Mercury in Traditional Tibetan Medicine – panacea or problem?

Sarah Sallon[1], Tenzin Namdul[2], Sonan Dolma[2], Pema Dorjee[2], Dawa Dolma[2], Tseten D. Sadutshang[3], Pnina Ever-Hadani[4], Tali Bdolah-Abram[1], Steven Apter[5], Shlomo Almog[6] .

1. Louis L. Borick Natural Medicine Research Center, (NMRC) Jerusalem, Israel
2. Clinical Research Dept., Men-Tsee-Khang, Tibetan Medical & Astrological Institutute, (MTK), Dharamsala, HP, India
3. Delek Hospital, Dharamsala HP, India
4. Braun School of Public Health Hadassah Hebrew University School of Medicine Jerusalem, Israel.
5. Dept. of Chemistry, University of Liverpool, Liverpool, U.K.
6. Dept of Toxicology, Sheba Medical Center Tel Aviv, Israel.

Running title: Mercury in Traditional Tibetan Medicine

Corresponding Author: Dr Sarah Sallon, Director, Louis L. Borick Natural Medicine Research Center, Hadassah Medical Organization, POB 12000 Jerusalem, 91120 Israel.
Tel; 972 2 6778372 Fax; 972 2 6429750
Email: ssallon@hadassah.org.il

ABSTRACT

SUMMARY

Symptoms of mercury toxicity, biochemical changes, and blood / urine mercury levels were evaluated in a small case series. Six patients attending Delek Hospital, Dharamsala, India, taking **mercury-containing** Traditional Tibetan Medicine (TTM), (Group I), were compared to 3 patients taking **non–mercury** containing TTM (Group II) and to 2 healthy volunteers (Group III). Quantitative estimates of mercury ingestion based on chemical analysis were compared to US regulatory standards.

Results

Group I were significantly older (mean 55 yrs) than other participants, took TTM on average for 51 months and had a mean of 2.5 non-specific, mercury-related symptoms. Group I had higher mean diastolic pressures (85 mm Hg) than Group II (73 mm Hg) ($p=0.06$) and more loose teeth. Mean daily mercury intake in Group I was 674 µg estimated as 10µg/kg /day. (Established ref. dose for chronic oral exposure; 0.3µg/kg /day). Blood mercury levels were non-detectable but mean urinary mercury levels for Group I were 67µg/L (EPA levels <20 µg /L). Renal and liver function tests were not significantly different between groups and within normal clinical range.

Conclusions

Prolonged ingestion of mercury containing TTM is associated with absent blood but relatively high urinary levels. Further studies are needed to evaluate toxicity and therapeutic potential.

Key words: Tibetan Medicine, Precious Pills, Mercury toxicity.

INTRODUCTION

The growing popularity of Asian traditional medicines has aroused concern over the presence of heavy metals added either as ingredients, or present unintentionally due to contamination [1-5]. Documented case studies have reported serious signs of toxicity from lead, arsenic and to a lesser extent mercury while random samples of herbal medicines collected in India and the US have revealed significant levels of heavy metals [6,-10]

Traditional Tibetan medicine (TTM) is an ancient holistic system of health care that utilizes a complex herbal and mineral pharmacopia[11,12].

Mercury is an important constituent of specific Tibetan medicines known as **Precious Pills,** multi–ingredient formulas used to treat a wide variety of conditions. Before mercury is incorporated into these pills however, it first undergoes a lengthy process of "detoxification" to produce **Tsothel**, a substance traditionally considered safe for patient use while possessing important therapeutic properties.[12,13,]

High levels of mercury have been detected in Tibetan medicines[10], however until now, specific evidence of toxicity due to mercury poisoning has not been documented. The current small case series represents the first time that Traditional Tibetan medicines (TTM) containing mercury have been chemically analyzed and their clinical, biochemical and toxicological effects evaluated in a small group of patients using them over a prolonged period of time.

METHODS

Study Design: An open, small case series of patients constituting the initial, feasibility stage of a large, future, prospective, clinical study.

Setting

The outpatients department of Delek Hospital, Dharamsala, Himachel Pradesh, India, a Western style hospital serving the Tibetan refugee, local Indian and tourist population.

