Gold nanoparticles: A therapeutic approach in murine carcinogenesis

Nabanita Maity [1], Mahuya Sengupta[1*]
[1]Department of Biotechnology, Assam University, Silchar, Assam, India.
Email Id of authors: nabnitaamaiity9@gmail.com, senguptamahuya35@gmail.com
*Corresponding author, Email: senguptamahuya35@gmail.com

In last decade, gold nanoparticles have gained attention in various platforms of biomedical science due to their high surface area to volume ratio than similar masses of bulk materials and adaptable optoelectronic properties due to their plasmon resonance, associated with particle size, shape and structure[1]. Gold is one the first noble metal, found to be reported as "colloidal gold" in Indian, Arabic and Chinese literature of V- IV centuries BC[2]. In Europe, gold was used to treat a number of nerve disorders, epilepsy and syphilis during Middle Ages[3]. There have been many studies, gold as potential photothermal and drug delivery agent in cancer theranostics[4]. Studies on intrinsic immunomodulatory properties of gold nanoparticles are very rare. Our study aims to elucidated therapeutic role of polyethylene glycol functionalized gold nanoparticles (PEG-GNRs) in 3-methylcholanthrene (MCA) induced mice model. This study focuses on the generation of an in vivo carcinogenesis by biweekly subcutaneous application of MCA for 12 weeks in 6-7 weeks old Swiss albino mice, followed by biweekly intravenous application of PEG-GNRs at a dose of 80 μM for 4 weeks. PEG coated gold nanorods were characterized via UV- spectrophotometric study. Isolated murine macrophages from spleen and liver of control, MCA and PEG-GNRs treated mice were subjected to various antioxidant (catalase), oxidative stress (lipid peroxidation and protein carbonylation) and immunomodulatory (nitric oxide) parameters assessment. MCA induced dysplastic changes and PEG-GNR restored tissue histology in liver and spleen were examined by H & E staining.

The results from PEG-GNRs treated murine carcinoma model shows that

a) Significant alterations in anti-oxidant parameter (catalase activity) is observed in both liver and spleen macrophages of mice. MCA induced stress increased catalase activity in both liver and spleen macrophages to combat the stress. Treatment with 80 μM PEG-GNRs decreased catalase level from (115.7±1.265 mg/dl) to (102.5±1.213 mg/dl) and from (116.7±3.03 mg/dl) to (100.8±2.296 mg/dl) in liver and spleen macrophages respectively.

b) Significant alterations in oxidative stress parameters like lipid peroxidation and protein carbonylation is observed. Treatment with 80μM PEG-GNRs decreased lipid peroxidation level from (80.53±2.606 mM/mg protein) to (36.67±3.399 mM/mg protein) and from (88.63±8.279 mM/mg protein) to (62.83±12.38 mM/mg protein) in spleen and liver macrophages respectively. Treatment with 80μM PEG-GNRs decreased protein carbonylation level from (139.47±1.606 mM/mg protein) to (72.93±6.317 mM/mg protein) and from (141.21±3.399 mM/mg protein) to (132.91±5.471 mM/mg protein) in liver and spleen macrophages respectively.

c) Nitric oxide is a signaling molecule that has an important role in various signaling pathways and immunological reactions. A significant result was seen in the nitric oxide (NO) level in macrophage treated with 80 μM PEG-GNRs. In this case, MCA stimulation decrease nitric oxide release in untreated cell significantly, however, subsequent treatment with PEG-GNRs increased nitric oxide release. Treatment with 80μM increased the production of NO from (36.18±3.097μM) to (75.31±3.461μM) and from (22.79±2.827μM) to (40.95±6.004μM) in spleen and liver respectively.

References

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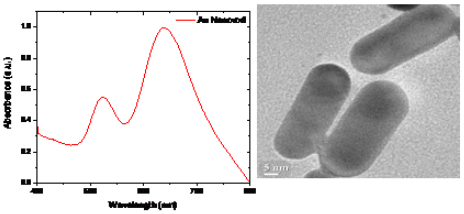

Fig 1: UV absorption spectra and TEM image of polyethylene coated gold nanorods.

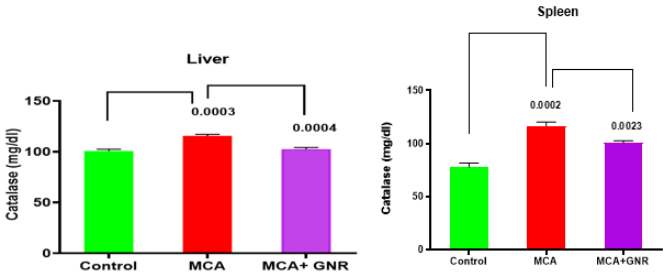

Fig 2: Catalase activity determined after treatment with selected concentration of 80 µM of PEG-GNRs (n=36)

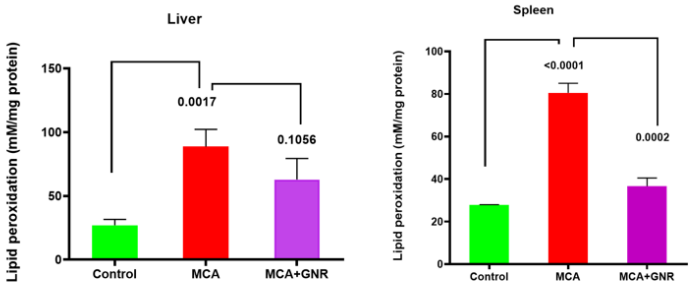

Fig 3: Lipid peroxidation activity determined after treatment with selected concentration of 80 µM of PEG-GNRs (n=36)

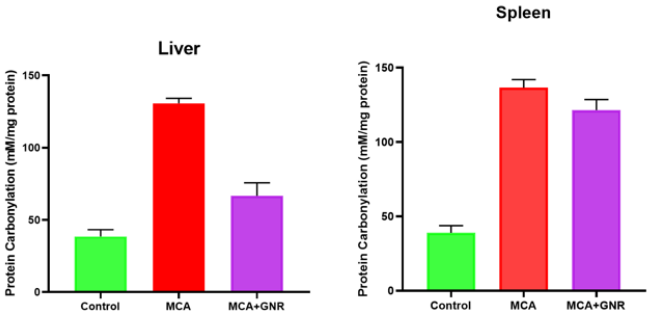

Fig 4: Protein carbonylation activity determined after treatment with selected concentration of 80 µM of PEG-GNRs (n=36)

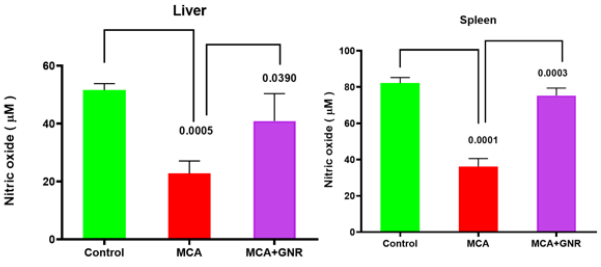

Fig 5: Nitric oxide activity determined after treatment with selected concentration of 80 µM of PEG-GNRs (n=36)