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GASTROPROTECTIVE EFFECTS OF NOVEL ANTIDOTAL COMBINATION IN RATS ACUTELY POISONED BY T-2 TOXIN

JAĆEVIĆ VESNA*, RESANOVIĆ RADMILA**, BOČAROV-STANČIĆ ALEKSANDRA***, ĐORĐEVIĆ SNEŽANA*, DRAGOJEVIĆ-SIMIĆ VIKTORIJA****, VUKAJLOVIĆ ANA* and BOKONJIĆ D*

*National Poison Control Centre, Military Medical Academy, Belgrade, Serbia
**University of Belgrade, Faculty of Veterinary Medicine, Serbia
***Bio-Ekološki Centar, Zrenjanin, Serbia
****Centre for Clinical Pharmacology, Military Medical Academy, Belgrade, Serbia

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The purpose of this experiment was to evaluate the antidotal potencies of methylprednisolone (soluble form, Lemod-solu®), nimesulide, N-acetylcysteine (Fluimucil®) and their combinations in rats treated with 1.0 LD_{50} (0.23 mg/kg) of trichothecene mycotoxin, T-2 toxin. Their antidotal efficacy was investigated by monitoring their effects on general condition, 24-hour-survival, body weight gain, food and water consumption and pathohistological changes in the gut of Wistar rats acutely treated with a single injection of T-2 toxin during a 4-week period. The highest protective index was obtained with methylprednisolone (2.43). Initial loss of body weight (after first 7 days) was found only in T-2 toxin group. During the whole experiment, in poisoned rats protected by methylprednisolone or methylprednisolone and nimesulide, a significant increase ($p<0.001$) in body weight gain, food and water consumption in comparison with T-2 toxin group was found. At the end of the experiment, N-acetylcysteine, nimesulide and their combination assured higher ($p<0.05$) weight gain, food and water consumption in comparison with T-2 toxin group. Signs of hemorrhagic diathesis and necrosis of the gut crypt epithelium and lymphoid tissues were found in the T-2 toxin group. Some of these histological alterations were presented in the gut of poisoned rats treated by nimesulide, N-acetylcysteine and their combination. The gut of T-2 toxin rats treated with a combination of methylprednisolone and nimesulide and especially methylprednisolone alone had a histological structure similar to the control group. These results clearly show that methylprednisolone, a well-known anti-inflammatory and immunosuppressive drug, exerts the best antidotal effect against T-2 toxin intoxication in rats.

Key words: gut, methylprednisolone, N-acetylcysteine, nimesulide, pathohistology, T-2 toxin

INTRODUCTION

T-2 toxin, a trichothecene mycotoxin, belongs to a diverse group of sesquiterpenoid metabolites that are produced by several *Fusarium* fungi found in food or the environment (Grove, 1993). T-2 toxin, as one of the most effective cytotoxic secondary sesqiterpenoid metabolites, produce a toxic reaction called mycotoxicosis after inhalation or consumption of contaminated food by humans and animals (Ciegler, 1980; Ueno, 1980; Pang *et al*., 1988; Josephs, 2004; Foroud and Eudes, 2009). However, some evidence has associated this toxin with alimentary toxic aleukia (ATA) (Joffe, 1974) and with chemical weapons (CW) incidents in Southeast Asia (Rosen and Rosen, 1982; Mirocha *et al*., 1983; Anonymous, 2003).

T-2 toxin, as well as the other trichothecene compounds, is highly toxic to eukaryotic cells, and this cytotoxicity depends on biochemical features characterized by a potent inhibitory effect on protein synthesis (Ueno, 1980; Iwahashi *et al.*, 2008). Its acute toxicity is higher than in other mycotoxins (Visconti, 1991). During the acute exposure to high doses of T-2 toxin, in animals exhibit "radiomimetic" symptoms, while extremely high doses can cause cardiovascular dysfunction resemble a shock-like syndrome that can result in death (Ueno, 1984; Doi *et al*., 2008). T-2 toxin induce some alterations in the membrane structure, which consequently stimulates lipid peroxidation. Once T-2 toxin crosses the plasma membrane and enters the cell it can ineract with a number of targets, including the ribosomes and the mitochondria (Wannemacher *et al*., 1991; Speijers and Speijers, 2004). Understanding the molecular and the cellular mode of action of T-2 toxin is very important for human health, as well as for the treatment of acute and repeated or subacute poisonings (Jaćević *et al.*, 2001b; Jaćević, 2005).

The aim of this study was to investigate the effects of soluble form of methylprednisolone (Lemod-solu®; MP), nimesulide (NM), N-acetylcysteine (Fluimucil®; NAC) and their combinations on general condition, 24-hours survival, body weight gain, food and water consumption and pathohistological changes in the gut of rats acutely poisoned with 1.0 LD_{50} T-2 toxin.

MATERIAL AND METHODS

Experimental animals and treatments

The experiment was performed on adult female Wistar rats 4 weeks old, weighing 180-200 g (Animal House, Military Medical Academy, Belgrade, Serbia). The animals were housed in plastic cages, under standard laboratory conditions (21ºC, 12/24-hours light/dark cycle, commercial food and tap water *ad libitum*) before being randomized into eight groups of animals. One day before the experiment, animals were fasting. During the subsequent experiment, they were fed with standard laboratory food *ad libitum*. They were allowed access to fresh tap water *ad libitum*.

In order to obtain the optimal doses of methylprednisolone (Lemod-solu®; MP), nimesulide (NM) and N-acetylcysteine (Fluimucil®; NAC), a range of their

doses was previously tested (Jaćević *et al*., 2001a). The best protecting doses of MP, NM and NAC were 40, 30 and 200 mg and these doses were chosen for this experiments (Table 1).

