Trending of Adulteration – ADR in Traditional Medicine & Health Supplement (TMHS) Products

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Overview

• Introduction
• Adulterant screening in NPCB
• ASEAN Post Marketing Alert System (PMAS)
• Adverse drug reactions associated with adulterated TMHS Products
• Challenges
• Conclusion
Introduction

• The use of TMHS products (a.k.a. Natural Health Products in some countries) is growing.
• Widely available in stores and on the internet.
• The World Health Organizations reported that 80 percent of the world’s population depends on herbal medicines.
• In Malaysia total of 21807 (TM) and *329 (HS) product being process and registered (cumulative figure)

* 2011 new code for HS
Traditional Medicine and Health Supplement Products (TMHS)

- **Traditional medicine** as defined under the Control of Drugs and Cosmetics Regulations 1984 means: Any product used in the practice of indigenous medicine, in which the drug consist solely of one or more naturally occurring substances of a plant, animal or mineral, of parts thereof, in the un-extracted or crude extract form, and a homeopathic medicine
Traditional Medicine and Health Supplement Products (TMHS)

- A Health Supplement (HS) means any product that is used to supplement a diet and to maintain, enhance and improve the health function of human body. It is presented in small unit dosage forms (to be administered) such as capsules, tablets, powder, liquids and shall not include any sterile preparations (i.e. injectables, eyedrops).

- TMHS have been subjected to pre-market approval and licensing for import and sale in Malaysia since 1992.

- Governed by various Acts
Traditional Medicine and Health Supplement Products (TMHS)

- Currently, method of evaluation for traditional medicines (TM) and health supplements (HS) – abridge evaluation
- Products with certain claims will be subjected to adulterant screening such as:
  - Men’s health e.g. sildenafil, tadalafil, analogues
  - Slimming e.g. sibutramine, fenfluramine
  - Muscle and joint pains e.g. NSAIDs, steroids
  - Cough and cold e.g. antihistamines
- Heavy metal analysis (routine test for TM)
- Microbial test (routine test for TM)
Why TMHS is popular?

• The perception of “natural means safe”. & “no side effect” (on long tradition of use history)

• Exaggerated claims of the products in the advertisement via internet and multi-level marketing implies as ‘cure for all” product.

• Many consumers want to find alternatives to allopathic medicines as result of their potential side effects especially for those with chronic illnesses.
Is TMHS really safe?
Potential risks of consuming TMHS

- Inherent toxicity
- Mis-identification of plant species
- ADULTERATION
- Contaminant
- Interaction
Health risks of **ADULTERATED** TMHS products

- Undeclared ingredients may not be recommended for certain disease or health condition
- Undeclared ingredients may not be authorised for sale due to related health concerns
- May contain a dose exceeds the maximum daily recommended dose
- Undeclared ingredients may not be
- Safety of analogues adulterants may not been known
- Multiple undeclared ingredients may increase the risk of possible interaction and serious health effect
Adulteration of TMHS products

- Products that are adulterated contains substances that are not declared on the label, including scheduled poison medicines or other potentially dangerous ingredients.
- It is considered as one of causes to the ADR cases.
- Consumer highly demand health products such as for weight loss, sexual enhancement, inflammatory conditions, treatment of diabetes have been considered the high risk products to be adulterated
Adulterant screening in NPCB
Adulteration Screening Unit

Responsibility

• Screening of adulterant in sample for:-
  – Registration
  – Surveillance
  – Enforcement
  – ADR
  – Complaint
Sample received

Number of Samples Received by Category (2006 - 2012)

