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Pharmacokinetic model of daily selenium intake from contaminated seafood in Taiwan

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Abstract

Contaminated seafood has been reported as an important source of human exposure to metals in Taiwan. Seafood represents a non-negligible source of selenium in the human diet. This study was designed to determine the concentration of selenium in different types of seafood and predict the concentration of selenium in the blood of Taiwanese using a one-compartment steady-state pharmacokinetic (PK) model. Samples involved three subgroups, including fish, crustaceans and bivalve molluscs. Quantitative analysis for selenium was performed using an ICP-AES (Perkin Elmer) instrument. Selenium concentrations in seafood ranged from 0.63 to 2.01 μg/g wet wt. The highest selenium concentration found in fish was 2.01 ± 0.36 μg/g wet wt in *Salmo salar* Linnaeus. In general, selenium concentration increased in the order of bivalve molluscs < crustacean < fish. The daily selenium intakes resulting from a high-seafood diet and an average diet were 145.2 and 60.2 μg/day, respectively. Daily selenium intake from seafood alone is higher than the US recommended daily allowance (RDA) of 55 μg/day and the World Health Organization (WHO) normative requirement of 40 μg/day. From PK model estimates, the concentrations of selenium in the blood of a typical seafood consumer and a high-seafood consumer were approximately 93 and 224 μg/l based on daily seafood intake of 60.2 and 145.2 μg/day, respectively.
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Keywords: Selenium; Seafood; Daily intake; Pharmacokinetic model

1. Introduction

Heavy metals are deleterious to biota in the world's marine and estuarine waters. Seafood is a primary source of protein for humans around the world. The consumption of contaminated seafood has been reported to be an important route of human exposure to metals in Taiwan. In our previous study, estimating total target hazard quotients (THQs) of tributyltin (TBT), copper, zinc, cadmium and inorganic arsenic caused by consuming contaminated oysters were 0.99 and 12.3 for the general population and Hsiangshan fishermen, respectively (Chien et al., 2002). THQ values greater than 1 indicate a likelihood of non-negligible adverse effects. Selenium is an essential human micronutrient, and selenium-rich diets appear to protect people against several types of cancer by the presence of the metal at active sites

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of glutathione peroxidase (Clausen et al., 1988; Schuckelt et al., 1991). The enzyme can protect against lipid peroxidiation-induced cell membrane damage, and reduce the potential of oxidative damage to DNA (Allan et al., 1999). Inverse relations exist between selenium intake/tissue levels and the incidence and mortality rate for several cancers (Comstockm et al., 1992). Selenium was associated with significant reductions in secondary end points of total cancer incidence, particularly lung, prostate and colorectal cancer, and lung cancer mortality (Clark et al., 1996). Selenium deficiency has been associated with Keshan disease, which mainly occurs in women of childbearing age and children in some areas of China (Yang et al., 1988). Thus, selenium is both a toxic and an essential element, depending on the amount, with dietary intake averaging 19 and 14 μg/day for adult men and women, respectively, protecting against disease (Yang et al., 1987). In 2000, the US Food and Nutrition Board established dietary reference intakes (DRI) according to selenium requirements of adults calculated from the RDAs for certain groups with special physiological requirements (Food and Nutrition Board, Institute of Medicine, 2000). The RDAs for selenium are 15–20 μg/day for infants, 20–30 μg/day for children, 40-55 μg/day for adults, 60 μg/day for pregnant women and 70 μg/day for lactating mothers. The Institute of Medicine recommends an intake of selenium for optimal health. An upper limit for safe intake was set at 400 μg/day.

People obtain selenium mainly through food, which varies widely in selenium content. Kidney, liver and seafood possess relatively high concentrations of selenium, ranging from 0.4 to 1.5 mg/kg. The range for cereals and gains is 0.1–0.8 mg/kg, and the concentration in fruits and vegetables is <0.1 mg/kg (WHO, 1987). Therefore, seafood represents a significant source of selenium in the human diet. The high consumption of seafood in Taiwan makes it essential to evaluate seafood selenium levels. However, very little information on the selenium concentration in food in Taiwan is available. Therefore, we analyzed selected seafoods for selenium content, quantified the dietary intake of selenium from seafood in the normal diet, and used a one-compartment steady-state pharmacokinetic (PK) model to estimate the concentration of selenium in the blood of Taiwanese who consume a typical amount or a large amount of seafood.