Patients

A volunteer non-randomized sample of 9 Tibetan patients attending Delek Hospital outpatient department, who in addition to taking conventional, western medications prescribed by Delek hospital physicians were also using TTM prescribed by traditional doctors from the nearby Men-Tsee-Khang (Tibetan Medical & Astrological Institute).

Study participants included 6 patients **(Group I**) regularly taking TTM in the form of "**Precious Pills**" which contained "detoxified" mercury as an ingredient and 3 patients **(Group II)** regularly taking TTM, without "detoxified mercury in its composition in which mercury was **not** an intentionally added ingredient.

In addition 2 volunteers **(Group III)** recruited from personnel working at MTKI, in good general health and taking neither Western nor Tibetan medicine served as controls for clinical, serum and urinary mercury evaluation.

Inclusion Criteria

- Regular use of **TTM** for at least **1 month** prior to the present study.

- The absence of any serious or life threatening disorders diagnosed in the period **before** commencing TTM therapy.
- Since patients were recruited from a western style OPD, several were also taking conventional medication in addition to TTM. These patients were included in the study but were requested to give the generic names, doses and duration of these medications to the research staff.

Exclusion Criteria
Documented evidence from Delek Hospital of Hepatitis A or B, a pre-existing kidney disease, psychiatric, neurological or serious cardiac condition, that pre-dated and was diagnosed according to conventional criteria prior to the current TTM treatment, carcinoma, HIV, or working in an environment exposed to mercury including the pharmacy of MTKI.

The study was approved by the local IRB /Ethics committee of Men-Tsee- Khang Institute of Traditional Tibetan medicine (MTKI) and Delek Hospital according to the Declaration of Helsinki.

All patients considered eligible for the study were requested to sign an informed consent form, following a full explanation of the nature and purpose of the study by the project's research staff.

Intervention
The 9 patients recruited into the study were questioned by local research staff from MTKI and Case Report Forms completed including demographic data, present and past conventional medical history, current treatment with TTM, including duration, dosage, frequency, name of formula and concomitant treatment if any, with conventional medication.

The presence of 23 non-specific symptoms of mercury toxicity compiled by the researchers from a review article on the subject [14], were evaluated by questioning each patient and included; metallic taste, burning sensation and/or mouth or throat pain, nausea, vomiting, hematemesis, diarrhea, abdominal pain, excess saliva, fatigue, depression, headaches, weakness, loss of concentration, easy blushing, extreme shyness, excessively emotional, anxiety, insomnia, anorexia, weight loss, delirium, and dizziness.

Patients **currently** suffering from any of the above symptoms were **retrospectively** questioned as to whether **these symptoms** had been present **before** or developed **after** taking TTM and whether at the present time, they would consider them to be **better, worse** or **unchanged** since TTM.

A general physical examination was performed by Western trained physicians working at Delek hospital who were informed only that the study participants were taking Tibetan Medicine but not whether this medication was mercury containing (Group I) or non mercury containing (Group II). Physicians conducted a full physical examination particularly for signs of mercury toxicity[14] including; cardiovascular evaluation (hypertension), dermatological examination (skin discoloration, rashes), neurological examination (abnormal reflexes, slurred speech, paralysis, tremor, peripheral sensory and motor neuropathy, tunnel vision) and oral examination evaluating presence of loose teeth, decay and dental fillings.

Any laboratory tests that patients had previously undertaken at Delek hospital or elsewhere were added to the Case Report Forms

Laboratory analysis
Blood for renal and liver function was taken from all patients in the study and evaluated in the laboratory of Delek hospital for levels of sodium, potassium, urea, creatinine, bilirubin, SGOT, gamma-GT, alkaline phosphatase and γGPT. Urine samples were obtained from participants and tested on site for the presence of red blood cells and protein, using a dip-sticks method.

