COMPARATIVE TOXICITY OF FOOD DYES ON LIVER AND KIDNEY IN GUINEA PIGS: A HISTOPATHOLOGICAL STUDY

V. Rus, C. Gherman, V. Miełauș, A. Mihalca, G. C. Nadăș

FACULTY OF VETERINARY MEDICINE CLUJ-NAPOCA

Summary

In food industry there are used substances from azoic dyes such as carmoisine and tartrazine. Therefore we decided to verify by a histological study, the effect of these two dyes, administered in drinking water in concentrations of 1, 2 and 3% for 3 weeks, on liver and kidney in guinea pigs. At the end of the experiment animals were euthanized and pieces of liver and kidneys were collected and histologically processed through inclusion in paraffin. For both liver and kidney we observed phenomena represented by stasis and oedema, congestion, hepatocyte and kidney apoptosis, with atrophy of renal corpuscles. Magnitude and severity of histopathological aspects observed were directly proportional to the concentration of the administered dyes.

Key words: carmoisine, tartrazine, guinea pigs, liver, kidney, histopathological study.

vasilerus2002@yahoo.com

Introduction

In the food industry there are a wide range of dyes, of which some azoic dyes, although it was said many years ago that they are carcinogens, at least in bladder cancer (McLean et al., 1964). In this category we chose to study carmoisine (E 122) and tartrazine (E 102).

Carmoisine is a synthetic red dye commonly used in Britain but banned in Sweden, USA, Austria and Norway. The most often is used as disodium salt. It seems that it is able to induce allergic reactions or intolerance especially among people with intolerance to aspirin, also signaling other reactions like skin rash similar to nettle-induced, including swelling of the skin. Asthmatics can react quite strongly to carmoisine (Wikipedia).

Tartrazine is used for coloring foods and beverages in yellow, but can also be used along Brilliant Blue FCF (E133) or Green S (E 142) to produce different shades of green. Tartrazine seems to cause many allergic reactions and food intolerance especially among people with asthma and those with aspirin intolerance (UK Food Guide). Tartrazine sensitivity symptoms occur either consecutively consumption of food or drinks containing tartrazine or skin exposure to substances containing tartrazine. After ingestion of tartrazine humans develop anxiety, headaches, blurred vision, itching, general weakness, heat waves, feeling of suffocation, purple skin patches and sleep disorders (UK Food Guide).

In young mice tartrazine have a noticeable effect on behavior (Tanaka 2006; Tanaka et al., 2008), while in rats has an inflammation effect on gastric mucosal increasing eosinophils and lymphocytes in the chorion, when administered in food a long time (Moutinho et al., 2007).

Aboel-Zahab and collaborators in a study on rats, in 1997, following the introduction in the diet of tartrazine, brown pigment deposits were observed in portal area and Kupffer cells and in interstitial tissue and tubular cells from urine tubes of the kidneys. Besides these aspects, were observed micro hemorrhages and congestion both at the liver and kidneys level. The authors stated that no
microscopic changes were observed in the stomach.

Other studies in rodents that have been administered carmoisine or tartrazine in different concentrations in food, revealed no microscopic changes in organs or development of neoplastic processes (Mannell, 1958; Bar and Grieptengrog, 1960; Manchon and LowYat, 1964; Gaunt et al., 1967).

Since literature data are sometimes contradictory, we considered it appropriate to test the effect of the two dyes on liver and kidney in guinea pigs.

**Materials and methods**

The experiment was conducted on 28 guinea pigs divided into 7 groups as follows: three groups treated with carmoisine (conc. 1%, 2%, 3%), three with tartrazine (conc. 1%, 2%, 3%) and one control group. Dyes were administered in drinking water ad libidum for 3 weeks. At the end of the experiment after anesthesia induced by administration of ketamine (100mg/kg body) and acepromazin (5mg/kg body) (Oana et al., 2006), rats were euthanized by neck dislocation followed by decapitation. In order to realize the histopathological examination, samples were collected from all animals studied, represented by fragments of liver and kidney slices thick as 5 mm. They were fixed for 24 hours in Stieve mixture, washed with ethylic alcohol, clarified with butyl alcohol and included in paraffin. 5 µm thick sections were stained with Goldner's trichromic method, and examined under a microscope Olympus BX 41.