2. Materials and methods

In order to study the dietary intake of selenium, a random representative sample of households throughout northern Taiwan was selected. Samples of seafood were obtained from September 2000 to July 2001 at fish markets, seaports and marine coastal areas of Taiwan. Samples involved three subgroups, including fish, crustaceans and bivalve molluscs. Samples were transferred to the laboratory immediately after collection, and flesh of samples were obtained, cleaned and homogenized. Wet weights were recorded and the tissue samples were placed into reaction flasks. Approximately 5 g of sample was digested with 15 ml of nitric acid at 200 °C. Hydrogen peroxide (H_2O_2) was added until a colorless liquid was obtained and the residual fluid was diluted to 25 ml with distilled water. Quantitative analysis for selenium was performed using an inductively coupled plasma-optical emission spectroscopy (ICP-AES; Perkin Elmer) instrument. Each sample was analyzed in triplicate. Standard reference materials SRM 1573a Oyster Tissue and DORM-2 were analyzed at regular intervals to ensure precision and accuracy of the analyses. Precision values for the reference material analyses were 90.7% and 104.29%, and accuracy values were 3.7% and 2.5%, respectively.

We contacted a total of 200 subjects from Taipei City to estimate individual seafood intake. Information on demographics and the frequency of fish, crustacean and bivalve mollusc consumption was obtained by questionnaire. Dietary fish intake was divided into five categories: <50; $50-<100$; $100-<150$; $150-<200$; and ≥ 200 g/day. Intake of crustaceans and bivalve molluscs was categorized into five groups: <50; $50-<100$; $100-<150$; $150-<200$; and ≥ 200 g/week, approximately equivalent to <1, 1, 2, 3 and ≥ 4 servings per week, respectively. The definition for typical consumers and high-seafood consumers was dietary intake of <50 g/day and ≥ 90 g/day, respectively. Dietary intake includes fish, crustaceans and

Table 1
Selenium concentration in seafood collected from supermarkets

Species	Number of samples	Selenium (μg/g wet wt.)	
		Mean ± S.D.	Range
Fish			
Salmo salar Linnaeus	6	2.01 ± 0.36	1.56–2.39
Scomberomorus commersoni	3	1.75 ± 0.13	1.66–1.90
Sebastiscus albofasciatus	5	1.55 ± 0.09	1.57–1.67
Eleutheronma tetradactylum Show	3	1.55 ± 0.15	1.44–1.72
Liza macrolepis	6	1.55 ± 0.22	1.20–1.77
Lateolabrax japonicus Cuvier	3	1.54 ± 0.14	1.43–1.70
Acanthopagrus latus	3	1.51 ± 0.02	1.49–1.53
Theragra chalcogramma	3	1.39 ± 0.07	1.33–1.47
Psenopsis anomale Temminck & Schlegel	6	1.36 ± 0.18	1.02–1.56
Plecoglossus altirelis Temminck & Schlegel	6	1.35 ± 0.05	1.26–1.41
Oncorhynchus mykiss	3	1.35 ± 0.15	1.18–1.47
Oreochromis sp.	3	1.34 ± 0.10	1.25–1.44
Larimichthys polyactis	5	1.34 ± 0.43	0.58–1.61
Taius tumifrons	7	1.33 ± 0.15	1.06–1.51
Priacanthus macranthus Cuvier	5	1.31 ± 0.16	1.13–1.48
Trichiurus lepturus	3	1.20 ± 0.10	1.13–1.32
Epinephelus mystacinus	3	1.17 ± 0.03	1.14–1.19
Mola mola Linnaeus	3	0.81 ± 0.11	0.71–0.93
Crustaceans			
Panulirus longipes	6	1.30 ± 0.30	0.87–1.76
Ovalipes punctatus	3	1.28 ± 0.11	1.15–1.35
Metapenaeus ensis	5	1.27 ± 0.22	1.00–1.38
Aristeus viritis	3	1.11 ± 0.31	0.91–1.47
Portunus sanguinolentus	4	1.09 ± 0.18	0.91–1.33
Bivalve molluscs			
Crassostrea gigas	21	1.18 ± 0.27	0.77–1.59
Raphia amabilis	3	1.33 ± 0.28	1.00–1.49
Ruditapes variegates	5	0.87 ± 0.20	0.67–1.20
Meretrix lusoria	10	0.73 ± 0.16	0.53–1.00
Amusium pleuronectes	2	0.63 ± 0.10	0.56–0.70
Haliotis diversicoloraquatilis Reeve	3	0.35 ± 0.03	0.84–1.00

