We have found a novel enzyme that exclusively decomposes selenocysteine into alanine and H₂Se in various mammalian tissues, and have named it selenocysteine lyase. The enzyme from pig liver has been purified to homogeneity. It has a molecular weight of approximately 85,000, and contains pyridoxal 5'-phosphate as a coenzyme. Its maximum reactivity is at about pH 9.0. Balance studies showed that 1 mol of selenocysteine is converted to equimolar amounts of alanine and H₂Se. The following amino acids are inert: L-cysteine, L-serine, L-cysteine sulfinate, selenocysteine, and L-ethyl-τ-l-selenocysteine, and L-selenohomocysteine. L-Cysteine (K_m, 1.0 mm) competes with τ-selenocysteine (K_m, 0.83 mm) to inhibit the enzyme reaction. The enzyme is the first proven enzyme that specifically acts on selenium compounds.

Selenium has been shown to be an essential micronutrient for mammals, birds, and several bacteria as reviewed by Stadtman (1) and Scott (2). The essentiality of selenium can be ascribed, at least partially, to the presence of enzymes that contain selenium as an integral component in these organisms. The selenium moiety of the following enzymes has been shown to be ascribed, at least partially, to the presence of enzymes that contain selenium as an integral component in these organisms: selenocysteine lyase, selenocystathionine γ-lyase, a-ketobutyrate reductase, and cystathionine β-synthase. Recent studies have shown that selenocysteine lyase from bovine liver catalyzes the reaction α-ketobutyrate + 2 H₂Se to L-lysine + L-cysteine. Selenocysteine lyase activity in the crude preparation of animal tissues was measured by determination of the homogenate system with a rat liver homogenate (7). During the course of study of these enzyme reactions, we have found that the far less efficient selenocysteine formation from the homogenate system is due to the presence of a novel enzyme in the homogenate system that decomposes specifically selenocysteine into alanine and H₂Se. All the enzymes acting on selenium compounds so far studied inherently act on sulfur compounds (1). We have named the novel enzyme selenocysteine lyase and have purified it to homogeneity from pig liver. We here describe distribution of the enzyme in mammalian tissues and the purification and properties of the pig liver enzyme.

**EXPERIMENTAL PROCEDURES**

**Materials**—S-L-selenocysteine (Sigma) was recrystallized from water to remove elemental selenium and some other contaminants. L-Selenocystathionine was synthesized as described previously (13). D-L-Selenocysteine was prepared from d-amino acid oxidase (Sigma), L-cysteine, and Na₂SeO₃. Alkaline dehydrase (EC 4.2.1.22) was prepared from hog kidney (14). S- and L-alanine and selenocysteines were purchased from Sigma; glutathione, Na₂SeO₃, and NaOH were from Aladdin, Tokyo, Japan. Cystathionine, L-homocysteine, L-homocystine, L-cystine, p-hydroxyphenylpyruvate, p-hydroxyphenylpyruvate aldolase, pyridoxal-5'-phosphate, pyridoxamine-5'-phosphate, and pyridoxamine-5'-phosphate deiminase were from Nakarai Chemicals, Kyoto. p-Hydroxyphenylpyruvate was prepared according to the method of Tietz et al. (15). The other chemicals were analytical grade reagents.

**Preparation of Cell-Free Extract**—The tissue extracts were prepared by homogenization of the frozen tissues at -4°C in 3 volumes of 0.25 M sucrose solution containing 5 mM potassium phosphate buffer (pH 7.4) and 0.1 mM EDTA. The homogenates were centrifuged at 40,000 × g for 20 min and the supernatant solution was dialyzed against 0.05 M potassium phosphate buffer (pH 7.4) containing 2 × 10⁻⁵ M pyridoxal-P and 0.1 mM EDTA.

**Assay of Selenocysteine Lyase**

All the reactions were performed in sealed tubes in which air was displaced by N₂. Substrates and selenium-containing compounds such as dL-selenocysteine were freshly prepared from the corresponding diselenides by reduction with 5 μl of diithiothreitol per ml of diselenide in 0.2 M Tricine/NaOH buffer (pH 8.5) or 0.2 M sodium pyrophosphate buffer (pH 8.5) and a cell-free extract. Selenocysteine or enzyme was omitted in a blank. After incubation at 37°C for 20 min, the reaction was terminated by addition of enzyme to the above solution.