Table 1. Effects of various regimens on 24h survival in rats poisoned with T-2 toxin

Regimens	T-2 toxin LD_{50} (mg/kg *sc*)	95% confidence limits	f(LD_{50})	Protective index
MP	0.44	0.35 - 0.55	1.25	2.43
NM	1.53	1.39 - 1.69	1.10	1.44
NAC	1.22	1.19 - 1.27	1.19	1.29
MP + NM	1.55	0.47 - 0.30	1.15	2.34
MP + NAC	0.76	0.51 - 1.12	1.48	2.16
NM + NAC	1.24	1.57 - 2.22	1.15	1.22

Rats were randomly allocated to eight groups, each of them consisting of 10 animals. Their treatments were: 1. Control group; 2. T-2 toxin, T2 (0.23 mg/kg sc); 3. T2 + MP (40 mg/kg im); 4. T2 + NM (30 mg/kg ip); 5. T2 + NAC (200 mg/kg im); 6. T2 + MP + NM; (7) T2 + MP + NAC and 8. T2 + NM + NAC. After recording 24-hour-survival rate, body weight gain, food and water consumption and pathohistological changes were monitored at the end of days 1, 7, 14, 21, and 28. General health condition of the animals was monitored daily throughout the whole experimental period (four weeks).

Study protocol

Study protocol was based on the Guidelines for Animal Study no. 282-12/2002 (Ethics Committee of the Military Medical Academy, Belgrade, Republic of Serbia).

T-2 toxin

T-2 toxin that was used in these experiments was produced in laboratory conditions from *Fusarium sporotrichoides* fungi, cultivated on synthetic GPY (glucose 5%, peptone 0.1%, yeast extract 0.1%, pH 5.4) medium. Extraction and crude purification of the toxin were performed by filtration, while definite purification and determination of T-2 toxin content were performed by gas chromatography with electron capture detection (GC-ECD) (Romer, 1987). T-2 toxin was preliminarily tested in animals in order to obtain its LD_{50} value (Litchfield and Wilcoxon, 1949; Jaćević *et al*., 2001a). It was thereafter used in the current experiment as a single dose of 0.23 mg/kg sc (1 LD_{50}).

Methylprednisolone

Commercially available formulation of methylprednisolone, Lemod-solu®, was used in these experiments. Lemod-solu® is methylprednisolone sodium succinate dissolved in 1 mL of 0.9% benzyl alcohol. This formulation contains 40 mg of active substance in 1 mL solution. The dose administered in these experiments was 40 mg/kg im.

Nimesulide

A dose of 30 mg/kg of commercially available formulation of nimesulide was used in these experiments. This powder was dissolved in 1 mL of 0.9% NaCl.

N-acetylcysteine

Commercially available formulation of N-acetylcysteine, Fluimucil®, was used in these experiments. This formulation contains 200 mg of active substance in 1 mL. The dose administered in these experiments was 200 mg/kg im.

Histopathological procedure

Animals were sacrificed after the end of the treatment on days 1, 7, 14, 21 and 28, respectively. The gut was excised and the samples fixed in 10% neutral formalin for 5 days. Transmural tissue samples were dehydrated in graded alcohol, xylol and embedded in paraffin blocks. Finally, 2-μm thick paraffin sections were stained by hematoxylin and eosin (H & E) method and analyzed (Olympus-2 microscope).

Quantitative analysis

The intensity of pathohistological changes in the gut's sampls was counted in 10 accidentally selected visual fields, magnified by 40x. The changes observed were scored by semiquantitative grading scales (gut damage score, GDS) showed in the Table 2.

Table 2. The semiquantitative grading scale - gut damage score (GDS)

Grade	Definition
0	Normal – normal histological structure
1	Mild damage – minority cells with degeneration and normal nuclear architecture
2	Moderate damage – Groups of cells (more than 50%) with marked citoplasmatic vacuolisation, transmural edema and hyperemia
3	Severe focal damage – majority cells with marked citoplasmatic vacuolisation and karyopicnosis, focal accumulation of inflammatory cells and focal haemorrhages
4	Severe diffuse damage – cystic deformation of stomach and small intestine glands, atrophy of intestinal villi and diffuse accumulation of inflammatory cells and diffuse haemorrhages
5	Tissue necrosis

Statistical analysis

Statistical evaluation was performed using commercial statistical software (Stat for Windows, R.4.5, Stat Soft, Inc., USA, 1993). Results are shown as the mean (X) ± the standard deviation (SD). Comparison of data was done by Student's t-test. The differences with values of $p<0.05$, $p<0.01$ and $p<0.001$ were considered significant. The one-way ANOVA + post-hock analysis (Tuckey's test)

were utilized to determine the significance of the differences in the severity of the gut damage scores among the various treatment groups. The differences with values of $p<0.05$ was considered significant.

RESULTS

General health of experimental animals

The clinical sings of acute intoxication such as vomiting, emesis, cyanosis, decreased body surface temperature and lethargy could be registered during the first day of study only in T-2 toxin-treated rats. In the surviving animals, during the 28-day period of observation, no significant changes of general health and appearance could be seen. All the rats were in good shape. Their hair, skin, visible mucosa and muscle tonicity were without any changes. Their movements and co-ordination were preserved and comparable to the control animals.

