Iodine concentrations in porcine blood, urine, and tissues after a single dose of iodised oil

I. HERZIG, B. PÍSAŘÍKOVÁ, I. DIBLÍKOVÁ, P. SUCHÝ

Veterinary Research Institute, Brno, Czech Republic.

ABSTRACT: Experimental groups of pigs were treated orally with 120 mg (Group O 120), or 480 mg (Group O 480) of iodine per animal, or intramuscularly with 240 mg (Group I 240) of iodine per animal. Iodine was administered in the form of iodised fatty acid esters (IFAE). The treatment resulted in significantly increased iodine concentrations in tissues and a single dose was sufficient to meet the requirement for the whole fattening period (180 days). Urinary iodine concentrations in all the experimental groups were higher than in the control group C receiving iodine only from conventional feed. Urinary excretion of iodine between days 2 and 5 was more distinctive in orally treated than in intramuscularly treated animals (Figure 1). Iodine concentrations at the end of the fattening period (day 180) were higher in the treated than in the control groups. The treatment effect was more marked in Groups O 480 and I 240 than in Group O 120. The dynamics of blood serum iodine concentrations was similar to urinary concentrations (Figure 2). Mean thyroid gland weights in the groups O 120, O 480, I 240, and C were 9.19, 8.51, 7.10, and 12.01 g, respectively. An opposite tendency was observed for iodine concentrations in thyroid gland dry matter (Figure 3). No effects of any of the treatments on total protein, albumin, total lipids, or cholesterol concentrations in blood serum were observed. Group C showed lower tissue iodine concentrations than any of the experimental groups. The only exception was hepatic tissue in which approximately the same iodine concentrations were found in all the groups. Data obtained in Groups O 120, O 480, and I 240 indicate that decisive for tissue concentrations was rather the dose of iodine than the route of administration. Iodine is stored above all in the thyroid gland and adipose tissue. As can be seen in Figure 4, its concentration was higher in muscles with a higher proportion of fat (neck) than in lean muscles (ham). ***For free full paper in pdf format see http://www.vri.cz/vetmed.asp***

Keywords: Lipiodol® UF; muscular and lipid tissues; thyroid gland; triiodothyronine; thyroxine; total protein; albumin; total lipids; cholesterol

INTRODUCTION

Low iodine intake and/or utilisation result in hypothyroidism manifested by health disorders which can be further aggravated by factors affecting iodine utilisation, such as strumigens. Strumigens can either reduce the amount of iodine utilisable by the thyroid gland, or affect iodine metabolism (McDowell, 1992; Pennington, 1988).

In the last decade, the conventional prophylaxis of human iodopoenia with potassium iodide in endemic iodine-deficient areas has been progressively replaced by oral or intramuscular administration of iodised fatty acid esters (IFAE) (Bourrinet *et al*., 1997; Delange, 1996; Zimmermann *et al*., 2000, and others). Todd and Dunn (1998) consider iodised salt and oil as the most effective means of prophylaxis of iodine deficiency.

The major benefit of IFAE is their long-term action after a single oral or intramuscular administration. Oral treatment is simpler, but its effect persists for a shorter period (Bourrinet *et al*., 1997; Furnee *et al*., 1995). Elnagar *et al*. (1995) demonstrated that the effect of single oral dose of IFAE containing 200 mg of iodine administered to adult humans persisted for one year. Mean efficacy period in children treated with IFAE containing 490 mg of iodine was 13.7 weeks when administered as a single dose and 9.9 weeks when the dose was split into halves. The effect of a single dose of triacyl glycerol fatty acid esters containing 675 mg of iodine persisted for 52.5 weeks. Dose splitting had no effect on retention and elimination of iodised oils and did not increase the treatment effect (Furnee *et al*., 1995).

Data on iodine concentrations in animal tissues and on the use of iodised oils in animals are rather scarce. Oral dose of 10 mg of iodine per 1 kg of pigs body weight resulted in a rapid increase of blood iodine concentration culminating during several days after the treatment and persisting for 2.5 months. Maximum io-

Supported by Ministry of Agriculture of the Czech Republic (Grants No. EP 9195 and No. M-03-99-01).

dine concentrations in blood serum of sheep given the same dose intramuscularly were observed on day 25 and the return to initial values after 5 months. Maximum concentrations in orally treated animals were reached within 17 days and a decrease was observed after 1.5 months (Chambon and Chastin, 1993). Azuolas and Caple (1984) demonstrated significantly higher milk iodine concentrations 16 months after a single intramuscular administration of 1 ml of iodised oil. Transplacental transfer of iodine and iodine secretion in milk was demonstrated in pregnant rabbits treated with iodised oil (Bourrinet *et al*., 1997).

