Potential of Malaysian herbs as Halal Pharmaceuticals

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INTRODUCTION

SCOPE OF PHARMACEUTICALS (API)

PROSPECTS OF MALAYSIAN HERBS

HALAL PHARMACEUTICAL ISSUES

OPPORTUNITIES AND POTENTIAL

REGULATORY STANDARD CHALLENGES

REFERENCE MONOGRAPHS

CONCLUSION
INTRODUCTION

• Herbal prospects worldwide
• Various product categories
• High demand & highly regulated
• Niche products under *halalan toyyiban* brands
SCOPE OF PHARMACEUTICALS

Pharmaceuticals consists of;

- synthetic chemicals,
- microorganisms,
- animal,
- plants,
- minerals and
- biologicals (vaccines, monoclonal antibodies etc).
The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) are two international instruments between countries and pharmaceutical inspection authorities.

The PIC/S is meant as an instrument to improve co-operation in the field of Good Manufacturing Practices between regulatory authorities and the pharmaceutical industry.
<table>
<thead>
<tr>
<th>Type of Manufacturing</th>
<th>Application of this Guide to steps (shown in grey) used in this type of manufacturing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Manufacturing</td>
<td>Production of the API Starting Material</td>
</tr>
<tr>
<td></td>
<td>Introduction of the API Starting Material into process</td>
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<tr>
<td></td>
<td>Production of Intermediate(s)</td>
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<td></td>
<td>Isolation and purification</td>
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<tr>
<td></td>
<td>Physical processing, and packaging</td>
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<tr>
<td>API derived from animal sources</td>
<td>Collection of organ, fluid, or tissue</td>
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<td></td>
<td>Cutting, mixing, and/or initial processing</td>
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<tr>
<td></td>
<td>Introduction of the API Starting Material into process</td>
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<tr>
<td></td>
<td>Isolation and purification</td>
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<tr>
<td></td>
<td>Physical processing, and packaging</td>
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<tr>
<td>API extracted from plant sources</td>
<td>Collection of plant</td>
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<tr>
<td></td>
<td>Cutting and initial extraction(s)</td>
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<td></td>
<td>Introduction of the API Starting Material into process</td>
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<tr>
<td></td>
<td>Isolation and purification</td>
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<tr>
<td></td>
<td>Physical processing, and packaging</td>
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<tr>
<td>Herbal extracts used as API</td>
<td>Collection of plants</td>
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<tr>
<td></td>
<td>Cutting and initial extraction</td>
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<tr>
<td></td>
<td>Further extraction</td>
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<tr>
<td></td>
<td>Physical processing, and packaging</td>
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<tr>
<td>API consisting of comminuted or powdered herbs</td>
<td>Collection of plants and/or cultivation and harvesting</td>
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<tr>
<td></td>
<td>Cutting/commining</td>
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<tr>
<td></td>
<td>Physical processing, and packaging</td>
</tr>
<tr>
<td>Biotechnology: fermentation / cell culture</td>
<td>Establishment of master cell bank and working cell bank</td>
</tr>
<tr>
<td></td>
<td>Maintenance of working cell bank</td>
</tr>
<tr>
<td></td>
<td>Cell culture and/or fermentation</td>
</tr>
<tr>
<td></td>
<td>Isolation and purification</td>
</tr>
<tr>
<td></td>
<td>Physical processing, and packaging</td>
</tr>
<tr>
<td>“Classical” Fermentation to produce an API</td>
<td>Establishment of cell bank</td>
</tr>
<tr>
<td></td>
<td>Maintenance of the cell bank</td>
</tr>
<tr>
<td></td>
<td>Introduction of the cells into fermentation</td>
</tr>
<tr>
<td></td>
<td>Isolation and purification</td>
</tr>
<tr>
<td></td>
<td>Physical processing, and packaging</td>
</tr>
</tbody>
</table>
PROSPECTS OF MALAYSIAN HERBS

• Plant based pharmaceuticals
• New sources of healthcare products
• New approaches and techniques are applied in screening indigenous medicinal plants.
TYPES OF HERBAL PREPARATIONS

