Introduction

Breast cancer is the most prevalent disease that holds second rank in the mortality rate of women (after lung cancer). In 2019, approximately 231,840 new breast cancer cases and 40,730 breast cancer deaths (40,290 women, 440 men) are estimated throughout the world. The World Health Organization (WHO) predicts that by 2050 there will be 27 million new cases of breast cancer and 17.5 million deaths from breast cancer per annum [1]. Therapeutic options for breast cancer are limited and associated with toxicities. Nanoparticles showed potential for treating or targeting breast cancer. Among the nanoparticles, various lipid nanoparticles are developed over the years for the breast cancer therapy, namely liposomes, solid lipid nanoparticles, nanostructured lipid carriers and lipid polymer hybrid nanoparticles [1-4]. Jose et al. [3] developed dual drug tamoxifen and imatinib which loaded temperature-sensitive liposomes for breast cancer treatment. Dual drug loaded liposomes have demonstrated synergistic growth inhibition against breast cancer cells MCF-7 and MDA-MB-231. Co-delivery of tamoxifen and imatinib can be produced using temperature-sensitive liposomes as a possible targeting strategy against breast cancer.

Targeted doxorubicin (DOX) encapsulating liposomes were built by loading tamoxifen (TMX) in bilayers which conferred on the liposomal surface estrogen receptor (ER) specificity and positive charge. TMX-DOX liposomes were found to be more effective in destroying MCF-7 cell compared to free tamoxifen by estimating the potential effects of these complexes on the cell death of human breast carcinoma (MCF-7) cell lines. The formulated tamoxifen liposomal conjugate was characterized by analytical techniques to determine its size, size-distribution, thermotropic changes and conformational changes along with possible cytotoxicity towards MCF-7 (breast cancer cell line) in vitro. The mean particle diameter was estimated to be 64.70±49.75 nm, 73.72±23.8 nm and 119±54.7 nm for blank liposomes, neutral and positively charged liposomes bound tamoxifen, respectively. As tamoxifen was introduced into positive liposomes, it resulted in noticeable broadening and shift to lower temperature at 135 °C compared to the main characteristic endothermic peak ($T_m$) of pure liposomes at 140°C, while the introduction of tamoxifen into neutral liposomes contributed to the disappearance of the main endothermic peak of pure liposomes. FTIR analysis revealed structural changes in vesicles after tamoxifen was incorporated into liposomes. The IC$_{50}$ value for tamoxifen in the cytotoxic assay with MCF-7 treated cells was 0.34 µg/ml, while tamoxifen-loaded neutrally or positively charged liposomes showed an increase of IC$_{50}$ value to 119.62 and 101.23 µg /ml, respectively. Current data suggests a new treatment regimen where free tamoxifen is substituted with liposomal tamoxifen to improve anticancer activity against MCF-7 cancer cell lines.

Keywords: Tamoxifen; charged Liposomes; DSC; FTIR; DLS; Cytotoxicity.
cells compared to DOX liposomes, as indicated by various studies of the in vitro cell line, and also showed superior ability to inhibit tumor growth in nude mice [4].

Fontana et al. [5] formulated solid lipid nanoparticles (SLNs) that contained tamoxifen citrate that were stable and demonstrated the sustained release in different in vitro aqueous media. Tamoxifen SLNs demonstrated extended release of intact medication in plasma, in effect, improved the medication bioavailability. In vitro anti-cancer tests on MCF-7 cell lines showed that the drug-loaded SLNs’ cytotoxic activity was significant compared to the free drug without affecting the bioavailability.

The developed Tamoxifen-loaded nanostructured lipid carriers (NLCs) targeted intestinal lymphatic systems by [6]. Tamoxifen-loaded NLCs showed a dose-dependent cytotoxicity in MCF-7 (acinar epithelium), but their activity decreased in ZR-75-1 (ductal epithelium).

