CROATICA CHEMICA ACTA
CCACAA **78** (3) 441–446 (2005)

ISSN-0011-1643
CCA-3033
Original Scientific Paper

Olive and Corn Oil Enriched Diets as Modulators of Mineral Content in the Submandibular Gland during Liver Regeneration*

Čedomila Milin,[a,] Marin Tota,[a] Robert Domitrović,[a] Radojka Pantović,[a] Jasminka Giacometti,[a] Mira Ćuk,[b] Ines Mrakovčić-Šutić,[b] Hrvoje Jakovac,[b] and Biserka Radošević-Stašić[b]**

[a]*Department of Chemistry and Biochemistry,*
[b]*Department of Physiology and Immunology, School of Medicine, University of Rijeka, HR-51000, Rijeka, Croatia*

RECEIVED NOVEMBER 26, 2004; REVISED JUNE 13, 2005; ACCEPTED JUNE 28, 2005

To estimate the role of the submandibular gland (SMG) in liver regeneration, i) the tissue mineral dynamics in SMG after 1/3 partial hepatectomy (pHx) and ii) the influence of olive (OO) and corn-oil (CO) enriched diets on these events were investigated. Different nutrition of BALB/c mice lasted 3 weeks, and the minerals in SMG were determined by microwave digestion and ICP spectrometry. The diet containing CO initially suppressed liver regeneration (after 24 h) and then, similarly to OO, increased liver growth (on day 7). In mice fed standard food, Zn^{2+} and Ca^{2+} accumulated in SMG and the concentration of Mg^{2+} decreased in the early phase of liver regeneration. These changes were, however, significantly less expressed in mice fed CO and OO enriched diets, suggesting that monounsaturated oleic acid (C18:1n-9) and polyunsaturated linoleic acid (C18:2n-6) might interfere with some metal-dependent activities of SMG that participate in the control of liver regeneration.

Keywords
olive and corn oil diets
submandibular gland
minerals
partial hepatectomy

INTRODUCTION

Liver regeneration that follows after partial hepatectomy (pHx) is a commonly used model for investigation of growth processes, during which the liver architecture remains intact and hepatocyte replication occurs in normal parenchyma.[1,2] The process is characterized by activation of a large number of genes, which are usually grouped into stages that correspond to the transition of hepatocytes from quiescence into the cell cycle (priming) and the progression of the committed hepatocyte through the G_1 phase to DNA replication and cell division.[3–5] Mediators such as tumor necrosis factor α (TNF-α) and interleukin 6 (IL-6) participate in the priming phase, while the progression through the cell cycle is driven by the hepatocyte growth factor (HGF) and transforming growth factor α (TGF-α). The termination phase is initiated by upregulation of TGF-β1 and activin, which suppress epithelial cell growth,[1–8] but the signals that precisely synchronize the start and the end of liver regeneration are still investigated.

These events are strongly influenced by tissue metals and metallothioneins,[9–15] as well as by the diets containing different quantities of mono-and polyunsaturated

* Dedicated to Professor Željko Kućan on the occasion of his 70th birthday. Presented at the Congress of the Croatian Society of Biochemistry and Molecular Biology, $HDBMB_{2004}$, Bjelolasica, Croatia, September 30 – October 2, 2004.

