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Abstract

Introduction: The chick embryo chorioallantoic membrane (CAM) is an extraembryonic membrane that is commonly used as an in vivo model. Ferromagnetic nanoparticles (FMN) represent an attractive option when it comes to targeted antitumor therapy. The aim of our study was to establish whether CAM is suitable as a model for testing biological properties, such as the biocompatibility and the bioavailability of the FMN.

Material & methods: Ten Eggs of White Leghorn chicken were incubated at 37.8°C for 13 days, in order to proceed to one or two daily intravascular injection of 0.2 ml of FMN for two consecutive days. Three embryos have been harvested on the second day after injection. Seven eggs were left incubated until the hatching stage. The harvested embryos have been sent for further histopathological studies H&E and Perls stainings.

Results: Injected embryos underwent a normal evolution and as a result a proper hatching. Histological studies have shown FMN deposits in the liver, as well as free nanoparticles in the blood stream.

Conclusions: The uninfluenced development of the injected embryos can be considered as a proof of biocompatibility and an open door for further studies. FMN deposits in viscerae can also be considered as a feasible biocompatibility.

Key Words

Biocompatibility; Bioavailability; Ferromagnetic nanoparticles; Embryo; CAM

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Introduction

The chick embryo chorioallantoic membrane (CAM) have been used as a model for studying development, biomaterial's properties, angiogenesis, photodynamic therapy, human tumor cell invasion and metastasis, microsurgical interventions[1-2]. Chick embryo CAM is an extraembryonic membrane that is commonly used as an in vivo model[3]. It offers an optimal access to a capillary rich vascular system (**Figure 1**), together with easy manageability, fast development and inexpensive costs. Ferromagnetic nanoparticles (**Figure 2**) are less than 1 micrometer particles and contains magnetic elements which allow us to manipulate them using magnetic field[4]. Thus, they represent an attractive option when it comes to targeted antitumor therapy[5].The aim of our study was to find out whether the CAM is suitable as a model for testing biological properties, such as the biocompatibility and the bioavailability of the

Figure 1: CAM

Figure 2: Ferromagnetic nanoparticles

ferromagnetic nanoparticles (FMN).

Material and Methods

Chick chorioallantoic membrane model

A number of ten White Leghorn chicken fertilized eggs were incubated in optimal conditions for hatching (37.8°C and 70% relative humidity) for 13 days, in order to proceed to one or two daily intravascular injection of 0.2 mL of FMN for two consecutive days (**Figure 3**). The eggs were daily examined and registered by a Carl Zeiss stereomicroscope equipped with a DCM 510

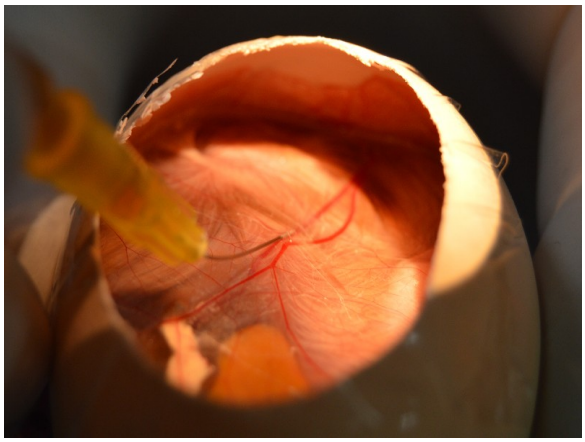

Figure 3

camera system. Three embryos have been harvested on the second day after injection. Seven eggs were left incubated until the hatching stage, additionally to analyse any potential morphological abnormalities that could appear during the embryos development. Blood samples, as well liver tissue samples of the harvested embryos where formaldehyde (4%) fixed and paraffin - embedded for further histopathological studies using hematoxylin-eosin and Perls stainings.

Results

In vivo observation

Injected embryos underwent a normal evolution and as a result a proper hatching, without showing any morphological abnormalities.