Zhang et al. [7] used emulsification-ultrasonication approach to encapsulate a water-soluble drug Mitoxantrone into lipid polymer nanoparticles (LPN). Mitoxantrone LPN increased cytotoxic activity in the MCF-7 and MCF-7-MX (multi-drug-resistant variant) as compared with free drug.

Liposomes are biocompatible and biodegradable, making them ideal for research in biomedicine. The unique feature of liposomes is their ability by nature to compartmentalize and solubilize both hydrophilic and hydrophobic matters. Phospholipids, which are amphiphilic molecules (with a hydrophilic head and hydrophobic tail) form the essential part of liposome. The hydrophilic part is predominantly phosphoric acid bound to a water-soluble molecule, while the hydrophobic portion consists of two fatty acid chains with 10-24 carbon atoms and 0-6 double bonds in each chain. When these phospholipids are dispersed in aqueous media, they form lamellar sheets such that the polar head group faces the aqueous region outwards, while the fatty acid groups face each other and eventually form spherical / vesicle structures called liposomes. The polar component remains in contact with aqueous region along with shielding of the non-polar part (located at an angle to the membrane surface) [8]. Coupled with biocompatibility and biodegradability, this unique feature makes liposomes very attractive as anticancer drug delivery vehicles [9-24].

Liposomes overcome the limitations of conventional chemotherapy by improving the bioavailability and stability of the drug molecules and minimizing side effects by site-specific targeted delivery of the drugs [15]. DaunoXome, Galen’s registered trademark, is the FDA-approved liposomal formulation of daunorubicin for the treatment of MCF-7-MX (Breast cancer cell line) in vitro.

Numerous studies have shown that cationic nanocarriers are more effective vehicles for drug delivery than conventional, neutral, or anionic liposomes, maybe due to the electrostatic interactions between the cationic liposomes, and the negatively charged cell membranes, the absorption of nanoparticles by adsorptive-mediated endocytosis is enhanced [23-24].

To our knowledge, no previous studies on the interaction of tamoxifen with positively charged phospholipids were performed from the perspective of the thermotropic phase behavior of phospholipids and to detect the changes of acyl chain conformations and characteristic PO2− bands in the polar heads of phospholipids. The formulated tamoxifen liposomal conjugate was characterized by analytical techniques to determine its size, size-distribution, thermotropic changes and conformational changes along with possible cytotoxicity towards MCF-7 (Breast cancer cell line) in Vitro.

The goal of this study was to determine whether neutrally or positively charged liposomes encapsulated with tamoxifen could inhibit the
proliferation of human breast cancer MCF-7 cell proliferation compared to free tamoxifen by estimating the potential effects of these complexes on the cell death of human breast carcinoma (MCF-7) cell lines.

**Materials and Methods**

**Chemicals**

Distearoyl phosphatidylcholine (DSPC) in powder form, with a molecular weight of 790.161 g, purity 99% (presented in Figure 1), and stearyl amine (SA), with molecular weight of 269.5 g and 99% purity were all purchased from Sigma (ST. Louis, Mo, USA). Tris base in powder form, molecular weight of 121.1 g, was purchased from CDH, New Delhi, India. Tamoxifen with a molecular weight of 371.515 g was purchased from EIPICO (Egyptian International Pharmaceutical Industries Co, Egypt). The molecular structure of tamoxifen is shown in Figure (2). Ethanol was of analytical grade and purchased from DaeJung Chemicals (Seohaean-ro, Gyeonggi-do, Korea). All other reagents and solvents used in this work were of research grade.

