

ORIGINAL RESEARCH ARTICLES

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# Analysis of mercury in Malaysian herbal preparations

HH Ang<sup>1</sup> and KL Lee<sup>1</sup>

## ABSTRACT

The DCA (Drug Control Authority) in Malaysia started implementing the phase three registration of traditional medicines on 1st January 1992 with special emphasis on the quality, efficacy and safety in all pharmaceutical dosage forms of traditional medicinal preparations. The rhizome of *Smilax luzonensis* is eaten as an aphrodisiac in the Malaysian community. This study was conducted to analyse the mercury content of 100 pharmaceutical dosage forms of *S. luzonensis* that were purchased in the Malaysian market, using cold vapour atomic absorption spectrophotometer. Results show that 86% of the products complied with the quality requirement for traditional medicinal preparations in Malaysia with particular reference to mercury content. Mercury, which has adverse effect on the male reproductive system, is present in 14% of the products examined, which calls for urgent action by the Malaysian government towards rectifying the abnormality.

## INTRODUCTION

The use of traditional and alternative medicine has increased worldwide.<sup>1-11</sup> However, the safety of alternative medicinal preparations for use has been questioned due to reports of unwanted side effects.<sup>12-18</sup> Therefore, a critical evaluation of their safety for use is extremely important.<sup>8,18,19</sup>

The Malaysia government started implementing the phase three registration of

traditional medicines on 1st January 1992 under the Control of Drugs and Cosmetics Regulation 1984. The regulation emphasises quality, efficacy and safety (including the detection of the presence of heavy metals) in all pharmaceutical dosage forms of traditional medicinal preparations.<sup>8,20-22</sup>

Malaysia is blessed with an abundance of varied medicinal plants, which places the country among the world's 12 mega biodiversity rich countries in terms of the number of plant species.<sup>23</sup> One of these herbal remedies is *Smilax luzonensis*, commonly known as *akar banar*,<sup>23,24</sup> *akar gadong tikus*,<sup>23,24</sup> *akar kelona betina*,<sup>23</sup> *akar semenjoh*,<sup>23</sup> *alok besil*,<sup>24</sup> *banar*,<sup>24</sup> *banar babi*,<sup>23-25</sup> *canar babi*,<sup>23</sup> *gadong jantan*,<sup>23,25</sup> *gadong tikus*,<sup>25</sup> *kelona betina*,<sup>25</sup> *kijil*,<sup>25</sup> *rancang tembaga*,<sup>25</sup> and *semenjoh*.<sup>25</sup> The rhizomes of this plant are used as sexual tonics<sup>25</sup> and as such various

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## KEY WORDS:

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<sup>1</sup>School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, 11800, Penang, Malaysia.

Correspondence: Dr H. H. Ang, Associate Professor, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, 11800, Penang, Malaysia. Tel: 04-6533888 ext. 2264; Fax: 04-6570017; E-mail: [hhang@usm.my](mailto:hhang@usm.my)

pharmaceutical preparations of the plant are available in the Malaysian market.

This study analysed the mercury content of 100 products (both registered and unregistered with the DCA Malaysia) in various pharmaceutical dosage forms of *S. luzonensis* using cold vapour atomic absorption spectrophotometer (CVAAS). The products were purchased in the Malaysian market using simple random sampling technique to ensure equal<sup>26</sup> and unbiased<sup>27</sup> selection of any sample.

## MATERIALS AND METHODS

All reagents used in this study were of analytical grade: hydrochloric acid (HCl) 37% (sp. gr. 1.33, Merck); nitric acid 65% (sp. gr. 1.40, Merck); stannous chloride dihydrate (BDH, Prod. 10270) and mercury stock solution 1000ppm (BDH, prod. 141454 K). All glass wares were soaked in aqua regia ( $\text{HCl}:\text{HNO}_3 = 3:2$ )<sup>28</sup> for two hours and then washed with deionised water (Deioniser Elga B113) prior to use.

One hundred medicinal preparations of *S. luzonensis*, either in single or combined preparations (Tables 1 and 2), were digested using freshly prepared aqua regia wet digestion. Approximately 1.5g of each sample was weighed and placed in 100ml quick fit round bottom flask, after which 25ml freshly prepared aqua regia was added. The mixture was then refluxed over water bath for 6–8 hours (or until the sample had completely dissolved in the aqua regia). The mixture was then allowed to cool and filtered; the residue was then washed with deionised water. The combined aqueous extract was then made up to 50ml with deionised water.

This extraction procedure was repeated for the same sample (replicate) and the blank (containing aqua regia only). Coarse particles such as tablets, pills or powders, capsules and other contents were grounded to fine powder or particles prior to wet digestion.

Following this, 1ml extract, blank or standard solution, was added to 70ml deionised

water in 150ml quick fit conical flask. Water was then added up to 2ml of 10% stannous chloride and aspirated by gas stream into the flameless pathway of the monochromatic light of GBC 906 AA model atomic absorption spectrophotometer (complete with in-built window-based 906 programme software). The absorbance was recorded when stable and the data were analysed. The operating procedures used were slit width: 0.5nm, current: 3.0mA and wavelength: 253.7nm.

