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Cisplatin and Metformin nano-cubosomes demonstrate higher cytotoxicity in CRC than individual drugs

Mona M Saber, Abdulaziz M Al-mahallawi, Noha N Nassar and **Samia A Shouman**
Cairo University, Egypt

Colorectal cancer (CRC) remains a leading cause of death worldwide. The use of cisplatin as an anti-cancer drug in CRC is correlated with severe adverse effects and drug resistance. Utilizing combination of anticancer agents can effectively kill cancer through multiple pathways; nonetheless, improvements in their delivery are needed. Nano-cubosomes, thanks to the advantages of their liquid crystalline porous nano-architecture and capability for multi-drug encapsulation, appear to be of interest as nanocarriers for anti-cancer therapies. Hence, delivering cisplatin, as nano-cubosomes, concomitantly with other chemo-dugs can lead to a rationally designed therapy for chemo-resistant cancers and might overcome problems associated with conventional cisplatin treatment. Therefore, we constructed nano-cubosomes bearing either cisplatin alone or cisplatin-metformin combination that are able to enhance drug transport to HCT-116 CRC cells. Results from this study revealed that nano-cubosomal formulations exhibited superior cytotoxic effect compared to unformulated cisplatin. This cytotoxic effect was profound upon incorporation of metformin, an mTOR inhibitor, in cisplatin nano-cubosomes. The induced CRC cell apoptosis was through inhibition of several metabolic pathways, namely, AMPK/mTOR and Akt/mTOR. Drug-loaded nano-cubosomes ensued depletion in glucose and energy levels that led to AMPK activation and thus mTOR inhibition. mTOR was additionally inhibited via suppression of p-Akt levels after nano-cubosomal treatment. Moreover, drug-loaded nano-cubosomes produced a notable escalation in ROS levels, evident as an increase in NADPH oxidase, inhibition of LDH and a consequential upsurge in caspase-3. These results demonstrated the influence exerted by cisplatin-loaded nano-cubosomes on CRC cell survival and enhancement of their cytotoxicity upon metformin addition.

Biography

Mona M Saber has completed her PhD from Cairo University in 2018. Currently, she is a lecturer at the Pharmacology and Toxicology department, of a premier research organization. She has published 2 articles related to colorectal cancer in the BMC Cancer journal. She spent 6 months in the institute of molecular medicine in Heinrich Heine University, Dusseldorf, Germany. This was a German Egyptian Research Short term scholarship funded by the DAAD (Deutscher Akademischer Austauchdienst). She has attended several international and national conferences including but not limited to; European cancer congress (ESMO 2015), 12th and 13th congress of EACPT, 2016 and 2017 conference of BGICC.

mona.magdy@pharma.cu.edu.eg

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