**Liposome preparation**

For the preparation of neutral small unilamellar vesicles (SUVs) liposomes, a mixture of Distearoyl phosphatidylcholine (DSPC) to tamoxifen at molar ratio 7:2 was used following the method of [25]. In round bottom flask (50 ml), 30 mg of DSPC and 4 mg tamoxifen (corresponds to 29 mol%) were mixed. One and a half mg of SA was added to the lipid composition to introduce a net positive charge. Then 20 mL of ethanol (EtOH) was added, and the flask was shaken until all lipids dissolved. The organic solvent was removed gradually using a rotary evaporator under vacuum to produce a uniform thin film of lipids on the inner wall of the flask. The lipid film was hydrated with Tris buffer (pH 7.4 at 37°C) in a water bath at 50°C for 15 min at 60 rpm to form multilamellar vesicles (MLVs) liposomes. MLVs were sonicated by using an ultrasonic homogenizer with Titanium probe (model 150VT, BioLogics, USA) at 50% amplitude with a pulse 90% at 42 °C, under nitrogen stream for 5 min to form small unilamellar vesicles (SUVs). Control empty liposomes were prepared following the same method as described above using only aliquots of DSPC.

![Figure 1. Schematic chemical structure of DSPC.](image1)

![Figure 2. The chemical structure of Tamoxifen.](image2)
Dynamic light scattering (DLS)
The mean particle size and size distribution of freshly prepared empty liposomes, and neutrally and positively charged liposomes encapsulated with tamoxifen were determined by dynamic light scattering using a particle sizing system (Nanotrac Wave II, Microtrac, USA) at 25°C in Tris buffer (pH 7.4). The measurements were performed in triplicate and an average size was determined.

DSC measurements
Differential scanning calorimetry (DSC) was carried out by using (model DSC-50, Shimadzu, Japan) calibrated with indium to investigate the thermal behavior of lyophilized samples of empty liposomes, and neutrally and positively charged liposomes encapsulated with tamoxifen. Analyses were performed using 5 mg of samples sealed in a standard aluminum pans. The thermogram of each sample covered the 25 - 200°C temperature range at a scanning rate of 3°C/min.

FTIR Spectroscopy
FTIR spectra of lyophilized samples of empty DSPC liposomes and those neutrally or positively charged liposomes encapsulated with tamoxifen deposited in KBr disks were recorded on a Jasco FT/IR-4100 spectrometer (Tokyo, Japan). Scanning was done in the range between 400–4,000 cm\(^{-1}\) at a speed of 2 mm/s, with a resolution of 4 cm\(^{-1}\) at room temperature.

In-Vitro cytotoxicity assay
Breast cancer cell line (MCF-7) was cultivated in a humidified incubator under 5% CO\(_2\) and 95% air at 37 °C in RPMI 1640 media supplemented with penicillin (100 IU/mL), streptomycin (100 μg/mL) and decomplemented fetal bovine serum (10%, v/v).

The drug treatments were performed in growth assays (96 well culture plates). Each drug at a calculated final concentration (50, 100, 200, 400, 800 and 1000 µg/ml), was added to the culture medium. The cell viability and proliferation (cell numbers) were measured using SRB (Sulfo-Rhodamine-B-stain) assay [26-27]. Using the method of Skehan et al., [26], the cytotoxic activity of free tamoxifen, neutrally or positively tamoxifen-loaded liposomes under test (50, 100, 200, 400, 800 and 1000 µg/ml) were added to the cell monolayer triplicate wells.

In an atmosphere of 5% CO\(_2\) and 37°C, monolayer cells were incubated with free tamoxifen, neutrally or positively tamoxifen-loaded liposomes, separately for 48 h. After 48 h, the cells were fixed, washed and stained with Sulfo-Rhodamine-B stain [28]. Excess stain was washed with acetic acid and attached stain was recovered with Tris- EDTA buffer. In an ELISA reader (ELISA-TECAN-SUNRISE, Germany), the optical density (O.D.) of each well was measured at 564 nm with an ELIZA microplate reader. In order to calculate the cell viability curve for MCF-7 cancer cell line after the treatment with free tamoxifen and those neutrally or positively tamoxifen-loaded liposomes, the relation between cell viability percentage (surviving fraction) and drug concentration was determined.

The percentage of cell survival was calculated using the following formula:

The IC\(_{50}\) values (the concentrations of drug required to produce 50 % inhibition of cell growth). The experiment was repeated 3 times for each individual drug.

