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The Toxicity of Doxorubicin Connected with Nanotransporters

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Abstract : Doxorubicin is one of the most commonly used and the most effective chemotherapeutic drugs. This antracycline drug isolated from the bacteria Streptomyces peuceticus var. caesius is sold under the trade name Adriamycin (hydroxydaunomycin, hydroxydaunorubicin). Doxorubicin is used in single therapy to treat hematological malignancies (blood cancers, leukaemia, lymphoma), many types of carcinoma (solid tumors) and soft tissue sarcomas. It has many serious side effects like nausea and vomiting, hair lost, myelosupression, oral mucositis, skin reactions and redness, but the most serious one is the cardiotoxicity. Because of the risk of heart attack and congestive heart failure, the total dose administered to patients has to be accurately monitored. With the aim to lower the side effects and to targeted delivery of doxorubicin into the tumor tissue, the different nanoparticles are studied. The drug can be bound on a surface of nanoparticle, encapsulated in the inner cavity, or incorporated into the structure of nanoparticle. Among others, carbon nanoparticles (graphene, carbon nanotubes, fullerenes) are highly studied. Besides the number of inorganic nanoparticles, a great potential exhibit also organic ones mainly lipid-based and polymeric nanoparticle. The aim of this work was to perform a toxicity study of free doxorubicin compared to doxorubicin conjugated with various nanotransporters. The effect of liposomes, fullerenes, graphene, and carbon nanotubes on the toxicity was analyzed. As a first step, the binding efficacy of between doxorubicin and the nanotransporter was determined. The highest efficacy was detected in case of liposomes (85% of applied drug was encapsulated) followed by graphene, carbon nanotubes and fullerenes. For the toxicological studies, the chicken embryos incubated under controlled conditions (37.5 °C, 45% rH, rotation every 2 hours) were used. In 7th developmental day of chicken embryos doxorubicin or doxorubicin-nanotransporter complex was applied on the chorioallantoic membrane of the eggs and the viability was analyzed every day till the 17th developmental day. Then the embryos were extracted from the shell and the distribution of doxorubicin in the body was analyzed by measurement of organs extracts using laser induce fluorescence detection. The chicken embryo mortality caused by free doxorubicin (30%) was significantly lowered by using the conjugation with nanomaterials. The highest accumulation of doxorubicin and doxorubicin nanotransporter complexes was observed in the liver tissue

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