Effects of different treatments on 24-hour-survival in rats

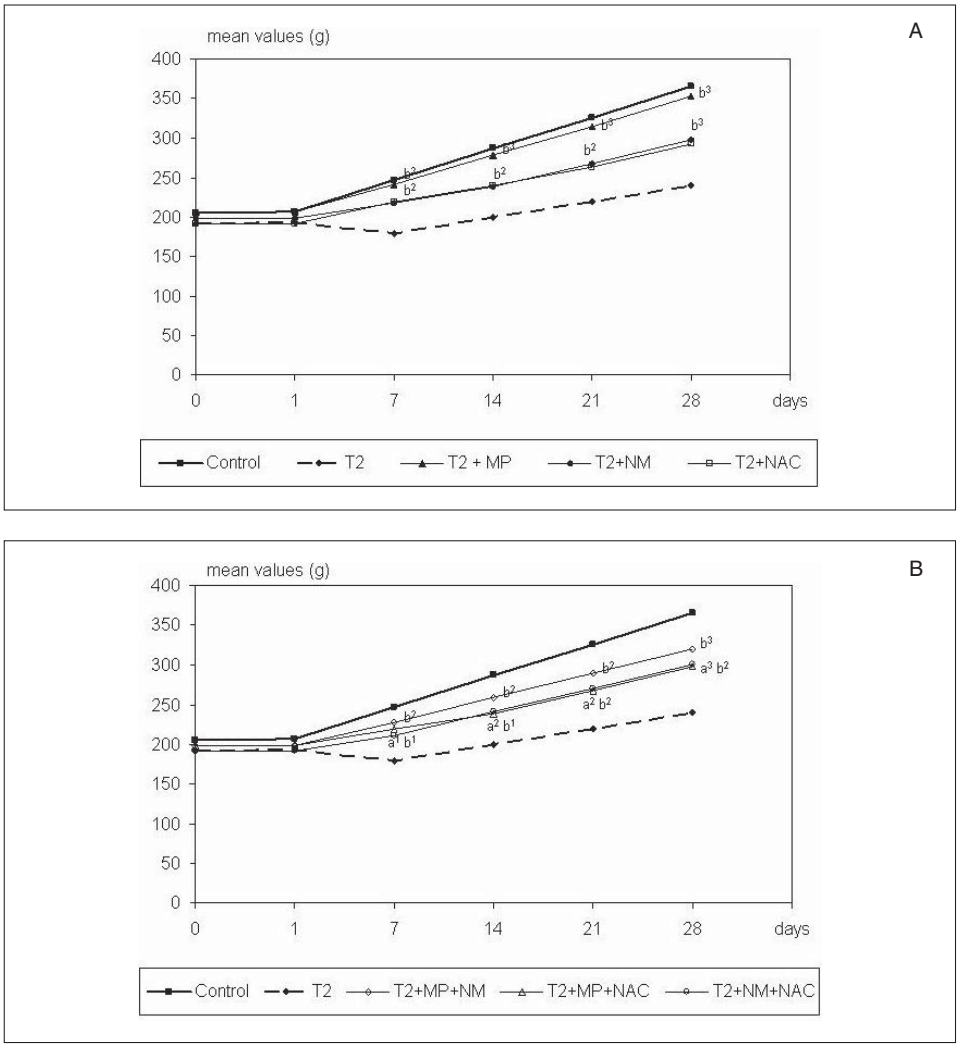
Registration of 24-hour-survival rates revealed that all the regimens significantly antagonized the lethal effects of T-2 toxin. Based on the results shown in Table 1, it could be seen that the highest protective index was obtained with MP (2.43), although this value was significantly different only from NM and NAC.

Effects of different treatments on body weight gain

In the second, poisoned but untreated group, T-2 toxin induced a decrease in body weight gain, in comparison with the control rats. Only animals from this group had a decrease in body weight gain, which was most prominent on the seventh day of the experiment. From days 7-28 a mild increase in body weight gain could be seen, but significantly smaller than in the groups treated with MP ($p<0.001$), NM, NAC and their combinations ($p<0.01$). The highest body weight gain was obtained with MP. The body weights of rats from that group were close to those of the control group and significantly higher from those in the group treated with T2 only ($p<0.001$). Increase in body weight gain was registered in the other two treated groups and the values obtained were significantly higher from those obtained in poisoned and untreated animals ($p<0.01$). Body weight in these groups increased significantly slower in comparison with the control group and the group treated with MP ($p<0.05$) (Figure 1A and B).

Effects of different treatments on food consumption

In animals treated with T-2 toxin only, during the period of the first week after poisoning, a significant decrease in food consumption could be seen. During the rest of the experimental period, a mild increase in food consumption could be registered, but significantly less than in the control group ($p<0.001$). The results presented in Figure 2A and B clearly show that food consumption in rats protected with MP or/and NM was very similar to the one in the control group during the whole 28-day period. In this group food consumption was increased in comparison with the poisoned group treated with NAC and after combined use of MP or NM and NAC ($p<0.01$).

