Effect of Goitrin on Iodine Absorption from the Gastrointestinal Tract of Chicks

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Abstract Effects of (—)-5-vinyl-2-oxazolidinethione (goitrin), a goitrogen in rapeseed, on iodine absorption from the gastrointestinal tract of the chicks were investigated, both *in vivo* and *in vitro*. A nonabsorbed marker technique (^{144}Ce) has been used to determine the net absorption and endogenous secretion of orally administered radioiodine. After 14 days feeding, secretion of iodine in the proventriculus and gizzard of the goitrin-fed chicks decreased and net absorption of iodine from jejuno-ileum increased as compared with the control chicks. Overall absorption of iodine in the diet was not depressed by prolonged administration of goitrin. On the other hand, it was proved that goitrin had a weak inhibitory action on iodine absorption from intestinal loops of lower jejuno-ileum of the chick *in situ* and from those of incubated *in vitro*. It therefore appears that metabolism of iodine in the goitrin-fed chicks was primarily affected by changes of thyroid function rather than by changes of iodine absorption from the gastrointestinal tract.

Iodine in the diet is absorbed from the gastrointestinal tract and then transported to the thyroid gland and utilized as an essential material for biosynthesis of thyroid hormone. In our previous reports^{1,2}, it has been confirmed that goitrin, a naturally occurring goitrogen in rapeseed, inhibits thyroid hormone biosynthesis and affects iodine metabolism in the chick. The objective of the experiment reported herein is to investigate the effects of goitrin on iodine absorption from the gastrointestinal tract of the chick.

Materials and Methods

Animal and diet: Single-Comb White Leghorn male chicks were fed a low-iodine diet (about 0.23 μg iodine/kg of diet) throughout the experiment. The diet was composed of yellow corn, 68; soybean meal, 17; alfalfa meal, 5; milk casein, 6; NaCl, 0.5; $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, 2.1; CaCO_3 , 1.4; vitamins and trace minerals, 0.1%.

Goitrogens and isotopes: Goitrin used in this experiment was prepared from rapeseed (*Brassica napus*) by the method of Astwood *et al.*⁵ Propylthiouracil (PTU) was purchased from Sigma Chemical Company, U.S.A. $^{144}\text{CeCl}_3$ was purchased from the Radiochemical Centre, England and Na^{125}I and Na^{131}I , from Dainabot RI Laboratory, Japan.

Experiment 1.

Iodine absorption and secretion in the gastrointestinal tract has been assessed by the use of ^{144}Ce as a reference substance. Chicks were fed the low-iodine diet containing 0.05% of goitrin or 0.0125% PTU from day-old and were simultaneously administered orally with ^{144}Ce

(4 μ Ci/day/bird) and ^{126}I (15 μ Ci/day/bird) for 4 days from 12th day of age. At the end of the experiment, chicks were killed by heart puncture and their gastrointestinal tracts were exposed. The duodenum was immediately divided into two segments and the jejuno-ileum was into five segments of equal length. The contents of each segment were removed by gentle manipulation and their radioactivity of ^{144}Ce and ^{126}I was counted in a well-type scintillation detector.

Experiment 2.

Iodine absorption from the intestinal loops *in situ* was determined by the method based on the report of CHUNG and VAN MIDDLESWORTH⁸¹. Each chick was anesthetized with ethylether and each 7 cm intestinal loop was prepared by tying two ligatures 8 cm apart. The loops of lower jejuno-ileum were irrigated with 5 ml saline solution. Radioiodine (^{131}I , 0.2 μ Ci) was injected into the loop with buffer solution. At the end of absorption period (1 hr), the intestinal loops were excised and the radioactivity remained in the loops was measured by a scintillation detector and calculated as follow;

$$\text{Absorption}(\%) = \frac{\text{Injected } ^{131}\text{I} - \text{Remained } ^{131}\text{I}}{\text{Injected } ^{131}\text{I}} \times 100$$

Experiment 3.

Iodine absorption from the intestinal loops was determined *in vitro* according to the report of WILSON and WISEMAN⁴¹. The jejuno-ileum was dissected and rinsed with saline solution containing 0.3% glucose. It was divided into 3 cm in length and each loop was ligatured at the both ends and then injected with buffer solution containing 0.01 μ Ci of ^{131}I , 0.01 mm of carrier iodine and 0.03% glucose. After weighing, the intestinal loops were incubated in 3 ml of KRP solution (pH 7.4) in 10 ml flasks which were kept at 37C in shaking water bath at approximately 100 oscillation per minute with O_2 as the gas phase. After incubation, intestinal loops were rinsed with small volume of buffer solution and weighed. Radioactivity in the inner liquid of each loop was measured and % of absorption was calculated.