Iodine concentration in animal food products can be effectively regulated by iodine intake from feeds. In mammals, approximately 80% of the total iodine amount is contained in the thyroid gland and the rest in soft tissues, particularly muscles and liver (Downer *et al*., 1981). Kaufmann and Rambeck (1998), who fed pigs a diet containing 30 mg of iodine per 1 kg, found higher concentrations of iodine in kidneys than in the liver, heart and muscles. No data on iodine concentrations in tissues of animals treated with IFAE were found in available literature.

The objective of the experiment was to establish whether a single oral or intramuscular administration of IFAE will meet the requirement of pigs for iodine for the whole fattening period and to identify tissues in which the treatment results in increased iodine concentrations.

MATERIAL AND METHODS

Animals

Twenty-four castrated male White Large × Landrace crosses with a mean body weight of 15.0 ± 2.62 were divided into four groups of six. During the experimental period, all the pigs were fed a diet without iodine supplementation, consisting of wheat (69.3%) barley (20.0%), extracted soybean meal (10.0%), dicalcium phosphate (0.5%), and iodine-free feeding salt (0.2%). Nutrients in the diet and its components (Table 1) were determined by methods laid down in the Czech Standard ČSN 46 7092 (1986) and Regulation No. 222/1996 of the Ministry of Agriculture of the Czech Republic. The pigs were fed twice a day (at 07.00 and 16.00) and the amounts of consumed feed were recorded on each feeding.

Iodine preparation and design of experiment

Six untreated pigs were used as the control group C. The pigs of group O 120 received a single oral dose of IFAE (Lipiodol® Ultra Fluid, Byk Gulden, France) containing 120 mg of iodine. The doses was contained in gelatine capsules and mixed with a small amount of feed. Group O 480 was given orally 480 mg of iodine per animal in the same way, and Group I 240 was treated intramuscularly with a single dose of 240 mg of iodine in IFAE. The experiments were carried out in the facilities of Veterinary Research Institute, Brno and principles of experiments on animals, laid down by Regulation No. 194/1996 of the Ministry of Agriculture of the Czech Republic, were strictly observed.

Table 1. Contens of nutrients, metabolisable energy and iodine per 1 kg of feed

	Feed – dry matter	
	original	absolute
Dry matter (g)	877.0	1 000.0
Crude protein (g)	183.2	208.9
Fat (g)	15.7	17.9
Fibre (g)	25.7	29.3
Ash (g)	29.9	34.1
NFE (g)	622.5	709.8
Organic matter (g)	847.1	965.9
TDN (g)	772.2	880.5
MEp (MJ)	13.57	15.47
Iodine (mg)	0.100	0.114

Urinary samples

Samples were collected on day 0 (before administration of IFAE), and daily during five four-day balance periods starting on days 2, 36, 66, 128, and 180. The pigs were kept in metabolic cages and urine was collected into calibrated vessels. Daily volumes of excreted urine were measured and daily means and means for each period were calculated. Iodine concentrations were determined in aliquots of pooled urine for each period.

Blood samples

Samples were collected from the jugular vein on day 0 and on the last day of each balance period.

Tissue samples

Samples of muscular (neck, ham), adipose (abdominal and back fat), and hepatic tissues, skin and the thyroid gland were collected after slaughter on day 180 of the experiment.

Analysis

All the samples were processed by dry alkaline ashing at 600°C and iodine concentrations were determined spectrophotometrically by the method of Sandell-Kolthoff (Bednář *et al*., 1964). The principle of the meth-

od, by which total inorganic and protein-bound iodine is determined, consists in iodine-catalysed reduction of Ce^{4+} to Ce^{3+} in the presence of As^{3+}. Blood serum samples were tested for total protein, cholesterol, and total lipid concentrations using the Bio-La sets (Lachema, Brno, Czech Republic), albumin concentration by the method of Dvořák (1981), and triiodothyronine (T_3) and thyroxine (T_4) by radioimmunoanalysis (Humalab, Košice, Slovakia). Specific gravity of urine was determined. The results were processed using the statistical and graphic software STAT Plus (Matoušková *et al*., 1992).

