

## Evaluation of the antitumor effect of trehalose in experimental models

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**Background:** Cancer continues to represent the main cause of mortality in the world, the second leading cause of death worldwide next to cardiovascular disease. Therefore, it is important to find effective non-toxic, inexpensive, and suitable neoadjuvant therapy with methotrexate (MTX) to decrease its dosage without lowering its chemotherapeutic efficacy. **Aim:** This study aimed to investigate the antitumor effect of trehalose (TRE) on mice bearing Ehrlich ascites carcinoma (EAC) and to test whether it can enhance the anticancer potential of MTX. **Materials and Methods:** In this experiment, mice were assigned into 8 groups were used for assessment of antitumor activity of TRE. The antitumor activity of TRE was assessed by measuring the survival time, counting tumor cells, monitoring autophagic activity at the cellular level by flow cytometry, monitoring autophagic and apoptotic regulated genes (Caspase 3, Bec1, and Bcl2 genes) by real-time PCR, as well as the biochemical parameters, oxidative stress markers in liver homogenate, complete blood picture (CBC) and histological studies of all groups. **Results:** Treatment of EAC mice with TRE or MTX alone or in combination resulted in a significant decrease in total, viable, and non-viable tumor cells count as well as the tumor volume in comparison with EAC mice. Treatment with TRE alone or in combination MTX induced a significant increase in the hepatic antioxidant status, a significant upregulation in the gene expression of caspase 3, with the highest expression in the combined group, as compared to the non-treated EAC group. On the other hand, the same treatments resulted in a significant downregulation of Bcl2 and Bec1 genes, with the lowest expression in the combined group. These results showed a significant decrease in autophagic activities in both TRE- and TRE+MTX -treated groups as compared to the non-treated EAC group. Histopathological examination revealed normal lobular architecture with central vein and radiating hepatic cell cords in normal control mice. **Conclusion:** TRE is considered as an autophagic inhibitor for cancer cells which could be used as a potential neoadjuvant for the antitumor drug, MTX, and probably other chemotherapeutic compounds. This new role of TRE coupled with its apoptotic induction property on tumor cells and lack of toxicity on normal cells increases the efficacy of an antitumor drug for treating a spectrum of cancers. (This Ph.D. thesis was approved by the Faculty of Science, Tanta University, Egypt by March 31, 2018).

**Keywords:** Apoptosis; Autophagy; Ehrlich ascites carcinoma; Methotrexate; Trehalose

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