Antitumor efficacy of Curcumin against MCF-7 using Nanotechnology

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ABSTRACT
Breast cancer is the most frequently diagnosed cancer and the main cause of cancer death in females worldwide, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths. Nanotechnology provides a unique approach and comprehensive technology against cancer through early diagnosis, prediction, prevention especially in breast cancer. Curcumin is that type of photochemical, it is derived from the rhizome of curcuma longa (which is also named turmeric) and was first isolated in 1910. Curcumin has traditionally been used as food additive or in many remedies around the world for thousands of years. The main purpose of this study is to investigate the effect of Curcumin synthesized by nanotechnology on human breast cancer cell line (MCF-7) proliferation. Firstly Curcumin was synthesized using nanotechnology as the nanoparticles (NPs) are usually non-toxic, biocompatible, non-immunogenic and biodegradable. And they may not be recognized by the host's defense mechanisms. The cytotoxicity of Curcumin nanoparticles (Cur-NPs) was investigated on the human breast cancer (MCF-7) cell line using the 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazoliumbromide (MTT) assay which showed the reduction of cell viability by reducing MCF-7 cell count to 50% (IC50) (127µg/ml). So, Curcumin nanoparticles (Cur-NPs) could be promising agent in breast cancer treatment. Further studies with in vivo models, are needed to confirm the antitumor efficacy of Cu-NPs in inhibition or prevention of breast cancer growth.

Keywords: Cur-NPs, MCF-7, MTTAssay, Nanotechnology.

Introduction
Breast cancer is the most frequently diagnosed cancer and the main cause of cancer death in females worldwide, representing 23% (1.38 million) of the total new cancer cases and 14% (458,400) of total cancer death cases (Ferlay et al., 2010). In Egypt breast cancer accounts for 32% among women (Ibrahim et al., 2014). Currently, the lifetime risk of developing breast cancer for women is 1/8. However, more than 40% of the affected patients are currently > 65 of age and remarkably, this group accounts for almost 60% of the total deaths from breast cancer (DeSantis et al., 2011 & Siegel et al., 2014).

In Egypt, breast cancer is estimated to be the most common cancer among females accounting for 37.7% of their total with 12, 621 new cases in 2008. It is also the leading cause of cancer – related mortality accounting for 29.1% of their total with 6546 deaths. The incidence to mortality ratio is poor (1.9:1) (Zeeneldin, 2012). The conventional breast cancer therapies (surgery, chemotherapy and radiotherapy) have limitations as they are not usually successful incurring metastatic stages (Skandarajah and Bruce, 2013) or they may be not targeted sufficiently. Nanotechnology has recently invaded the field of breast cancer which may overcome the limitations of the conventional breast cancer therapies which attributed to the advantages of nanoparticles of having high surface area to volume ratio which allowing many functional groups to be attached to a nanoparticle, which also can seek out and bind to certain tumor cells (Seleci et al., 2016). Curcumin is that type of photochemical, it is derived from the rhizome of curcuma longa (which is also named turmeric) and was first isolated in 1910. Curcumin has traditionally been used as food additive or in many remedies around the world for thousands of years (Anand et al., 2008). The major components of curcumin are approximately 77% diferuloylmethane (curcumin I), 17% demethoxycurcumin (curcumin II) and 3%
bisdemethoxycurcumin (curcumin III). Several studies have shown that curcumin I is more active than curcumin II and III. (Liu and Hong, 2006; Sandur et al., 2007). Curcumin has been shown to possess anticancer, antioxidant, anti-inflammatory, ant proliferative, and antifungal activities, suggesting broad potential applications for the treatment of various malignancies, inflammatory diseases and fungal infections (Chandran and Goel, 2012; Gupta et al., 2012; Kunwar et al., 2012; Lee et al., 2013; Moghadamtousi et al., 2014). Previous studies that were conducted on Curcumin have shown that it has potential chemopreventive and therapeutic value against a wide variety of cancers, including breast, cervical, colon, gastric, hepatic, ovarian, pancreatic and prostate cancer cell lines (Lee et al., 2013; Moghadamyousi et al., 2014; Sandur et al., 2007).

In the current study, Curcumin nanoparticles (Cur-NPs) were synthesized by the mean of green nanotechnology a clean approach to minimize potential environmental and human health risks associated with the manufacture and use of nanotechnology products. So Cur-NPs were synthesized by lactic acid bacteria Lactobacillus strain according to method described by Philip, (2009). Then the size and zeta potential of the Cu-NPs were measured and their cytotoxicity was investigated in vitro against the human breast cancer cell line (MCF-7) using MTT assay.