Results and Discussion
Dynamic light scattering (DLS) of a solid/liquid system, is a technique that is used in particle size measurement [28]. The results of particle size measurement of freshly prepared neutrally or positively charged liposomes doped with tamoxifen as opposed to empty liposomes are presented in Figure 3. The particle size distribution of all tested liposomal formulations showed unimodal symmetrical distribution pattern. The size distribution of empty liposomal samples clustered at a mean size diameter of about 64.70±49.75 nm with 0.394 PDI Figure 3A. Polydispersity index (PDI) effectively accounts for particle homogeneity of colloidal suspension. Values greater than 0.7 designate that the sample is probably not stable for the DLS technique. The encapsulation of tamoxifen into neutrally charged liposomes resulted in an increase in the calculated mean size diameter of blank liposomes from 64.70±49.75 nm to 73.72±23.8 nm with 0.477 PDI Figure 3B. Such results may indicate
that the liposomes may be physically conjugated with tamoxifen at the surface and the molecule of tamoxifen appears to interact to a large extent with the lipid bilayer which could explain why the size is increased.

Once tamoxifen was encapsulated into positively charged liposomes, the mean vesicle sizes increased significantly (119±54.7 nm with 0.734 PDI) (Figure 3C). These results indicate that the inclusion of tamoxifen into positive liposomes increased the spacing between the adjacent bilayers resulting in the formation of liposomes bigger in size compared with the control ones. The increase of particle size may be due to stronger electrostatic repulsive force occurring between the DSPC N(CH₃)₃⁺ group and the tamoxifen NH₃⁺ group within the lipid bilayer of liposomes. Table (1) summarizes the particle size for each formulation of tamoxifen-loaded liposomes as compared to empty liposomes. However, there are some conflicting results on the average particle size of tamoxifen loaded liposomes.

The DSPC vesicles have been used as model membranes because this phospholipid can mimic many aspects of biological membranes, being one of their most abundant constituents.

Upon dehydration pure DSPC vesicles when submitted to DSC analysis, showed a main endothermic peak at 140°C (Figure 4), which is in agreement with [29,30]. The pre-transition temperature (T_p) was around 60°C for pure DSPC liposomes. The incorporation of tamoxifen into positively charged liposomes exhibited distinct broadening and shift to lower temperature (135 °C) of the main endothermic peak of pure DSPC
TABLE 1: Particle size distribution measured by dynamic light scattering (DLS) for different liposomal formulations.

<table>
<thead>
<tr>
<th>Liposomal formulation</th>
<th>Average size vesicles (nm)</th>
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<tbody>
<tr>
<td>Empty liposomes</td>
<td>64.70±49.75</td>
</tr>
<tr>
<td>Tamoxifen neutral liposomes</td>
<td>73.72±23.8</td>
</tr>
<tr>
<td>Tamoxifen positive liposomes</td>
<td>119±54.7</td>
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</table>

that exists at 140 °C, its intensity was markedly depressed of about 90% when compared to pure DSPC. This result indicated that tamoxifen had a substantial impact on the acyl chains of DSPC bilayers, and that their presence reduced the cooperative transition of the lipid acyl chains. The lowered temperature of the main DSPC transition process indicated that there was a likelihood that tamoxifen incorporation would cause the formation of acyl chains in a disordered and loose state. These findings were in agreement with previous studies [31-33]. The pre-transition temperature was around 60°C either for pure DSPC liposomes or those doped with tamoxifen. Broadening of the main transition peak by the presence of tamoxifen (TAM) especially for 6 mol%, 9 mol% and 15 mol% concentrations was an indicative of model membrane destabilization, indicating that this drug was intercalated within the lipid bilayer [32].

Compared with positively charged liposomes, the greater impact of tamoxifen could be observed upon its incorporation into neutral liposomes. The incorporated tamoxifen probably conjugated with the lipid bilayers, interacted with them to a large extent, and disturbed them which resulted in the disappearance of the main characteristic endothermic peak of pure DSPC that exists at 140 °C. This phenomenon can be explained by solubilization of tamoxifen that was dispersed in an amorphous nature in the molten liposomes ensured a significant interaction of tamoxifen with DSPC liposomes.