** Author to whom correspondence should be addressed. (E-mail: cedo@medri.hr)

fatty acids (MUFA and PUFA, respectively),[16–22] since they might be responsible for structural integrity and enzyme activities involved in transduction signals, transcription and replication of factors during cell proliferation and apoptosis. Contributing to this field, we previously reported on the activation of a zinc-dependent hepatothymic axis after pHx,[23] as well as on the additional hepatectomy-induced changes in concentrations of Zn^{2+}, Fe^{2+}, Mg^{2+} and Ca^{2+} in regenerating liver, thymus and spleen.[24] It the latter study, we reported also on the marked pHx-induced changes in the metal tissue dynamics at the level of the submandibular gland (SMG), suggesting that during liver regeneration these metals might be important regulators of exocrine and endocrine functions of salivatory glands. The latter finding was not too unexpected owing to the presence of a large body of evidence demonstrating that SMG is a crucial part of the cervical sympathetic trunk-submandibular gland neuroendocrine axis, involved in maintaining systemic homeostasis after tissue damage, inflammation and other »stress conditions«,[25–29] as well as owing to the fact that SMGs are the main source of the epidermal growth factor (EGF) and other growth factors involved in the control of liver regeneration.[1–8,30–33] To our knowledge, however, no previous experimental evidence showing the effects of pHx on metals tissue dynamics of the salivary gland has been reported. In an attempt to extend our knowledge about the regulatory effects of metals on SMG functions during liver regeneration, in the present study we investigated the influence of diets containing different quantities of mono-and polyunsaturated fatty acids (MUFA and PUFA, respectively) on these events, because of their known influence on oxidative stress and lipid peroxidation, matrix metalloproteinases, signal transduction pathways, cytokine production, *etc*.[16–22]

The data showed that the dynamics of tissue metals in SMG was sensitive to diets enriched with olive and corn, indicating the participation of MUFA and PUFA in this control.

EXPERIMENTAL

Animals

Mice of BALB/c strains, aged 2–3 months, were used in the experiment. They were housed in groups 6–8, kept under standard conditions and exposed to a natural day-night cycle. Animals were bred and maintained according to the »Guide for Care and Use of Laboratory Animals« (NIH, 1996), and the ethical committee for handling laboratory animals of the School of Medicine, University of Rijeka, approved the study.

Feeding Procedure

During the three research weeks, animals were fed standard laboratory pellets or diets enriched with olive or corn oil (5 g addition to 100 g of standard pellet), containing predominantly oleic acid (C18:1n-9) or linoleic acid (C18:2n-6), respectively.

Partial Hepatectomy

Under ether anesthesia, mice were subjected to 1/3 pHx after removal of the median liver lobe. To avoid possible diurnal variability, all operations were performed between 8:00 – 9:00 a.m. Animals were sacrificed by bleeding on days 1, 2, 7 and 15 after pHx and compensatory liver growth was calculated from the wet and dry weights of the remaining and removed liver.

Tissue Sample Preparations for Liberalization

The submandibular gland of mice sacrificed by exsanguinations was carefully removed using plastic instrumentation. Tissue samples were selected and prepared as previously described.[34] Briefly, 20–50 mg of the SMG was dried at 105 °C for 5 hours. After that, 3 ml of conc. HNO_3 (»Kemika« d.d., Zagreb, Croatia) and 0.5 ml of 30 % H_2O_2 (»Kemika« d.d., Zagreb, Croatia) were added. Microwave digestion occurred in the MLS – 1200 Mega, Microwave Digestion System with MDR Technology, under the following conditions: 5 min at 300 W, 30 s at »zero« W, 5 min at 600 W and 1 min of ventilation. After cooling for 15 min, samples were transferred into flasks and filled with distilled/demineralizated water to the mark of 10 ml.

Inductively Coupled Plasma Spectrometry (ICP)

Liquid samples were introduced into the apparatus by pneumatic nebulization, which is the most popular way because of its desirable characteristics (relatively good stability, rapid change-over and no memory effects with specificity in operation). Measurements were performed using a PHILIPS PU 7000-ICP Spectrometer, by the ASTM D 19756-91 method (power 1 kW, coolant 12 L/min, nebulizer 38 psi) and a wavelength of 213.856 nm. Single zinc standard (Merck, Darmstadt) of 1000 ppm was diluted to obtain appropriate standard concentrations. Lower detection limit was 0.05 ppm and r.s.d. was 3 %.

Statistical Analysis

The data were analyzed using the Sigma Plot Scientific Graphing System, Version 8.0. Statistical significance was calculated by two-tailed Student's t-test for unpaired samples. Data are reported as mean +/– SEM. The results were considered statistically significant at $p<0.05$.