For urinary inorganic mercury levels, a freshly voided urine sample was collected in a standard glass test tube from each of the participants and 2 controls. For blood inorganic mercury concentrations, an additional 5 cc of venous blood was taken from participants and controls and added to an EDTA tube placed on ice. All samples were refrigerated at 4^0C for the duration of the study. For transportation to Israel, blood and urine samples were packed on ice, and taken by an air courier to Israel, where they were delivered by hand to the Dept. of Toxicology, Sheba Medical Center, Tel Aviv, Israel

Analysis of whole blood and urine for inorganic mercury concentrations was performed using Flow Injection Mercury System (FIMS) equipped to an Atomic Absorption Spectrometer (Perkin Elmer Analyst 800 A). (Detection limit of 0.4μg/L).

Materials
All Traditional Tibetan Medicines taken by the study participants was locally made in the pharmacy of MTKI and consisted of complex formulas containing a variety of herbal and minerals ingredients formulated according to classical Tibetan pharmacopoeial texts.[11]

Mercury in the form of **"Tsothel",** or "**Detoxified mercury**" was an ingredient of specific Tibetan Medicines known as **"Precious Pills"** of which the following 4 varieties were used by Group I patients in the current study; *Tso-Tru Dashel, Mangjor Chemno , Ratna Sanphel,* and *Jumar 25* [15] .

Chemical Analysis
Analysis of the 4 types of Precious Pills used in the study all containing detoxified mercury (Tsothel) and a sample of **Tsothel** alone in the form of a fine black powder, was performed at the Chemistry Dept. of Liverpool University, UK.
All Samples were digested in a microwave accelerated reaction system using nitric acid (3 mls), hydrochloric acid (2 mls) and hydrofluoric acid (1ml) followed by micro-wave for 40 minutes at 200^0C producing a clear precipitate free solution.
Analysis of mercury and other heavy metals were performed on ICPAES (Inductivity Coupled Plasma Atomic Emission Spectrometer) Spectro. CCD model and analyzed against standard calibration lines. Carbon, hydrogen and nitrogen were analyzed by decomposing samples at high temperature (1050^oC) and any carbon present detected as $C0_2$, hydrogen as H_20 and nitrogen as N_2, using a CHN Analyzer (Carlo Erba model 1106).

Data Analysis
The non-parametric Mann-Whitney Test was used to compare quantitive, continuous variables between Groups I and II and the Kruskal-Wallis Test between 3 groups. For qualitive variables the Fishers Exact Test was applied.

RESULTS

Group I was significantly older (mean 55 yrs ± SE 6.4) compared to Group II (26.7yrs ±SE 5) and Group III (32.5yrs ± SE 0.5) (p=0.05). Mean duration of treatment with TTM, was 51 months for Group I (range 2-96 mths) and 24 mths for Group II.(range 0.5 – 72mths) (NS). **(Table 1)**

Group I had an overall prevalence of 10.9 %, non-specific, mercury related symptoms (15 out of a possible total of 138 (23x6)) with a mean of 2.5 symptoms /patient, (±SE 0.22) (range1-3). The most common symptoms reported were headaches (5 patients), weakness (2), nausea (2), dizziness (2), insomnia (2), blushing (1), depression (1).
Group II had a prevalence of 21.7% mercury related symptoms (15 out of a possible total of 69 (23x3)) with a mean of 5 symptoms/patient (± SE 2.3) (range 1-9).(p=0.058). **(Table 2)**

In Group I only 4 symptoms (2.3%) developed **after** taking TTM compared to 3 (4.7%) in Group II **(NS),** none of which were reported as worsening during treatment.
The mean **systemic blood pressure** in Group I was 122.5 mm Hg (±SE 5), Group II 106 mm Hg (±SE 7) and Group III 122 mm Hg (±SE 2.5) **(NS)**. Group I had higher mean **diastolic** pressures 85mmHg (±SE 2.2) compared to Group II, 73 mmHg (±SE 3.3)) and Group III, 75 mmHg (±SE 5). (p=.062).

At the time of the study two patients in Group I were concurrently treated with conventional medication for **essential hypertension.**

Group I patients had significantly more **loose teeth** than Group II. (83% v 0%) (p=.015) together with some evidence of decay. No significant differences in the prevalence of fillings were found.

Other aspects of Physical examination including skin evaluation were normal, with the exception of a slight tremor detected in a single Group I patient who was concurrently taking the drug Nifedipine for hypertension.

