



Distribution and toxicity of mercury in rats after oral administration of mercury-contaminated whale red meat marketed for human consumption

T. Endo ^{a,*}, Y. Hotta ^a, K. Haraguchi ^b, M. Sakata ^a

^a Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, 1757 Ishikari-Tobetsu, Hokkaido 061-0293, Japan

^b Daiichi College of Pharmaceutical Sciences, 22-1 Tamagawa-Cho, Minami-Ku, Fukuoka 815-8511, Japan

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10 Abstract

11 Toothed-whales and dolphins have been hunted for human consumption in Japan, and their muscles (red meats) are
12 highly contaminated with mercury (Hg). We investigated the distribution and toxicity of Hg in rats after oral admin-
13 istration of Hg-contaminated whale red meat marketed for human consumption in Japan. Rats were orally adminis-
14 tered the red meat homogenate for seven consecutive days (0.5 g red meat/kg-bw/day). The red meat administered to
15 rats contained 81 µg/g of total mercury (T-Hg) and 13.4 µg/g of methyl mercury (M-Hg). This dose corresponds to
16 the human consumption of 210 g red meat/60 kg-bw/week, exceeding by about 29 times the provisional tolerable weekly
17 intake of M-Hg at 1.6 µg/kg-bw/week set by JECFA [JECFA, 2003. Joint FAO/WHO expert committee on food addi-
18 tives. 61st meeting, Rome]. Twenty-four hours after the last administration, the distribution of T-Hg in rat organs and
19 biochemical parameters in serum were analyzed. The administration of red meat significantly elevated T-Hg concentra-
20 tions in the liver, kidney, erythrocytes, cerebral cortex and medulla oblongata from the control levels but did not elevate
21 the T-Hg concentration in serum, showing the typical distribution pattern of M-Hg, not of inorganic Hg. The admin-
22 istration slightly but significantly increased GTP activity and P concentration and decreased BUN concentration in
23 serum, although no abnormalities were observed in rat body weight gain and movement during the 7 days. The occa-
24 sional consumption of red meat from small cetaceans, therefore, could pose a health problem for not only pregnant
25 women but also for the general population.

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27 **Keywords:** Methyl mercury; Inorganic mercury; Whale, dolphin; Red meat; Human consumption

29 1. Introduction

30 Toothed-whales and dolphins have traditionally been
31 hunted for human consumption along the coast of Ja-

pan. The main species of small cetaceans taken in these 32
are; Dall's porpoise (*Phocoenoides dalli*), Baird's beaked 33
whale (*Berardius bairdii*), short-finned pilot whale 34
(*Globicephala macrorhynchus*), pantropical spotted dol- 35
phin (*Stenella attenuata*), Risso's dolphin (*Grampus gris-* 36
eus), rough-toothed dolphin (*Steno bredanensis*), striped 37
dolphin (*Stenella coeruleoalba*), bottlenose dolphin 38
(*Tursiops truncatus*), and false killer whale (*Pseudorca* 39

* Corresponding author. Tel.: +81 1332 3 1211x3158; fax: +81 1332 3 1376.

E-mail address: endotty@hoku-iryo-u.ac.jp (T. Endo).

crassidens) (Iwasaki et al., 2002). Japanese small-type coastal whaling supplied about 730 tonnes of odontocete products such as red meat, blubber, skin and others, and drive- and harpoon-fisheries supplied a further 900 tonnes in 2000 (Fujise and Goto, 2002).

45 High levels of toxic substances are reported to be
46 accumulated in the bodies of odontocete species, reflect-
47 ing their position at the top of the marine food chain
48 and their relative longevity (Haraguchi et al., 2000; Sim-
49 monds et al., 2002). Among these toxic substances, the
50 mercury (Hg) burden is prominent. A high level of Hg
51 is known to accumulate not only in the internal organs
52 of small cetaceans but also in the muscle or 'red meat',
53 the most popular product consumed in Japan (Endo et
54 al., 2002, 2003b, 2004). In response to the Minamata
55 tragedy, a methyl mercury (M-Hg) poisoning by eating
56 contaminated fishes, the Japanese Ministry of Health
57 and Welfare (JMHW) set the provisional permitted lev-
58 els of total mercury (T-Hg) and M-Hg in fish and shell-
59 fish at 0.4 and 0.3 µg/wet g, respectively (JMHW, 1973).
60 All T-Hg concentrations (Endo et al., 2003b) and M-Hg
61 concentrations (our unpublished data) in the red meat
62 samples originating from toothed-whales and dolphins
63 exceeded these permitted levels.