RESULTS

Changes in Liver Regeneration Induced by Olive and Corn Oil Enriched Diets

Partial hepatectomy in the control mice provoked a very fast growth of the liver remnant in the first 24 h, increasing the regenerating index, calculated as the ratio of the

remaining to removed liver mass, to 2.75 (Figure 1). A new increase of liver mass was observed again in the interval between postoperative (p.o.) days 7 and 15, when the regenerating index reached the value of 4.4. The corn oil enriched diet significantly decreased the early phase of liver regeneration, ($p<0.001$), but on p.o. day 7 increased regenerating indices were noticed ($p<0.001$) in mice fed both experimental diets.

Changes in Tissue Dynamics of Zinc, Calcium, Magnesium and Iron in the Submandibular Gland Induced by pHx and by Diets

Submandibular gland masses were found to be unaffected by pHx and either type of diet (Figure 1), but marked changes were observed in the tissue metal content in SMG (Figure 2). In mice fed standard diet during liver regeneration, concentrations of Ca^{2+} ($p<0.001$) and Zn^{2+} ($p<0.01$) went up, while that of Mg^{2+} decreased ($p<0.01$). Changes lasted until the p.o. day 7 and then returned to the initial values. Both diets influenced this dynamics, diminishing the accumulation of Zn^{2+} and Fe^{2+} (from p.o. days 1–7), and after the p.o. day 2 also the accumulation of Ca^{2+}. Some differences were also noticed between the effects of the two diets, since in corn-oil fed mice the initial values of Zn^{2+} and Fe^{2+} were changed even before pHx (time 0), while on the p.o. day 7 the inhibiting effects of olive-oil diet on Zn^{2+}, Ca^{2+}, and Fe^{2+} accumulation were more expressed. In contrast, after the olive-oil-enriched diet, higher accumulation of Mg^{2+} was recorded 48 h after pHx ($p<0.05$).

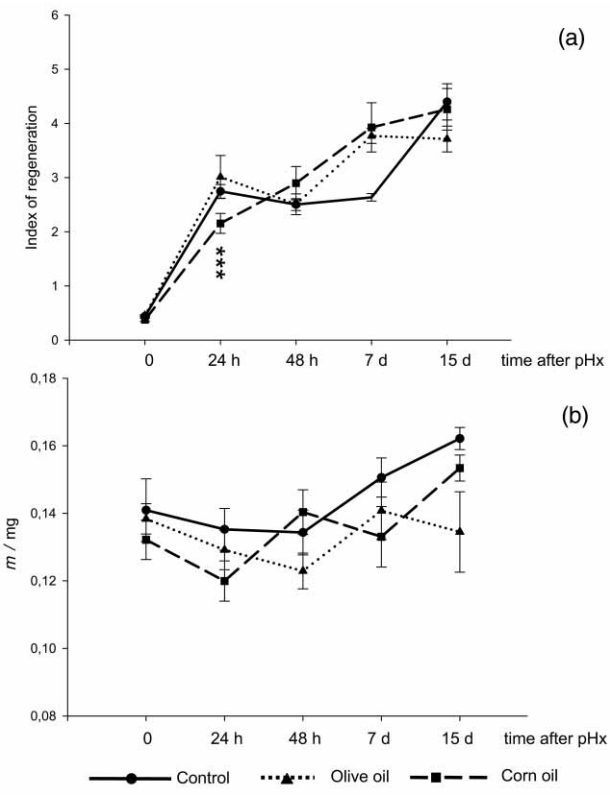

Figure 1. a) Dynamics of liver regeneration, presented as the regeneration index (calculated as the ratio of remaining liver mass to removed liver mass). b) Changes in wet masses of the submandibular gland in partially hepatectomized (pHx) mice fed different diets for 3 weeks before pHx. Data are mean ± SE of 4–6 mice. *** $p<0.001$.

DISCUSSION

The data show that metal tissue kinetics in SMG is markedly affected by pHx and additionally changed by olive and corn oil enriched diets, suggesting that the submandibular salivary glands have an active lipidic metabolism, which is sensitive to dietary fatty acid intake and local turnover of Zn^{2+}, Fe^{2+}, Ca^{2+} and Mg^{2+}. The complex relationship of the estimated metals,[9–15] as well as dietary lipids,[16–22] to almost all steps of cell biology allows, however, only speculation about the significance of our findings.