RESULTS AND DISCUSSION

Iodine concentrations in urine and blood serum and selected parameters of homeostasis were monitored in groups of swine after a single oral or parenteral administration of iodised oils. The monitoring was concluded by determination of iodine concentrations in selected tissues after slaughter.

Urinary iodine concentrations

During the first balance period (days 2–5), the urinary iodine concentrations were highly significantly higher ($P < 0.01$) in the experimental than in the control groups. The effect was more distinctive in Groups O 120 and O 480 than in Group I 240. The subsequent balance periods were characterised by a progressive decrease in urinary iodine concentrations which was again more distinctive in Groups O 120, and O 480. At the end of the experiment (day 180), urinary iodine concentrations in all the experimental groups (41 µg/l for O 120, 164 µg/l for O 480, and 148 µg/l for I 240) were higher than in the control group (18 µg/l). The difference was more distinctive in Groups I 240 and O 480 (Figure 1).

Due to the significant correlation between iodine intake and excretion, urinary iodine concentration is the most accurate indicator of biological availability of dietary iodine and of the iodine status of the organism (Phillips *et al*., 1988; Furnee *et al*., 1995; Herzig *et al*., 1996; Ingenbleek *et al*., 1997). The rate of urinary iodine excretion after oral intake depends on many factors including the iodised oil type, goitre, infection by intestinal parasites, sex, amount of adipose tissue, season, and feeding of cassava (Furnee, 1997; Furnee *et al*., 1997). In lactating females, a considerable amount of iodine is excreted in milk.

Blood serum iodine concentration

The dynamics of iodine concentrations in blood serum was similar to that found in urine. Control pigs showed very low concentrations indicative of an insufficient intake of dietary iodine throughout the experimental period (Figure 2). Well balanced concentrations were found in Group I 240. The results have confirmed the assumption that a single intramuscular or a higher oral dose of IFES can ensure an appropriate iodine status for the whole fattening period. This conclusion is consistent with the data of Chambon and Chastin (1993),

