THE CONSEQUENCES ON BLOOD GSH DYNAMICS ON WISTAR FEMALE RATS AT AD LIBITUM CHROMIUM (VI) ADMINISTRATION DURING THE GESTATION AFTER THE WEAN

CONSECINŢELE APORTULUI DE CROM (VI) ASUPRA DINAMICII GSH-ULUI SANGUIN DUPA INŢARCARE, ADMINISTRAT FEMELELOR WISTAR, AD LIBITUM, IN TIMPUL GESTAŢIEI

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Chromium (VI) is a widely used industrial chemical, extensively used in paints, metal finishes, steel including stainless steel manufacturing, alloy cast irons, chrome, and wood treatment. In nature chromium occurs in divalent, trivalent and hexavalent forms. Hexavalent chromium predominates over the trivalent form in natural waters. We have studied the influence of potassium dichromate ($K_2Cr_2O_7$) on blood GSH values in rats. This study was carried out on 28 Wistar adult female rats, divided in 3 experimental groups (E) and one control group (C). The rats were feed with 25ppm (LOAEL), 50ppm and 75ppm potassium dichromate, ad libitum, in drinking water, during the gestation. The control batch received tap water. Reduced glutathione (GSH) was measured quantitatively after the wean using a Perkin-Elmer spectrophotometer, through Beutler et al. method, at 412nm. This study reports that potassium dichromate exposure induced the depletion of blood GSH because Cr(VI) can generate reactive oxygen species (ROS). It can induce oxidative stress and toxicity.

Keywords: GSH, potassium dichromate, oxidative stress, female rats.

Introduction

Numerous evidence suggests that exposure to diverse environmental toxicants, including heavy metals, polyhalogenated or polycyclic aromatic hydrocarbons, may involve events which include production of reactive oxygen species (ROS) and oxidative stress leading to lipid peroxidation (Bagchi, 1998a, 2002), DNA-SSB (single strand breaks) and fragmentation (Stohs, 1997), membrane damage with decreased membrane fluidity, apoptosis (cell death) (Stihs,

1995), glutathione depletion (Bagchi, 1996a), altered calcium homeostasis (Bagchi, 1997, 1998a, b), induction of stress/heat shock protein (HSP) (Von Burg, 1993), stimulation of oncogene expression and inhibition of tumor suppressor genes (Schwarz, 1995).

The pollution of water resources by toxic chemical pollutants continues to occur. The domestic and industrial effluents are the main sources responsible for the contamination of aquatic environment (Claxton, 1998; White, 1998).

Chromium exist predominantly in two valence states. Cr^{3+} is an essential micronutrient, Cr^{6+} is carcinogenic. The most dominant form of Cr^{6+} in neutral aqueous solution is chromate, $(CrO_4)^{2-}$, who can readily cross cellulare membranes via non-specific anion carriers (Danielsson, 1982).

Materials and Methods

This study was carried out on 28 adult white Wistar adult female rats, divided in 3 experimental groups (E_1, E_2, E_3) and one control group (C).

The experimental groups are:

- E_1 = female rats – exposed for 3 weeks, during the gestation, to 25ppm Cr^{+6} (LOAEL) form ($K_2Cr_2O_7$) in drinking water, ad libitum.
- E_2 = female rats – exposed for 3 weeks, during the gestation, to 50ppm Cr^{+6} form ($K_2Cr_2O_7$) in drinking water, ad libitum.
- E_3 = female rats – exposed for 3 weeks to 75ppm Cr^{+6} form ($K_2Cr_2O_7$) in drinking water, ad libitum.
- Control batch (C) – female rats – maintained tape water without Cr^{+6}.

Potassium dichromate was administered to the adult female rats in drinking water, ad libitum, during the gestation. The rats were euthanatized after the wean, the blood samples being used for determinations.

GSH was measured quantitatively at a Perkin-Elmer spectrophotometer through Beutler et al. method (Beutler, 1963), at 412nm of yellow color developed by adding 5,5'-dithiobis(2-nitrobenzoic acid) to sulphahidryl compounds. The results were expressed as μmol GSH/gHb. Hemoglobin (Hb) was determined through Drabkin method (Ghergariu, 2000) at the automatic analyzer MS-9 VET.

Results and Discussion

Chromate is a known carcinogen. The toxicity of chromate may be mediated by the reaction of chromium(VI) with glutathione (GSH) to generate relatively stable chromium(V) complexes and other more reactive intermediates (O'Brien, 1989). The toxicity of chromate may be mediated by the reaction of chromium(VI)

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The blood test results are presented in Tables 1 and Figure 1.

Table 1.

GSH values in the control group (C) and experimental groups (E_1, E_2, E_3) after the wean.

Group	GSH (μmol/gHb)		
	X±Sx	DS	Confidence level 95%
C	0.65±0.01	0.01	0.01
E_1(25ppm)	0.64±0.01	0.01	0.01
E_2(50ppm)	0.59±0.01	0.01	0.01
E_3(75ppm)	0.53±0.01	0.01	0.01

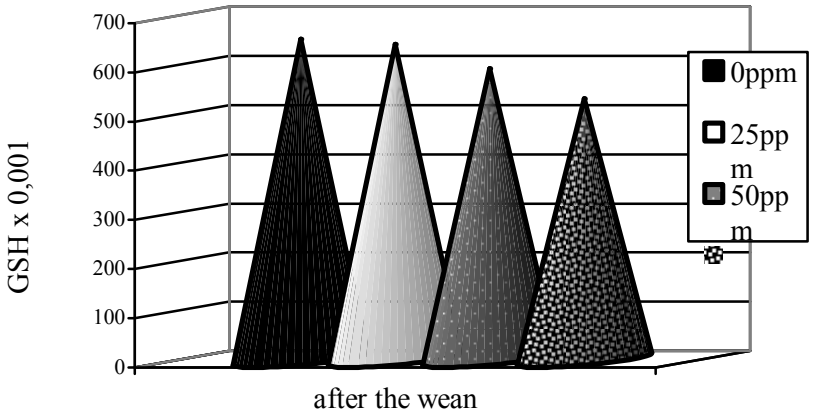

Fig.1. GSH value in the control and experimental groups

Reactive intermediates, generated during the reduction of chromate by GSH, include thionyl radicals and two relatively stable Cr^{+5} species, $[CrOCl_4]^-$. Mixtures of Cr^{+6} and GSH and a Cr^{+5} complex of GSH, $Cr(V)GSH_n$, are capable of causing strand breaks in DNA, internucleosomal DNA fragmentation, inhibition of macromolecular synthesis and apoptosis (Barceloux, 1999). This is because reactive intermediates generated during the reduction of chromium(VI) provide one route by which the genotoxicity of chromate may be expressed (O'Brien, 1989).

Conclusions

Hexavalent chromium (Cr^{6+}) is a potent teratogen. He is significantly reduced to trivalent state by glutathione (GSH) in all tissues. During this reduction process, chromium may interact with cellular macromolecules and DNA.

The reaction of GSH with chromate is complex . The exact species generated in these reactions are not yet fully identified.

The consequences of ad libitum $K_2Cr_2O_7$ administration at 25, 50 and 75ppm during three weeks to adult white Wistar female rats, during the gestation, was the induced oxidative stress, the inhibition of GSH regeneration, a limited decrease of GSH values in E_1, E_2, E_3 groups.

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