As a key organ in the neuro-immuno-regulatory network,[25–29] the SMGs play an integral role in physiological adaptations and contribute to the maintenance of systemic homeostasis, particularly under the 'stress conditions' seen during tissue damage and inflammation. Behaving as an endocrine gland, SMG produces and secretes a large number of physiologically active proteins and peptides, such as growth factors, homeostatic proteases, and regulatory peptides, which subserve a range of biologic functions not directly associated with the alimentary digestive system, indicating that they possess endocrine functions. Furthermore, the synthesis and release of these SMG-derived factors are regulated by hormonal and neural mechanisms,[25–29] which ensure a prompt response of SMG to various stressful stimuli.

Owing to the fact that they accumulate biologically active peptides and hormones, such as the epidermal growth factor (EGF), nerve growth factor (NGF), TGF-α, TGF-β and HGF,[25–33] it was suggested that the liver was a major target of factors released from the submandibular salivary glands. The existence of a proposed SMG-liver axis was especially evident in sialoadenectomized mice, which showed a transient wave of apoptosis in the liver, followed by alterations in cellularity, and delayed liver regeneration.[35–37]

It may be also relevant for our data that EGF, secreted from SMG, might affect the adipose tissue development and lipolysis stimulated by isoproterenol and glucagon, interfering with the signal transduction between lipolytic hormone receptors and adenylate cyclase.[38] Further, the evidence showed that the fatty acid composition of the submandibular salivary gland and synthesis of a great variety of its lipids might be strongly dependent on the dietary intake of PUFA, which were in this way able to modulate the growth of salivary gland tumors.[39]