<table>
<thead>
<tr>
<th>Year</th>
<th>Registration</th>
<th>Surveillance</th>
<th>Complaint</th>
<th>Enforcement</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>2144</td>
<td>2737</td>
<td>119</td>
<td>192</td>
<td>31</td>
</tr>
<tr>
<td>2007</td>
<td>2076</td>
<td>2294</td>
<td>149</td>
<td>268</td>
<td>7</td>
</tr>
<tr>
<td>2008</td>
<td>1487</td>
<td>2296</td>
<td>132</td>
<td>408</td>
<td>53</td>
</tr>
<tr>
<td>2009</td>
<td>1116</td>
<td>2236</td>
<td>103</td>
<td>1099</td>
<td>0</td>
</tr>
<tr>
<td>2010</td>
<td>748</td>
<td>2190</td>
<td>116</td>
<td>660</td>
<td>8</td>
</tr>
<tr>
<td>2011</td>
<td>607</td>
<td>2026</td>
<td>83</td>
<td>212</td>
<td>31</td>
</tr>
<tr>
<td>2012</td>
<td>604</td>
<td>1883</td>
<td>71</td>
<td>211</td>
<td>61</td>
</tr>
</tbody>
</table>
Statistic on adulterated samples

Number of Samples Tested and Adulterated (2006-2012)

- No. of samples tested
- No. of samples adulterated

Year | Samples Tested | Samples Adulterated
--- | --- | ---
2006 | 339 | 75
2007 | 728 | 114
2008 | 593 | 138
2009 | 1203 | 184
2010 | 1358 | 308
2011 | 769 | 273
2012 | 799 | 133
Statistic on adulterated samples

No. of Test Done for Different Types of Adulterants (2011-2012)

Categories of adulterant

- Steroid
- Non-steroidal anti-inflammatory drugs (NSAIDS)
- ED drugs
- Slimming agents
- Antihistamine
- Antidiabetic
- Statin
Popular adulterants

**Steroid**
Dexamethasone

**Erectile dysfunction drugs**
Sildenafil, tadalafil dan analog

**Antihistamine**
Chlorpheniramine, dextromethorphan, promethazine

**NSAIDs**
Phenylbutazone

**Analgesic**
Paracetamol

**Slimming Agents**
Sibutramine, N-desmethylysibutramine (analog sibutramine)

**Antidiabetic**
Metformin, Glibenclamide, Ripaglinide

**Statin**
Lovastatin
Combination of adulterant

- Chlorpheniramine + Dexamethasone
- Dexamethasone + Ibuprofen + Chloramphenicol + Chlorpheniramine
- Chlorpheniramine + Dexamethasone + Betamethasone + Prednisolone
- Paracetamol + Phenylbutazone
- Promethazine + Dextromethorphan + Chlorpheniramine
- Dexamethasone + Chlorpheniramine + Dextromethorphan
- Dexamethasone + Chlorpheniramine + Dextromethorphan + Promethazine
ASEAN Post Marketing Alert System (PMAS)
ASEAN PMAS

• Communication tools for ASEAN members in exchanging information with respect to health products especially involving in safety issues
• TMHS products also included in this activities and currently only few TMHS products reported under this tools.
No. of alert under PMAS for TMHS products 2012 (Jan – Dis)

No. of alert under PMAS for TMHS 2012

- Traditional medicine
- Health Supplement

- ~14 product adulterated with scheduled poison
- ~2 detected with high mercury level
- ~1 contaminant with Clostridium spp. (Thailand)

Bar chart showing the number of alerts for TMHS products in Malaysia, Singapore, and Thailand.
Type of adulterants under PMAS for TMHS products 2012 (Jan – Dis)

![Bar chart showing types of adulterants detected under PMAS 2012](chart.png)
ADR associated with adulterated TMHS Products
ADR MONITORING SYSTEM IN MALAYSIA

Reporter:
- a) Health professionals
- b) Product Registration Holder
- c) Consumer

ADR Report – Manual form: faks (03-79567151), emel (fv@bpfk.gov.my) & online reporting via www.bpfk.gov.my

National ADR Monitoring Centre

Drug Control Authority (DCA)

Malaysian ADR Advisory Committee (MADRAC)

WHO

Policy Implementation

Recommendation

Feedback
ADR REPORTS RECEIVED (YEAR 2000-2012)

- 2011: ADR due to adulterated products: 11
- 2012: ADR due to adulterated products: 12
Reported Cases

Famous adulterant detected in Malay Traditional Medicine product known as Makjun/Tonik