**Results and discussions**

In control group animals no structural changes were identified by histopathology in the liver or kidney, suggesting that the animals studied were healthy and the conditions under which the experiment was conducted were proper.

In experimental animals we noticed changes from discrete to pronounced, both in animals treated with carmoisine and those with tartrazine. Changes in the liver are discrete in animals which have consumed carmoisine and tartrazine in concentration of 1%. They consist of slight congestion, in both intralobular and extralobular vessels and discrete perivascular edema. In the external third of lobules we observed some apoptotic hepatocytes. For the concentration of 2 %, the liver vascular phenomena are more pronounced, capillary congestion is present in many lobules, determining a slight compression atrophy of hepatocyte cords. Hepatocytes in various stages of apoptosis were observed in small numbers within the liver lobe, the number of hepatocytes in apoptosis being greater at the lobe periphery. Both hepatocyte apoptosis and congestive phenomena are more pronounced in the group that received carmoisine 2% (Fig. 1) compared to that consumed 2% tartrazine (Figure 2). For 3% concentration, liver lesions are more advanced than in other concentrations. Congestion is especially pronounced in group treated with carmoisine 3% (Fig. 3), and at the level of the portobiliar space is currently present a perivascular and pericanalicular oedema more pronounced in group treated with carmoisine.

Changes in the kidney are somewhat comparable to those of liver, meaning that there is congestion of different intensities and perivascular edema. In addition to these, abnormal glomerular filtration and glomerular or tubular stasis were observed. In animals treated with low dose (1%), vascular congestion is relatively moderate and for the group treated with carmoisine 3% (Fig. 3), and at the level of the portobiliar space is currently present a perivascular and pericanalicular oedema more pronounced in group treated with carmoisine.
nephrocite apoptosis appears. Concentration of 3% led to the kidney level the most pronounced changes. Renal corpuscles atrophy is present in both groups, for the group treated with tartrazine having in addition several corpuscles and tubular necrosis (Fig. 6).

Changes induced by the two tested substances in the liver of guinea pigs are largely similar. They begin with vascular changes, evidenced by congestion, stasis and edema. Along with these aspects of apoptosis are present and affects some hepatocytes without an increased number. The intensity of these phenomena is directly proportional to the administered dose, the most pronounced being recorded from animals which have received the concentration of 3% for both substances tested. Although the sequencing of events seems comparable to the two substances, among them there are some difference in that the lesions produced in the liver are more advanced in case of carmoisine administration. In case of the liver histopathological aspects are mostly reversible, with no major organ function disorders, so removing these substances from the diet will be followed by structural recovery.

Effect of test substances is comparable also for kidney, where changes are highly comparable and dose dependent. Here also exist differences between the two substances, but the toxicity is higher for tartrazine and not for carmoisine as in case of the liver. Furthermore, some changes in the kidney are irreversible, with the decommissioning of the structures affected. It is primarily about renal atrophy corpuscles determining their functional removal. Microscopic aspects of guinea pigs groups captured that were administered tartrazine, are similar to those described by Aboel-Zahab et al. (1997), in a study on rats, only those obtained by us in guinea pigs are more advanced, especially in the kidney.

![Fig. 1. Moderate vascular congestion (white arrow) and diffuse hepatocyte apoptosis (black arrow) - carmoisine 2% (Goldner's Trichromic stain, ob. 10X)](image1)

![Fig. 2. Discrete vascular congestion (white arrow) and diffuse hepatocyte apoptosis (black arrow) - 2% tartrazine (Goldner's Trichromic stain, ob. 10X)](image2)

![Fig. 3. Marked hepatic congestion (white arrow) - 3% tartrazine (Goldner's Trichromic stain, ob. 10X)](image3)
Conclusions

Dyes studied were found to have hepatotoxic and nephrotoxic action, causing congestion, stasis and edema in the liver and kidney and hepatocyte and kidney apoptosis and atrophy of some renal corpuscles.

Action of both substances tested is comparable to a point and the amplitude and extension of lesions is largely proportional to dose.

Comparative assessment of the effect of the two substances tested revealed that hepatotoxic action is more pronounced in group treated with carmoisine, while tartrazine has increased nephrotoxic action compared with carmoisine.

Acknowledgements

This research was funded by C.N.M.P., contract number 51-072/2007.

References


http://www.ukfoodguide.net/e102.htm.