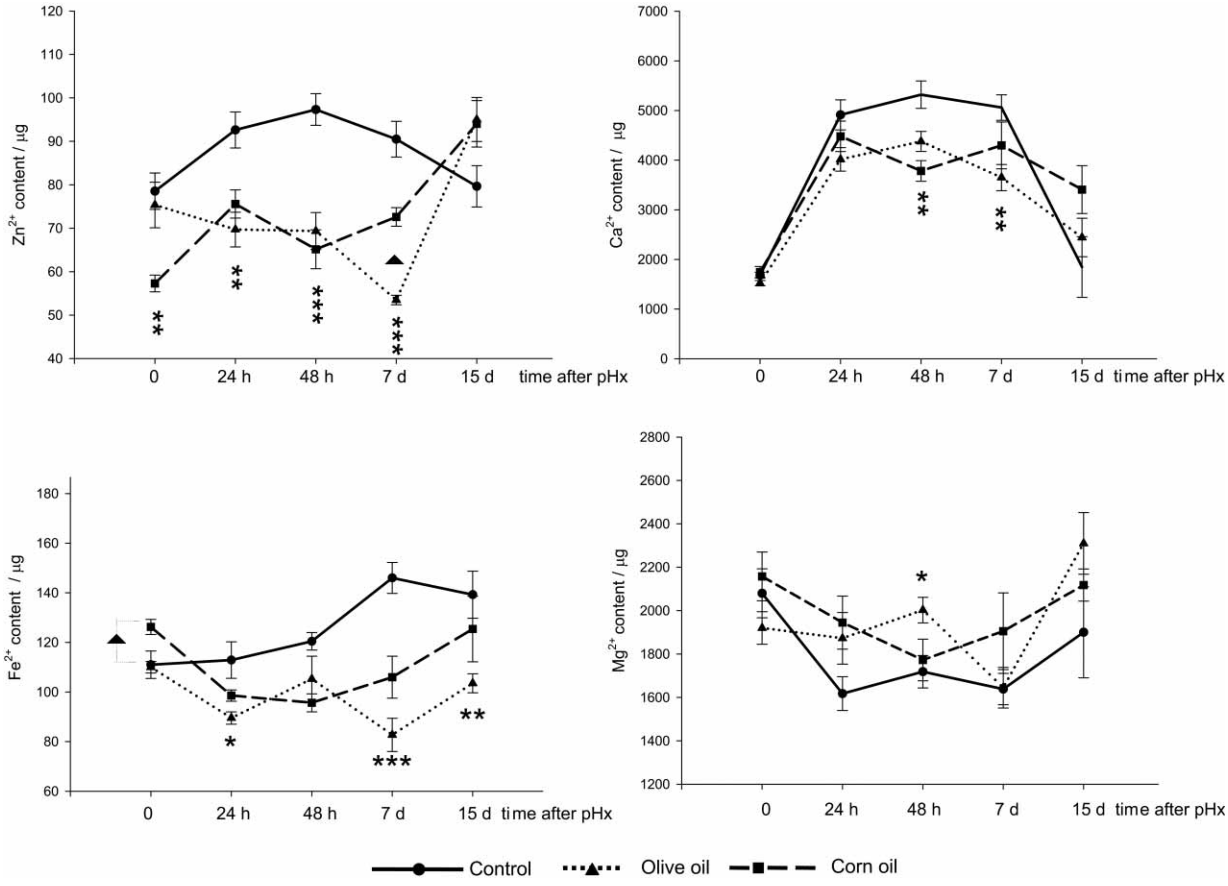

Figure 2. Metal tissue content in the submandibular gland of pHx mice fed the standard diet or diets enriched with olive (OO) or corn oil (CO) for 3 weeks before pHx. Data are mean ± SE of 4–6 mice. *** $p<0.00$; ** $p<0.01$; * $p<0.05$ (compared to the control group); ▲$p<0.05$ (comparison between the OO and CO fed groups).

The herein presented data show that dietary intake of MUFA or PUFA may modulate also the tissue dynamics of several trace metals in SMG after pHx, indicating that some of their effects might be Zn^{2+}, Fe^{2+}, Mg^{2+} or Ca^{2+}-dependent.

Namely, supporting the extensive literature data of the effects of trace elements on all aspects of cell biology,[9–15] our data showed that liver regeneration was followed by marked changes in the SMG mineral content, emphasizing the regulatory role of Zn^{2+}, Ca^{2+}, Fe^{2+} and Mg^{2+} for the processes activated by pHx.[24] Thus, as presented in Figure 2, immediately after pHx, an initial increase in the concentrations of Zn^{2+} and Ca^{2+} and a decrease in the Mg^{2+} content was found in the control group of mice, suggesting that these metals influenced the production or release of factors involved in the initiation of liver growth. However, as recently reported,[24] in the late phase of liver regeneration in mice fed the standard diet, highly significant negative correlations were found between the concentrations of Zn^{2+}, Fe^{2+}, Ca^{2+} and Mg^{2+} in SMG and the index of liver growth, indicating that these metals participated also in reestablishment of new morphostasis after pHx. Since marked changes in metal tissue kinetics were simultaneously visible also in the regenerating liver, thymus and spleen, we hypothesized that these interconnected changes occurred as a consequence of the breakdown of tolerance to self antigens and/or activation of cytokine and growth-dependent pathways after pHx,[24] in which an important role might be that of the metallothionein (MT) gene induction by stress mediators, or by EGF or TGF-α, which were able to induce MT gene expression in cultured rat hepatocytes in parallel with DNA synthesis.[9,3,40–47]

As presented here, olive and corn-oil enriched diets, containing oleic acid (C18:1, ϖ-9 MUFA) and linoleic acid (C18:2, ϖ-6 PUFA), respectively, additionally changed the SMG mineral content. Thus, the corn-oil enriched diet significantly diminished the early phase of liver regeneration, while both diets increased the regeneration indexes on the p.o. day 7 (Figure 1). Simultaneously, both types of diet markedly diminished the accumulation of Zn^{2+}, and Fe^{2+} and Ca^{2+} and increased the early accumulation of Mg^{2+} in SMG after pHx (Figure 2), pointing to interconnection between the metabolism of metals and fatty acids in SMS and supporting the extensive evidence of the modulation of cellular activities by nutrients.[9–19,36–43]

