin nanocapsules (Table 4).

From the Table 4 it can be inferred that zeta potential of ellipticine loaded cyclodextrin nanocapsule is +10.21 Mv which indicates increase in particle size of due to cyclodextrin adsorption over nanocapsule surface. This layer is expected to take place and also a complementary anti-cancer activity from kitosan, an established caspase-3 activator, because of incorporation of PEG into intestinal mucosa via opening tight links.

Table 4. Characterization parameters of ellipticine loaded cyclodextrin nanoparticles

<table>
<thead>
<tr>
<th>Measuring parameters</th>
<th>Ellipticine loaded cyclodextrin nanocapsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean particles size</td>
<td>200±7.5</td>
</tr>
<tr>
<td>Zeta potential</td>
<td>+10.21±0.8a</td>
</tr>
<tr>
<td>Polydispersity index</td>
<td>0.13±0.07a</td>
</tr>
</tbody>
</table>

*a*wherein ‘a’ indicates difference between formulations

The entrapment efficiency and associated drug percentage was determined of the Cyclodextrin nanocapsules and PEG-cyclodextrin (CD) nanocapsules. The cationic PEG - cyclodextrin nanocapsules and anionic cyclodextrin nanocapsules were further compared. Table 5 represents the percentage of drug entrapment efficiency and percentage of associated drugs.

Table 5. Entrapment and associated drug percentage of nanocapsules

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Entrapment efficiency</th>
<th>Associated drug percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD nanocapsules</td>
<td>40±2.4</td>
<td>35±1.5a</td>
</tr>
<tr>
<td>PEG-CD nanocapsules</td>
<td>56±2.2</td>
<td>43±0.4a</td>
</tr>
</tbody>
</table>

From the Table 5 it is inferred that, entrapment efficiency of PEG-CD nanocapsules is 56±2.2% as compared to CD nanocapsules whose entrapment efficiency is 40±2.4. Similarly, Associated drug percentage (%) of PEG-CD nanocapsules is 43±0.4a % as compared to CD nanocapsules i.e. 35±1.5a %. PEG coated CD nanocapsules does not contribute to rise in drug loading, because lipophile CPT compound is effectively enclosed within core nanocapsule by adsorbing or imprisoning in smaller quantities in PEG aliphatic chains, because such hydrophilic polymer does not trigger the strongly lipophilic product molecule.

In-vitro drug ellipticine release from CD-PEG nanocapsules were determined in Phosphate buffer (PBS) at physiological pH and acidic pH.
1.3 for mimicking the environment within blood and stomach of humans respectively. Fig. 1a and b shows the average percentage of ellipticine release from nanocapsules w.r.t time. From the Fig. 1a it may be concluded that, no release of ellipticine from nanocapsules in first 3 hrs. This may be due to polymeric walls that prevents the release from acidic environment. In comparison, releasing media of pH 7.4 is seen to release around 35% of ellipticine from formulations within first two hours and to detect full release of enclosure within 50 hours. Reports display a safe release profiles for both formulations (Fig. 1b).

Cell line L930 for polymeric toxicity testing is approved cell line of USP and is therefore utilized in such study to determine if nanocapsules toxicity is correlated or not with polymeric material. Furthermore, L930 cells with MTT check have been tested for their cytotoxicity by blank anionic and cationic cyclodextrin nanocapsules. Fig. 2 Shows cell viableness of fibroblast L930 at dilution levels of 1:5, 1:10, 1:20, 1:40 and 1:80 after 2 days of cell incubation with unloaded cyclodextrin nanocapsules. There was no substantial difference in cell viableness of each concentration measured among anionic and cationic cyclodextrin nanocapsules (P>0.05). The sensitivity of blank nanocapsules was also shown to amount dependent and blank nanocapsules could be considered protected through dilution limit of 1:10 v / v (concentration is 2.525 μg / mL).

Fig. 3 demonstrates viableness of MCF-7 tumor cells with DMSO tainted solutions at dilution rate 1:10 after 48 hours incubation. In contrast with ellipticine solution, cytotoxic activity of anionic and cationic solutions has been observed at concentrations of 5,125 μg / mL. Incubation duration is based on both double-time of MCF-7 cell lines and release quality. C I ell line of MCF-7 doubled over 35 hours, while ellipcitine had been released continuously from nanocapsules over 48 hours, which indicates that accumulation within cells required an extended exposure.
Fig. 2. Representation of percentage of cell viability of CD nanocapsules and PEG coated CD nanocapsules against L930 cells after 48 hrs of incubation. Mean results are represented by data.

Fig. 3. Representation of %cell viability of MCF cancer cell lines with Ellipticine loaded nanocapsule and unloaded nanocapsule by comparing with ellipticine nanocapsule prepared at similar concentration. Data represents the mean results wherein it indicates that ellipticine loaded nanocapsule (CD-PEG nanocapsule) is required in less amount to attain percentage viability.

From the all analysis it was observed that, PEG coated cyclodextrin nanocapsule was significant as they allow penetration of drugs into cells more efficiently. This may be attributable due to cellular adhesions and increased residence duration at surfaces given by PEG polymer thereby proving to be an effective method of drug delivery. The percentage release of the drug ellipticine from CD-PEG nanocapsule was observed in both acidic and basic media wherein it was observed that, 50% of drug was release in 48 hrs under acidic condition while 90% of drug was released in 48 hrs. This indicates that basic conditions are more suitable for drug release. Also Polyethylene glycol (PEG) loaded and unloaded nanoparticles were compared for cell viability in L930 Cells and MCF cells where it was observed that, 15µg of CD-PEG nanocapsule complex was sufficient enough for viability of both L930 and MCF cells.

Many doxorubicin (DOX) centered nanoparticles have been developed so far for example DOX-conjugated gold nanoparticles that significantly inhibited tumor development in mouse and humans [11], but the cyclodextrin modified with PEG is more potent due to stealth and bioavailability of PEG which lacks in contention drug formulations. Thus, it can be concluded that, the cyclodextrin modified with PEG is potent for delivering the drug to the target site.

4. CONCLUSION

Development of sophisticated pharmacological nano- carriers for treating cancer has been in
demand from many decades. In this research a new kind of drug delivery carrier has been evaluated for providing delivery of anti-cancer agents to their target site. This work was the first time in vitro to grow and test the CPT-loaded amphiphilic CD nanocapsules in oral chemotherapy. These findings suggest that CD nanocapsules provide a modern approach to produce secure and efficient oral chemotherapy. In the present work, elepticin loaded nanocapsule were synthesized and evaluated in vitro for their effective drug delivery for treating lung cancer. The results procured from the present work indicates that cyclodextrin nanocapsules offer naive strategy for providing safe and advantageous chemotherapies for curing lung carcinoma.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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