**Method A:** Assay of Crude Tissue Preparation—Selenocysteine lyase activity in the crude preparation of animal tissues was measured by determination of the aspartate formed. The reaction mixture (final volume, 1.0 ml) contained 2 μmol of dL-selenocysteine, 5 μmol of diithiothreitol, 0.01 μmol of pyridoxal-P, 60 μmol of pyrophosphate buffer (pH 8.5), and a cell-free extract. Selenocysteine or enzyme was omitted in a blank. After incubation at 37°C for 20 min, the reaction was terminated by addition of 0.1 ml of 50% trichloroacetic acid, followed by centrifugation. An aliquot of the supernatant solution was subjected to amino acid analysis (see below).

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Selenocysteine Lyase

The reaction mixture contained 5 pmol of selenocysteine, 5 pmol of dithiothreitol, 0.01 pmol of pyridoxal-P, 0.02 mg of bovine serum albumin (Sigma), 60 pmol of Tricine/NaOH buffer (pH 8.5), and enzyme in a final volume of 0.5 ml. The purified selenocysteine lyase is labile when the protein concentration is low. Bovine serum albumin (0.02 mg/ml) effectively protects the enzyme from inactivation. After incubation at 37°C for 20 min, 3.5 ml of 5% lead acetate solution in 0.1 N HCl was added to the reaction mixture. Lead acetate solution gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used. M, Selenocysteine, L-selenohomocysteine, L-cysteine, and the other thiol compounds (2 pmol/m) of the reaction mixture gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used. M, Selenocysteine, L-selenohomocysteine, L-cysteine, and the other thiol compounds (2 pmol/m) of the reaction mixture gave no precipitate under the conditions.

The reaction mixture contained 5 pmol of dithiothreitol, 200 pmol of dithiothreitol, 0.01 mol of pyridoxal-P, 0.02 mg of bovine serum albumin (Sigma), 60 pmol of Tricine/NaOH buffer (pH 8.5), and enzyme in a final volume of 0.5 ml. The purified selenocysteine lyase is labile when the protein concentration is low. Bovine serum albumin (0.02 mg/ml) effectively protects the enzyme from inactivation. After incubation at 37°C for 20 min, 3.5 ml of 5% lead acetate solution in 0.1 N HCl was added to the reaction mixture. Lead acetate solution gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used. M, Selenocysteine, L-selenohomocysteine, L-cysteine, and the other thiol compounds (2 pmol/m) of the reaction mixture gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used.

Selenocysteine remaining in the reaction mixture of selenocysteine lyase was derivatized into Se-ethylselenocysteine with ethyl iodide. The reaction mixture contained 5 pmol of dithiothreitol, 2.80 × 10^{-6} mol of pyridoxal-P, and enzyme in a final volume of 0.5 ml. The purified selenocysteine lyase is labile when the protein concentration is low. Bovine serum albumin (0.02 mg/ml) effectively protects the enzyme from inactivation. After incubation at 37°C for 20 min, 3.5 ml of 5% lead acetate solution in 0.1 N HCl was added to the reaction mixture. Lead acetate solution gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used. M, Selenocysteine, L-selenohomocysteine, L-cysteine, and the other thiol compounds (2 pmol/m) of the reaction mixture gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used.

The reaction mixture contained 5 pmol of dithiothreitol, 200 pmol of dithiothreitol, 0.01 mol of pyridoxal-P, 0.02 mg of bovine serum albumin (Sigma), 60 pmol of Tricine/NaOH buffer (pH 8.5), and enzyme in a final volume of 0.5 ml. The purified selenocysteine lyase is labile when the protein concentration is low. Bovine serum albumin (0.02 mg/ml) effectively protects the enzyme from inactivation. After incubation at 37°C for 20 min, 3.5 ml of 5% lead acetate solution in 0.1 N HCl was added to the reaction mixture. Lead acetate solution gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used. M, Selenocysteine, L-selenohomocysteine, L-cysteine, and the other thiol compounds (2 pmol/m) of the reaction mixture gave no precipitate under the conditions. Elemental selenium (5 mg) also did not react with lead acetate under the acidic conditions used.
**RESULTS**

