Can nanographene cross placental barrier?

Graphene is an upcoming revolutionized 2D material that has sketched its importance across a wide spectra of interdisciplinary arenas due to its distinguishing properties. Being a sp2 hybridized allotrope of carbon with a honeycomb lattice structure; it possess superior electrical/ thermal conductivity, mechanical strength and exceptional optical properties. Graphene is therefore going to revolutionise the whole scientific era in the very recent times especially in material science, electronics and biomedical technology due to these stringent characteristics. As a result of this there is high chance of accidental as well as intentional exposure of graphene and its derivatives evoking toxic responses in the biological system. Due to very limited data availability about the toxicity and related aspects of graphene derivatives, necessity of intact studies has become a raising concern. Herein reported an effective green strategy for the synthesis of pluronic-P123 stabilised reduced graphene oxide (rGO-P), which was followed by a rarely explored area of toxicological research of feto-placental transmission and developmental toxicity.

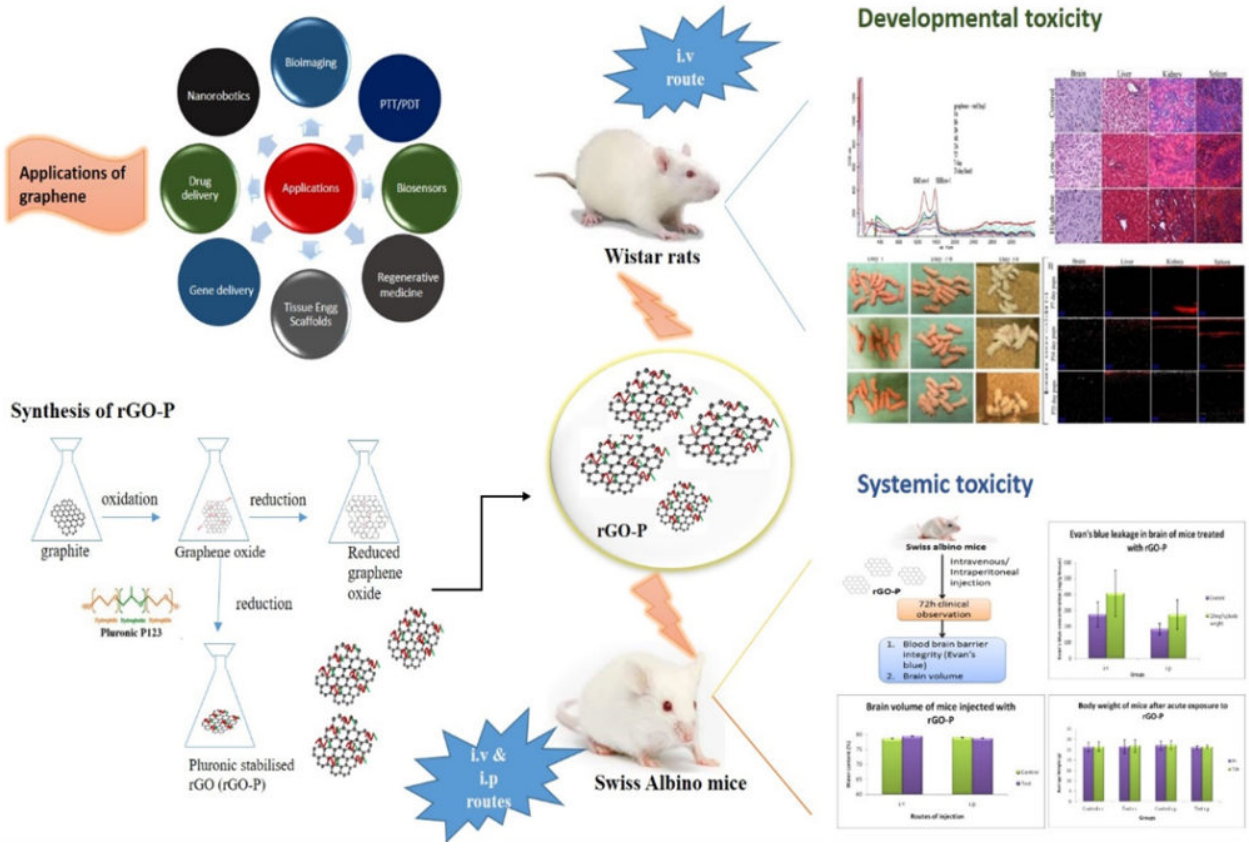

Fig. 1. Complications of graphene oxide in biological system.

To date, to the best of available literatures, very limited reports have been available regarding the

placental translocation efficacy and developmental intriguing potential of graphene derivatives in living system. Therefore, the present study has aimed at synthesis of pluronic stabilised reduced graphene oxide and its feto-placental transmission mediated developmental toxicity involving biodistribution, blood/renal clearance and histopathological examination of vital tissues.Natural graphite was oxidized using dimanganeseheptoxide and exfoliated to obtain hydrophilic GO, which has numerous oxygen functional groups that maintains a hydrophilic consistency. GO further get reduced by a green route of reduction using ascorbic acid reducing agent, to form black aggregates of hydrophobic rGO.Pluronic-P123 was used to maintain the colloidal stability. The as synthesized rGO was conjugated with P123 with assisted bath sonication technique forming rGO-P. Reduction and pluronic-P123 stabilisation are effective strategies adopted for avoiding aggregation and provide with excellent water dispersibility for graphene nanoparticles.Reduction and surface functionalization were confirmed by various sophisticated characterisation techniques such as FTIR, Raman Spectroscopy, XPS *etc.,*

PC-12 cells served as the major subject cell lines for *in vitro* studies confirming cytotoxic and proliferative potential of the material. Major *in vivo* studies were categorised into (i) Acute toxicity studies in Swiss Albino mice and (ii) feto-placental transmission mediated developmental toxicity studies in Wistar rats. Swiss Albino mice were administered with 10mg/kg body weight rGO-P to study blood brain barrier integrity confirming leakage of brain contents. Wistar rats were administered with 5mg/kg and 10mg/kg body weight of rGO-P during organogenesis period for developmental toxicity study. All the rat dams were subjected to caesarean followed by euthanization.Bio distribution studies and histopathological examination of major tissues confirmed the presence of material in vital organs of dams.Biodistribution studies using Confocal Raman mapping indicated that rGO-P circulated in the blood and localized in the brain, liver, spleen, kidney and bone marrow of rat pups shows a clear cut evidence of crossing the placental barrier to enter into the foetus. Even then pups and rats were healthy throughout the experimental period. Balance beam test was conducted to analyse possible motor co-ordination defects in pups due to presence of rGO-P in brain of pups. None of the results were controversial confirming lack of issues with motor co-ordination and development. All the oxidative stress parameters and non enzymatic antioxidants remained intact in the brain and liver of all the experimental animals also shows a good sign.

Current trend in science and technology focussed more on graphene like 2D materials and their derivatives and has even entered into biomedical technology also. Generally, before validating any material safe for biomedical applications, prior safety evaluations has become a must follow criterion. Lack of in-depth knowledge about the potent developmental toxic responses that can be evoked by graphene nanoparticles makes the present study worthwhile for futuristic applications. Therefore the results of the present study propose that pluronic stabilised reduced graphene oxide is a potent candidate material that can be applied safely for various applications in biomedical and healthcare modalities.

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