Laboratory tests
Mean serum levels for liver and renal function tests were within the normal clinical range and did not differ significantly between groups. All urine samples were negative for red blood cells and protein.

Blood mercury levels were **non-detectable** in all groups. **Mean urinary mercury** levels for Group I were 67 µg/L (±SE37.3) (range 0 –173 µg/L), Group II 1.7 µg/L (1 sample positive) and non detectable in Group III. Environmental Protection Agency (EPA), Biological Exposure Index (BEI) for urinary mercury levels in chronic oral exposure is <20 µg/L[16]

Chemical Analysis.
The composition of the mercury containing powder **Tsothel** demonstrated: mercury 44.7%, calcium 1%, sulfur 42.5%, silver 0.4%, iron 1.5% and copper 0.5%. Most mercury was in the form of mercuric sulfide (HgS) with smaller amounts as mercuric sulphite ($HgSO_3$) and mercuric sulphate ($HgSO_4$).

Analysis of the 4 types of **Precious Pills** used by Group I patients is shown in **Table III**. Mercury content ranged from 1.4 -2.3mgs.

Calculation of daily mercury ingestion compared with regulatory standards

The mean **weekly** consumption of mercury in Group I was calculated as **4720 µg** (range 2300-9800 µg) equivalent to **674µg/day** (range 329-1400µg) **(Table 4).**
Assuming an average body weight of participants as 70kgs, the average intake of mercury in Group 1 was estimated as approx. **10µg/kg/day (range 4.7-20µg/kg/day).**
Environmental Protection Agency (EPA) established reference doses (RfDs) for oral chronic exposure is 0.3 µg/kg/day for mercuric chloride[16]

DISCUSSION

In this small case series, the toxicological effects of mercury were evaluated in patients taking Precious Pills, a form of Traditional Tibetan Medicine (TTM). Although representing only the feasibility stage of an intended larger clinical trial, these initial findings present for the first time a chemical analysis of Precious Pills and a preliminary attempt to correlate their high mercury content ranging from 1.4-2.3 mgs with potential toxicity in patients.

Mercury toxicity is essentially a multi-system disorder with symptoms of acute and chronic poisoning associated with often wide spread deposition of mercury in various tissues[7]. Clinically elemental, inorganic or organic mercury poisoning can be accompanied by central nervous system dysfunction, renal damage ranging from asymptomatic, reversible proteinure to fully developed nephrotic syndrome, oedema and hypoproteinemia, as well as liver damage and characteristic skin rashes.[17]

In the current study, 6 patients taking Precious Pills for an average of over 4 yrs, had a mean daily estimated intake of mercury of approx. 10 µg/kg/day an amount well above the EPA established reference doses for mercuric chloride of 0.3 µg/kg/day[16]. Although this ingested mercury appeared to be mainly in the form of mercuric sulphide, toxic effects at these levels whatever the counter ion in the mercury salt have been well documented in the past.[18-20]

Despite this prolonged intake however, blood levels of mercury in this case series were non-detectable by Atomic absorption spectrometry although urine levels, (mean 89 µg/L), were significantly greater than the normal reference levels (<20 µg/L)[16.]

These findings suggest that while most of the ingested mercury from Precious Pills, probably in the form of mercuric sulfide (Hgs), is harmlessly excreted in the stool, some mercuric compounds are absorbed.

Amongst Group I patients, renal and liver dysfunction based on serum examination was not demonstrated, findings which cannot be wholly explained by our exclusion criteria. Although patients with serious kidney disease were not enrolled in the current study this exemption was applied only to participants with pre-existing conditions where conventional diagnosis had pre-dated TTM treatment.

Patients did demonstrate several non-specific signs and symptoms of mercury toxicity. Group I patients had more loose teeth and higher mean diastolic pressures levels (although within normal limits for age) than Group II. In addition a single Group I patient concurrently using Nifadapine for hypertension, exhibited a slight tremor.

Group I patients however, were significantly older (55 yrs) than the other participants and both essential hypertension [21, 22,] and poor dental care [23] have been documented as common amongst older Tibetans. Nifadapine a calcium channel blocker used for hypertension has also been associated with tremor [24]

The prevalence of other non-specific symptoms of mercury toxicity obtained from questionnaires was low in Group I (2%), with no symptoms reported as worsening and dermatological signs not detected.