Then 10g stannous chloride dihydrate ( $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ ) was dissolved in 20ml hot concentrated HCl and diluted to 100ml with deionised water. The resulting solution was heated with a metallic tin until the precipitate disappeared. It was stored in a glass bottle containing tin powder.

Mercury stock solution (1000ppm) was diluted serially to produce a standard solution of 0.1µg/ml. This was followed by adding 70ml deionised water into each of the seven 150ml quick fit conical flasks. They were then added to 0, 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0ml 0.1µg/ml of mercury stock solution to produce 0, 0.05, 0.1, 0.15, 0.2, 0.25 and 0.30µg of mercury respectively. Also, 2ml of 10% stannous chloride was added to each flask, after which they were aspirated by a gas stream into the flameless pathway of the monochromatic light. Absorbance was recorded when stable and the data were analysed.

## RESULTS

### Mercury content evaluation

Table 1 shows that 14 out of the 100 products (14%) contained 0.51–1.23ppm mercury and, therefore, do not comply with the quality requirement for traditional medicines in Malaysia, which should not exceed 0.5ppm for mercury.<sup>30-33</sup> Six of the 14 products were already registered with the DCA Malaysia; these were capsule rancang tembaga extra ( $0.51 \pm 0.21$ ppm mercury), ace capsule rancang tembaga ( $0.53 \pm 0.12$ ppm mercury), ummira rancang tembaga plus ( $0.68 \pm$

Table 1 Content of mercury in *S. luzonensis* preparations in Malaysia

Status of registration	Number complying <sup>a</sup>	Number not complying <sup>a</sup>	Total
Registered	14 <sup>b</sup>	6 <sup>c</sup>	20
Unregistered	72 <sup>b</sup>	8 <sup>d</sup>	80

<sup>a</sup> ≤ 0.5ppm mercury<sup>30-33</sup>; <sup>b</sup> ≤ 0.5ppm mercury; <sup>c</sup> 0.51–0.68ppm mercury; <sup>d</sup> 0.56–1.23ppm mercury

Detection limit is defined as the concentration that will produce an absorbance signal three times the standard deviation of the blank.<sup>29</sup>

$$\text{Detection limit (instrument and sample)} = \frac{\text{Detection limit of instrument} \times \text{dilution factor}}{\text{Sample weight}} = 0.1\text{ppm}$$

0.11ppm mercury), gold box rancang tembaga plus ( $0.62 \pm 0.12$ ppm mercury), maajun pak tani rancang tembaga ( $0.61 \pm 0.12$ ppm mercury) and maajun petani rancang tembaga ( $0.56 \pm 0.21$ ppm mercury).

The remaining eight of the 14 products were available in the Malaysian market nationwide but were not registered with the DCA Malaysia. These were: super capsule rancang tembaga ( $0.70 \pm 0.03$ ppm mercury), great capsule rancang tembaga ( $0.63 \pm 0.12$ ppm mercury), tender capsule rancang tembaga ( $0.73 \pm 0.12$ ppm mercury), extra capsule rancang tembaga ( $0.56 \pm 0.12$ ppm mercury), force capsule rancang tembaga ( $1.23 \pm 0.23$ ppm mercury), super capsule rancang tembaga plus ( $0.61 \pm 0.24$ ppm mercury), force capsule rancang tembaga plus ( $0.78 \pm 0.11$ ppm mercury) and jiwa super capsule rancang tembaga ( $0.88 \pm 0.12$ ppm mercury).

Only 86% of the products available in Malaysian markets complied with the maximum level of mercury content required for traditional medicines in Malaysia.

## DISCUSSION

The use of aqua regia in acid digestion could ensure total extraction of metals from both inorganic and organic samples and virtually eliminates loss of mercury, compared to conventional wet digestion.<sup>34</sup> CVAAS is the predominant technique for mercury

analysis,<sup>29,35-38</sup> due to its high selectivity and sensitivity. The sensitivity of the CV technique is far greater than can be achieved by the conventional AAS because it has 100% sampling efficiency, since all the mercury in the sample solution placed in the reaction flask is chemically atomised and transported to the sample cell for measurement.<sup>29</sup>

The general belief that herbal preparations are natural and, therefore, inherently safe,<sup>39-41</sup> harmless<sup>42</sup> and without any adverse effects is sometimes unfounded.<sup>22</sup> Toxic effects of herbal preparations have been attributed to several factors including contamination by mercury. Mercury poisoning through traditional Chinese,<sup>43-47</sup> Indian<sup>48,49</sup> and Malaysian<sup>50</sup> medicines have been reported. In addition, mercury is capable of inducing sperm abnormality in human,<sup>51</sup> whilst higher blood mercury concentration is associated with male infertility.<sup>52</sup> Other studies have shown that membranes of acrosomal cap, the midpiece and the tail of human sperm are potential binding sites for mercury.<sup>53</sup>

Therefore, the DCA Malaysia has specified that the validity of pharmaceutical products (non-poisons) should be limited to a maximum of five years. Applicants will have to submit an application for re-registration and re-assessment of the quality, efficacy and safety of their products. In addition, the DCA may reject, cancel or suspend the registration of any product if the need arises.<sup>54</sup>

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