FTIR, which was used to examine the wavenumber of the vibrational modes of the different functional groups to detect any structural alterations in vesicles of liposomal membrane structure could confirm these observed changes in the present DSC study.

FTIR spectra of empty lyophilized DSPC liposomes was compared with neutrally or positively charged liposomes doped with tamoxifen samples in two distinct spectral regions, namely 3500–2800 cm⁻¹ (Figure 5), and 1800–1200 cm⁻¹ (Figure 6).

The spectrum of the DSPC liposomes displayed the FTIR peaks of highest absorption, especially those corresponding to the symmetric and antisymmetric PO₂⁻ stretching vibrations at 1090 and 1220 cm⁻¹, respectively. The peak noticed near 1470 cm⁻¹ is due to CH₂ bending vibration and that at 1734 cm⁻¹ is due to the carbonyl stretching vibration C=O. Two peaks relative to the symmetric and antisymmetric stretching vibrations of the CH₃ in the acyl chain around 2850 and 2920 cm⁻¹, respectively were apparent. These data are in accordance with the data reported in the literature (34).

The peaks of the symmetric and antisymmetric stretching vibrations of CH₃ have been used as a sensitive indicator of the ordering of the alkyl chains. A change in the wavenumber of the antisymmetric CH₂ stretching bands in the acyl chain appearing in Figure 5 was induced after the encapsulation of tamoxifen into positively charged DSPC liposomes, suggesting that tamoxifen creates a conformational disorder within the acyl chains of phospholipids. The peak at 2920.66 cm⁻¹ for the pure DSPC is shifted towards higher wavenumber 2922.66 cm⁻¹ for tamoxifen liposomes implanted with positive charge. This result indicates that the number of gauche conformers may be increased which implies an increase in the disorder of the bilayer and thereby destabilization of the system in the gel phase (Figure 5) [35]. The increase in the wavenumber represents an increase in the number of gauche conformers indicating that tamoxifen disorders the membrane.

The present findings were consistent with FTIR spectroscopy results obtained by Bilge et al., [32] which showed that the increasing concentrations of tamoxifen (TAM) (except one mol percent) increased the wavenumbers of CH₃ stretching modes, suggesting a disordering effect for DSPC MLVs in both the gel and liquid crystalline phases. Except for one mol percent, the bandwidth values of the CH₃ stretchings increased when TAM concentrations for DSPC liposomes
increased, indicating an increase in liposome dynamics.

To monitor the average trans/gauche isomerization in the systems, the wavenumbers of the CH$_2$ stretching bands of acyl chains depended on the degree of conformational disorder and, hence the wavenumber values could be used [36]. The CH$_2$ scissoring vibration modes which are located at 1464.67 cm$^{-1}$ is affected by the incorporation of tamoxifen into DSPC liposomal preparation. The wavenumber was shifted to higher values at 1468.53 cm$^{-1}$ after the encapsulation of tamoxifen into positively charged DSPC liposomes. This implied the presence of disordering effect in acyl
chain packing in the gel phases of phospholipids, in accordance with DSC studies. Upon the encapsulation of tamoxifen into neutrally charged DSPC liposomes, the wavenumber was shifted towards higher values at 1466.6 cm\(^{-1}\). This result assumes that the molecules of tamoxifen induce a slight disorder in the hydrocarbon as they may act as small spacers of the polar head group (Figure 6) These findings are in accordance with previous studies [31-33].

The interaction of tamoxifen with the glycerol backbone near the interfacial region, the C=O stretching band was analyzed. The wavenumber value of C=O group was shifted to higher degrees (from 1734.66 cm\(^{-1}\) to 1736.58 cm\(^{-1}\)) for the neutral liposomes sample containing tamoxifen, without any evidence of hydrogen bonding formation. The wavenumber value of C=O group exhibited a shift towards higher value (from 1734.66 cm\(^{-1}\) to 1737.55 cm\(^{-1}\)) for the positive liposomes sample containing tamoxifen, implying dehydration about these functional groups in the interfacial region of the lipid membranes. Therefore, any effects in the spectra of this region can be attributed to an interaction between tamoxifen and the interfacial region of the membrane (Figure 6) [31-32].