64 The highest concentrations of T-Hg and M-Hg,
65 found in the boiled whale liver sold for human consump-
66 tion, were 1980 µg/wet g and 23.5 µg/wet g, respectively
67 (Endo et al., 2002). T-Hg and M-Hg concentrations in
68 this boiled liver exceed the Japanese permitted levels of
69 these Hg by about 5000 times and 80 times, and the sin-
70 gle oral administration of this liver to rats caused the
71 acute toxicity by inorganic Hg (I-Hg), even though most
72 of the Hg in the liver exists as the less toxic compound
73 HgSe (Endo et al., 2003a). In response to our prelimin-
74 ary survey, the fishery cooperative in Wakayama Prefec-
75 ture forbade the sale of whale liver and kidney for
76 human consumption under voluntary regulation.

77 Although T-Hg level of odontocete red meat was
78 markedly lower than that of the boiled liver, M-Hg level
79 in the red meat was of similar magnitude to that in the
80 boiled liver (Endo et al., 2004). The highest concentra-
81 tions of T-Hg in the red meat were found in false killer
82 whale from Okinawa Prefecture: This red meat con-
83 tained 81.0 µg/wet g of T-Hg and 13.4 µg/wet g of M-
84 Hg, exceeding the Japanese permitted levels in seafood
85 by about 200 and 46 times, respectively (Endo et al.,
86 2003b). Thus, chronic toxicity due to occasional con-
87 sumption of Hg-contaminated odontocete meat could
88 occur. In spite of these high levels of T-Hg and M-Hg,
89 odontocete red meats are commercially available in Jap-
90 an without any regulation. As far as we know, there
91 are few experimental data on the distribution and toxic-
92 ity of Hg after oral ingestion of the whale red meat.
93 The aim of the present study was to investigate the dis-
94 tribution of Hg as well as biochemical parameters for
95 Hg-toxicity in serum and urine after oral administration

of Hg-contaminated whale red meat to rats for seven 96
consecutive days. 97

2. Materials and methods 98

99 Red meats originating from false killer and minke 99
whales marketed for human consumption were pur- 100
chased from retail outlets in Nago, Okinawa Prefecture, 101
and Shiogama, Miyagi Prefecture, Japan. The red meat 102
from the false killer whale contained 81.0 µg/wet g of T- 103
Hg, 13.4 g/wet g of M-Hg, 15.2 µg/wet g of selenium (Se) 104
and 0.18 µg/wet g of cadmium: the molar ratio of T-Hg 105
to Se in this red meat was 2.13 and the percentage of M- 106
Hg in the T-Hg was 16.5 (Endo et al., 2003b). In con- 107
trast, the red meat from the minke whale contained only 108
trace amounts of T-Hg (0.15 µg/wet g) and M-Hg 109
(0.12 µg/wet g). These red meats were homogenized in 110
distilled water (10% w/v) just before oral administration 111
to the rats. 112

113 Male Wistar ST rats (4 weeks) were purchased from 113
Shizuoka Laboratory Animal Center (Shizuoka, Japan). 114
The rats were separately housed in metabolic cages under 115
air-conditioned and light-controlled conditions and 116
were allowed access to a commercial solid diet (Oriental 117
Yeast Co. Ltd. Type MF) and water. Zinc and Se contents 118
in the diet are reported to be about 53 ppm and 119
0.4 ppm, respectively. Following acclimatization for a 120
week, the rats weighing about 100 g were orally admin- 121
istered one of the red meat homogenates or saline (con- 122
trol) at a rate of 0.5 ml homogenate per 100 g body 123
weight (0.5 g red meat/kg-bw) for seven consecutive 124
days. During the experimental period, the rats were al- 125
lowed access to the solid diet and water, and urine was 126
collected. Twenty-four hours after the last administra- 127
tion (the eighth day), the rats were killed by blood sam- 128
pling via the abdominal aorta. All experimental 129
procedures were approved by the Ethics Committee of 130
the Health Sciences University of Hokkaido. 131

132 According to our previous report (Endo et al., 132
2003a), we determined some selected biochemical 133
parameters in serum and urine to investigate Hg-toxicity 134
due to the whale product consumption. Serum paramet- 135
ers analyzed were glutamic oxaloacetic transaminase 136
(GOT), glutamic pyruvic transaminase (GPT), alkaline 137
phosphatase (ALP) and lactate dehydrogenase (LDH) 138
activities, and urea nitrogen (BUN), creatinine (CRN), 139
inorganic phosphorus (P), Na⁺, K⁺ and Cl⁻ concentra- 140
tions. Urinary parameters analyzed were *N*-acetyl-β-D- 141
glucosaminidase (NAG) activity, albumin (ALB) 142
concentration and ratios of above electrolytes (Na⁺/K⁺ 143
and Na⁺/Cl⁻). Urine samples collected for 24 h after 144
the last administration were pooled for the analysis. 145

146 T-Hg concentrations in the liver, kidney, erythro- 146
cytes, serum, cerebral cortex and medulla oblongata 147
were determined using a Rigaku Mercury Analyzer 148

SP-2. DOLT-2 (National Research Council of Canada) was used as an analytical quality control sample for determination of T-Hg. T-Hg concentrations presented are based on wet weight.