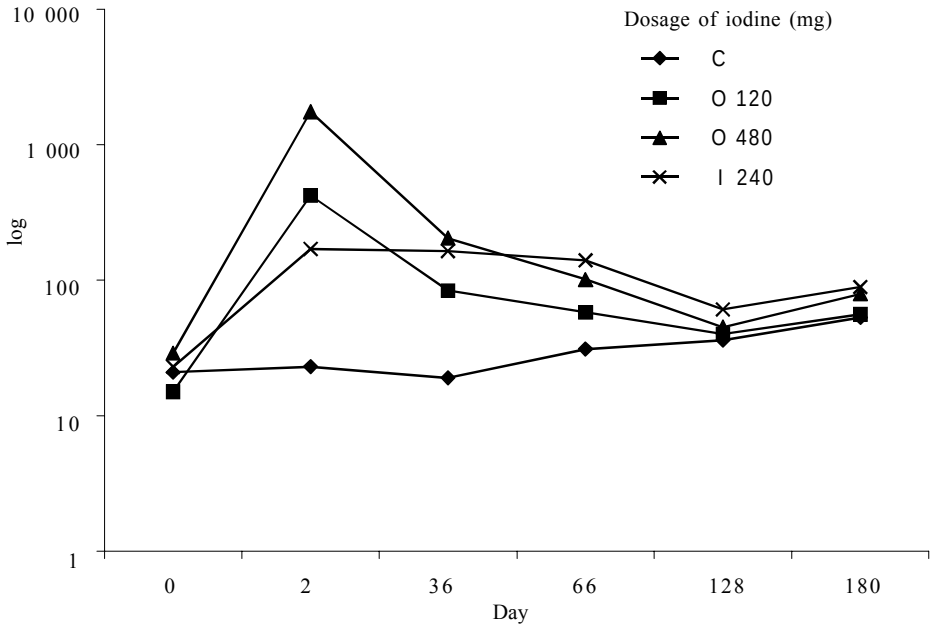

Figure 1. Urinary iodine concentrations in pigs

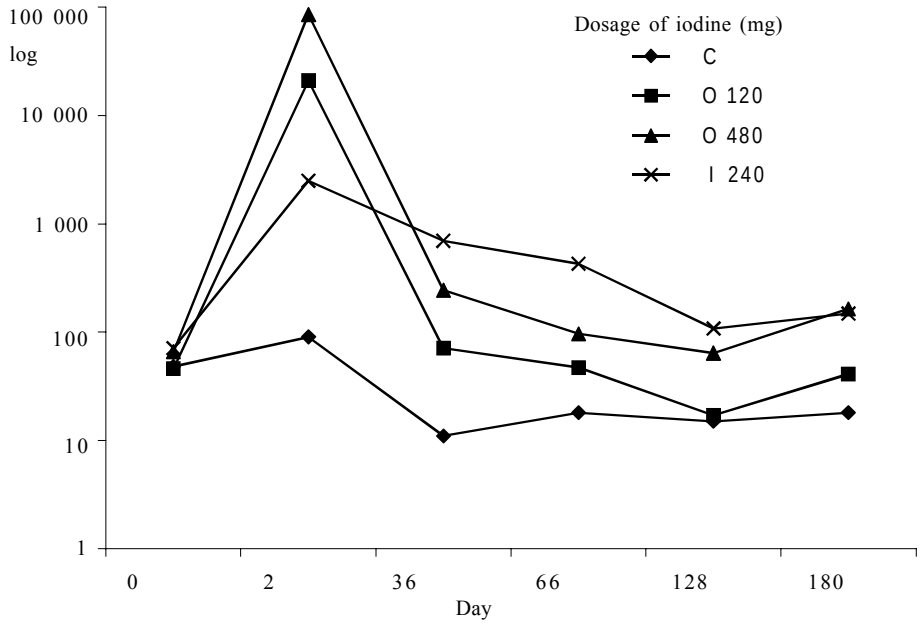

Figure 2. Blood serum iodine concentrations in pigs

who found increased blood serum iodine concentrations in pigs persisting for 2.5 months.

Thyroid gland hormones and parameters of homeostasis

Variations of T_3 concentrations throughout the experimental period were approximately the same in all the groups and no significant difference was demonstrable between the control and the experimental groups. T_4 concentrations began to increase almost linearly in all the experimental groups on day 128 from 6.5 to 52.4 nmol per l. At the end of the experiment (day 180) the concentrations were lower than in the preceding period. The very low concentrations in the control group (6.3 to 19.8 nmol/l) were indicative of iodine deficiency.

The administration of IFAE had no effect on concentrations of total proteins, albumin, total lipids, or cholesterol in blood serum. Total protein and albumin concentrations rose regularly up to day 180 from 54.4 to 69.4 g/l and from 13.0 to 20.8 g/l, respectively. Total lipid concentrations decreased moderately from day 0 to day 36 and then increased up to day 180 from 3.5 to 3.6 g/l. The same tendency was observed for cholesterol (from 2.3 to 3.2 nmol/l). No significant differences were found either between the control and any of the experimental groups or between the experimental groups. None of the concentrations exceeded the respective reference range (Tlučhoř, 2001).