Mechanisms by which MUFA and PUFA affect the metal tissue dynamics in SMG during liver regeneration are, however, still unclear, since they might be connected with the effects of dietary fats on the tissue fatty-acid composition in SMG, as well as by direct and indirect effects of both FA and trace metals on immune and inflammatory responses, activated by pHx. Thus, dietary FA incorporated into membrane lipids can change membrane fluidity and affect intercellular interactions, receptor expression, nutrient transport, as well as the signal transduction pathways regulated by several metal-containing enzymes.[48,49] Further, the concentration and composition of dietary fat (FA and cholesterol) can alter the serum-lipoprotein profile, as well as the eicosanoids production, which influence the numerous activities of innate and adaptive immunity.[16–22] In general, eicosanoids derived from ϖ-3 PUFA are less potent mediators of inflammation than those derived from arachidonic acid (C20:4, ϖ-6) or linoleic acid (C18:2, ϖ-6), but increased PUFA intake increases also the oxidative stress, which can cause lipid peroxidation and modulate a number of genes involved in the inflammatory response, including those encoding for TNF-α, IL-lα, IL-1β, IL-6, and PDGF. Additionally, dietary fatty acids and their oxidation products are ligands for the peroxysome proliferator-activated receptors, and nuclear transcription factors, which regulate a variety of anabolic and catabolic functions in different cell types.[16–22,45–47]

Since tissue metals are involved in almost all steps of the cited mechanisms, acting as cofactors for enzymes, having the central or modulatory role in their activities, as well as in structural stabilization and functional regulation of numerous transcription factors involved in cell proliferation and apoptosis,[9–15,36–50] it is obvious that regulatory pathways exerted by the olive and corn oil enriched diet in our experiments might involve very different mechanisms, which include a series of events related to activation of SMG itself, but also to participation of other regulatory factors in the neuroendocrine-immune circuit activated during liver regeneration.[9,13,25–29,51]

Regardless of the unknown mechanisms of actions, we would like to conclude that our data emphasize that pHx induces significant and interconnected changes in the tissue concentrations of Zn^{2+}, Fe^{2+}, Ca^{2+} and Mg^{2+} in SMG, which might be additionally modulated by olive and corn enriched diets, indicating participation of the salivatory gland in the control of growth and regulatory effects of micronutrients and MUFA and PUFA in this organ.

Acknowledgements. – This work was supported by grants from the Croatian Ministry of Science (projects No. 0062002 and 0062018).