bivalve molluscs. The ratios of male/female were 32:68 and 26:74 for typical consumers and high-seafood consumers, respectively. Continuous data were analyzed using ANOVA and Scheffe's test. Student's *t*-test was used to determine differences in daily intake between the two seafood consumer groups.

3. Results and discussion

3.1. Concentrations of selenium in seafood

Selenium seafood concentrations are summarized in Table 1. In general, selenium concentrations ranged from 0.63 to 2.01 μg/g wet wt., and increased in the order: bivalve molluscs < crustaceans < fish. The highest selenium concentration (2.01 ± 0.36 μg/g wet wt.) in fish occurred in *Salmo salar* Linnaeus and the lowest (0.81 ± 0.11 μg/g wet wt.) was observed in *Mola mola* Linnaeus. The molluscs, *Haliotis diversicoloraquatilis* Reeve, had the lowest concentration of selenium (0.35 ± 0.03 μg/g wet wt.) among all the samples.

Selenium concentrations in marine organisms are listed in Table 2. In France, the seasonal variation in selenium concentration of mussels (*Mytilus edulis*) and oysters (*Crassostrea gigas*) was examined in the Bay of Bourgneuf (Amiard et al., 1993). Mussels and oysters contained selenium at concentrations of 2–13 and 3–6 μg/g dry wt., respectively. The wet weight/dry weight ratios were 4.1–10.5 and 3.5–11.9, respectively. Data from the US National Oceanic and Atmospheric Administration (NOAA, 1986–1993) for selenium in Eastern oysters (*Crassostrea virginica*) ranged from 2.4 to 3.5 μg/g dry wt. The US Food and Drug Administration (FDA) conducted a survey of selenium in fresh clams and oysters collected from US coastal areas. Levels of selenium were 0.50±0.10 and 0.53±0.10 μg/g wet wt. in Eastern and Pacific oysters, respectively; levels in hardshell and softshell clams were below the detection limit (Capar and Yess, 1996). A recent study in Greenland reported selenium concentrations in marine fish (<0.20 μg/g wet wt.), shrimp (1.57±0.28 μg/g wet wt.), Icelandic scallops (0.47±0.06 μg/g wet wt.) and blue mussels (0.90±0.02 μg/g wet wt.) (Johansen et al., 2000).

3.2. Estimating daily intake of seafood

Fig. 1 shows the consumption of crustaceans, bivalve molluscs and fish among the general population and those with a high-seafood diet in Taiwan. The consumption rate in the general population increased in the order: crustaceans < bivalve molluscs < fish, which was the same as that found for heavy seafood consumers, although the intake of heavy consumers was 2.0–2.7-fold greater than that of the general population ($P<0.05$). Daily selenium intake was calculated based on the concentration of selenium in the seafood.

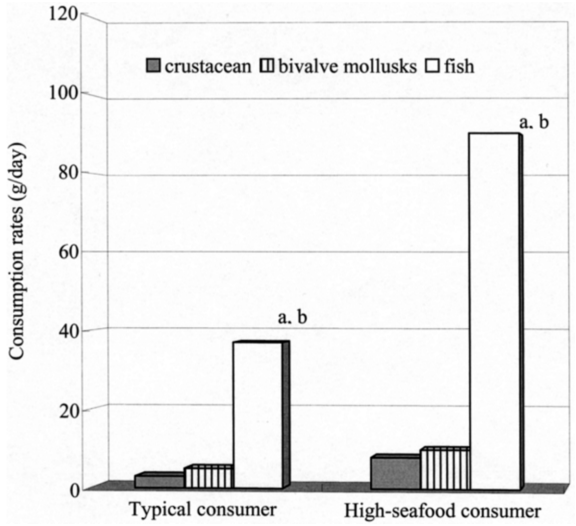

Fig. 1. The average consumption rate of cruatacean, bivalve mollusks and fish among typical consumers and high-seafood consumers in Taiwan. [a]$P<0.05$ compared with other consumption rate by Scheffe's test. [b]$P<0.05$ compared with typical consumer and high-seafood consumer by Student's *t*-test.