Whether the above findings are due to prolonged mercury ingestion or secondary to other factors however cannot be conclusively answered from this study. A case series such as this with small groups, uncontrolled for age, general health or use of conventional medicines and not fully blinded evaluations presents significant limitations to interpretation. In addition the ability of patients to accurately relate their symptoms introduces a significant recall bias making the data derived from the questionnaires of limited validity. Nevertheless we do believe that these early findings have raised a number of important questions relating to the inclusion of mercury compounds in Traditional Tibetan Medicines.

Mercury's disruption of normal cell physiology is thought to arise principally from its covalent binding to sulphydral groups (SH) and to phosphyl, and amide groups, interactions considered to cause the toxic effects associated with mercuric compounds through widespread disruption of enzyme systems, transport mechanisms, membranes and cell structure[25].

Although beyond the range of this study, it is possible to speculate that under certain circumstances, the mercury salts in Precious Pills that appear to be absorbed but rapidly cleared from the blood, could possess some form of bio-activity. Whether this activity is toxic or actually underlies a potentially therapeutic effect remains to be investigated.

Precious Pills are complex formulas containing many botanical and mineral ingredients and are traditionally used to treat a wide range of conditions including blood disorders, cancer, neurological problems, allergies, arthritis, chronic wounds as well as use as tonics and antidotes to chemicals and poisons[11-13].

Mercury is an important constituent of Precious Pills, however while elemental mercury is considered extremely toxic in Tibetan Medicine, its "detoxified" form, **Tsothel**, produced by a complex process which takes several months, is considered an important therapeutic substance that is safe for oral ingestion[13,14] .

In view of the growing popularity of Traditional Tibetan medicine in the West and the increasing numbers of patients traveling to Asia for treatment, there is no doubt that further research needs to be performed on these medications

A much larger prospective, controlled, blinded clinical study should be undertaken in patients taking mercury containing TTM to assess toxicity, with periodic assessments of biochemical and clinical markers, as well as serial documentation of mercury levels in serum, urine, hair and other tissues. In addition, laboratory studies should be performed evaluating the bio-activity of Precious Pills and *Tsothel* particularly for their anti-inflammatory and anti-cancer activity.

Acknowledgements

The authors gratefully wish to thank the following: Prof Stanley Roberts of The University of Liverpool for helpful advice and the generous use of his facilities, Mr. Sandup Lhatse (Director) and the staff of Men-Tsee-Khang (Tibetan Medical & Astro. Instt.), Delek hospital, Dharamsala for their cooperation throughout the project, Ms. Sarah Furst for typing this manuscript. **Financial disclosure:** No relevant financial interest by any of the authors. **Funding/Support:**

The study was supported by The Louis L. Borick Foundation, Los Angeles and the Charles Gartner Foundation Dallas, Texas. **Permission for reproduction of Copyright materials:** Permission for reproducing the copyrighted material is given by Dr Sallon (contributing author) and all co -authors. **Role of Sponsor:** Hadassah Medical Organisation had no role in the design and conduct of the study, the collection, management, analysis and interpretation of the data, or preparation, review or approval of the manuscript for submission. **Study Disclaimer:** The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the US Environmental Protection Agency.

REFERENCES

1. Hardy AD, Sutherland H, Varshnov, R, Worthing M. **A report on the Composition of mercurials used in traditional medicines in Oman.** J. Ethnopharmacology 1995; **49:**17-22.

2. Kang Yum, E, Oransky SH. **Chinese patient medicines as a potential source of mercury poisoning.** Veterinary and Human Toxicology 1992; **34**:235-238.

3. Aslam M, Davis S, Healy M. **Heavy metals in some Asian medicines and cosmetics.** Public Health 1979; **93 :**274-284.

4. Ernst E. **Heavy metals in Ayurvedic herbs.** European Journal of Clinical Pharmacology. 2002 ;**57**:891-896.

5. Saper RB, Kales S, Paquin J. **Heavy Metal Content of Ayurvedic Herbal Medicine Products** JAMA 2004; **292**:2868-28736.

