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Uptake, delivery and anticancer activity of thymoquinone nanoparticles in breast cancer cells

Hala Gali-Muhtasib[1], **Isabelle Fakhoury**[1], **Walid Saad**[1], **Kamal Bou Hadir**[1], **Peter Nygren**[2] and **Regine Schneider-Stock**[3]
[1]American University of Beirut, Lebanon
[2]Uppsala University, Sweden
[3]University Erlangen-Nuremberg, Germany

Thymoquinone (TQ) is a promising anticancer molecule but its development is hindered by its limited bioavailability. Drug nanoparticle formulation is commonly used to overcome low drug solubility, limited bioavailability and nonspecific targeting. This project aimed at synthesizing different TQ nanoparticles (TQ-NP), characterizing them and assessing their uptake and delivery mechanisms as well as their anticancer potential in a panel of breast cancer cells. TQ-NP was prepared by flash nanoprecipitation. Dynamic light scattering and scanning electron microscopy were used for the characterization of the size, morphology and stability of the NPs. The anticancer activity was assessed by MTT. The uptake and subcellular intake mechanism of fluorescent TQ-NP were evaluated by both fluorometry and confocal microscopy. Four different TQ-NPs were formulated. The average diameter size ranged between 45-130 nm. All TQ-NPs were stable and had high entrapment efficiency (75-80%) and loading content (36-50%). *In vitro*, TQ-NP had equal or enhanced anticancer activity effects compared to TQ, in MCF-7 and aggressive MDA-MB-231 breast cancer cell lines. No significant cytotoxicity of the blank NP was noted. The uptake of fluorescent TQ-NP occurred in a time and concentration dependent manner. Treatment with inhibitors of endocytosis revealed the involvement of caveolin mediated endocytic pathway in TQ-NP uptake. This was also confirmed by subcellular localization findings, showing the colocalization of TQ-NP with both caveolin and transferrin as well as with the early and late markers of endocytosis, EEA-1 and lamp-1 proteins. Altogether, the results describe an approach for the enhancement of TQ anticancer activity and uncover the mechanisms behind cell-TQ-NP interaction, uptake and biodistribution.

Biography

Hala Gali-Muhtasib is currently a Professor of Cell Biology at the American University of Beirut. She has received her PhD from Kansas State University, USA. Her research interests are in studying the role of natural products in cancer prevention and therapy. Her research focuses on cancer chemoprevention and chemotherapy; in particular, study of plant derived compounds. She has explored novel drugs that inhibit the mechanisms involved in colon cancer such as naturally occurring plant tannins, vitamin E and essential oils of the Lebanese sage plant, thymoquinone extract from black seed and extracts from Lebanese indigenous plants, all of which are ingested regularly by humans and thus may hold promise as anticancer agents. Her efforts have been directed towards understanding the cellular and molecular mechanisms of action of various anticancer agents using cellular biology techniques as well as an emerging array of molecular technologies. She has numerous publications on mechanisms of action of anticancer drugs. She is the recipient of three research achievement awards, Suad Al-Sabbah, Abdul Hameed Shoman Prize for Young Arab Researchers and ISESCO Science Prize for contributions in Biology.

amro@aub.edu.lb

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