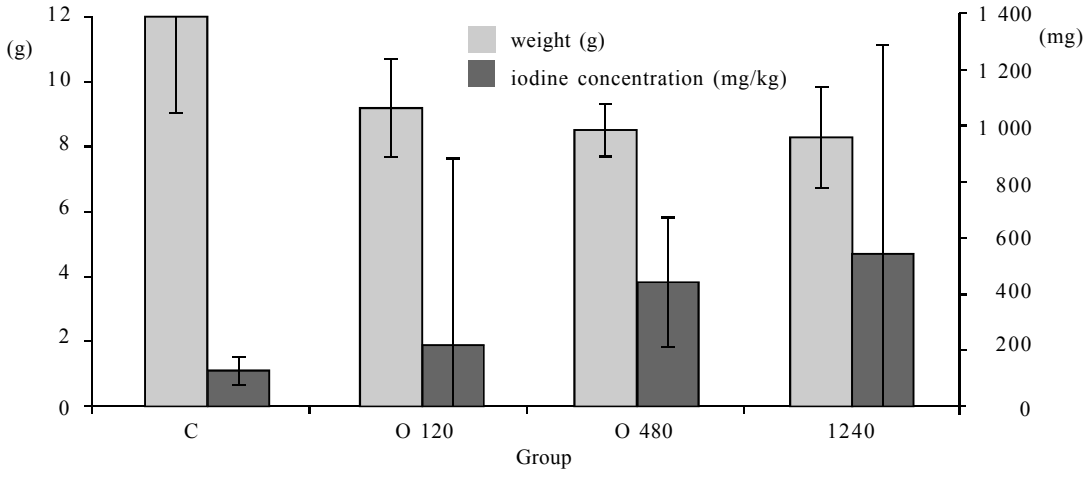

Figure 3. Thyroid gland weight and iodine concentration

Thyroid gland weight and iodine concentration

The highest mean thyroid gland weight was found in Group C (12.0 ± 2.97 g). The corresponding vales for Group O 120, O 480, and I 240 were 9.2 ± 1.50, 8.5 ± 0.81, and 8.3 ± 1.54 g, respectively (Figure 3). The values for Groups O 480 and I 240 were significantly ($P < 0.05$) lower than those for controls. Iodine concentrations in thyroid gland dry matter in Groups C, O 120, O 480, and I 240 were 127 ± 50 g/kg, 489 ± 665 g/kg, 442 ± 231 g/kg, and 742 ± 520 g/kg, respectively.

Iodine concentrations in selected tissues after slaughter

Group C showed lower tissue iodine concentrations than any of the experimental groups (Figure 4). The only exception was hepatic tissue in which approximately the same iodine concentrations were found in all the groups. The hepatic tissue apparently does not rank among significant stores of iodine from iodised oils. Degradation products of thyroid hormones are excreted in bile. Data obtained in the experimental groups indicate that decisive for tissue concentrations was rather the dose of iodine than the route of administrations. The analyses were done to identify tissues from which iodine was released during the fattening period. The results indicate that the major iodine reservoirs are the thyroid gland and adipose tissue. This finding is also supported by differences in iodi-ne concentrations between muscles with higher proportions of fat (neck) and lean muscles (ham) (Table 2).

The natural source of iodine present in foods and feeds is soil. The results of a survey conducted by WHO have confirmed that Central Europe must be regarded as an area with endemic prevalence of goitre (Luckas, 1986). Due to the geological structure and distance from the sea, the iodine content in the soil in the Czech Re-

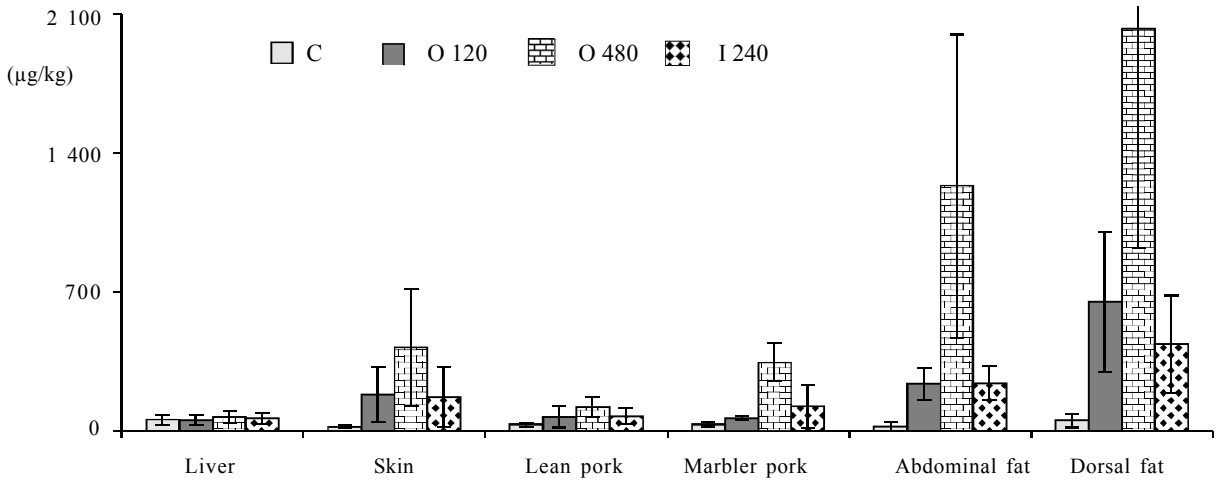

Figure 4. Iodine concentrations in selected porcine tissues

Table 2. Iodine concentrations in porcine tissues (µg/kg fresh tissue) on day 180 after administration of IFAE

