Case study: fatal poisoning by malathion

T.S. Thompson a,*, R.G. Treble a, A. Magliocco b, J.R. Roettger a, J.C. Eichhorst a

a Saskatchewan Health, Provincial Laboratory, 3211 Albert Street, Regina, Saskatchewan, Canada S4S 5W6
b Department of Pathology, College of Medicine, University of Saskatchewan, B419 Health Sciences Building, 107 Wiggins Road, Saskatoon, Saskatchewan, Canada S7N 5E5

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Abstract

A case involving a fatal poisoning (suicide) by the insecticide malathion is described. The intact insecticide was found in the post-mortem blood and gastric contents at concentrations of 1.8 and 978 μg/ml, respectively. None of the insecticide was found in the autopsied liver tissue. Gas chromatography–mass spectrometry (GC–MS) techniques were used for the identification and quantification of malathion in the body fluids. © 1998 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Malathion, or O,O-dimethyl-S-(1,2-dicarbethoxyethyl)phosphorodithioate, is one compound of a general class of chemicals commonly referred to as organophosphorous insecticides (OPs). It is frequently used for the control of insects on fruits and vegetables. Malathion has also been used to control mosquitoes, flies, miscellaneous household insects, animal parasites, and human head and body lice [1]. Malathion is non-systemic and kills insects by direct contact or through vapour action. It is the active ingredient in numerous general use pesticide formulations and can be purchased at many different types of retail outlets.

*Corresponding author.

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In comparison with other OPs such as parathion or mevinphos, malathion has a low mammalian toxicity. This is largely due to the presence of enzymes which are capable of hydrolyzing the carboxyl groups to yield the mono- and dicarboxylic acid analogs of malathion. Experimental studies and occupational exposure indicate that malathion is only slightly toxic. Symptoms of organophosphate poisoning include defecation, urination, lacrimation, muscular twitching, and convulsions [2]. Although the convulsions may be tonic (limbs stretched and rigid), they are more likely to be clonic (rapid repetitive movement) in nature. The sequence of events leading up to death generally consist of inhibition of cholinesterase, acetylcholine accumulation, disruption of nerve function (centrally or peripherally), respiratory failure, and ultimately asphyxiation. It has been estimated that the lethal dose in man is approximately 60 g [3].

Malathion is generally considered to be one of the safest of the OP insecticides, however there have still been numerous cases of either accidental or intentional poisoning. From 1957 to 1961 and 1965 to 1966, there were 63 reported accidental poisonings (ten fatalities) and 480 suicide or homicide attempts (404 deaths) in Japan [2]. In Guyana during 1959 to 1964 malathion poisoning claimed the lives of 46 individuals, 43 of which were suicidal in nature [2]. A subsequent report, also based in Guyana, described 264 cases of suicides that resulted from malathion poisoning [4]. This study included clinical characteristics and examined the role of sociocultural factors in the occurrence of suicidal poisonings involving malathion. During a two-year period, a Sri Lankan hospital encountered 92 cases of OP insecticide poisoning [5]. Malathion was the insecticide involved in eight of these poisonings. Most malathion poisonings in the United States are accidental in nature and involve children [1].

There have been several confirmed cases (i.e., where malathion was determined to be present in bodily fluids and tissues) in which an individual has committed suicide by ingesting products containing this chemical [3,6–8]. In separate cases of attempted suicide, two men drank unknown quantities of malathion [9]. One man spent 20 days in the hospital on a respirator and subsequently required surgery to repair lung damage. The other man was found in a coma and was hospitalized for 13 days. After an extended illness which included 6 days in the hospital, a 26-year old man admitted to having attempted to commit suicide by intramuscular injection of 3.0 cc of malathion [10]. In a similarly unusual case, a man attempted to commit suicide by intravenously injecting a solution of 50% malathion into his forearm [11].

1.1. Case history

The body of a 40-year old woman was discovered by her husband lying face down on the floor of their barn loft at approximately 8:00 p.m. On the counter adjacent to the body was an open 500-ml bottle of malathion pesticide with 50 to 100 ml of liquid still inside and with the cap on the counter. In addition there was an Exxacto brand retractable utility knife with protruded blade, a pack of cigarettes, and several smoked cigarette ends. Multiple slash wounds were noted on her left wrist, and there was a small amount of blood on the floor and her hand. There were no signs of other trauma or of a struggle.
The woman lived with her husband and two children aged 14 and 16 years on a half section grain farm. She had developed a major affective disorder with paranoid features in October 1994. This was treated at the time with hospitalization, antidepressants and antipsychotic agents (Zoloft and Haldol). She had a possible previous suicide attempt in December 1994 when she took an overdose of her medication. Following treatment her status improved to the point where medication was withdrawn one year later in December 1995. Unfortunately, she reported a return of depression 5 months later, one week prior to her death. She contacted her primary care physician by telephone and her antidepressant medication was resumed. However, she never picked up the prescription renewal.