Table 2 shows the chemical shifts observed for tamoxifen after the incorporation into neutrally and positively charged DSPC liposomes.

Table 2

<table>
<thead>
<tr>
<th>Drug Concentration</th>
<th>Neutally Charged DSPC</th>
<th>Positively Charged DSPC</th>
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<tbody>
<tr>
<td>50 µg/ml</td>
<td>1247 cm(^{-1})</td>
<td>1248 cm(^{-1})</td>
</tr>
<tr>
<td>100 µg/ml</td>
<td>1246 cm(^{-1})</td>
<td>1246 cm(^{-1})</td>
</tr>
<tr>
<td>200 µg/ml</td>
<td>1245 cm(^{-1})</td>
<td>1245 cm(^{-1})</td>
</tr>
<tr>
<td>400 µg/ml</td>
<td>1244 cm(^{-1})</td>
<td>1244 cm(^{-1})</td>
</tr>
<tr>
<td>800 µg/ml</td>
<td>1243 cm(^{-1})</td>
<td>1243 cm(^{-1})</td>
</tr>
<tr>
<td>1000 µg/ml</td>
<td>1242 cm(^{-1})</td>
<td>1242 cm(^{-1})</td>
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The potential cytotoxic activity of tamoxifen has been investigated using cell viability (in vitro cytotoxicity SRB) assay at different drug concentrations of free tamoxifen or tamoxifen combined with neutrally or positively charged liposomes against breast carcinoma (MCF-7) cell lines [26]. At zero concentration of each drug untreated cells served as controls. The MCF-7 cancer cell lines were incubated separately with the same series of different drug concentrations 50, 100, 200, 400, 800 and 1000 µg/ml, for 48 h (Figure 7).

![Fig. 6. The magnified part (1800–1200 cm) of FTIR spectra of empty DSPC and DSPC/ Tamoxifen in different liposomal formulations.](image-url)
TABLE 2. The chemical shifts observed for tamoxifen after the incorporation into neutrally and positively charged DSPC liposomes.

<table>
<thead>
<tr>
<th>Peak assignment</th>
<th>Wavenumber (cm(^{-1}))</th>
<th>Wavenumber (cm(^{-1}))</th>
<th>Wavenumber (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Empty Liposomes</td>
<td>Tamoxifen neutral liposomes</td>
<td>Tamoxifen Positive liposomes</td>
</tr>
<tr>
<td>Antisymmetric stretching vibration of the CH(_2) in the acyl chain</td>
<td>(2920–3000)</td>
<td>2920.66</td>
<td>2920.66</td>
</tr>
<tr>
<td>CH(_2) scissoring vibration</td>
<td>(1456-1470)</td>
<td>1464.67</td>
<td>1466.6</td>
</tr>
<tr>
<td>Carbonyl stretching vibrations (C=O)</td>
<td>(1730–1740)</td>
<td>1734.66</td>
<td>1736.58</td>
</tr>
<tr>
<td>Anti-symmetric PO(_2) stretching vibration</td>
<td>(1220-1245)</td>
<td>1246.75</td>
<td>1238.08</td>
</tr>
</tbody>
</table>

