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Fish oil as chemosensitizer: Targeting onset of drug resistance in colon cancer cells

Isha Rani, Bhoomika Sharma, Satinder Kaur, Sandeep Mahiwal and Navneet Agnihotri
Panjab University, India

Antineoplastic resistance continues to be a major impediment in medical oncology. The current strategies have been mainly focused on use of chemosensitizers to combat cancer resistance. Our previous studies demonstrated that fish oil (FO) rich in n-3 PUFAs act as a potential chemosensitizer against colon cancer cells. The mechanistic hypothesis may be effective strategy of fish oil as chemosensitizer in abrogating/delaying onset of drug resistance. Therefore, the present study is designed to understand the role of fish oil as an adjuvant to circumvent the mechanisms of drug resistance in experimental colon carcinoma. The colon cancer was induced by 1,2- dimethylhydrazine (DMH)/dextran sulfate sodium (DSS) and further animals were treated with 5-FU, FO and 5-FU+FO regimens. The principle mechanisms which promote/enable drug resistance were delineated by analyzing variations in the expression of drug transporters and membrane characteristics, drug and its metabolites distribution at target sites and cancer stem cells expression using various methods. We observed that nutritional intervention of fish oil along with 5-FU decreased the expression of drug efflux transporters (ABCB1, ABCC5) and increased the cellular uptake of drug and its metabolites at target site. In addition, synergism of 5-FU and FO decreased the expression of cancer stem cells which are generally spared by chemotherapeutic treatment due to drug resistance. The combinatorial regimens also overcome drug resistance by modulating biophysical properties of membrane and altering membrane composition. The use of fish oil as chemosensitizer with an acceptable safety profile may be an appropriate strategy to improve clinical potential in cancer resistant therapy.

singlaisha8@gmail.com

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