Histological analysis

Histological studies have shown free nanoparticles deposits in the liver (**Figure 4**) and Kupffer & Hepatocytes cells (**Figure 5**), as well as free nanoparticles in the blood stream (**Figure 6**). Nanoparticle deposits from the liver were dose-dependent.

Discussion and Conclusions

In this study we have shown that chick embryo chorioallantoic membrane is suitable as a model for testing biocompatibility and bioavailability of ferromagnetic nanoparticles, due to unaffected

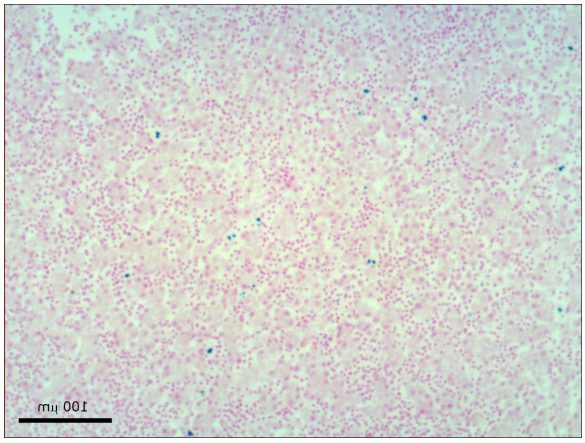

Figure 4: Nanoparticles deposits. Liver

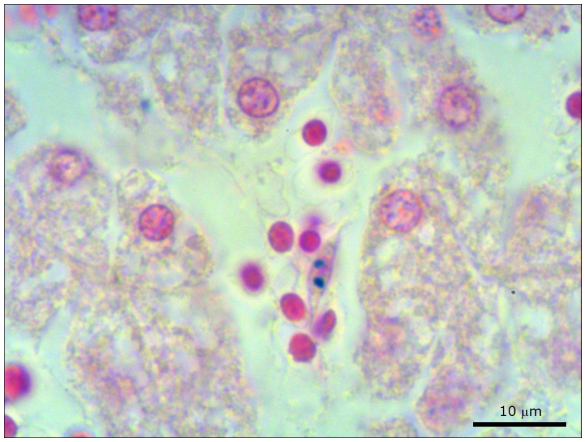

Figure 5: Kupffer and Hepatocytes cells

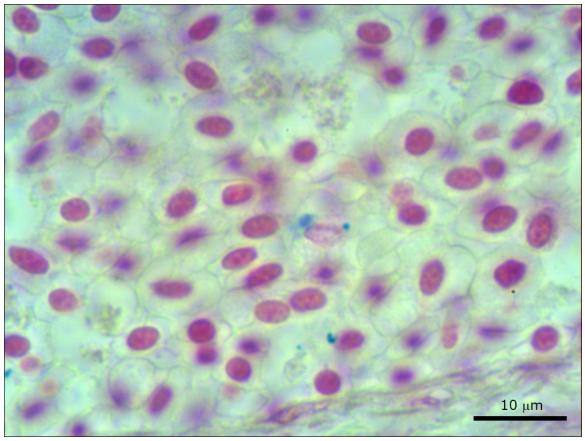

Figure 6: Blood stream - Monocytes

development of the embryos and large distribution throughout the fluids and tissues of the body. Nanoparticle interactions with biological systems still remains relatively unknown, although their ability of cell membrane penetration has been proven [6]. Such feature as high surface to volume ratio makes them very catalytic, which seems to be a strong argument against their biosafety[7]. However, in our study chick embryos injected with FMN hatched and survived without any morphological abnormalities.

In conclusion, the uninfluenced development and hatching of the embryos injected with FMN can be considered as a proof of biocompatibility and an open door for further studies. Nanoparticle deposits in viscerae can also be considered as a feasible biocompatibility. Nevertheless, caution should be exerted when extrapolating these results to another animal model or human system. As a limitation of our study are the unknown long-term effects on development of the chick.

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