**Enzymatic Cleavage of Selenocysteine**

When DL-selenocysteine was incubated with a rat liver homogenate in the reaction mixture of Method A (see "Experimental Procedures"), the formation of alanine and H\textsubscript{2}Se was observed. H\textsubscript{2}Se was identified with 5,5'-dithiobis(2-nitrobenzoic acid) in a Thunberg tube containing the reaction mixture in the main compartment and a mixed solution (2 ml) of 20 \(\mu\)mol of 5,5'-dithiobis(2-nitrobenzoic acid) and 40 \(\mu\)mol of potassium phosphate buffer (pH 7.4) in the head compartment. After the tube was evacuated thoroughly, the reaction was started by tipping DL-selenocysteine into the main compartment and performed at 37 °C. The 5,5'-dithiobis(2-nitrobenzoic acid) solution in the head compartment was colored yellow \((\lambda_{max} 412 \text{ nm})\) after 3 h, indicating that volatile H\textsubscript{2}Se formed from selenocysteine reduced 5,5'-dithiobis(2-nitrobenzoic acid). The production of H\textsubscript{2}Se was also confirmed by the yellowish brown colloidal formation with lead acetate under the acidic conditions (see "Experimental Procedures"). After 8 h, the reaction was terminated by the addition of 0.1 ml of 50% trichloroacetic acid. Alanine produced in the reaction mixture was identified by amino acid analysis (retention time, 46.0 min) and gas chromatography of the N-heptafluorobutyryl n-propyl ester (retention time, 5.0 min). The mass spectrum of the N-heptafluorobutyryl n-propyl ester of the reaction product coincided with that of authentic alanine. We could not observe the alanine formation in the control experiments with boiled rat liver homogenate (boiled for 5 min), with water substituted for DL-selenocysteine, or with a rat liver homogenate and with L-cysteine for DL-selenocysteine.

Balance studies show that substantially equivalent amounts of alanine (0.93 pmol) and H\textsubscript{2}Se (1.04 pmol) are produced from DL-selenocysteine (2.0 pmol) with a rat liver homogenate (8.4 mg as protein) in the reaction mixture of Method B at 37 °C for 1 h. The alanine produced was reduced quantitatively with alanine dehydrogenase which specifically acts on L-alanine and H\textsubscript{2}Se. This reaction apparently is a reduction, and we mentioned briefly the enzyme as "selenocysteine reductase" in a previous paper (7). However, it is impossible to distinguish H\textsubscript{2}Se from Se\textsuperscript{6} by any available method containing the present reactants. The presence of reductants in the reaction system is required to make selenocysteine from selenocysteine, and to prevent selenocysteine from oxidation. Elemental selenium is reduced to H\textsubscript{2}Se by the reductants. In addition, selenocysteine, the substrate, serves also as a good reductant. Thus, we cannot decide whether H\textsubscript{2}Se or Se\textsuperscript{6} is the actual product of the enzyme reaction. We have tentatively termed the enzyme selenocysteine lyase. A possible systematic name of the enzyme is selenocysteine-hydrogen selenide-lyase (alanine-forming) or selenocysteine-selenium-lyase (alanine-forming).

**Selenocysteine Lyase Activity of Several Mammalian Tissues**

The selenocysteine lyase activity was found in several animal tissues when assayed by the production of alanine from selenocysteine (Method A) (Table I). We could not observe the formation of alanine from cysteine with all the rat tissues, bovine liver, and pig liver. We have also found that selenocysteine is \(a\beta\)-eliminated too slowly with the homogenates of the above mammalian tissues to affect the amount of alanine formed from selenocysteine (0–5% of the selenocysteine lyase reaction rate). Thus, the formation of alanine through a trituration of the reaction of selenocysteine and selenocysteine is not possible. We have found that selenocysteine lyase activities of livers and kidneys are generally higher than those of other tissues. Significant activity was also detected in the thymus, testis, and spleen of the individual.