Results

Experiment 1.

Average ratios of orally administered ^{126}I and ^{144}Ce in the gastrointestinal contents are shown in Fig. 1. ^{144}Ce is used as the reference and is assumed to move with the ingesta, to be uniformly mixed and to be unabsorbed. The values in Fig. 1, which are greater than 100% indicate net endogenous secretion and the values less than 100% indicate net absorption.

$$\begin{aligned} \text{Percent concentration } ^{126}\text{I} \text{ in sample in relation} &= \left(\frac{^{144}\text{Ce}}{^{126}\text{I}} \text{ diet} \right) \div \left(\frac{^{144}\text{Ce}}{^{126}\text{I}} \text{ section} \right) \times 100 \\ \text{to intake with } ^{144}\text{Ce} \text{ as a reference material} &= \left(\frac{\text{Ingesta } ^{126}\text{I}}{\text{Administered } ^{126}\text{I}} \% \right) \div \left(\frac{\text{Ingesta } ^{144}\text{Ce}}{\text{Administered } ^{144}\text{Ce}} \% \right) \times 100 \end{aligned}$$

From Fig. 1, it is apparent that there are net secretion of iodine in the proventriculus, gizzard and duodenum, and net absorption of iodine in the jejuno-ileum, colon and rectum. In the goitrogen administered chicks, ratios were decreased in sections from the proventriculus to duodenum as compared with those of the chicks in the control group. There were no marked differences between ratios in gastrointestinal tract in goitrin- and PTU-administered chicks except in the lower duodenum.

Experiment 2.

Iodine absorption (disappearance of ^{131}I from the intestinal loop) was relatively rapid and

Goitrin on Iodine Absorption

Fig. 1. Effect of goitrogen on average ratios of administered ^{125}I and ^{144}Ce (expressed as percentages) in the gastrointestinal contents of six chicks dosed ^{125}I and ^{144}Ce for four days. Vertical bars indicate standard deviation of the mean.

nearly 100% of the injected ^{131}I was disappeared from the loop within 2 hours. The effect of goitrin on iodine absorption for 1 hour was assessed in loops injected with ^{131}I and 5 mm of goitrin. Injection of goitrin significantly ($P < .01$) depressed the iodine absorption from the intestinal loops as shown in Table 1.

Experiment 3.

Radioiodine (^{131}I) absorption was increased as a function of the incubation time. Effect of goitrin on absorption of iodine from the intestinal loop *in vitro* was investigated in 1 hour incubation (Table 2). Injection of 2 mm goitrin into the loops depressed the iodine absorption to 75% and 50% of those of the control loops in chicks of 3 weeks and 7 weeks old, respectively.

Table 1. Effects of goitrin on absorption of iodine for 1 hour through the intestine of chicks with the loop technique

Addition	No of chicks	Absorption (%)
—	5	94.3 ± 3.4 ¹⁾
Goitrin 5 mm	5	85.7 ± 4.4*

¹⁾ Mean ± standard deviation

* Significant at the 1% level

Table 2. Effects of goitrin on absorption of iodine for 1 hour through the intestinal loops of chicks *in vitro*

Age (week)	Addition	No of chicks	Absorption (%/100 mg intestine)
3	—	4	29.0 ± 4.1
3	Goitrin 2 mm	4	21.3 ± 3.0*
7	—	4	18.8 ± 3.6
7	Goitrin 2 mm	3	8.8 ± 3.1*

* Significant at the 5% level

Discussion

There exist considerable literatures on iodine absorption in rats⁸⁻⁸⁾, but little work has been done on iodine absorption in chicks except of SHIBATA and IKEDA⁹⁾. It is clearly shown

in experiment 1 that the major site of iodine absorption in the chick is the lower jejuno-ileum and this is in agreement with the above report⁹⁾. It has been reported that orally administered ^{144}Ce was not absorbed from the intestine of cattle^{10,11)}, and chicks¹²⁾, and it was proved in this study that ^{144}Ce could be used as a nonabsorbed reference substance in chicks. No radioactivity was detected in the blood, muscle, liver and kidney of the chick after 2 days of daily oral administration of ^{144}Ce .

