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Experimental treatment of breast cancer-bearing BALB/c mice by artemisinin and transferrin-loaded magnetic nanoliposomes

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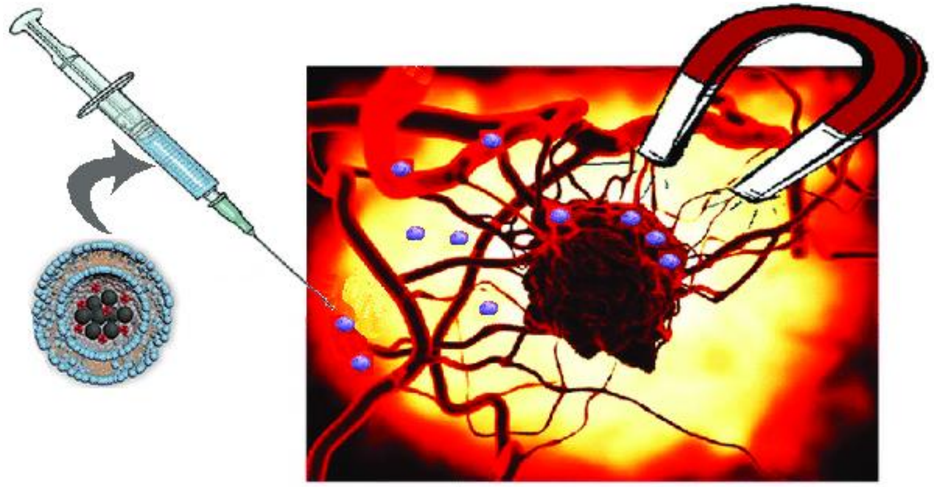

PURPOSE

The combination of artemisinin and transferrin exhibits versatile anticancer activities. In previous, we successfully prepared artemisinin and transferrin-loaded magnetic nanoliposomes and evaluated their anti-proliferative activity against MCF-7 and MDA-MB-231 cell lines *in vitro*.[1] In this study, we investigate the *in vivo* anti-breast cancer activity of artemisinin and transferrin-loaded magnetic nanoliposome against breast transplanted tumors in BALB/c mice model.

METHODS

The artemisinin and transferrin-loaded magnetic nanoliposomes were prepared by our previous described method. [1]

The contents of the artemisinin, transferrin and magnetic iron oxide in the nanoliposomes were evaluated using high performance liquid chromatography (Perkin Elmer, USA) and spectrophotometer (Shimadzu, Japan), respectively. Then, the loading efficiency of artemisinin, transferrin, and magnetic iron oxide was calculated.

The magnetic properties and morphology of prepared nanoliposomes were analyzed by vibrating sample magnetometer (Meghnatis Daghigh Kavir Co., Iran) and cryo-transmission electron microscopy (cryo-TEM), respectively.

Breast cancer bearing mice were divided into 6 groups and treated daily with different administration modalities as follows: Group 1, intravenous (i.v.) administration of control nanoliposomes (without artemisinin and transferrin) under an external magnetic force; group 2, i.v. administration of free artemisinin, transferrin and magnetic iron oxide without a magnetic force; group 3, i.v. administration of free artemisinin, transferrin and magnetic iron oxide under an external magnetic force; group 4, i.v. administration of artemisinin and transferrin-loaded magnetic nanoliposomes without a magnetic force; group 5, i.v. administration of artemisinin and transferrin-loaded magnetic nanoliposomes under an external magnetic force; the control group, i.v. administration of 1 mL PBS solution. In groups 1, 3 and 5 as an external magnetic force, a piece of magnet (1 by 1 by 0.3 cm) was placed at the breast tumor site. In groups 1-5, the dose of artemisinin, transferrin, and magnetic iron oxide were fixed at 100, 102.4 and 79.44 µg/1 mL PBS, respectively. All preparations were administered via the tail vein as a short infusion. These mice were used for subsequent experiments.

