CHROMIUM OXIDE NANOPARTICLE DISTRIBUTION: AN MRI STUDY IN RATS

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Introduction:

Chromium exists in two major oxidation states Cr(III) and Cr(VI). The toxicity of chromium depends on its oxidation states. Chromium Cr(VI) causes cancer and is toxic to kidneys, liver, lungs and skin, while Chromium oxide (Cr_2O_3) Cr(III) strongly affects immune system including sensitization and allergies, reproduction and fertility, kidney and renal system and skin [1]. The present study is aimed at finding out the distribution of Cr_2O_3 nanoparticle (NP) when administered intraperitoneal, intravenous, intramuscular, oral and dermal routes in rats using MRI technique.

Materials & methods: A total of fifteen Male wistar rats were used for the study and they were grouped in five categories i.e. intraperitoneal, intravenous, intramuscular, oral and dermal. The rats in each group were weighed and were administered Cr_2O_3 NP intraperitoneally, intravenously, intramuscularly, orally and dermally. 100 µg/ml doses of Cr_2O_3 NP (176 nm) were prepared in saline. 100µg/100g body weighted dose of Cr_2O_3 NP was administered for each rat. The images were recorded after three hour from Cr_2O_3 NP administration. A standard anesthesia was prepared using Xylazine and ketamine in 1:10 and 100ul/100gm body weighted dose was administered to each rat before placing in MRI probe. All the brain and thigh along with testicular region images were recorded using 9.4 Tesla Bruker Biospin NMR wide bore (80mm) spectrometer with micro-imaging accessories and a 35 mm proton volume resonator was used for the study. The T_1 weighted axial section images were recorded (TR = 600 msec, TE = 20 msec, FOV = 3.8 cm, 256×256 matrix, 2 mm slice thickness, NEX = 2, total scan time = 5 min)

Results:

Preliminarily studies were performed in order to observe the effect of contrast of Cr_2O_3 NP in an *in-vitro* by making use of phantom containing Cr_2O_3 NP suspended in the agarose gel with different concentrations and only agarose gel which served as control. The MR images of the phantom did not show any significant contrast. However, an in-vivo situation viz intramuscular administration of the Cr_2O_3 NP to rats to the thigh region showed time dependent linear increase in the contrast in the images of the thigh region {B (after 15 min), C (2nd day) and D (5th day)} with respect to the control (A) as shown in Fig-1.

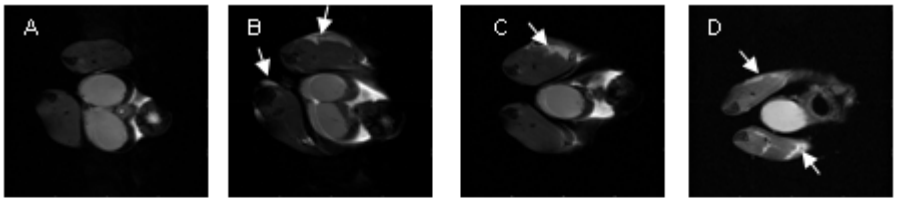

Fig-1: T_1 weighted images of the thigh region of the rat in intramuscular administration of Cr_2O_3np. → refers to the portion where the enhanced contrast was observed

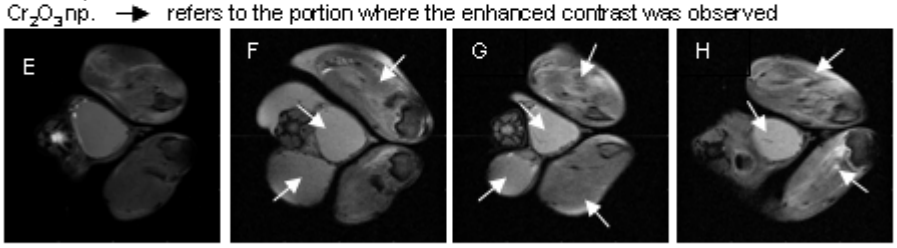

Fig-2: T_1 weighted images of the thigh and testicle region of the rat in dermal application of Cr_2O_3 np. → refers to the portion where the enhanced contrast was observed

The time dependent spread of the positive contrast was mapped in the T_1 weighted images till the fifth day indicating the distribution of Cr_2O_3 NP. The images of brain and thigh along with testicles for all the fifteen rats were obtained before administering Cr_2O_3 NP; these images were served as controls. This study went for a five days with daily administrating Cr_2O_3 NP three hr prior to obtaining the images. Dermal application only showed significant contrast in thigh and testicles {F (2nd day, G (3rd day) and H (4th day)} with respect to the control (E) as shown in Fig-2 respectively.

Discussion:

Dermal and intramuscular application of Cr_2O_3 NP to the thigh region showed consistent time dependent linear increase in the contrast in the images of both thigh and testicles. Whereas, no significant contrast was observed for intraperitoneal, intravenous and oral administration. This presence of contrast in the images suggested that Cr_2O_3 in an *in-vivo* may form a suitable soluble macro molecular complex with protein or lipoprotein and thus may be responsible for generating contrast in the images. The dermal administration results indicated that Cr_2O_3 NP are efficiently being absorbed by the skin followed by its uniform distribution in the thigh and testicles, while in intramuscular administration there was an uniform distribution. These observations may further be utilized for future toxicological studies of Cr_2O_3 NP.

References:

1. Michael.J.Decelanko., William.E.Rinehart., Roger J.Hilaski., Roger B.Thompson and Eckhard loser. Thirteen-week subchronic rat inhalation toxicity study with a recovery phase of trivalent chromium compounds, Cr_2O_3 and basic chromium sulfate, Toxicology sciences, **(52)**: 278 (1999).