**TABLE I**

| Tissues | Rat \(^a\) | Dog | Mouse | Guinea pig | Pig | Cat | Rabbit | Bovine | Monkey |
|---------|---------|-----|-------|------------|-----|-----|--------|--------|--------|
| Liver   | 5.5     | 10  | 9.7   | 15         | 8.2 | 1.6 | 17     | 3.5    | 9.9    |
| Kidney  | 4.9     | 4.5 | 8.9   | 14         | 3.6 | 1.9 | 17     |        |        |
| Pancreas| 8.0     |     | 3.0   | 0.21       |     |     |        |        |        |
| Adrenal | 3.5     |     |       |            |     |     |        |        |        |
| Heart   | 0.90    |     | 0.81  |            |     |     |        |        |        |
| Lung    | 2.0     |     | 1.2   |            |     |     |        |        |        |
| Testis  | 0.83    |     |       |            |     |     |        |        |        |
| Thymus  | 0.93    | 0.96|       |            |     |     |        |        |        |
| Spleen  | 1.7     |     | 6.0   |            |     |     |        |        |        |
| Muscle  | 1.4     |     | 1.8   |            |     |     |        |        |        |
| Fat     | 0.57    |     |       |            |     |     |        |        |        |
| Blood\(^b\) | 0   |     |       |            |     |     |        |        |        |

\(^a\) Average values of two rats are given. For the other animals, the values were obtained from the individual.

\(^b\) From whole blood was dialyzed against 0.01 M potassium phosphate buffer (pH 7.4). After centrifugation, the supernatant solution was examined.

**TABLE II**

| Purification of selenocysteine lyase | Step | Total protein mg | Total activity units | Specific activity units/mg | Yield %
|-------------------------------------|------|------------------|-----------------------|---------------------------|-------|
| 1. Crude extract                    | 651,000 | 13,600 | 0.021 | 100
| 2. Heat treatment                   | 271,000 | 7,300  | 0.027 | 54
| 3. Ammonium sulfate fractionation   | 103,000 | 6,290  | 0.061 | 46
| 4. DEAE-cellulose                   | 5,840  | 2,980 | 0.53  | 22
| 5. First hydroxyapatite             | 425    | 1,360 | 3.2   | 10
| 6. Second hydroxyapatite            | 240    | 1,210 | 5.0   | 9.0
| 7. Sephadex G-200                   | 27.2   | 635   | 23    | 4.7
| 8. Third hydroxyapatite             | 7.6    | 278   | 37    | 2.0

**Step 8: Third Hydroxyapatite Column Chromatography**—The enzyme solution was applied to a hydroxyapatite column (1.2 \(\times\) 13 cm) equilibrated with 0.01 M buffer. The enzyme was eluted with 0.04 M buffer at a flow rate of 0.4 ml/h. The active fractions were collected and concentrated by ultrafiltration.

**Activity Staining**

About 0.05 unit of the enzyme was subjected to disc gel electrophoresis by a modification of the procedure of Davis (19). After electrophoresis, the gel was soaked briefly with water and soaked in 5 mM lead acetate solution in 0.1 M HCl. Active protein bands were colored yellowish brown. Yellow precipitate due to the complex of diithiothreitol with lead acetate, which appeared on the gel surface, was rapidly diminished.

**Selenocysteine Lyase Activity in Various Mammalian Tissues**

The enzyme activity was measured by determination of alanine formed by amino acid analysis (Method A). The tissue extracts were prepared by centrifugation of the homogenates as described under "Experimental Procedures."
was found in rat pancreas, rat adrenal, and dog pancreas. However, no activity occurred in rat blood and rat fat. We have chosen pig liver for the purpose of purification of the enzyme in view of easy availability and abundance of enzyme activity.

Purification of Selenocysteine Lyase from Pig Liver

The pig liver enzyme was purified as described above and a summary of the purification is presented in Table II. About one-half of the enzyme activity was lost by heat treatment of the enzyme at 50 °C for 30 min (Step 2 of the purification), but this treatment was essential to perform the subsequent column chromatographies effectively. The purified enzyme, which contains pyridoxal-P as described below, is completely devoid of the following activities: cystathionine y-lyase, cystathionine β-synthase, serine dehydratase, cysteine las, aspartate β-decarboxylase, kynureninase, alamine aminotransferase, and serine hydroxymethyltransferase.

The purified enzyme can be stored at −20 °C for a few weeks without loss of activity when protein concentration is more than 0.5 mg/ml, whereas it is inactivated significantly by freezing in a dilute solution (less than 0.06 mg/ml). However, the enzyme is fully stable in the presence of 20% sucrose, 20% glycerol, or 1% crystalline bovine serum albumin under the same conditions. Therefore, the enzyme was routinely stored in a deep-freeze (−20 °C) in the presence of 20% sucrose until use.