1- Gharib A, Faezizadeh Z, Mesbah-Namin SA, Saravani R (2014). **Preparation, characterization and *in vitro* efficacy of magnetic nanoliposomes containing the artemisinin and transferrin**. DARU J Pharm Sci 22 (1), 44

RESULTS

Physicochemical properties of nanoliposomes

The entrapment rate of artemisinin, transferrin and magnetic iron oxide in the nanoliposomes was 83.06% ± 0.53%, 80.12% ± 0.12% and 66.14% ± 0.42%, respectively. The average size, zeta-potential and polydispersity index of nanoliposomes were 95.06 ± 0.15 nm, −1.40 ± 0.22 mv and 0.19 ± 0.09, respectively. In this study, the results from nanoliposomes size distribution showed a monomodal pattern. The magnetic properties of the nanoliposomes were analyzed by vibrating sample magnetometer at room temperature. The saturation magnetizations for nanoliposomes were 30.5 electromagnetic units per gram (emu/g) and the cryo-TEM analysis showed that the nanoliposomes have a fine spherical shape and rough surface (Fig. 1).

Tumor distribution of artemisinin and transferrin, and magnetic iron oxide

The plasma stability of artemisinin, transferrin, and magnetic iron oxide in the loaded form without an external magnetic force was significantly higher than those of free form. When compared to the free artemisinin and transferrin, the i.v administration of artemisinin and transferrin-loaded magnetic nanoliposomes followed using the magnetic field approximately produced 10- fold higher levels of artemisinin and transferrin in the tumors (Fig. 2).

Suppressive effects on primary tumor growth

All combined artemisinin and transferrin preparations could significantly suppress primary tumor growth compared to the control group. At 15 days after treatment, the artemisinin and transferrin-loaded magnetic nanoliposomes combined with an external magnetic force not only completely suppressed the growth of primary tumor but also reduced the tumor volume in tumorized mice (Fig. 3). In the presence of an external magnetic force, a significant difference was observed between antitumor effects of magnetic artemisinin and transferrin nanoliposomes and other examined groups ($p < 0.01$).

Histologic examination

Fifteen days after treatment, the central region of the tumor mass treated with artemisinin and transferrin-loaded magnetic nanoliposomes under the magnetic force was found with many apoptotic cells and some viable tumor cells (Fig. 4).

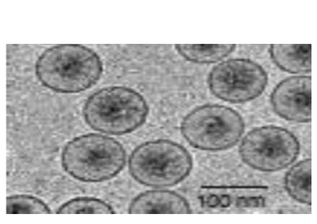

Fig. 1

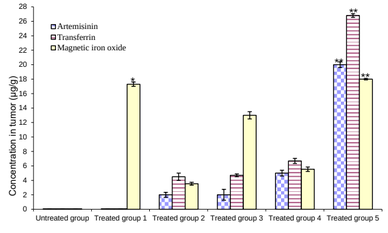

Fig. 2

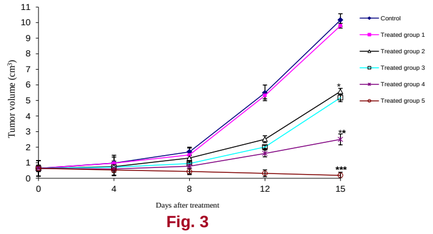

Fig. 3

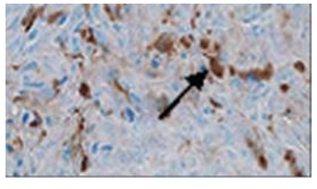

Fig. 4

CONCLUSION

In the presence of a magnetic force, we successfully investigate the *in vivo* anti-breast cancer activity of artemisinin and transferrin-loaded magnetic nanoliposomes. Altogether, in the presence of an external magnetic field, the systemic chemotherapy with magnetic nanoliposomes containing artemisinin and transferrin could effectively reduce the breast tumor mass in the treated mice.

ACKNOWLEDGEMENT

The author gratefully acknowledges financial support from the Iran National Science Foundation (INSF) under grant agreement no: 91001200.