**Dexamethasone**, detected in various product’s name under medicine known as “Makjun” Majun Dua Istimewa, Maajun Burung Unta, Makjun Taufiq Dua Istimewa, Maajun Kuat Khasiat Sakit Pinggang & Maajun Tolak Angin
## Reported Cases

<table>
<thead>
<tr>
<th>No</th>
<th>Suspected Traditional Medicines (Adulterant)</th>
<th>Reported Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Madu Adunan Herba (Dexamethasone)</td>
<td>Acute jaundice and hepatitis</td>
</tr>
<tr>
<td>2</td>
<td>Jamu Tradisional Asam Urat Jaya Asli (Phenylbutazone)</td>
<td>Epidermal necrolysis, Jaundice, Eosinophilia, Rash maculo-papular, Stevens Johnson’s Syndrome, Dress Syndrome</td>
</tr>
<tr>
<td>3</td>
<td>Pil Haruan (Chlorpheniramine)</td>
<td>Unexpected Therapeutic Effect (general well being)</td>
</tr>
<tr>
<td>4</td>
<td>Air Ikan Haruan (Dexamethasone)</td>
<td>Hypotension, Pneumonia, Cushing’s Syndrome</td>
</tr>
<tr>
<td>5</td>
<td>Tonik Warisan Banjar (Dexamethasone)</td>
<td>Weight increase, moon face</td>
</tr>
<tr>
<td>6</td>
<td>Pil ibu gamat ratu mahsuri (Dexamethasone &amp; Chlorpheniramine)</td>
<td>Unexpected Therapeutic Effect (Asthma)</td>
</tr>
</tbody>
</table>
Reported Cases

Adulterants detected in Traditional Chinese Medicine (TCM) product

- **Dexamethasone & Chlorpheniramine** detected in product name as Twin Bee Wang Ling
- **Dexamethasone** - Xue Ya Gao Zhong Feng Qing Cao Yao Cao
- **Dexamethasone & Chlorpheniramine** Seven Leave Ginseng
Reported Cases

Adulterants detected & suspected in Traditional Chinese Medicine (TCM) product

- Positive Piroxicam & suspected Cortisone in product Ji Xue Teng

- For joint pain

ADR reported: Breath shortness
Reported Cases

Adulterants detected in other unregistered products

Maca Tongkat Ali
ADR reported: Myalgia, Joint Stiffness & Pain in Limb
Positive: Tadalafil

Vimax Capsule
ADR Reported: Dizziness & Eye pain
Positive: Sildenafil

PS-
ADR Reported: Blood glucose decreased
Positive: Repaglinide
ADR due to adulterated food products

- **Adulteration with sex stimulant**
  - Mentalk Candy
  - Goji Yumberry Powder
  - Hotton Vitality Candy
  - Kopi Tenaga Tok Lebai Plus
  - Kopi Pahlawan

- **Adulteration with anti obesity**
  - Lax 9
  - NP Trimz
Trending Summary

- An increasing trend over the years especially for the highly demand consumer products

- Implicated products mostly for sexual enhancement, pain relieving, slimming and for increase energy products

- Common adulterants were found to be therapeutic substances associated with the specific indications of the products such as adulterant for sexual enhancement drugs (sildenafil, tadalafil), pain relieving drugs (dexamethasone, piroxicam) and slimming drugs like sibutramine

- Foods and herbs which have been claimed to be aphrodisiacs also in trending to be adulterated with therapeutic substance.
Challenges

• Emerging of new therapeutic substances have been added as adulterants sometimes without any correlation with the product indication/substances.

• Drug analogues in sexual enhancement & slimming products is alarmingly high. Such analogues are difficult to detect by ordinary laboratory methods.

• Adulteration in product fall under category of Food-Natural Health Product Interface ??. Few products still under investigation food based product with added collagen, glutathione, botanical beverages

• Enhance the work systems in terms of work in close collaboration with other health stakeholders and various partners (agencies and community organizations)
CONCLUSION

Industry

Public

QUALITY, SAFETY & EFFICACY

Health Professionals

Regulators
Is everybody’s responsibility!
Thank you for your attention