Sample	Group			
	C (n = 6)	O 120 (n = 6)	O 480 (n = 6)	I 240 (n = 6)
Marbled pork (neck)	35 ± 12.6^{A}	65 ± 10.4^{A}	346 ± 94.6^{B}	125 ± 110.6^{A}
Lean pork (ham)	32 ± 9.7^{A}	70 ± 50.4	122 ± 51.3^{B}	75 ± 37.8
Liver	56 ± 25.9	55 ± 24.4	70 ± 31.3	64 ± 26.3
Dorsal fat	53 ± 35.0^{A}	651 ± 352.4^{A}	2 026 ± 1101.9^{B}	438 ± 245.6^{A}
Abdominal fat	23 ± 22.7^{A}	238 ± 79.4^{A}	1 236 ± 763.4^{B}	242 ± 84.5^{A}
Skin	21 ± 8.9^{a}	184 ± 136.9^{b}	421 ± 293.0^{b}	171 ± 149.6^{b}

The values designated by different small letters are significantly different ($P < 0.05$)
The values designated by different capitals are significantly highly different ($P < 0.01$)

public is insufficient for saturation of the food chain. Considering the mineralogical structure, the major part of the Czech Republic, composed of crystallite and volcanic rocks, is affected by moderate to distinctive iodine deficiency. Although iodine content in sedimented rocks is generally higher, in this case it is still insufficient. Therefore, the necessary level of iodine intake is ensured for the human population by salt iodisation and for the animal population by inclusion of iodine compounds into mineral supplements. However, salt consumption and thereby also iodine intake, are currently decreasing owing to the campaign against cardiovascular diseases. Much attention is paid to the enhancement of the thyroid gland function in foetuses and new-born babies by sufficient intake of iodine in pregnant and lactating women (Anonymous, 1996).

The demand for iodine in animals is further increased by the action of natural and anthropogenic goitrogenic factors. Much attention is paid in the Czech Republic to meet the demand for iodine in animal populations (Herzig *et al*., 1996, 1999, 2000; Kroupová *et al*., 1998; Kursa *et al*., 1997; 2000), because, apart from the effect on animal health, a low iodine concentration in foods of animal origin aggravates iodine deficiency in the human population.

REFERENCES

Anonymous (1996): Safe use of iodized oil to prevent iodine deficiency in pregnant women. WHO, Geneva. Bull. World. Health. Organ., *74*, 1–3.

Azuolas J.K., Caple I.W. (1984): The iodine status of grazing sheep as monitored by concentrations of iodine in milk. Aust. Vet. J., *61*, 223–227.

Bednář J., Röhling S., Vohnout, S. (1964): Příspěvek ke stanovení proteinového jodu v krevním séru. Českoslov. Farm., *13*, 203–209.

Bourrinet P., Dencausse A., Cochet P., Chastin I., Bonnemain B. (1997): Secretion in milk and transplacental transfer of two iodized oils, Lipiodol UFR® and Oriodol®, in rabbits. Biol. Neonate, *71*, 395–402.

Chambon C., Chastin I. (1993): Animal studies of iodized oils: Iodine disposition and physiological effects. In: Delang F. *et al*. (ed.): Iodine Deficiency in Europe. Plenum Press, New York. 159–165.

Delange F. (1996): Admistration of iodized oil during pregnancy: a summary of the published evidence. WHO, Geneva. Bull. World. Health. Organ., *74*, 101–108.

Downer J.V., Hemken R.W., Fox J.D., Bull L.J. (1981): Effect of dietary iodine on tissue iodine content of the bovine. J. Anim. Sci., *52*, 413–417.

Dvořák M. (1981): Stanovení koncentrace albuminu v krevní plasmě prasat s použitím bromkresolové zeleně. Vet. Med. (Praha), *26*, 481–489.

Elnagar B., Eltom M., Karlsson F.A., Ermans A.M., Gebre-Medhin M., Sourdoux P.P. (1995): The effects of different doses of oral iodized oil goiter size, urinary iodine, and thyroid-related hormones. J. Clin. Endocrinol. Metab., *80*, 891–897.

