EFFECTS OF ALKOXY-GLYCEROLS - ECOMER®- ON THE ACCUMULATION OF MERCURY IN RATS AFTER A SINGLE DOSE OF METALLIC MERCURY

Bengt Fredin, LDS

Department of Physiological Chemistry IV

University of Lund

Box 94, 221 00 LUND, Sweden

Abstract:

Male rats were exposed to a single dose of metallic mercury. Half the rats were in addition given a shark liver oil extract of alkoxy-glycerols - Ecomer®- in the feed daily, starting three days before the mercury dose was administrated. The post mortem concentrations of Hg were increased in blood, brain, heart and kidney of all animals supplied with Hg compared to control animals and among the Hg exposed rats the Hg-concentrations were found lower in animals supported by Ecomer®.

Introduction:

The absorption of metallic mercury in the gastrointestinal tract has been considered unimportant (1). In consequence mercury and mercury compounds have been frequently used i medicine. It might be of historical interest to note that metallic mercury was used in large doses in the treatment of ileus and for centuries metallic mercury dispersed in sheeps fat was the medicine against syphilis. Mercury has survived in medicine mainly in preserving agents and in diuretics. In dentistry, however, mercury is still used in large quantities as the dominating w/w component in dental amalgam.

The alkoxy-glycerols were discovered by Tsujimoto & Toyama in 1922 (2). In 1962 Hallgren and Larsson analyzed the alkoxy-glycerol ethers in the liver oils of elasmobranch fish (3) and the natural occurence of the compounds in man and cow (4).

Ecomer® is an extract of alkoxy-glycerols from livers of Greeland shark containing metoxysubstituted alkoxy-glycerols.

Ecomer® has been reported to have beneficial effects in the treatment of some forms of cancer (5,6,7) and to improve immune reactivity (8). Dental amalgam fillings continuously leak mercury (9). Mercury, whether inhaled, swollowed or directly penetrating oral tissues, is by the author considered a potential risk of poisoning.

A pilot study on man indicated a rapid influence on the fecal excretion of mercury after taking Ecomer®(10).

The intention of this study was to investigate the eventual influence of Ecomer® on the retention of mercury, following exposure to metallic mercury, since health improvments had been reported by self diagnosed "oral galvanists" using Ecomer®.

Materials and methods:

Twenty-two laboratory, pellet-fed male rats of a weight around 250 g in series 1 and around 300 g in series 2 were used in the study. Six animals were untreated controls, the other sexteen were supplied with a single dose of 14 mg metallic mercury given under anaesthesia by a sond into the ventricle in a solution of triglycerids:

1,9% C_6 - capron -
77,7% C_8 - capryl -
19,6% C_{10} - caprin -
0,8% C_{12} - lauryl -
mol. weight = 538

The mercury was vibrated for five minutes with the triglycerids before insertion. Half the number of the Hg-supplied animals were given 30 µl Ecomer® a day in the feed, starting 3 days before the mercury dose was given. The investigation was run in two series of animals on different occasions with eight Hg-exposed rats in each group. 48 hours after the Hg-supply the rats were sacrified and blood, brains, heart and kidney removed for analysis of their Hg-content. The samples were frozen in coded vessels until analyzed by A.A.S. (Elementanalys AB).

Results:

Table 1 (Hg-content ng g^{-1})

Exposed rats:	A = 14 mgHg + Ecomer®				B = 14 mgHg			
	Brain	Kidney	Heart	Blood	Brain	Kidney	Heart	Blood
Series 1	44	1 230	31	31	33	1 520	44	31
	35	0 880	22	28	40	1 860	48	40
	33	1 330	23	33	53	1 660	35	32
	51	1 950	28	36	82	2 450	44	53
Series 2	1	1 210	100	49	3	950	110	53
	1	715	86	65	3	810	130	58
	3	820	90	53	4	945	110	54
	3	940	160	41	4	605	170	69

Table 2

Untreated controls (Hg-content ng g^{-1})

Brain	Kidney	Heart	Blood
2,3	12	6	19
2,3	37	10	11
< 1	140	7	10
< 1	73	8	10
< 1	94	16	21
< 1	96	5	18

There are obvious differences in the Hg-levels between animals in the first and the second series. Differences in weight, food composition, and individual variations in absorption, metabolism and excreation of Hg in the animals might be part of an explanation (11,12).