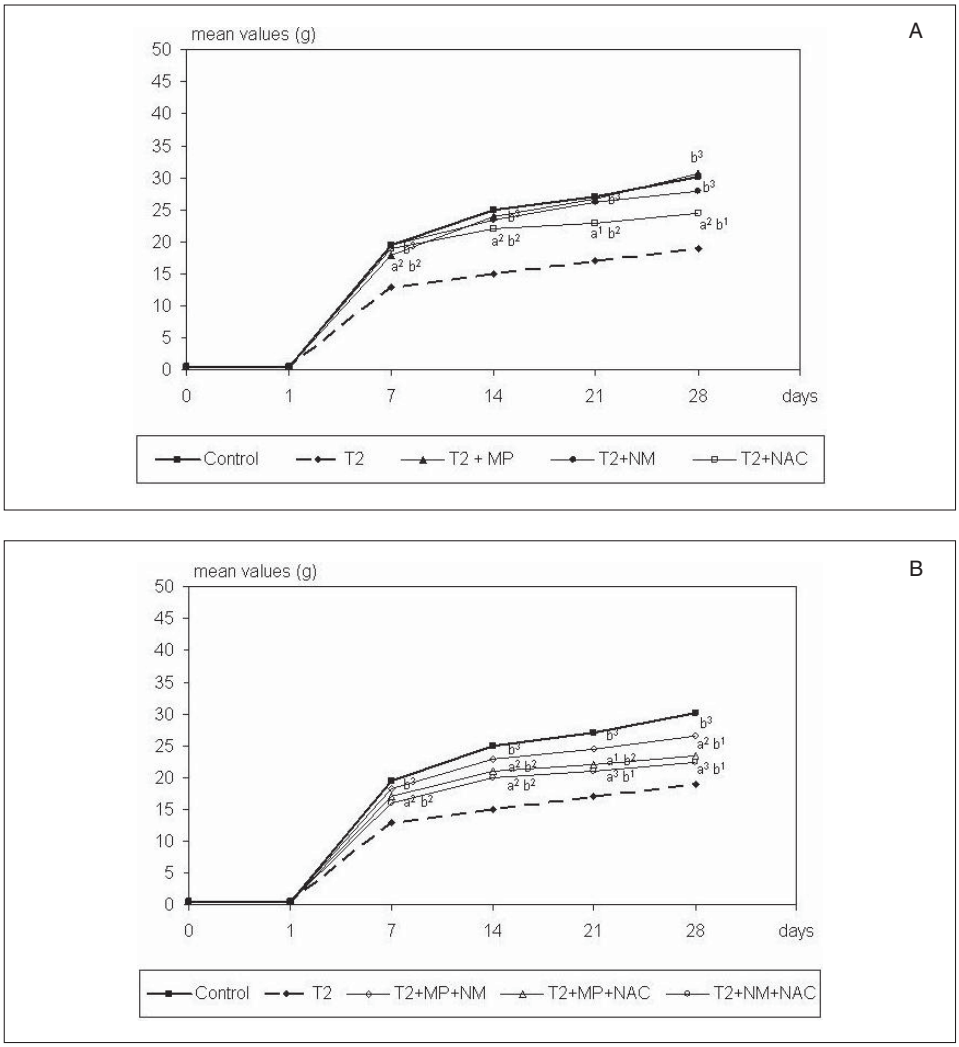


$a^{1, 2, 3}$ - $p<0.05$, 0.01, 0.001 vs control group; $b^{1, 2, 3}$ - $p<0.05$, 0.01, 0.001 vs T2 group

Figure 1A and B. The changes in body weight gain in control, T2 or/and MP, NM, NAC rats

Effects of different treatments on water consumption

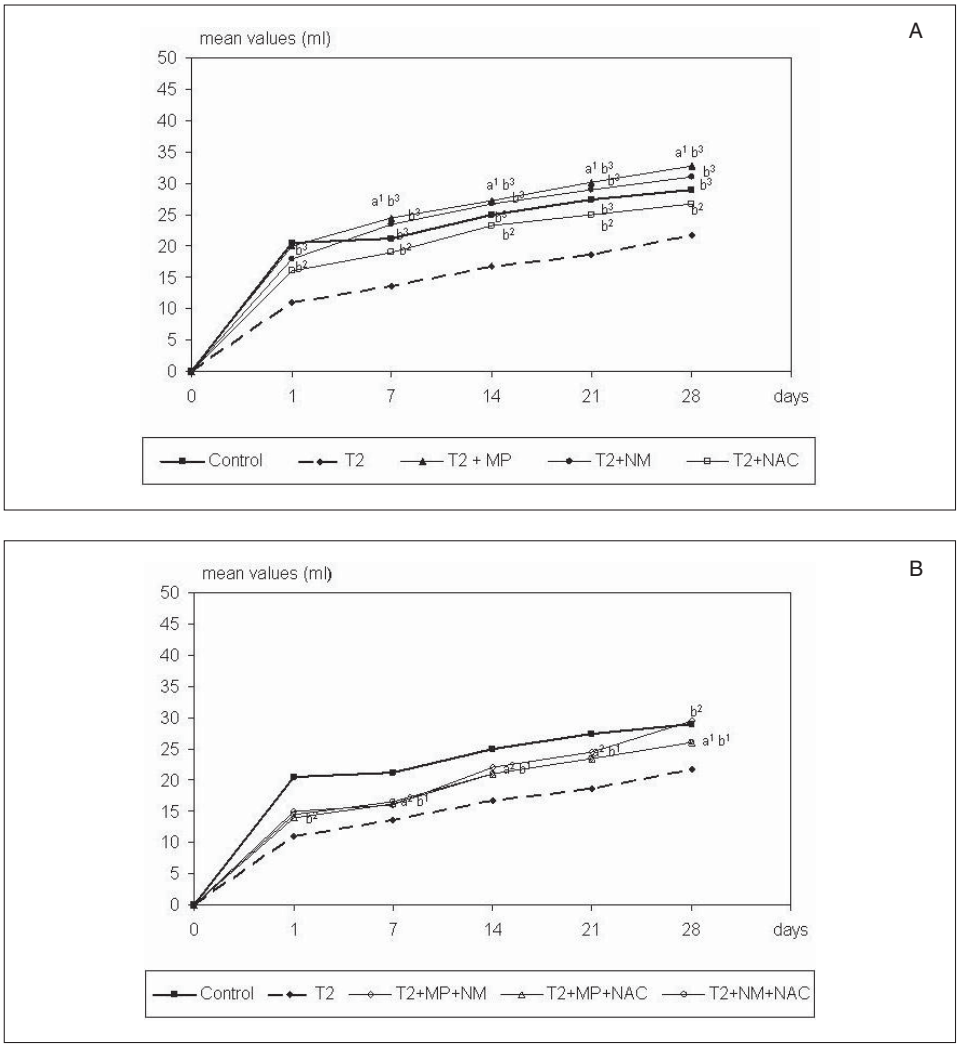
Single injection of MP or NM in poisoned rats significantly increases the volume of consumed water in comparison with the animals that received T-2 toxin only ($p<0.001$).