Furnee C.A. (1997): Prevention and control of iodine deficiency: A review of a study on the effectiveness of oral iodized oil in Malawi. Eur. J. Clin. Nutr., *51*, 9–10.

Furnee C.A., Pfan G.A., West C.E., van der Haar F., van der Heide D., Hautvast J.G. (1995): New model for describing urinary iodine excretion: its use for comparing different oral preparations of iodized oil. Am. J. Clin. Nutr., *61*, 1257–1262.

Furnee C.A., West C.E. Haar F., Hautvast J.G. (1997): Effect of intestinal parasite treatment on the efficacy of oral iodized oil for correcting iodine deficiency in schoolchildren. Am. J. Clin. Nutr., *66*, 1422–1427.

Herzig, I., Říha, J., Písaříková, B. (1996): Urinary iodine levels an intake indicator in dairy cows. Vet. Med. – Czech, *41*, 97–101.

Herzig I., Písaříková B., Kursa J., Říha J. (1999): Defined iodine intake and changes of its concentration in urine and milk of dairy cows. Vet. Med. – Czech, *44*, 35–40.

Herzig I., Písaříková B., Kursa J., Suchý P. (2000): Utilisation of iodine from different sources in pigs. Arch. Anim. Nutr., *55*, 179–189.

Ingenbleek Y., Jung L., Férard G., Bordet F., Goncalves A.M., Dechoux L. (1997): Iodised rapeseed oil for eradication of serve endemic goitre. Lancet, *350*, 1542–1545.

Kaufmann S., Rambeck W.A. (1998): Iodine supplementation in chicken, pig and cow feed. J. Anim. Physiol. Anim. Nutr., *80*, 147–152.

Kroupová V., Kratochvíl P., Kaufmann S., Kursa J., Trávníček J. (1998): Metabolická odezva aditivního příjmu jodu u nosnic. Vet. Med. – Czech, *43*, 207–212.

Kursa J., Herzig I., Kroupová V., Kratochvíl P., Trávníček J. (1997): Consequences of iodine deficiency in cattle in some regions of Czech Republic. Scientia Agric. Bohemica, *28*, 105–117.

Kursa J., Trávníček J., Rambeck W.A., Kroupová V., Vítovec J. (2000): Goitrogenic effects of extracted rapeseed meal and nitrates in sheep and their progeny. Vet. Med. – Czech, *45*, 129–140.

Luckas B. (1986): Nachweis und Bestimmung von Jod in speisesalzen durch Ionenpaar-Chromatografie. Dtsch. Lebensm. Rdsch., *82*, 357–361.

Matoušková O., Chalupa J., Cígler M., Hruška K. (1992): STAT Plus – Manual (in Czech). 1st ed. Veterinary Research Institute, Brno. 168 pp.

McDowell L.R. (1992): Iodine. In: Minerals in Animal and Human Nutrition. Academic Press, New York. 224–245.

Pennington J.A.T. (1988): Iodine. In: Smith K.T. (ed.): Trace Minerals in Foods. Marcel Dekker, New York. 249–289.

Phillips D.I., Lusty T.D., Osmond C., Church D. (1988): Iodine supplementation: comparison of oral or intramuscular iodized oil with oral potassium iodine. Int. J. Epidemiol., *17*, 142–147.

Tlučhoř V. (2001): Hodnocení biochemických výsledků ve veterinární medicíně z pohledu jedince a stáda. Krmivářství, *5*, 18–20.

Todd C.H., Dunn J.T. (1998): Intermittent oral administration of potassium iodine solution for the correction of iodine deficiency. Am. J. Clin. Nutr., *67*, 1279–1283.

Zimmermann M., Adou P., Torresani T., Zeder C., Hurrell R. (2000): Low dose oral iodized oil for control of iodine deficiency in children. Brit. J. Nutr., *84*, 139–141.

Czech Standard ČSN 46 7092, 1986.

Regulation No.194 of Ministry of Agriculture of Czech Republic, 1996.

Regulation No.222 of Ministry of Agriculture of Czech Republic, 1996.

Received: 01–08–02

Accepted after corrections: 01–08–27

Corresponding Author:

Doc. MVDr. Ivan Herzig, CSc., Veterinary Research Institute, Hudcova 70, 621 32 Brno, Czech Republic
Tel. +420 5 41 32 12 41, fax +420 5 41 32 12 29, e-mail: herzig@vri.cz