REFERENCES

1. N. Fausto, A. D. Laird, and E. M. Webber, *FASEB J.* **9** (1995) 1527–1536.
2. G. K. Michalopoulos and M. C. DeFrances, *Science* **276** (1997) 60–66.
3. B. A. Haber, K. L. Mohn, R. H. Diamond, and R. Taub, *J. Clin. Invest.* **91** (1993) 1319–1326.
4. A. M. Diehl and R. M. Rai, *FASEB J.* **10** (1996) 215–227.
5. E. M. Webber, J. Bruix, R. H. Pierce, and N. Fausto, *Hepatology* **28** (1998) 1226–1234.
6. N. Fausto, *Hepatology* **39** (2004) 477–487.
7. J. H. Albrecht and L. K. Hansen, *Cell. Growth Differ.* **10** (1999) 397–404.
8. D. B. Stolz, W. M. Mars, B. E. Petersen, T. H. Kim, and G. K. Michalopoulos, *Cancer Res.* **59** (1999) 3954–3960.
9. E. Mocchegiani, D. Verbanac, L. Santarelli, A. Tibaldi, M. Muzzioli, B. Radošević-Stašić, and Č. Milin, *Life Sci.* **61** (1997) 1125–1145.
10. L. Rink and P. Gabriel, *Proc. Nutr. Soc.* **59** (2000) 541–552.
11. P. J. Fraker and L. E. King, *Annu. Rev. Nutr.* **24** (2004) 277–298.
12. A. S. Prasad, *Met. Ions Biol. Syst.* **41** (2004) 103–137.
13. E. Mocchegiani, R. Giacconi, E. Muti, C. Rogo, M. Bracci, M. Muzzioli, C. Cipriano, and M. Malavolta, *Ann. N.Y. Acad. Sci.* **1019** (2004) 127–134.
14. M. D. Lastra, R. Pastelin, A. Camacho, B. Monroy, and A. E. Aguilar, *J. Trace Elem. Med. Biol.* **15** (2001) 5–10.
15. H. Tapiero and K. D. Tew, *Biomed. Pharmacother.* **57** (2003) 399–411.
16. D. S. Kelley, *Nutrition* **17** (2001) 669–673.
17. R. F. Grimble, *Proc. Nutr. Soc*. **60** (2001) 389–397.
18. R. F. Grimble, *Nutrition* **14** (1998) 634–640.
19. P. Evans and B. Halliwell, *Br. J. Nutr.* **85** (2001) S67–74.
20. D. Hwang, *FASEB J.* **3** (1989), 2052–2061.
21. H. Tapiero, G. N. Ba, P. Couvreur, and K. D. Tew, *Biomed. Pharmacother.* **56** (2002) 215–222.
22. P. C. Calder and R. F. Grimble, *Eur. J. Clin. Nutr.* **56** (2002) S14–19.
23. Č. Milin, B. Radošević-Stašić, D. Verbanac, R. Domitrović, M. Petković, M. Ćuk, Z. Trobonjača, J. Varljen, and D. Rukavina, *Croat. Chem. Acta.* **68** (1995) 559–567.
24. Č. Milin, M. Tota, R. Domitrović, J. Giacometti, R. Pantović, M. Ćuk, I. Mrakovčić-Šutić, H. Jakovac, and B. Radošević-Stašić, *Biol. Trace Elem. Res.* **107** (2005) 1–19.
25. M. Mori, Y. Takai, and M. Kunikata, *Acta Histochem. Cytochem.* **25** (1992) 325–341.
26. R. Mathison, J. S. Davison, and A. D. Befus, *Immunol. Today* **15** (1994) 527–532.
27. E. Sabbadini and I. Berczi, *Neuroimmunomodulation* **2** (1995) 184–202.
28. C. Rougeot, I. Rosinski-Chupin, R. Mathison, and F. Rougeon, *Peptides* **21** (2000) 443–455.
29. O. Amano and S. Iseki, *Anat. Sci. Int.* **76** (2001) 201–212.
30. P. Skov Olsen, S. Boesby, P. Kirkegaard, K. Therkelsen, T. Almdal, S. S. Poulsen, and E. Nexo, *Hepatology* **8** (1988) 992–996.
31. S. Noguchi, Y. Ohba, and T. Oka, *J. Endocrinol.* **128** (1991) 425–431.
32. M. Jo, D. B. Stolz, J. E. Esplen, K. Dorko, G. K. Michalopoulos, and S. C. Strom, *J. Biol. Chem.* **275** (2000) 8806–8811.