Even among the untreated control animals unequalities in the Hg-content were observed. The two first control animals in table 1 belong to the animals of the first series, the others to series two. Essential is, however, the divergence in Hg-content in mercuryexposed animals with and without supply of alkoxyglycerols comparing animals in the same series.

Statistical evaluation:

Statistical evaluation of the results was made by means of the Wilcoxon-Mann-Whitney (WMW) rank sum test; one-sided p-values were computed. When ties occurred mid-ranks were used. A non-standard computer program provided p-values that are exact also in the mid-rank case.

Analysis of one single organ in one single series is a question of comparing two random samples, each of size 4.

Results (p-values):

	Brain	Kidney	Heart	Blood
Series 1	27,1%	10,0%	1,4%	20,0%
Series 2	8,6%	24,3%	8,6%	11,4%

Thus heart in series 1 gave the only significant difference. For each single organ the information from the two series was then combined; this was done simply by using the previously used ranks (assigned within each series separately) as data, giving two samples, each of size 8, to be compared by means of the WMW test.

Result (p-values):

	Brain	Kidney	Heart	Blood
Series 1+2	5,6%	5,7%	0,2%	4,5%

Finally the information from the four organs was combined. The method for doing that was to sum, for each animal separately, the ranks that the four organs were given in the previously mentioned ranking within organ and series; these rank sums were considered as two samples, each of size 8, and compared by means of the WMW test.

Result (p-values):

	All organs
Series 1+2	0,2%

Discussion:

The absorption of metallic Hg in the rats is not considered negligible comparing exposed animals to controls. The solubility of mercury in fat might affect the degree of absorption. The reduced conc. in heart-tissue of the Hg-exposed animals supplied with Ecomer® in the feed is notable. The capability of Ecomer® to reduce the Hg-conc. in rats exposed to a single dose of metallic mercury - as observed in blood, brain, heart and kidney in this study - is statistically significant, although the underlying mechanisms at present are unknown.

ACKNOWLEDGEMENT

I wish to thank Research Engineer Lennart Krabisch, Department of Physiological Chemistry, University of Lund, for practical advices and fruitful discussions, Professor Sven Brohult, Bromma, for encouraging support and Dr Jan Lanke, Department of Statistics, University of Lund, for statistical evaluation.

References:

(1) Bornmann G., Henke G., Alfes H. & Mollman H.: Über die enterale Resorption von metallischen Quecksilber. Arch. Toxicol. 26:203-209, 1970.

(2) Tsujimoto M. & Toyama Y.: Über die unverseifbaren Bestandteile (höheren Alkohole) der Haifish - und Rochen - leberöle. J. Chemische Umschau, XXIX:27-29, 1922.

(3) Hallgren B. & Larsson S.: The glycerol ethers in the liver oils of elasmobranch fish. Journal of Lipid Research, 3:31-38, 1962.

(4) Hallgren B. & Larsson S.: The glycerol ethers in man and cow. Journal of Lipid Research 3:39-43, 1962.

(5) Brohult A. & Holmberg J.: Alkoxyglycerols in the treatment of leukopenia caused by irradiation. Nature:1102, 1954.

(6) Brohult A.: Alkoxyglycerols and their use in radiation treatment. Acta Radiol, Suppl. 223, 1963.

(7) Brohult A., Brohult J., Brohult S. & Joelsson I.: Reduced mortality in cancerpatients after administration of alkoxyglycerols. Acta Obstet. Gynecol. Scand. 65:779-785, 1986.

(8) Boeryd B., Nilsson T., Lindholm L., Lange S., Hallgren B. & Ställberg C.: Stimulation of immune reactivity by methoxy-substituted glycerol ethers incorporated in the feed. Eur. J. Immunol.,8:678-680, 1978.

(9) Fredin B.: Studies on the mercury release from dental amalgan fillings,1987 (manuscript accepted for publication).

(10) Fredin B.: Preliminary observations of rapid effects of Ecomer® on the excretion of man (A pilot study),manuscript, 1988.

(11) Tamashiro H., Arakaki M., Akagi H., Hirayama K. & Smolensky M.H.: Methyl mercury toxicity in spontaneously hypertensive rats (SHR). Bull. Environ. Contam. Toxicol., 36:668-673, 1986.

(12) Fredin B.: The distribution of mercury in various tissues of Guinea-pigs after application of dental amalgam fillings (A pilot study). Sci. Total Environ., 66:263-268, 1987.