Statistical analysis was carried out with the Statcell program using Fisher's PLSD test or Scheffe's *F* test, depending on sample size, and *p* values of less than 0.05 were considered significant.

3. Results and discussion

Fig. 1 shows the distribution of T-Hg after the oral administration of red meats originating from minke and false killer whales for seven consecutive days. The administration of false killer whale meat markedly elevated T-Hg concentrations in erythrocytes, liver and kidney relative to control rats (saline administration), and slightly but significantly elevated those in the cerebral cortex and medulla oblongata. However, administration of this red meat did not substantially elevate T-Hg concentrations in the serum. T-Hg concentrations in the serum after the administration of false killer whale meat as well as minke whale meat and saline were near or below the detection limit (0.1 ng/mg). Preferential accumulation of Hg in erythrocytes (Fig. 1) is a typical distribution pattern of M-Hg in whole blood, but not of inorganic mercury (I-Hg) (Sweet and Zelikoff, 2001; Clarkson, 2002). No significant increases in T-Hg concentration relative to control rats were observed in the rat organs after the administration of minke whale meat.

Changes in biochemical parameters in serum after the oral administration of red meats originating from minke and false killer whales for seven consecutive days are shown in Table 1. Compared with saline administration,

the administration of false killer whale meat slightly but significantly increased GTP activity and P concentration and decreased BUN concentration. No significant changes were observed in the parameters after the administration of minke whale meat.

The administration of false killer whale meat did not change the values of the urinary parameters analyzed such as urinary volume, urinary excretion of NAG and ALB, and the ratios of Na^+ to K^+ and Na^+ to Cl^- in the urine (data not shown). Urinary excretion of NAG, a lysosomal enzyme, is considered the most sensitive indicator of I-Hg intoxication (Langworth et al., 1992). These results for urinary parameters are consistent with the typical distribution pattern of M-Hg after the administration of the false killer whale meat (Fig. 1). As expected, the administration of minke whale meat did not change these parameters.

No differences were observed in the body weight gain of rats fed false killer whale meat, minke whale meat and saline after the seven consecutive days (the average of body weight gain was about 60 g), and no symptoms of Hg-toxicity were observed in the movements of rats fed minke and false killer whale meats. Thus, there appears to be little fear of acute intoxication associated with this level of consumption of Hg-contaminated odontocete red meat although T-Hg concentrations in erythrocytes, liver, kidney and brain tissues were significantly elevated (Fig. 1) and some parameters in the serum (GPT, BUN and P) were marginally changed (Table 1).

In a previous study, we administered boiled whale liver containing 1980 $\mu\text{g}/\text{wet g}$ of T-Hg, 23.5 $\mu\text{g}/\text{wet g}$ of M-Hg and 656 $\mu\text{g}/\text{wet g}$ of Se to rats (po) (Endo et al., 2003a). A single administration of this liver (2 mg red meat/kg-bw) changed all the above mentioned urinary biochemical parameters, suggesting acute renal dysfunction by I-Hg. The amount of T-Hg ingested by the single administration of whale liver was about 14 times more than the total amount of T-Hg from false killer whale meat administered in the present study, whereas the amount of M-Hg ingested was almost the same. The large excess amount of I-Hg ingested by the single administration of whale liver may thus be the cause of the renal dysfunction observed previously.

People living in the Faroe Islands, Denmark, have traditionally eaten pilot whales, and the consumption of this whale is one of the main sources of Hg in human diets. The average T-Hg and the percentage of M-Hg in the T-Hg found in the red meat from pilot whales caught off the Faroe Islands were reported to be 3.3 $\mu\text{g}/\text{wet g}$ and about 50%, respectively (Clarkson, 2002). The government of the Faroe Islands issued recommendations concerning the consumption of pilot whale products by the public to prevent the chronic intoxication by M-Hg as well as PCBs, suggesting that adults should only eat the blubber and meat once or twice a month,

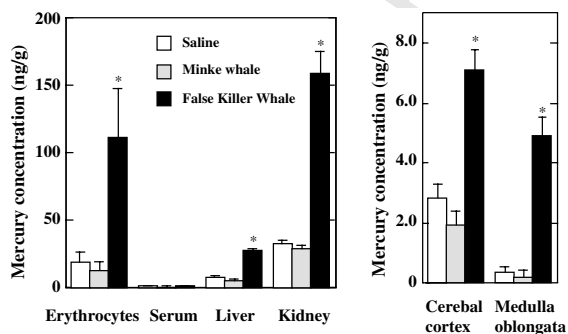


Fig. 1. Distribution of mercury after the oral administration of whale red meat for seven consecutive days. Rats were administered homogenate of red meat originating from minke whale, false killer whale, or saline (control). Each bar represents the mean \pm SD for 5 rats. *Significantly different from saline ($p < 0.05$).