$a^{1, 2, 3}$ - $p<0.05$, 0.01, 0.001 vs control group; $b^{1, 2, 3}$ - $p<0.05$, 0.01, 0.001 vs T2 group

Figure 2A and B. The changes in food consumption in control, T2 or/and MP, NM, NAC rats

During the whole four-week period, these values were slightly higher than those in control animals ($p<0.05$). NAC also increased water consumption ($p<0.01$), as well as the combined treatment ($p<0.05$) during the whole course of the experiment (Figure 3A and B).



$a^{1, 2, 3}$ - $p<0.05, 0.01, 0.001$ vs control group; $b^{1, 2, 3}$ - $p<0.05, 0.01, 0.001$ vs T2 group

Figure 3A and B. The values in water consumption in control, T2 or/and MP, NM, NAC rats

Pathohistological analysis of the gut in the control groups

Microscopic examination of the stomach and small intestine of control animals showed no changes (Figure 4, 5).

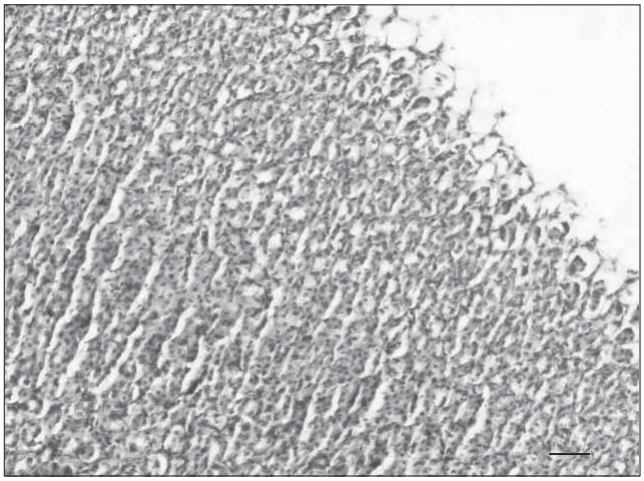


Figure 4. Histological section of the stomach in control rats sacrificed after 24h shows normal structure (HE, 10x), scale bar = 10 μm

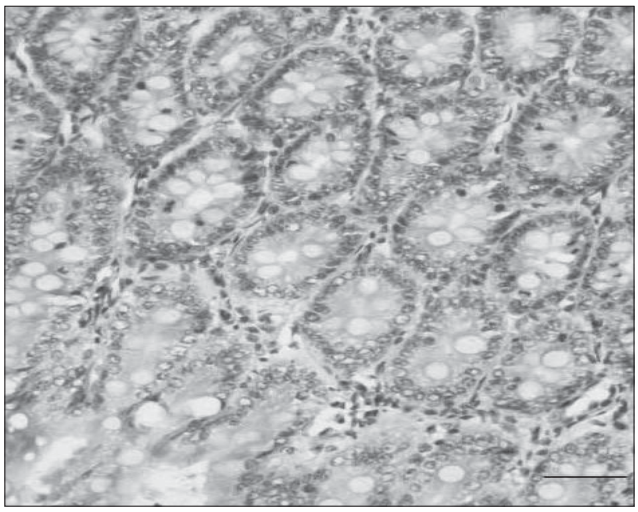


Figure 5. Histological section of the small intestine in control rats sacrificed after 24h shows normal structure (HE, 20x), scale bar = 10 μm

Pathohistological analysis of the gut in T-2 toxin group

The gut alterations detected in poisoned animals ranged from degeneration to diffuse necrosis and massive circulatory changes. These changes were the most prominent in *the tunica mucosa* and *the tunica submucosa* of the digestive system. In the group of animals sacrificed on the seventh day of the experiment

alterative changes were predominant, including intracellular edema and degeneration. These irregular, round to ovoid cells were characterized by dissolution and granularity of cytoplasm. In the majority of these epithelial and glandular cells nuclear pleomorphism was present, with large, round to rectangular shapes and prominent nucleoli (Figure 6). The most intensive

Figure 6. Histological section of the stomach in T2-treated rat sacrificed on the 7th day shows ulceration in *the tunica mucosa* (HE, 10x), scale bar = 10 μm

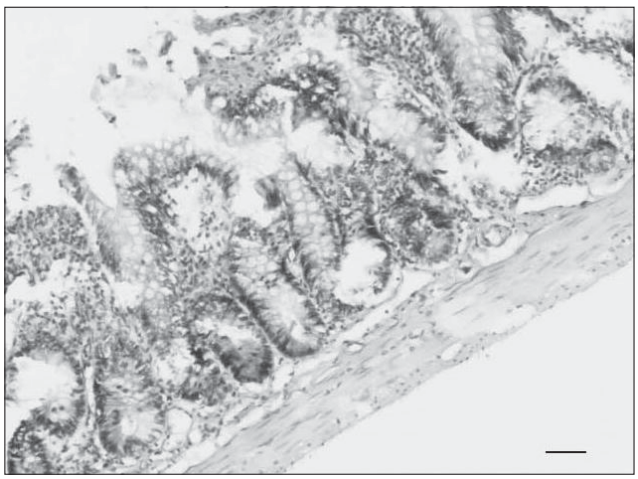


Figure 7. Histological section of the small intestine in T2-treated rat sacrificed on the 7th day shows necrosis of *the villi intestinales* (HE, 10x), scale bar = 10 μm

changes were seen in *the tunica mucosa* of the ileum that covers the lymphatic tissue of rats sacrificed on the 7th day after treatment (GDS = 5.0) (Figure 7, 8). Epithelial cells of villi intestinales were totally desquamated. Atrophic *villi intestinales* were rounded, finger-like, dendritic or papillomatous. In these areas Lieberkühn's crypts were enlarged and filled with necrotic glandular cells debris. Depletion of the lymphocytes was found in the lymphoid follicles of Payer's patches. Thickening of the blood vessels with vacuolation of the endothelial cells was observed. The most striking findings are the presence of diffuse hemorrhagic foci in *the tunica submucosa*. During the 4-week period in the gastrointestinal tract T-2 toxin caused diffuse epithelium deficit, erosions, ulcerations, hyperemia, transmural edema, atrophy of intestinal villi and cystic deformation of the stomach and the small intestine glands with diffuse accumulation of polymorphonuclear cells. The described pathohistological changes were less intensive in comparison with the poisoned group sacrificed on the 7th day of the study (GDS = 3.5) (Figure 8).