Properties of Purified Enzyme

Purity and Molecular Weight—The purified enzyme was found to be homogeneous by disc gel electrophoresis (Fig. 1). The single protein band stained with Amido black corresponded to the band stained by selenocysteine lyase activity. Homogeneity of the enzyme was demonstrated also by ultracentrifugation. The enzyme sedimented as a single and symmetrical peak during the sedimentation velocity run (Fig. 1). The sedimentation coefficient (s20, w) was calculated to be 5.5 S (20 °C; 10 mM potassium phosphate buffer (pH 7.4) containing 2 × 10−5 M pyridoxal-P, 0.1 M KCl, and 0.01% 2-mercaptoethanol; protein concentration, 2.0 mg). The molecular weight of the enzyme was estimated to be approximately 93,000 by the Sephadex G-200 gel filtration method. A molecular weight of 85,000 ± 3,000 was obtained also by the sedimentation equilibration method, assuming a partial specific volume of 0.74. Polycrystalline gel electrophoresis in sodium lauryl sulfate gave a single major band that had an estimated molecular weight of 48,000. Therefore, the enzyme probably consists of two subunits with identical molecular weight.

pH Optimum—The enzyme showed the maximum reactivity at about pH 9.0 when measured in Tricine/NaOH (pH 7.0–9.0) and glycine/NaOH (pH 8.5–11.0) buffers.

Substrate Specificity—The ability of the enzyme to catalyze cleavage of various amino acids, in particular selenocysteine derivatives, was investigated. The enzyme was found to act specifically on selenocysteine to produce alanine and H2Se. From double reciprocal plots for the relationship between velocity and substrate concentration, the Michaelis constant for L-selenocysteine was calculated to be 0.83 mM. The following amino acids were inert: L-cysteine, L-serine, β-chloro-L-alanine, L-cystine sulfinate, S-methyl-L-cysteine, and Se-ethyl-DL-selenocysteine. Neither α-aminobutyrate nor H2Se (nor H2S) was formed from the following amino acids or their derivatives: L-selenohomocysteine, L-homocysteine, and selenocysteamine. When dithiothreitol was omitted in the reaction mixture, no enzymatic cleavage was observed for DL-selenocysteine, L-cystine, L-selenohomocysteine, and selenocystamine. L-Cysteine was found to behave as a competitive inhibitor against DL-selenocysteine (K1: 1.0 mM). None of the following compounds inhibited the enzyme reaction with 4 mM DL-selenocysteine: 5 mM L-serine, L-alanine, L-homocysteine, L-selenohomocysteine, and H2Se, and 10 mM glutathione.

Stoichiometry—Experiments to establish the stoichiometry of the enzymatic cleavage of selenocysteine were performed with a twice larger scale reaction mixture than that of Method B. The ratio of the amount of selenocysteine consumed to the amounts of alanine and H2Se formed was approximately 1:1:1 (Table III). Amounts of dithiothreitol in 5 mM excess over selenocysteine were routinely used to form selenocysteine as a substrate in the reaction mixture. In order to investigate the role of dithiothreitol in the enzyme reaction, we followed the reaction in the absence of extra dithiothreitol. When dithiothreitol was added in the reaction mixture with a molar ratio of 2.2 or 1.5:2 against DL-selenocysteine, and determined with lead acetate prior to addition of enzyme, no reduced form of dithiothreitol remained in the reaction mixture. However, the enzyme reaction proceeded with virtually the same velocity as in the presence of 5 mM excess amounts of dithiothreitol over selenocysteine. Thus, the presence of extra dithiothreitol is not essential for the enzymatic cleavage of selenocysteine.

Role of Pyridoxal-P as a Cofactor—The absorption spectrum of selenocysteine lyase has an absorption maximum at 420 nm, which is characteristic of pyridoxal-P enzymes (Fig. 2). The enzyme, incubated with 10 mM hydroxylamine solution (pH 7.2), followed by dialysis against three changes of the standard buffer for 12 h, had no activity in the absence of added pyridoxal-P and no longer exhibited the absorption maximum at 420 nm. Activity was about 94% restored by addition of 2 × 10−5 M pyridoxal-P. The Km value for pyridoxal-P was estimated to be 3.3 × 10−7 M. The following vitamin B6 derivatives (2 × 10−5 M) were not effective as a cofactor: pyridoxal, pyridoxamine 5′-phosphate, pyridoxine, and pyridoxine 5′-phosphate. Reduction of the holoenzyme with sodium borohydride resulted in disappearance of the absorption