Table 2
Comparison of selenium concentrations in marine organisms in different studies

	Concentration (μg/g)	Reference
France		Amiard et al., 1993
Mytilus edulis[a]	2–13	
Crassostrea gigas[a]	3–6	
US NOAA		NOAA, 1986–1993
Eastern oyster *Crassostrea virginica*[a]	2.4–3.5	
US FDA		Capar and Yess, 1996
Eastern oyster[b]	0.4–0.6	
Pacific oyster[b]	0.43–0.63	
Greenland		Johansen et al., 2000
Fish[b]	<0.20	
Shrimp[b]	1.29–1.85	
Iceland scallop[b]	0.41–0.53	
Blue mussel[b]	0.88–0.92	

[a] Dry weight basis.
[b] Wet weight basis.

Table 3
Estimated intake of selenium from seafood in Taiwan

Seafood type	Se concentration (μg/g wet wt.)	Estimated intake of Se (μg/day)			
		Typical population		High-seafood consumer	
		Mean	95th percentile	Mean	95th percentile
Crustaceans	1.20	3.60	13.9	9.60	25.2
Bivalve molluscs	0.96	4.80	13.9	9.60	33.6
Fish	1.40	51.8	160	126	332
Total		60.2	187.8	145.2	390.8

Table 3 shows the estimated intake of selenium from seafood in Taiwan. The daily selenium intake for the high-seafood consumer (145.2 μg/day) was 2.4-fold greater than that for the typical consumer (60.2 μg/day). For typical and high-seafood consumers, daily selenium intake was estimated to be 187.8 and 390.8 μg/day, respectively, for the 95th percentile of seafood consumption. The selenium intake of a Japanese fisherman may be as high as 500 μg/day (Simonoff and Simonoff, 1991). In Greenlanders, the calculated selenium intake was 4569 μg/week per person from marine food in the Disko Bay region in 1995–1996, equaling 652.7 μg/day per person (Johansen et al., 2000). Thus, the intake of selenium from seafood in Taiwan is far below the amount in Greenlanders.

Table 4 shows the daily selenium intake in different countries. Estimates of daily intake and comparison of dietary standards for selenium are shown in Fig. 2. One study estimated the daily selenium requirements for New Zealanders using two approaches. A 'lower estimated requirement' was based on data from WHO, the Food and Agriculture Organization (FAO) and the International Atomic Energy Agency (IAEA), which used

Table 4
Comparison of daily selenium intakes from other countries

Country	Daily selenium intake (μg/day)	Reference
Canada	110–220	Simonoff, 1990
USA	60–150	Oster and Prellwitz, 1989
China	11–116	Yang et al., 1983, 1988
Greece	110	Bratakos and Ioannou, 1991
Finland	90	Varo, 1993
Netherlands	72	Van Dokkum et al., 1989
Mexico	60.6–72.9	Valentine et al., 1994
Japan	69	Suzuki et al., 1988
India	61.9	Mahapatra et al., 2001
Belgium	28.4–61.1	Robberecht and Deelstra, 1994
France	48	Pelus et al., 1994
Germany	38–48	Oster and Prellwitz, 1989
Sweden	44	Beker and Kumpulainen, 1991
Italy	43	Allegrini et al., 1985
UK	29–39	MAFF, 1997; Church et al., 1998
Portugal	37	Reis et al., 1990
Spain	35	Díaz-Alarcón et al., 1996
England	35	Brown et al., 2000
New Zealand	29	Duffield et al., 1999
Taiwan	60–145	This study, estimated seafood intake

