



## Chemotherapeutic activity of silybin liposomes combined with Doxil in TUBO breast cancer cell bearing mice

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### Abstract

According to different studies, high intake of natural products is associated with reduced cancer risk. It is suggested that the specific concentrations of phytochemicals may have cancer chemo-preventive effects without causing significant levels of toxicity. Nowadays, there is an increasing emphasis on combination chemotherapy using cytotoxic and natural chemotherapeutic agents. The successes of combination chemotherapy suggested that all cancers could be treated by providing the correct combination of drugs at the correct doses and correct intervals of administration. Silybin is the active ingredient of *Silybum marianum* that has been used in traditional medicine because of its liver protective effects in different countries. It can also modulate imbalance between cell survival and apoptosis through interference with expressions of cell cycle regulators and proteins involved in apoptosis. In present study, nano-liposomal formulations containing silybin have been prepared and their anti-tumor activities alone and in combination with doxil were assessed in a mouse TUBO breast tumor model. After injection of liposomes, tumor size and survival were monitored on 3 occasions a week for 100 days. The results of *in vivo* studies showed that anti-tumor efficacy of silybin liposome formulations alone in treated mice were not significantly more than control animals on day 27. In the other two groups, the efficacy of doxil and doxil-silybin ( $p < 0.001$ ) liposomes were significantly more than control animals. Also according to our data, even 100 days after inoculation, 83% animal survival was observed in doxil-silybin liposome were used simultaneously but in case of doxil alone, the survival percentage reached to almost 40% and for silybin liposomes alone reached to 20%. Therefore there is a significant difference between survival percent in control group with doxil alone ( $p < 0.001$ ) and doxil-silybin liposomes combination ( $p < 0.001$ ). The survival percent of the control group reached to zero, on around 40 days after tumor inoculation. In conclusion, these results indicated that

combination therapy using Doxil and silybin can induce improvement in chemotherapy of treated mice.

Cancer is that the second reason for death worldwide. it's expected that its incidence is growing worldwide because of the aging of the population. Despite intensive analysis aimed toward discovering metastatic tumor agents and completely different enhancements created in therapy regimens, cancer treatment these days is inadequate: it's not terribly effective and in the midst of many facet effects. Indeed, most therapy agents effectively target quick dividing cells and there's no distinction in their practicality between cancerous cells and also the quick growing traditional cells. Therefore, traditional cells are broken and a large sort of facet effects, like instinctive reflex, nausea, cardiotoxicity, hepatotoxicity, nephrotoxicity, ototoxicity, immunological disorder, myelosuppression, hemorrhage, anemia, deficiency disease, and non-specific neurocognitive issues ar ascertained. One prototypical example of cytotoxic medicine is antibiotic drug (DXL). it's Associate in Nursing growth anthracycline antibiotic unremarkably wont to treat a spread of cancers. Despite the introduction of antibiotic drug against malignant tumors, its use in clinical therapy is proscribed because of progressive and clinically important cardiotoxic effects. The on top of mentioned unhealthful manifestations clearly recommend that there's Associate in Nursing pressing want for nontoxic and clinically effective treatments of cancer that eliminate issues related to standard chemotherapies. One of the most reasons for failure in cancer treatment is high toxicity, development of resistance, and low response rates of therapy in solid tumors. it's clear that the dose of a medicament could be a vital consider each its effectiveness and toxicity. within the low doses, it'll not be effective against tumors, however with increasing the dose, the toxicity signs ar outstanding. In recent years, with the aim of developing a lot of efficacious ways whereas reducing general

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toxicity, efforts are directed toward combination medical care. present agents with completely different mechanisms of action and non-overlapping toxicities, are urged as a promising candidates in synergistic combination medical care of cancer. Several experimental studies urged victimisation combination of low unhealthful natural compounds like polyphenols, to scale back the desired dose of cytotoxic agents within the treatment of cancer. Silymarin (SLM) is a lively extract from the seeds of the plant milk weed (Silybum Marianum). The plant milk weed has been utilized by human race for a protracted time as a food in some components of the globe. SLM extract and its main part, silybin, are acknowledged for their inhibitor, hepatoprotective and chemoprotective effects. Recently, increasing evidences highlighted important anti-neoplastic activity of those agents in an exceedingly sort of in vitro and in vivo cancer models, together with skin, breast, lung, colon, bladder, and prostate.

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