![Fig. 1. Sedimentation pattern (A) and disc gel electrophoresis (B) of selenocysteine lyase. A, the picture was taken 53 min after achieving top speed. B, a sample of the enzyme preparation (30 μg) was electrophoresed under the conditions of Davis (17).](image-url)
The pathways of selenocysteine synthesis may be possible. Selenomethionine, which was reported to be detoxified through methylation (28), is remarkable cleavage of selenocysteine by selenocysteine lyase and some other enzyme orientation into protein. Stadtman (25) has briefly reported a direct incorporation hypothesis, and an excess of it is incorporated into the proenzyme to form the selenocysteine residue. Two possibilities were presented for attention has been given to the pathway of synthesis of the selenocysteine residue. These results suggest that the borohydride reduces the aldimine linkage formed between the 4-formyl group of pyridoxal-P and an ε-amino group of a lysine residue at the active site to yield the aldimine linkage as in other pyridoxal-P enzymes thus far studied.

**DISCUSSION**

Since selenocysteine was demonstrated as an essential constituent in polypeptide chains of several proteins, considerable attention has been given to the pathway of synthesis of the selenocysteine residue. Two possibilities were presented for the mechanism of selenocysteine residue synthesis of rat liver glutathione peroxidase: the post-translational Se incorporation to some precursor amino acid (e.g. dehydroalanine and cysteine) residue (23), and the direct incorporation of selenocysteine to the enzyme protein (24). The wide distribution of selenocysteine lyase demonstrated here may interfere with the exact observation of selenocysteine formation and incorporation into protein. Stadtman (25) has briefly reported a remarkable cleavage of selenocysteine by Clostridium sticklandii cells. Thus, it is requisite to take a breakdown of selenocysteine by selenocysteine lyase and some other enzyme into consideration for investigation of the mechanism of selenocysteine incorporation into protein.

Evidences have been obtained to show that selenocysteine is synthesized from selenomethionine derived from a diet (26) in the analogous pathway to the sulfur counterparts as follows: selenomethionine → Se-adenosylselenomethionine → Se-adenosylselenohomocysteine → selenohomocysteine → selenocystathionine → selenocysteine (1, 7, 27), although other pathways of selenocysteine synthesis may be possible. Selenocysteine thus formed probably is incorporated into glutathione peroxidase or some other selenoprotein according to the direct incorporation hypothesis, and an excess of it is decomposed by selenocysteine lyase to alanine and H2Se, which was reported to be detoxified through methylation (28). Alternatively, according to the post-translational Se incorporation hypothesis, H2Se produced from selenocysteine by the enzyme is converted to the actual Se precursor to be incorporated into the proenzyme to form the selenocysteine residue. Based only on the Km value for l-selenocysteine (0.83 mM) and the Kc value for l-cysteine (1.0 mM) obtained in vitro, the enzyme probably acts on selenocysteine very slowly in vivo, because the concentration of selenocysteine in the tissues is lower than the Km value. However, the total activity of enzyme is most likely sufficient to metabolize a small amount of selenocysteine in the tissues. Further investigation, e.g. on the localization and compartmentation of the enzyme, the substrate, and the inhibitors, is needed to shed light on the physiological function of the enzyme.

The enzyme acting on sulfur compounds (e.g. mammalian cystathionine γ-lyase (7) and bacterial L-methionine γ-lyase (29)) work on the selenium analogs, although enzymes specific for selenium compounds have been considered (25). The indiscriminate catalytic action of enzymes on sulfur and selenium compounds probably is concerned at least partly in the toxicity of selenium compounds. Selenocysteine lyase, which does not act on cysteine at all, is unique with respect to the substrate specificity.

The selenocysteine lyase reaction is exceptional among those of the pyridoxal-P enzymes so far studied. The enzyme resembles the bacterial aspartate β-decarboxylase (EC 4.1.1.12) (30) in the reaction mechanism where a moity binding to 50% of the substrate is cleaved to produce alanine. The following two mechanisms for the selenocysteine-lyase reaction are possible. Elemental selenium is released enzymatically from selenocysteine and reduced to H2Se nonenzymatically with selenocysteine or dithiothreitol contained in the reaction mixture. Alternatively, selenocysteine and dithiothreitol serve as reducing agents in the enzyme reaction and H2Se is produced inherently. The detailed mechanism of the enzyme reaction is currently under investigation.

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