6. Marcus DM, Grollman AP .**Botanical medicine : the need for new regulations.** New Eng J. Med 2002 ;**347**:2073-2076

7 Clarkson T, Magos L, Myers G. **The Toxicology of Mercury – Current exposures and Clinical Manifestations**. New Eng. J. Med. 2003 ; **349**:18 1731-1736

8. Traub SJ, Hoffman RS, Nelson LS. **Lead toxicity due to use of an Ayurvedic compound** (abstract) J. Toxicol Clin. Toxicol. 2002; **1**: 40:322

9. Kew J, Morris C, Aihic A. **Arsenic and mercury intoxication due to Indian ethnic medicines.** British Medical Journal 1993; **306**:506-507

10. Moore C, Adler R. **Herbal vitamins; lead toxicity and developmental delay.** Pediatrics 2000 ; **106**:3:600-2

11 .Rinpoche R. **Formulation of Precious Pills in Tibetan drugs.** In: Tibetan Medicine. 215-217. Welcome Institute of The History of Medicine Publications, London. 1973

12 . Aschoff J **.Tibetan medicine and mercury – Mercury in Tibetan "Precious Pills".** Neuro-www.mgh.harvard.edu/neurowebforum/ generalfeedbackarticles .1996

13. Choedrak T **.The Rainbow Palace** ; 124-127 Bantam Books UK**,** 2000

14. Graeme AK., Pollack CV. **Heavy metal toxicity part I :Arsenic and Mercury.** J. Emergency Med 1998; 16: 45-46.

15. Dept. of Pharmacy, Consumer Information Service, Men-Tsee-Khang Institute of Traditional Tibetan Medicine and Astrology .**Contents of Precious Pills**. Pub. Men-Tsee-Khang, India,2003.

16. US Enviromental Protection Agency, Integrated Risk Information System;
At http:/wwwepa.gov/iris. (Accessed March 8, 2005)

17.Winship KA. **Toxicity of mercury and its inorganic salts** Adv. Drug. Reac. Acute Poisoning Rev. 1985; 4:129-60.

18 McAuliffe CA, **The Chemistry of Mercury**. Macmillan, London ,
1977

19. Greenwood N N, Earnshall A . **Chemistry of the Elements** 1422 **,** Pergamon Oxford, 1986,.

20 Friberg L T, Vostal J. **Mercury in the Environment** CRC Press, Cleveland, 1972

21 . Zhuang L,Cui C, Chen Y, et al**. Genetic Basis of essential hypertension in Tibetans**. Zhongua Yi Xue Za Zhi, 2002; **82**:1009-12

22. Malhotra RP, Sehgal AK, Krishan I**. Cardiovascular Epidemiology in Refugee Tibetans in India** J. Assoc Physicians India 1965; **13**:101-7

23. Robertson JA, Reade PC, Steidler NE, et al. **A dental survey of Tibetan children in Dharamsala.** Community Dent Oral Epidemiol. 1989; **1**: 44-6l

24. Topaktas S, Onur R, Dalkara R. **Calcium channel blockers and essential tremor.** European Journal of Neurology. 1987 **27**(2):114-119

25. Young-Jin Sue. **Mercury***;* In *:*The clinical Basis of Medical Toxicology;1239-1248 N.Y. Pergamon Press,*1991*

TABLE I

Demographic details of patients and controls

	Patient .No	Age (yrs)	Sex	Occupation	Reason for consulting Traditional Tibetan doctor	TTM#	Duration of TTM treatment (mths)	Conventional medical diagnosis	Medication Conventional
Group I Mercury containing) (Precious pills	1	28	M	Office worker	Digestive problem	T	30	Past history of typhoid	None
	2	69	M	Retired soldier	,Lower back pain Indigestion	T	96	None	None
	3	67	M	Monk	Arthritis	.J.T.R	60	problem Arthritis cervical disc	Analgesics
	4	48	M	Security guard	Severe lower back and knee pain	.J.T	96	Tuberculosis ,Sinusitis cervical disc problem	Anti TB analgesics
	5	66	M	Monk	headache ,Neck pain Gastritis	J,R,M	24	Hypertension Cervical spondylosis	Hypotensive
	6	52	M	Office worker	fever ,Hypertension Oedema	*J	2	Hypertension	Hypotensive (Nifadepine)
mercury -non)Group II containing Tibetan medicine	7	34	F	Office worker	Gastric ulcer	G,Y,T	72	None	None
	8	17	F	Student	Lower back pain	.P.D	0.5	None	None
	9	29	F	ice workerOff	Indigestion	SH.D.S	1	None	None
Group III Controls	10	33	M	Office staff				None	None
	11	32	M	administrator				None	None