33. J. L. Cruise, S. J. Knechtle, R. R. Bollinger, C. Kuhn, and G. K. Michalopoulos, *Hepatology* **7** (1987) 1189–1194.
34. D. Verbanac, Č. Milin, R. Domitrović, J. Giacometti, R. Pantović, and Z. Ciganj, *Biol. Trace Elem. Res*. **57** (1997) 91–96.
35. I. Buira, E. Poch, O. Sanchez, G. Fernandez-Varo, M. Grau, F. Tebar, I. Ramirez, and M. Soley, *J. Cell Physiol.* **198** (2004) 12–21.
36. D. E. Jones Jr., R. Tran-Patterson, D.-M. Cui, D. Davin, K. P. Estell, and D. M. Miller, *Am. J. Physiol. Gastrointest. Liver. Physiol.* **268** (1995) G872–G878.
37. L. Lambotte, A. Saliez, S. Triest, D. Maiter, A. Baranski, A. Barker, and B. Li, *Hepatology* **25** (1997) 607–612.
38. F. Tebar, I. Ramirez, and M. Soley, *J. Biol. Chem.* **268** (1993) 17199–17204.
39. A. B Actis, C. B. López, S. Joekes, and A. R. Eynard, *Prostaglandins, Leukotrienes and Essential Fatty Acids* **61** (1999) 259–265.
40. P. Moffat and F. Denizeau, *Drug Metabolism Rev.* **29** (1997) 261–307.
41. C. O. Simpkins, *Cell. Mol. Biol.* **46** (2000) 465–488.
42. W. Maret, C. Jacob, B. L. Vallee, and E. H. Fischer, *Proc. Natl. Acad. Sci. USA.* **96** (1999) 1936–1940.
43. J. Zeng, R. Heuchel, W. Schaffner, and J. H. Kagi, *FEBS Lett.* **279** (1991) 310–312.
44. R. Shimoda, W. E. Achanzar, W. Qu, T. Nagamine, H. Takagi, M. Mori, and M. P. Waalkes. *Toxicol. Sci.* **73** (2003) 294–300.
45. M. Sato, M. Sasaki, and H. Hojo, *Metallothionein III*, Birkhaüser Verlag, Basel, 1993, p. 125.
46. A. Molotkov, N. Nishimura, M. Satoh, and C. Tohyama, *Life Sci.* **66** (2000) 963–970.
47. E. Mocchegiani, R. Giacconi, C. Cipriano, M. Muzzioli, N. Gasparini, R. Moresi, R. Stecconi, H. Suzuki, E. Cavalieri, and E. Mariani, *Exp. Gerontol.* **37** (2002) 349–357.
48. C. Kerkhoff, T. Vogl, W. Nacken, C. Sopalla, and C. Sorg, *FEBS Lett.* **460** (1999) 134–138.
49. T. Dudev and C. Lim, *Chem. Rev.* **103** (2003) 773–788.
50. M. P. Vaquero, *J. Nutr. Health Aging* **6** (2002) 147–153.
51. R. Giacconi, C. Cipriano, M. Muzzioli, N. Gasparini, F. Orlando, and E. Mocchegiani, *Mech. Ageing Dev.* **124** (2003) 371–378.

SAŽETAK

Modulacijsko djelovanje prehrane maslinovim i kukuruznim uljem na sadržaj minerala u submandibularnoj žlijezdi nakon parcijalne hepatektomije

Čedomila Milin, Marin Tota, Robert Domitrović, Radojka Pantović, Jasminka Giacometti, Mira Ćuk, Ines Mrakovčić-Šutić, Hrvoje Jakovac i Biserka Radošević-Stašić

Istražujući ulogu submandibularne žlijezde (SMG, submandibular gland) u regeneraciji jetre ispitivali smo: 1) dinamiku promjena u koncentracijama minerala u tkivu SMG nakon 1/3 parcijalne hepatektomije (pHx) i 2) učinke dijeta s većim sadržajem maslinovoga (OO, olive oil) i kukuruznoga ulja (CO, corn oil) na ove procese. BALB/c miševi hranjeni su različitim dijetama tijekom 3 tjedna, a minerali u SMG određivali su se mikrovalnom digestijom i ICP spektrometrijom. Dijeta obogaćena CO smanjivala je početnu fazu regeneracije jetre (nakon 24 h), a obje dijete povećavale su rast jetre nakon 7 dana. U kontrolnih miševa u ranoj fazi regeneracije jetre u SMG nakupljali su se Zn^{2+} i Ca^{2+}, a smanjivala se koncentracija Mg^{2+}. Ove promjene bile su značajno manje izražene u miševa hranjenih CO i OO-dijetama, pa je pretpostavljeno da oleinska (C18:1n-9) i linolna (C18:2n-6) masna kiselina utječu na određene, o metalima ovisne, putove kojima SMG sudjeluje u kontroli regeneracije jetre.