Table 1

Biochemical parameters in serum after the oral administration of red meats originating from minke and false killer whales and saline

	Saline	Minke whale	False killer whale
GOT	79.7 ± 5.4	80.6 ± 8.1	84.1 ± 6.7
GPT	46.7 ± 3.4	47.1 ± 4.5	53.1 ± 4.9*
ALP	1681 ± 264	1815 ± 255	1797 ± 257
LDH	272 ± 143	265 ± 148	251 ± 164
BUN	19.4 ± 1.0	19.9 ± 1.9	17.8 ± 0.8*
CRN	0.44 ± 0.05	0.46 ± 0.05	0.47 ± 0.05
Na ⁺	140 ± 1	142 ± 2	141 ± 2
K ⁺	5.2 ± 0.3	5.2 ± 0.3	5.3 ± 0.4
Cl ⁻	104 ± 1	105 ± 2	104 ± 1
Ca ²⁺	5.2 ± 0.1	5.1 ± 0.2	5.1 ± 0.2
P	8.0 ± 0.5	8.4 ± 0.6	8.9 ± 0.5*

GOT, GPT, ALP and LDH activities are expressed as U/l. BUN, CRN, and P concentrations are expressed as mg/dl. Na⁺, K⁺, Cl⁻, and Ca²⁺ concentrations are expressed as mEq/l. The data represent the mean ± SD for 7 rats.

* Significantly different from saline ($p < 0.05$).

and pregnant and nursing women should not eat the meat at all (Anonymous, 1998). In 2003, a joint FAO/WHO Expert Committee on Food Additives (JECFA) re-evaluated the provisional tolerable weekly intake (PTWI) of M-Hg to protect the developing fetus, and JECFA revised the PTWI from 3.3 µg/kg-bw/week to 1.6 µg/kg-bw/week (JECFA, 2003). In this study, we orally administered false killer whale meat to rats for seven consecutive days (0.5 g red meat/kg-bw/day). This dose corresponds to the consumption of 210 g of red meat per 60 kg-bw per week, which exceeds the revised PTWI of M-Hg by 29-fold, and thus could cause neurodevelopmental disorders in a developing fetus.

In concert with our previous reports (Haraguchi et al., 2000; Endo et al., 2002), the Japanese Ministry of Health, Labour and Welfare (JMHLW) investigated contamination levels of T-Hg and M-Hg in five species of toothed whales, and advised pregnant women to limit consumption of whale meats originating from sperm whale, short-finned pilot whale, bottlenose dolphin, and Baird's beaked whale, based on the PTWI of M-Hg at 3.3 µg/kg-bw/week (JMHLW, 2003): Most of the contaminated samples among these four species originated from bottlenose dolphins, and the average of M-Hg was 6.6 µg/wet g (0.61–9.7, $n = 5$). According to our data, all T-Hg concentrations (Endo et al., 2003b) and M-Hg concentrations (our unpublished data) in the red meat samples originating from nine species of toothed-whales and dolphins exceeded the Japanese permitted level for fish and shellfish, and Hg contamination levels were higher in false killer whales than in bottlenose dolphins. The size and scope of the Government survey were limited, and soon after the Government recommendation the PTWI of M-Hg was revised from 3.3 µg/kg-bw/week to 1.6 µg/kg-bw/week to protect against neurodevelopment disorders in the foetus. The

revised recommendation for pregnant women is necessary.

Choy et al. (2002) investigated the relations among infertility, whole blood concentration of T-Hg, and dietary seafood consumption in Hong Kong, and reported that higher blood concentrations of T-Hg are associated with male and female infertility and higher seafood consumption is associated with elevated T-Hg concentrations in the infertile population. For instance, T-Hg concentrations in male whole blood in the control and infertile groups were 31.2 and 40.6 nmol/l (6.24 and 8.12 ng/ml), respectively. From the data on T-Hg concentrations in erythrocytes and serum (Fig. 1) and 40% hematocrit, the estimated T-Hg concentrations in the whole blood of rats fed saline and minke and false killer whale meats are 7.7, 5.1 and 45 ng/ml, respectively. The estimated T-Hg concentration in rats fed the false killer whale is markedly higher than the T-Hg concentration in the Hong Kong male infertile group although the species difference must be considered. Thus, not only pregnant women and women of childbearing age but also men who want children should restrict their consumption of Hg-contaminated toothed-whale products.

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