 # TTM = Traditional Tibetan Medicine; T=Tso-Tru Dashel, **R**=Ratna Samphel, **J**=Jumar 25, **M**=Mangjor Chemno (Precious Pills containing **detoxified mercury (Tsothel))**
S=Sedok 5, **D**=Dhadan, **P**=Padrak, **SH**=Shiru**, T**=TKEA8, **Y**=Yaril 13 **G**=Ghiuam 9 (Tibetan formulas without added detoxified mercury)
* All Precious pills used by Group I were taken **once a week** with the exception of Patient 6* who took **J** (Jumar 25) daily.

TABLE 2

Comparison of non-specific symptoms of mercury toxicity between patient groups

Symptoms [#]	Group I (n=6)*	Group II (n=3)	P

Overall number **(%)** Mean no./ patient	15 (10.9%) 2.5 (± 0.022)	15 (22%) 5 (±2.3)	0.058
No. developing only after taking TTM (%) Mean no./patient	4† (2.3%) 0.7 (±0.3)	3 (4.7%) 1 (±1)	NS
No. present before taking TTM (%) Mean no. /patient	11 (8.0) 1.83 (±0.54)	12. 0 (17%) 4 (±1.5)	NS

Based on 23 non–specific symptoms of mercury toxicity[14]. For Group I the maximum possible no. of symptoms was 138 (6x23), and for Group II, 69 (3x23) .

† None reported as worsening * missing data = 1

TABLE 3

Chemical Analysis of Precious Pills

Precious Pill (mgs)	Mercury Content	Other Substances †
1. Tso-Tru Dashel (86.3)	**2.66% = 2.3 mg**	**Carbon, 37%, H_2, 6%, N_2, 0.99% Calcium, 6.4%, Sulphur, 0.88%**
2. Mangjor Chemno (131)	**1.57% = 2.1 mg**	**Carbon, 35.5% H_2, 4.7%, Calcium, 3.4% Fe, 1.05%, Phosphorus, 1.06% Sulphur, 0.86%**
3. Ratna Samphel (109.6)	**1.33% = 1.5 mg**	**Carbon, 36% H_2, 5.2% N_2, 1.6% Calcium, 3.2% Sulphur, 0.87% Phosphorus, 1.15% Iron, 0.94%**
4. Jumar 25 (121)	**1.15% = 1.4 mg**	**Carbon, 34.12% H_2, 4.5% N_2, 0.83% Calcium, 5.7% Sulphur, 0.77% Iron, 1.01% Phosphorus, 0.74% Barium, 0.45%**

† All samples also contained low levels (ppm) of **Al Ma, Mn, Si, Cu and Zn**

TABLE 4

Amount of mercury ingested by Group I patients from Precious Pills and serum and urinary mercury levels

Patient	Name of Precious Pill	Amount of mercury/ pill (µgs)	Amount of mercury ingested / week (µgs) ‡	Serum mercury levels (µg/L)	Urine * Mercury levels (µg/L)
1	Tso-Tru Dashel	2300	2300	ND	ND
2	Tso-Tru Dashel	2300	2300	ND	-
3	Tso-Tru Dashel Jumar 25 Ratna Sampel	2300 1400 1500	5200	ND	38
4	Tso-Tru Dashel Jumar 25	2300 1400	3700	ND	173
5	Jumar 25 Mangjor Chemno Ratna Sampel	1400 2100 1500	5000	ND	57
6	Jumar 25	1400	9800	ND	-

ND= Non-detectable

‡ All patients ingested Precious Pills on a once/week basis with the exception of patient 6 who took Jumar 25 daily

* Missing data =2