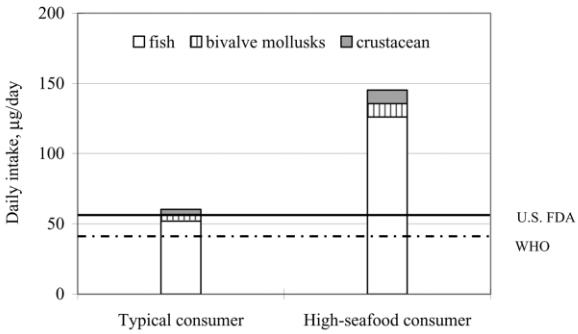

Fig. 2. Estimation of daily intake from seafood and comparison of dietary standards for selenium. WHO, normative requirement (1995). US FDA, recommended daily allowance (2000).

the selenium intake necessary to reach two-thirds of maximal glutathione peroxidase (GSHPx) activity as the criterion for the normative requirements (WHO/FAO/IAEA, 1996). An 'upper estimated requirement' was calculated as the daily intake for maximal GSHPx activity for optimal health, derived from the US RDAs (Combs, 1994). The upper and lower estimated requirements were 90 and 39 μg/day Se, respectively, for New Zealanders (Duffield et al., 1999). Our study reveals that the daily selenium intake in Taiwanese from seafood alone (60–145 μg/day) is higher than the US RDA of 55 μg/day and the WHO normative requirement of 40 μg/day. However, dietary standards for selenium throughout the world differ considerably.

The total daily intake of selenium in people of southeastern Spain was 35.46 μg/day, based on intake of 15.78 μg/day from fish, 1.21 μg/day from vegetables and fruits, and 18.47 μg/day from meat, organ meats and sausages (Díaz-Alarcón et al., 1996). The daily intake of selenium was 34 μg/day in the UK, based on intake of 9.9 μg/day from bread and cereals, 4.7 μg/day from meat and meat products, 5.7 μg/day from poultry and fish, 4.63 μg/day from fruit and vegetables, and 5.5 μg/day from milk and milk products (Barclay et al., 1995). The bioavailability of selenium in food is the fraction of ingested selenium that is absorbed and transformed into a biologically active form (Cantor et al., 1975a,b; Simonoff and Simonoff, 1991; Yoshida et al., 1993 Levander and Burk, 1994). In addition to the quantity of the mineral in the diet, its oxidation state will increase or decrease its absorption from foods (Turnlund, 1991). A new study has found that selenium ingested as a pure compound may not protect as well as selenium consumed in food. Some factor associated with whole foods must increase selenium availability or boost its anticancer properties (Janet, 2001). Thus, available dietary selenium depends on the chemical form of selenium and the type of foods consumed.

3.3. Modeling the impact of seafood on human selenium body burden

Mahapatra et al. (2001) used first-order kinetics to evaluate turnover time of selenium in blood, which they calculated to be 17 days. We applied that value in a one-compartment steady-state pharmacokinetic (PK) model to predict the concentration of selenium in the blood of Taiwanese. The model for estimating turnover time is:

$$\tau = C_p V_D / IF$$

where τ is the reciprocal of the biological decay constant of selenium (17 days); C_p is the steady-state concentration of selenium in blood (μg/l); V_D is the apparent volume of blood in the body (estimated at 5.5 l); I is the intake through ingestion (μg/day); and F is the uptake fraction into the blood through ingestion (estimated at 50%). The concentration of selenium in blood under steady-state conditions for the general population and heavy seafood consumers was approximately 93 and 224 μg/l based on daily selenium intake of 60.2 and 145.2 μg/day, respectively. The estimated selenium values for Taiwanese adults were higher than the level of 76 μg/l found for Czech Republic adults (Benes et al., 2000).

The difference between a beneficial dose and a toxic dose of selenium is very small. Selenium has a large number of biological functions in the human body. It catalyzes intermediate metabolic reactions and inhibits the toxic effects of other heavy metals, such as arsenic, cadmium and mercury. Our results estimate that the daily intake of selenium for consumers with a high-seafood diet and a typical diet is 145.2 and 60.2 μg/day, respectively, indicating that seafood is an important source of selenium in the diet of the Taiwanese.

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