At autopsy the body was clothed, and multiple slash wounds and hesitation marks on the left wrist were noted (Fig. 1). There was incontinence of feces and urine. There was a strong chemical odour typical of malathion emanating from the body. The pupils measured 3 mm in diameter bilaterally. There was bilateral pulmonary congestion (left lung 470 g, right lung 560 g) and thick mucoid material in the airways. The stomach contained approximately 100 ml of cloudy brown fluid. There were no other physical abnormalities. Material was collected for toxicology studies. Microscopic examination revealed only pulmonary congestion, the liver was unremarkable.

As a result of the suspected poisoning by malathion, autopsy blood, gastric contents, and liver tissue were submitted to the Provincial Health Laboratory. Each of the samples were extracted according to the procedures outlined below and subsequently analyzed by GC–MS.

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Fig. 1. Wrist slash (self-inflicted) with hesitation marks.
2. Materials and methods

2.1. Reagents

All organic solvents used in this study were distilled-in-glass and suitable for pesticide residue analysis. An authentic neat standard (>95% purity) of malathion was obtained from the PolyScience Corporation (Niles, IL). Hexachlorobenzene (HCB), which was used as an internal standard for the GC–MS analysis, was purchased as a neat solid (>95% purity) from Ultra Scientific (North Kingston, RI).

2.2. Extraction of blood

Two portions of the post-mortem blood sample plus an aliquot of blood taken from a non-exposed individual were extracted. The latter blood sample was processed with the samples and acted as a reagent blank. Briefly, 1-ml aliquots of post-mortem blood and the control blood were extracted with 3×1-ml portions of methyl t-butyl ether (MTBE) in clean centrifuge tubes using a rocking mixer. The MTBE extracts were dried over anhydrous sodium sulphate. The final volume of each extract was adjusted to 10 ml using MTBE.

2.3. Extraction of gastric contents

Two portions of gastric contents were processed by taking 1-ml portions of the fluid and diluting each to 10 ml with distilled water in 15-ml centrifuge tubes. The diluted gastric contents were extracted with 3×3-ml aliquots of MTBE by gently mixing the contents using a rocking mixer. The resulting emulsions were broken up by centrifuging the tubes for 10 min at 2500 rpm. The MTBE extracts were dried over anhydrous sodium sulphate and the final volume of each extract was adjusted to 10 ml.

2.4. Extraction of liver tissue

Liver tissue was homogenized along with water (1:3 w/v liver:water) using a high speed blender equipped with a low-volume mixing chamber. Two 1-ml aliquots of the homogenate were pipetted into 15-ml centrifuge tubes. Using distilled water, the total volume of each solution was adjusted to 10 ml. The dilute homogenates were extracted with 3×3-ml portions of MTBE with the aid of the rocking mixer. As for the gastric contents, emulsions formed by the mixing were dissipated by centrifugation. The extracts were dried over anhydrous sodium sulphate and the final volumes were adjusted to 10 ml.

2.5. GC–MS analysis

All analyses were performed using a benchtop GC–MS system which consisted of a Fisons 8000 series gas chromatograph interfaced to a Fisons MD800 quadrupole mass spectrometer. The GC was equipped with a split/splitless injection port which was
operated in the splitless mode (purge time set at 1 minute) and maintained at a
temperature of 220°C. All chromatographic separations were achieved using a 15 metre
DB-5MS fused-silica capillary column having an inner diameter of 0.25 mm and a
stationary phase film thickness of 0.25 microns. A Fisons AS800 autosampler was used
to inject 1.0 µl of each extract into the GC–MS. The oven temperature profile consisted
of an initial temperature of 120°C ramped at 15°C/min to a final temperature of 300°C
which was held for an additional 5 min.

The mass spectrometer was operated in the electron impact ionization mode with the
electron energy set to 70 eV. The mass spectrometer was tuned and calibrated using
perfluorotributylamine. All samples were initially screened using a cyclical scan mode
where \( m/z \) values from 50 to 400 AMU were monitored in a period of 0.8 s.

Malathion quantities were determined using an internal standard calibration procedure.
All standard solutions of malathion were made up to a final volume of 10 ml. A 50-µl
aliquot of a standard containing 1.6 µg/µl of HCB was added to each sample extract
and standard solution. Based on the integrated peak areas for the reconstructed ion
chromatograms corresponding to \( m/z \) 284 for HCB and \( m/z \) 173 for malathion, a
three-point calibration curve of relative response factor versus malathion concentration
was established. Relative response factors were calculated for each sample and the
corresponding malathion concentration was determined from the calibration curve. Two
calibration curves, one for the blood and liver samples and another for the gastric
contents, were utilized since the latter had much higher malathion levels than the former.