Materials and Methods

I. Chemicals
Curcumin was purchased from Sigma – Aldrich Company, Saint Louis, Missouri, USA.

II. Cell line
Human breast cancer (MCF-7) cell line was obtained from VACSERA Tissue Culture Unite

III. Synthesis and characterization of Cur-NPs.
Lactobacillus strain will be inoculated into sterile MRS and 2gm of wet biomass will be collected in a 500- ml Erlenmeyer flask mixed with100 ml of 1m M of Curcumin (Cur) and incubated at 37°C under agitation (200 rpm) for 24h. Ultrasonic disruption of cells will be carried out with an ultrasonic processor (Sonics & Materials Inc, vibra cell T.M., USA). The sonicated samples will be centrifuged at 15,000 rpm for 30 minute 4°C to remove cell - debris. The resulting aqueous solution will be filtered through a 0.22 μm Millipore filter before use (Philip, 2009).

IV. Zeta potential and size distribution of the Cu-NPs, were characterized using the Malvern Zetasizer Nano ZS (United Kingdom).

V. Cu-NPs cytotoxicity on MCF-7 cell line
Cytotoxicity of Cu-NPs was investigated on the human breast cancer (MCF-7) cell line using the 3- (4,5-dimethylthiazol-2-yl) - 2,5- diphenyl tetrazolium bromide (MTT) assay (Wilson et al., 1990) which based on the mitochondrial dehydrogenase conversion of the MTT to a blue formazan product in the viable cells by an enzyme present in the mitochondria of viable cells. The colorimetric changes of blue formazan dissolved in dimethyl sulfoxide (DMSO) were measured spectrophotometrically at 590 nm using enzyme-linked immunosorbet assay (ELISA) plate reader DV990BV4 micro plate reader from Gio.deVita E C.S.r.l (Rome, Italy) and data were analyzed using 990 win 6 software.

Results
I - Dynamic light scattering (DLS) of the Cur-NPs were analyzed by DLSZ etasizer(ZS) for size determination and the results revealed that Cur-NPs size ranged from 85-120 nm as shown in the Figure 1.
II. Cytotoxicity of Cur–NPs against MCF-7

Cytotoxicity of Cu- NPs against MCF-7 using MMT assay showed the reduction of cell viability relative to control and the concentration of Cur-NPs which reduced MCF-7 cell count to 50% (IC50) was (127µg/ml) and shown in table (1).

Table 1: Antitumor efficacy of Cur- NPs against human breast cancer cell line (MCF-7).

<table>
<thead>
<tr>
<th>Cur-NPs conc. (µg/ml)</th>
<th>Viability % S.D.</th>
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<tbody>
<tr>
<td>500</td>
<td>23.491.53</td>
</tr>
<tr>
<td>250</td>
<td>35.280.94</td>
</tr>
<tr>
<td>125</td>
<td>49.031.71</td>
</tr>
<tr>
<td>62.5</td>
<td>70.461.92</td>
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<tr>
<td>31.25</td>
<td>87.520.75</td>
</tr>
<tr>
<td>15.6</td>
<td>95.340.21</td>
</tr>
<tr>
<td>7.8</td>
<td>99.170.09</td>
</tr>
<tr>
<td>3.9</td>
<td>1000</td>
</tr>
<tr>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

Discussion

Breast cancer is the field of medicine with the greatest presence of nanotechnological therapeutic agents as it offers potential solutions to the historical challenge that has rendered breast cancer (Tanaka et al., 2009) as overcoming of the limitations of the conventional breast cancer therapies (surgery, chemotherapy and radiotherapy). Surgery is effective only in the area of the primary tumor (Custodio et al., 2013), Chemotherapy kills both of normal and malignant cells as chemotherapeutic agents enter the blood stream and distribute throughout the body attacking many types of proliferating cells not only cancer cells (Aparo and Geol, 2012). So the medical applications of nanoparticles are growing, as they have the potential to offer novel methods of non-invasive cancer detection, diagnosis, and treatment. Tumor targeting ligands, such as antibodies, peptides, or small molecules, can be attached to nanoparticles for targeting of tumor antigens and vasculatures with high affinity and specificity. In addition, diagnostic agents (i.e. optical, radiolabels, or magnetic) and chemotherapeutic drugs can be integrated into their design for more efficient imaging and treatment of the tumor with fewer side effects (Deshpande, 2016).

Nanoparticles (NPs) can be synthesized by chemical and physical approaches that are often expensive, labor-intensive and potentially hazardous to the environment and living organisms (Makarov et al., 2014) and since NPs revolutionize a series of medical tools and procedures, they became be synthesized biologically via Eco-friendly, cost-effective methods using microorganisms, enzymes, fungus and plants or plant extracts (Hasan, 2015) in a technology called green synthesis or biosynthesis.

All efforts in the world tend to use natural products for either protection (prevention) or treatment of several diseases. One of bioactive compound called Curcumin (Cur) (diferuloylmethane) signaling pathway was further found as the potential molecular mechanism of Curcumin to regulate cell cycle arrest in vitro.
Conclusion

Curcumin nanoparticles (Cur-NPs) could be promising agent in breast cancer treatment. Further studies within vivo models, are needed to confirm the antitumor efficacy of Cur-NPs in inhibition or prevention of breast cancer growth.

References