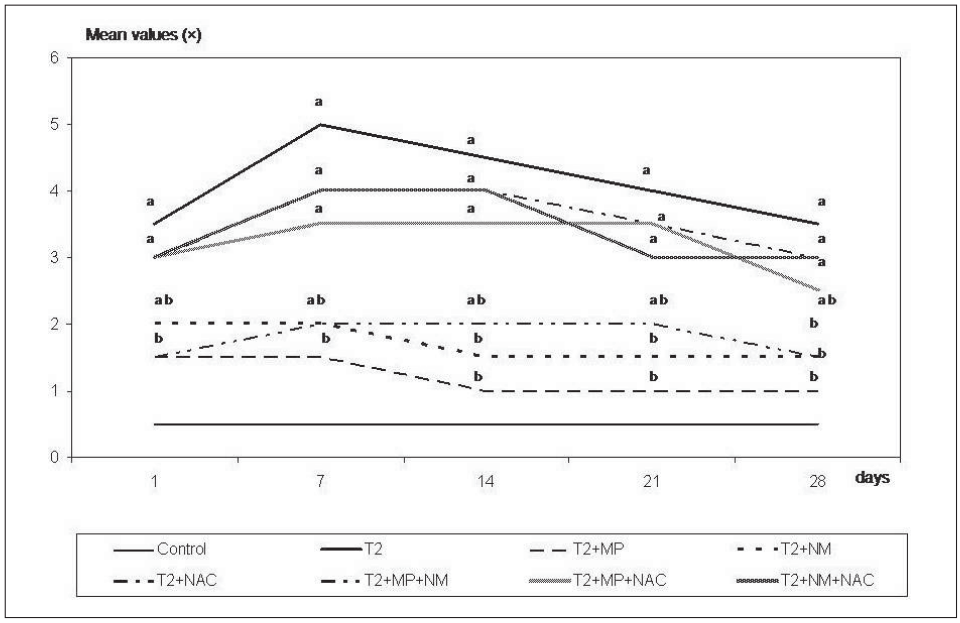


Figure 8. Influence of T2 or/and MP, NM, NAC on the gut damage scores (GDS) in rats (× ± SD)

Pathohistological analysis of the gut of rats treated with T-toxin and methylprednisolone, nimesulide or/and N-acetylcysteine

The histological changes observed from the gut section of these animals varied from intracellular edema to focal necrosis of epithelial cells and mild hemorrhagic infiltration. These areas were present in the focal part of *the tunica*

mucosa and some layers of *the tunica submucosa*. Dissolution and granularity of cytoplasm were observed in 50 percent of the stomach and small intestine. The minority of these cells were irregular, round to ovoid. However, a small number of

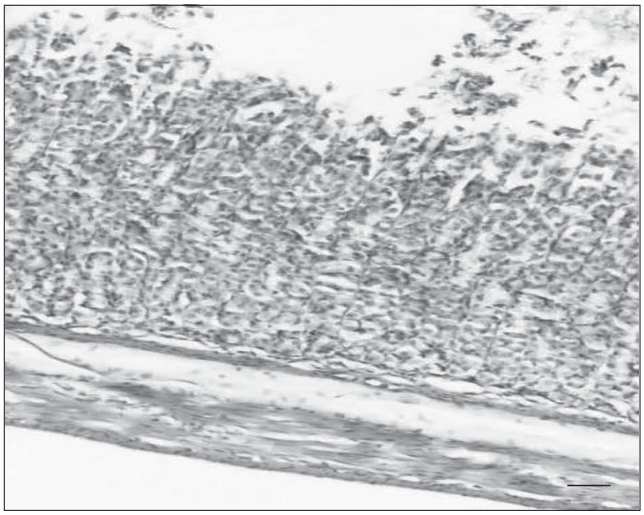


Figure 9. Histological section of the stomach in rats treated with T2 and MP + NM sacrificed on the 7th day shows hyperemia and edema of *the tunica mucosa* and *the tunica submucosa* (HE, 10x), scale bar = 10 μm

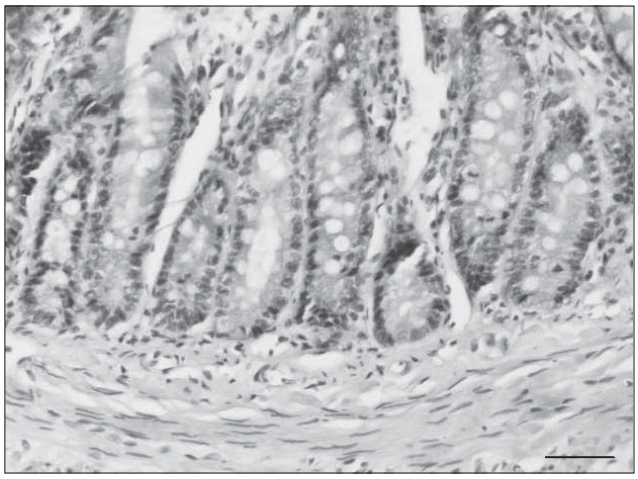


Figure 10. Histological section of the small intestine in rats treated with T2 and MP + NM sacrificed on the 7th day shows polymorphonuclear infiltration in the stroma of the *villi intestinales* (HE, 20x), scale bar = 10 μm

glandular cells with nuclear pleomorphism and large, round to rectangular shapes and prominent nucleoli could be seen. The presence of polymorphonuclear cell infiltration, diffuse hyperemia and hemorrhagic foci were more prominent in the poisoned group treated with NM or NAC, only. In the group of poisoned animals protected with MP or their combinations with NM and NAC