3. Results

Post-mortem blood, gastric contents, and liver tissue were analyzed for the intact
insecticide. The results of the analyses are presented in Table 1. The average
concentration of malathion in the blood was found to be 1.8 µg/ml. Fig. 2 illustrates the
total ion chromatogram (TIC) for a blood extract plus the two reconstructed ion
chromatograms corresponding to the quantification ions for malathion and HCB (which
elutes at approximately 4.7 min. The mass spectrum of the component eluting at 6.7 min
is given in Fig. 3 along with the best match obtained from the computerized search of a
database containing over 60,000 spectra. The mass spectrum of the suspect component
was confirmed to be malathion (a probability of 968 out of a possible 1000 was assigned
to the quality of the match based on the search algorithm). The GC retention behaviour

<table>
<thead>
<tr>
<th>Fluid/tissue</th>
<th>Malathion concentration</th>
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<tbody>
<tr>
<td></td>
<td>Duplicate A</td>
</tr>
<tr>
<td>blood</td>
<td>1.9 µg/ml</td>
</tr>
<tr>
<td>gastric contents</td>
<td>975 µg/ml</td>
</tr>
<tr>
<td>liver</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND=not detected.
Fig. 2. (a) Total ion chromatogram; (b) reconstructed ion chromatogram for m/z 173; and (c) reconstructed ion chromatogram for m/z 284 of blood contents extract.
was confirmed by injecting a standard solution of malathion under identical operating conditions.

The gastric contents had an average malathion concentration of 978 μg/ml. Fig. 4 shows the TIC and the two quantification ion RICs for one of the gastric contents.
Fig. 4. (a) Total ion chromatogram; (b) reconstructed ion chromatogram for $m/z$ 173; and (c) reconstructed ion chromatogram for $m/z$ 284 of gastric contents extract.
extracts. Neither of the duplicate liver sample extracts were found to contain detectable quantities of malathion. It was estimated that the method detection limit was approximately 1 μg/g.

4. Discussion

The high concentration of intact malathion in the gastric contents is consistent with other cases in which individuals have committed suicide by ingesting large quantities of malathion. Jadhav reported six cases of fatal malathion poisoning where the concentration of malathion in the gastric contents were found to range from 452 to 989 μg/ml [3]. In another report involving 4 cases of suicide, malathion levels in the stomach contents ranged from 310 to 12 960 μg/ml [6]. Post-mortem stomach contents containing up to 54 000 μg/ml of malathion were discussed by Lewin [7]. Malathion was found at a concentration of 2110 μg/ml in the stomach contents of a suicide victim in Japan [8].

The level of malathion found in the post-mortem blood was considerably lower than those reported in six cases reported by Jadhav [3] and 4 cases by Farago [6]. In the six suicides discussed by Jadhav et al., the concentration of malathion in blood ranged from 175 to 517 μg/ml. Farago reported levels in blood which ranged from 100 to 1880 μg/ml. However, in another report of three suicides, concentrations of malathion in blood ranged from 0.67 to 5 μg/ml [7]. Suzuki and co-workers found malathion in post-mortem blood of a suicide victim at a concentration of 1.89 μg/ml [8]. Our data would appear to be consistent with the findings of these latter two reports.

Interestingly, there does not appear to be any relationship between the levels of malathion found in the gastric contents and blood of suicide victims. The ratio of malathion found in gastric contents as compared to blood was found to range from 1.2:1 up to 80 000:1 [3,6–8].

The determination of the intact insecticide in autopsied liver tissue has produced markedly different results in the various reported cases of malathion poisoning. Jadhav reported malathion concentrations ranging from 198 to 383 μg/g [3] while Farago reported levels ranging from 200 to 1700 μg/g [6]. Lewin found malathion at a concentration of 2.4 μg/g in a liver sample taken from a poisoning victim [7]. In a document profiling the properties and toxicity of malathion, brief mention is made of a case where an individual had ingested a large quantity of malathion [12]. The intact insecticide was found at high concentrations in the stomach and intestines and at much lower levels in fat tissue. No malathion was detected in the liver.

The differences in the levels of malathion which were found in the body fluids and tissues analyzed in this case and in cases reported in the literature will be due to a number of factors. Obviously different quantities of malathion were consumed in each case. As Lewin suggested, differences in autopsy results will also arise from variations in the intervals between ingestion and death [7]. Differences in the intervals between the time of death, the subsequent autopsy, and the final laboratory preparation and analysis may also affect the levels found. In this case, the deceased had slit her wrists in addition to consuming the solution of malathion.
References