At the lower concentration roughly at 200 µg /ml, MCF-7 treated cells with neutrally or positively charged liposomes loaded with tamoxifen showed cell viability of about 20% as compared to free tamoxifen of about 38 % (Figure 7). Higher cytotoxic efficacy was observed above 200 µg /ml against MCF-7 cell lines treated with tamoxifen-loaded liposomes when compared to free tamoxifen. At the highest tamoxifen-loaded liposomes concentration (1000 µg/ml), MCF-7 treated cells showed cell viability of approximately 10 %, at 48 hours of incubation. While for free tamoxifen treated cells, the cell viability was approximately 40 % at the same concentration (1000 µg/ml) (Figure 7). The increase in tamoxifen concentration (200 to 1000 µg /ml) in liposomes increased growth inhibition from 80% to 90%. In contrast, addition of tamoxifen at higher concentration range (2 to 10 µM) in liposomes increased the growth inhibition from 6.1 % to 33.2 % \(^{[3]}\). The decrease in cell viability that accompanied by the administration of tamoxifen-loaded liposomes as compared to the free tamoxifen could be attributed to the sustained release of the encapsulated tamoxifen from liposomes then diffused passively into the cells, or the liposomes might be directly internalized by endocytosis. Bhatia et al., \(^{[37]}\) aimed to explore the in vitro cytotoxicity of developed liposomal systems of tamoxifen employing the human breast cancer MCF-7 cell line. The findings showed that the viability of MCF-7 cells with encapsulated tamoxifen versus free drug was strongly inhibited by composition based. The encouraging findings from their work reveal immense potential in the treatment of breast cancer from lipid-based vesicular systems.

IC\(_{50}\) value for tamoxifen in the cytotoxic assay with MCF-7 treated cells was 0.34 µg/ml, while tamoxifen-loaded neutrally or positively charged liposomes showed an increase of IC\(_{50}\) value to 119.62 and 101.23 µg /ml, respectively. This increase in IC\(_{50}\) value can be attributed to tamoxifen’s lipo-solubilized state due to its imprisonment in multiple vesicle lipid domains (Figure 10). The latter was achieved in the presence of bilayered systems’ aqueous and nonaqueous phases, a condition best appropriate for better drug interaction with cells. In addition, phospholipid is considered to be a significant component of both the vesicular and cell membrane structures. It may help in generating and retaining the required physicochemical state of the drug for its improved biological interactions. This would lead to facilitate cell penetration of the encapsulated drug and to increase tamoxifen efficacy. Zeisig et al., \(^{[38]}\) demonstrated for the first time that tamoxifen-containing liposomes can be prepared that are sufficiently active to significantly reduce resistance to tamoxifen in several in vivo xenografts of human breast cancer.

**Conclusion**

The present study shows that a combination of tamoxifen with liposomes shows synergistic growth inhibitory activity on breast carcinoma...
Fig. 7. Cytotoxicity of free Tamoxifen, Tamoxifen bound neutrally or positively charged liposomes against breast carcinoma (MCF-7) cell lines; incubated for 48 h with different concentrations (50, 100, 200, 400, 800 and 1000 µg/ml). The cell viability was determined using the SRB assay. The data represent mean ± standard error of triplicate experiments.

Fig. 8. IC50 chart with significant values for free Tamoxifen and Tamoxifen bound neutrally or positively charged liposomes against breast carcinoma (MCF-7) cell lines by using SRB assay, 48 h post-treatment.

(MCF-7) cell lines via induction of cytotoxicity and may be a promising approach to treat breast cancer, although more studies are needed. The current data suggest a novel formulation of liposomal tamoxifen that is replaced by free tamoxifen to raise its anticancer activity against MCF-7 cancer cell lines. This would improve the therapeutic index of tamoxifen and is a proof of principle in support of administering liposomally co-encapsulated drug.

Conflict of interest: The author alone is responsible for the content and writing of this paper.

References


Cytotoxic Activity of Tamoxifen Bound Liposomes Against Breast Cancer...

Anacemeha lana an haifeen min nata ne kasar da ke cikin maya abinda da liko yaya kare naka da ke cikin maya abinda da liko yaya kare kamar tarnatarki shiyyar.

MCF-7

Ture garko wannan abinda da liko yaya kare kamar tarnatarki shiyyar, wannan abinda da liko yaya kare kamar tarnatarki shiyyar.

140

Tm

135

IC50

MCF-7