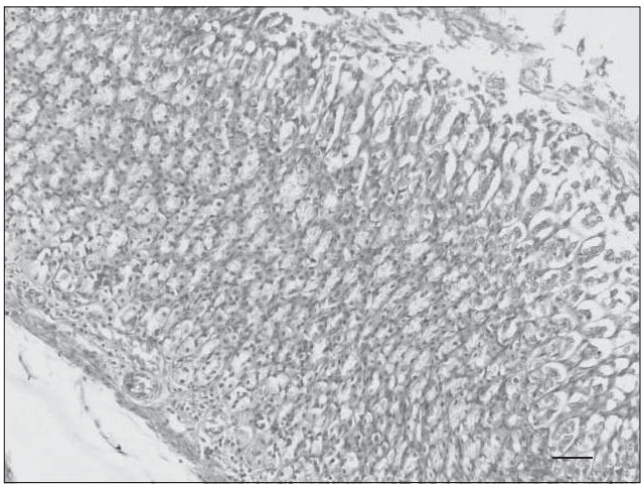


Figure 11. Histological section of the stomach in rats treated with T2 + MP sacrificed on the 7th day shows discreet edema of the stomach glands (HE, 10x), scale bar = 10 μm

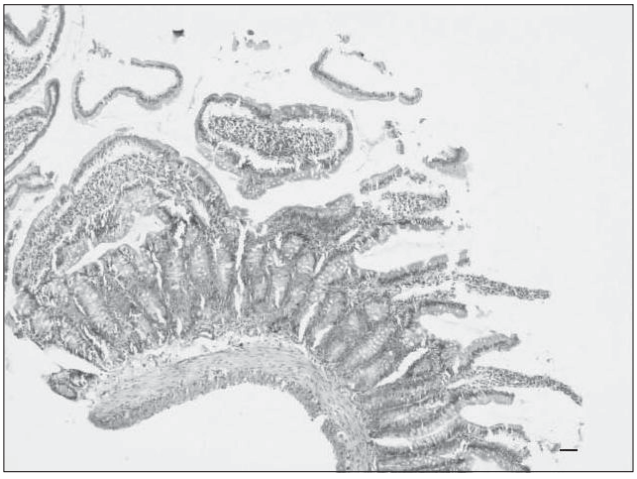


Figure 12. Histological section of the small intestine in rats treated with T2 + MP sacrificed on the 7th day shows a mild edema in *the tunica submucosa* (HE, 5x), scale bar = 10 μm

described histological changes were the smallest. After the 4-week period, the guts of rats treated with combination of MP and NM (Figure 9, 10) and especially MP alone (Figure 11, 12) had a histological structure similar to the control group (GDS=1.0) (Figure 4, 5, 8).

DISCUSSION

The experimental model adopted for this study was that described by Jaćević *et al*., 2001a; Jaćević *et al*., 2001b, and similarly to it, our current results have shown that a single injection of 0.23 mg/kg sc T-2 toxin produced sings of systemic toxicity in rats.

In the present study the first clinical sings of acute intoxication, such as: vomiting, cyanosis, decreased body surface temperature, lethargy and death of experimental animals have been registered by the end of the 2 hours after administration of T-2 toxin, only. Our own results, as well as others (Lorenzana *et al*., 1985a; Pang *et al*., 1988) support the statement that the pathogenesis of acute general toxicity is often multifunctional. In our experiments, the intensity of clinical symptoms did correlate with the degree of the alterations found in the gut.

Considering T-2 toxin general toxicity (Speijers and Speijers, 2004), one of the most important target organs in T-2 toxin poisoning is the digestive system (Jaćević *et al*., 2003). In our study, signs of inflammation, degeneration and rapid loss of normal cell architecture could be found in the stomach and the small intestine of T-2 toxin treated rats sacrificed after the end of day 1. Similar pathohistological alterations, small zones of mucosal necrosis and ulcerations with picnotic nuclei and karyorrhexis in the epithelial cells of the *tunica mucosa* and in the crypt cells of the small intestine, have been reported in the swine acute T-2 toxin poisoning (Weaver *et al*., 1978; Marrs *et al*., 1986), as well as in rats (Jaćević, 2006). T-2 toxin-induced histological alterations in the gut mucosa are not due to direct local effects, only (Schiefer and Hancock, 1984). These authors suggested that gross histological changes in the gut, combined with other characteristic changes of T-2 mycotoxicosis, imply that generalized radiomimetic effect might be induced by biliary excretion of the biologically active T-2 toxin metabolites.

If the disease lasted long enough (Sklan *et al*., 2003) - 28 days in our experiment - pathohistological changes in the gut of T-2 toxin-poisoned rats ranged from diffuse epithelium deficit, erosions, ulcerations, hyperemia, transmural edema, atrophy of villi intestinales, cystic deformation of the stomach and the small intestine glands with diffuse accumulation of polymorphonuclear cells. Thickening of the blood vessels with vacuolization of the endothelial cells was observed, too. It was suggest that T-2 mycotoxin may have a direct toxic effect on the capillaries and increase their permeability thus leading to diffuse infiltration with the mononuclear cells (Jaćević, 2001b; Jaćević, 2005).