SHIBATA and IKEDA⁹⁾ reported that a little absorption of iodine was found in the proventriculus and gizzard of chicks. It is, however, considered that in the proventriculus and gizzard secretion of iodine exceeds absorption of iodine as clearly shown in Fig. 1. It is conceivable that elevated rate of secretion of iodine in the duodenum originated in greater amount of iodine secretion in bile. Phase of secretion and absorption of iodine in the gastrointestinal tract of the goitrogen administered chicks was clearly different from those in the control chicks. In our previous papers^{1,2)}, it was shown that overall metabolism of iodine was changed by prolonged feeding of goitrogen. Iodine seems to be absorbed relatively rapid in the chick since 90% of the injected ^{131}I was disappeared from the loop *in situ* in 1 hour after injection. Similar results were reported by SHIBATA and IKEDA⁹⁾. Injection of goitrin (5 mm and 2 mm) depressed the iodine absorption from the lower jejuno-ileum *in situ* and *in vitro*. It would be calculated that the concentration of goitrin (2-5 mm) administered in these experiments *in situ* and *in vitro* was approximately equivalent to the concentration of goitrin in the intestine when chicks were fed the diet containing 0.05-0.1% goitrin.

Referring to the effect of goitrogen on iodine absorption from the intestine, it has been reported that anion-type goitrogens, such as KClO_4 , KSCN and greater amount of KI , depressed the iodine absorption in rats^{8,7)}, and chicks⁹⁾. Furthermore, it has been reported that secretion of iodine into gastric juice was decreased by the administration of KClO_4 and KSCN in chicks¹³⁾, and methylthiouracil (MTU), a goitrogen which belongs to thion-amide drugs as goitrin, had no effect on iodine absorption in rats and in chicks⁹⁾. However effect of goitrin on iodine absorption has not yet been reported. In this experiment, it was ascertained that goitrin inhibits the iodine absorption from the intestine of chicks; but the difference in effects on iodine absorption between goitrin and MTU could not be interpreted clearly.

Overall percentage of net absorption of iodine could be estimated from the absorption coefficient in the colon in experiment 1. The absorption coefficients in the colon of both goitrin- and PTU-administered chicks were higher, but not significant, than those in the control chicks. This fact indicated that overall absorption of iodine was not depressed by prolonged administration of goitrogen. The above concept might be supported by our previous finding¹⁾ that the excretion of ^{131}I into the chick droppings was depressed by goitrin-feeding. In view of the above results, it may be suggested that the metabolism of iodine in goitrin-fed chicks was not primarily affected by changes of iodine absorption from the gastrointestinal tract.

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ニワトリ消化管におけるヨウ素吸収に対する Goitrin の影響

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菜種粕中に存在する抗甲状腺物質である(一)-5-Vinyl-2-oxazolidinethione (Goitrin) がヒナのヨウ素代謝に影響を与えることはすでに報告したので, ニワトリの消化管からのヨウ素の吸収に対する Goitrin の影響を白色レグホーン種雄ヒナを用いて検討した. Goitrin を14日間投与したヒナにおける放射性ヨウ素 (^{131}I) の吸収と排泄の様相を, 非吸収 Index として ^{144}Ce を用いて検討した. 腺胃・筋胃および十二指腸ではヨウ素の吸収よりも排泄が多く, 空回腸部で著しいヨウ素の吸収がみられた. Goitrin の投与により腺胃および筋胃へのヨウ素の排泄が減少し, 空回腸部におけるヨウ素の吸収が増加す

る傾向がみられたが, 飼料中ヨウ素のみかけの吸収率は Goitrin 投与で低下しなかった. ヒナの空回腸部の loop からのヨウ素 (^{131}I) の吸収を *in situ* および *in vitro* 培養条件下で測定した. いずれの条件下においても Goitrin (2 mm と 5 mm) はヨウ素の吸収を若干抑制することが確かめられた. したがって, Goitrin はヒナ消化管においてヨウ素吸収抑制作用を示すが, Goitrin 投与によるニワトリの体内ヨウ素代謝の変化は, 消化管におけるヨウ素の吸収に因るよりも, 主に甲状腺機能の変化に起因することが示唆された.