Biosafety of graphene oxide in an in-vivo murine model

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INTRODUCTION Graphene is a highly conductive and adhesive biomaterial that can be modified due to its physicochemical properties. The salient features of graphene can be seen through reports of antibacterial [1] and anticancer activities [2], making it a promising candidate for several biomedical applications, including tissue engineering scaffolds [3]. However, contradictions in literature due to potential toxicity from residual impurities and inconsistent therapeutic dosage reports make it a challenge to translate its application into humans, hence, we investigate here the biocompatibility of graphene oxide (GO).

METHODS This study compared commercial graphene oxide (GO-CBG) and graphene oxide synthesized in the lab (GO-P1_2) in an *in vivo* rat model for histopathological examinations. This work was approved by the Novosibirsk Institute of Cytology and Genetics bioethical committee (№63, 09.10.2020). Briefly, adult male rats (n=70) were injected (IV) with sterile water (control group; n= 10), graphite(n= 20), GO-CBG(n=20), or GO-P1_2(n=20) at a dose range of 0.5mg/kg to 75mg/kg for 2 weeks. The organs(heart, kidney, liver, spleen and lungs) were retrieved for morphological analysis, along with brain tissue to determine blood-brain barrier (BBB) penetration.

RESULTS No mortality or signs of overdosing were observed in any group. Comparative analysis of mice that received 50mg/kg and 75mg/kg of GO revealed no significant changes in any organ tissues except in lung tissue. Slight changes in the morphology in the GO P1_2 group and large conglomerates in the GO CGB group were observed (Figure 1). The quantity of GO varied across the tissues: GO P1_2 group showed larger quantities of GO compared to GO CBG group, except in the heart where no difference was seen. GO P1_2 was concentrated in the liver (cytoplasm of Kupffer cells), spleen and lungs (walls of alveolar sacs), while the heart and kidney tissues had minimal traces of either substance. No traces were seen in the brain tissue suggesting no penetration of BBB.

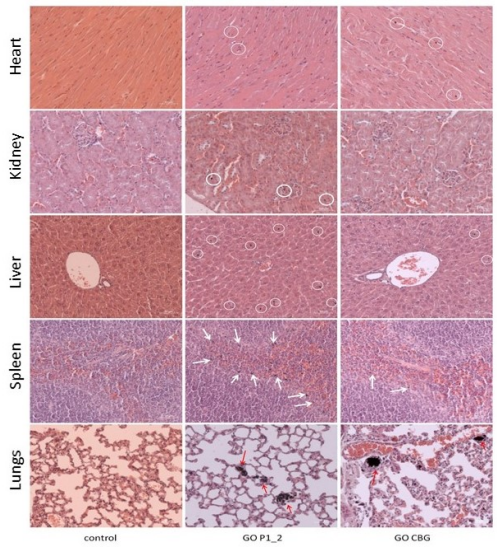

Figure 1 Tissues of a mouse that received an intravenous injection of GO at the highest dosage of 75mg/kg. White circles, white arrows and red arrows show GO particles. Image is obtained at x20 magnification.

DISCUSSION & CONCLUSION The study did not show any apparent difference in this dosage range. Accumulation of GO in most organs coincides with the localization of macrophages which can be helpful in future application. The changes in the morphology of lung tissue can neither be pathological or normal, but large conglomerates in the pulmonary vessel may lead to thrombosis and impair lung function. Additional research on acute toxicity study in higher doses is required.

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