In our experiments, the best protective effects were produced by the soluble form of methylprednisolone. The single administration of methylprednisolone significantly decreased the general toxic effects of T-2 toxin. In these gut sections histological changes observed varied from intracellular edema to focal necrosis of

the epithelial cells and mild hemorrhagic infiltration. These areas were present in the focal part of *the tunica mucosa* and some layers of *the tunica submucosa*. Although the degree of intensity and quality of these pathohistological changes was similar to the ones observed in the poisoned rats protected with methylprednisolone and their combinations with nimesulide and N-acetylcysteine described, but the intensity of these histological changes were stronger. These results corroborate the existence of the antidotal efficacy of prednisolone and dexamethasone in mice (Mutoh *et al*., 1988) and of dexamethasone in rats poisoned with T-2 toxin (Tremel *et al*., 1985). Our result is probably a consequence of the fact that even the soluble form of methylprednisolone acts long enough to cover the peak of the T-2 toxin harmful effects. Kown glucocorticoids inhibit both the early and the late manifestation of inflammation (Barnes and Adcock, 1993; Smith, 1996; Sugita-Konishi, 2001).

Single administration of nimesulide significantly decreased the toxic effects of T-2 toxin, too. N-acetylcysteine and its combination with methylprednisolone or nimesulide showed a mild increase in body weight gain, food and water consumption, as well as histological changes in the gut of rats support the facts that they have a complex role in protection of animals against T-2 toxin (Atroshi *et al*., 2000; Dannhardt and Kiefer, 2001).

As it is well known, among the nonsteroidal anti-inflammatory drugs (NSAIDs), NM is a selective COX-2 inhibitor. The dose and route of NM administration employed in this experiment was in accordance with the literature data (Gupta *et al*., 1999; Wallace *et al*., 1999). Since an attempt to use a COX-2 selective antidotal dose of 5-10 mg/kg NM (Wallace *et al*., 1999) failed, it implies that COX-2 is not a pathway important for the pathophysiology of T-2 toxicosis. On the other hand, N-acetylcysteine (NAC), the acetylated derivative of the amino acid L-cysteine, is an excellent source of sulfhydryl (SH) groups, and is converted in the body into metabolites capable of stimulating glutathione (GSH) synthesis, promoting detoxification, and acting directly as free radical scavengers (Kelly, 1998). Free radical damage initially induced by T-2 mycotoxins can be propagated and magnified by lipid peroxidation chain reactions (Rizzo *et al*., 1994). Although some differences could be seen among the three antidotal regimens investigated. The therapeutic mechanism of these drugs is different and often multifunctional, as well as the pro-inflammatory mechanism of T-2 toxin (Meky *et al*., 2001).

This result is probably a consequence of the fact that methylprednisolone acts long enough to cover the peak of the T-2 toxin harmful effects. On the other hand, nimesulide and N-acetylcysteine does start to act soon enough to counteract the first T-2 toxin-induced manifestation of poisoning, but not the later ones. However, this choice could be important for the treatment of repeated or subacute poisonings.

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Address for correspondence:
Vesna Jaćević, DVM., PhD, pathologist, assistant professor
Department for experimental toxicology and pharmacology
Institute for toxicology and pharmacology
National Poison Control Centre
Military Medical Academy
Crnotravska 17
11000 Belgrade, Serbia
E-mail: petmedic@net.yu

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Jaćević Vesna *et al.*: Gastroprotective effects of novel
antidotal combination in rats acutely poisoned by T-2 toxin

GASTROPROTEKTIVNI EFEKAT NOVIH ANTIDOTSKIH KOMBINACIJA KOD PACOVA AKUTNO TROVANIH T-2 TOKSINOM

JAĆEVIĆ VESNA, RESANOVIĆ RADMILA, BOČAROV-STANČIĆ ALEKSANDRA, ĐORĐEVIĆ SNEŽANA, DRAGOJEVIĆ-SIMIĆ VIKTORIJA, VUKAJLOVIĆ ANA i BOKONJIĆ D

SADRŽAJ

Cilj ovog rada je bio da se ispitaju efekti metilprednizolona (solubilni oblik, Lemod-solu®), nimesulida, N-acetilcisteina (Fluimucil®) i njihovih kombinacija kod pacova tretiranih sa 1,0 LD_{50} (0,23 mg/kg) trihotecenskog mikotoksina T-2. Antidotski efekat je ispitivan praćenjem njihovog uticaja na opšte stanje, 24-voro časovno preživljavanje, telesnu masu, potrošnju hrane i vode i patohistološke promene u digestivnom traktu tokom 4 nedelje, kod pacova, soj Wistar, kojima je jednokratno aplikovan T-2 toksin. Najveći zaštitni efekat ispoljio je metilprednizolon (2,43). Gubitak telesne mase, tokom prvih 7 dana ustanovljen je samo u T-2 toksin grupi. Tokom čitavog eksperimenta, u grupama trovanih pacova koji su štićeni metilprednizolonom ili metilprednizolonom i nimesulidom, ustanovljeno je značajno povećanje ($p<0,001$) telesne mase, potrošnje hrane i vode, u poređenju sa T-2 toksin gropom. Na kraju ispitivanog perioda, N-acetilcistein, nimesulid i njihova kombinacija obezbedili su takođe porast ($p<0,05$) telesne mase, potrošnje hrane i vode u poređenju sa T-2 toksin grupom. Znaci hemoragične dijateze i nekroza epitelnih žlezdica digestivnog trakta uočeni su u T-2 toksin grupi. Blage histološke promene bile su prisutne u digestivnom traktu trovanih pacova tretiranih nimesulidom, N-acetilcisteinom i njihovom kombinacijom. Histološka građa digestivnog trakta trovanih pacova koji su štićeni metilprednizolonom i nimesulidom, a posebno sa metilprednizolonom bila je slična kao u kontrolnoj grupi. Prikazani rezultati jasno ukazuju da je metilprednizolon, dobro poznat anti-inflamatorni i imunosupresivni lek, ispoljio najbolji zaštitni efekat kod pacova akutno trovanih T-2 toksinom.