Phytomedicine
Standardized extract (100)
Freeze dried (40)
Extract (25)
Tincture, Juice (10)
Dried powder (10)
Fresh (2)

Value added
• The Malaysian herbs are a rich source of such pharmaceuticals
• Currently being researched to produce value added products
• As health supplements, nutraceuticals and phytopharmaceuticals.
HALAL PHARMACEUTICAL ISSUES

- *Shariah* compliant pharmaceutical products
- Halal source or origin
- Safe, quality & efficacy
- Manufacturing process regulated & monitored
• Halal pharmaceuticals is a niche area.
• Halal assurance fully controlled & monitored
• Sourcing of unadulterated halal assured raw materials (API, excipients, etc)
• Industry responding positively
• CCM the champion for halal pharmaceuticals
Developing Halal Standard for the Pharmaceutical Industry

• CCM is now going a notch higher from being a manufacturer of Halal pharmaceutical products to getting involved in the development of Halal standard for the pharmaceutical industry.
• The standard will further protect the interests of Muslim consumers in particular and all consumers in general the world over.
intoxicants

• Herbs having *khamar*-like effects are categorised as intoxicants affecting the central nervous systems are questioned.
• Poisonous plants avoided
LISTS OF PROHIBITED HERBAL PLANTS IN HERBAL PREPARATIONS
LISTS OF PLANTS CONTAINING SCHEDULE POISONS UNDER POISONS ACT 1952 (REVISED 1989)

• Aconitum
• Asidosperma quebracho
• Atropa belladona
• Black nightshade
• Berberis
• Calabar bean (Physostigma venenosum)
• Cabola albarrane (squill)
• Chondodendron tomentosum
• Colchicum autumnale
• Datura metel
• Datura stramonium
• Digitalis purpurea folium
• Drimia maritima (Squill)
• Ephedra Herbs
• Foxglove leaf
• Gelsemium sempervirens
• Hyoscyamus muticus
• Hyoscyamus niger

• Larrea tridenata
• Larnea mekicara
• Lobelia inflata
• Lobelia nicotianifolia
• Nicotinana tabacum (solanine)
• Nux Vomica
• Papaver somniferum
• Physostigma venenosum (Calabar Bean)
• Pilocarpus microphyllus
• Puasinystalia yohimbe
• Rauwolfia serpentina
• Rauwolfia vomitoria
• Schoenocaulonofficinale
• Scillae bulbus (Squill)
• Solanum nigrum (Black nightshade)
• Strychnos nuxvomica
• Urginea maritima (Squill)
• Urginea Scill (Squill)
• Valerian extract (Valepotriates)
• Valerian (Valepotriates)
PLANTS NOT ALLOWED

- *Dryabalanops aromatica & Borneolum syntheticum*
  - Contains camphor and borneol not allowed in oral preparations.

- Chapparal (*Larrea tridentate* and *Larrea mexicana*)
  - Reported to cause liver damage.

- *Hydrastis canadensis*
  - Reported to cause nerve system disruptions.

- *Magnolia officinalis*
  - Reported to cause kidney damage.

- *Stephania tetrandra*
  - Reported to cause kidney damage.

- *Piper methysticum* (kava-kava)
  - Reported to cause liver damage.

- Aristolochic Acid, [Attachment A](#) & [Attachment B](#)
  - Reported to cause kidney damage.
OPPORTUNITIES AND POTENTIAL

• The potential of Malaysian medicinal plants as halal pharmaceuticals can be enhanced
• proper strategies and funding mechanisms in place
• industry is a highly regulated
• fulfillment of various standards set by the regulatory agencies
REGULATORY STANDARD CHALLENGES

- Standards related to good practices in farming (GAP), post harvesting, extraction and drying, formulation and manufacturing (GMP)
- QC and standardisation
- Preclinical studies
- GLP assured
- Comply with international standards.
STANDARDIZATION OF *ORTHOSIPHON STAMINEUS* RAW MATERIAL AND PRODUCTS

### PHYSICAL PARAMETERS
- **NOMENCLATURE**
  *Orthosiphon stamineus* Benth
- **MICROSCOPY**
  Diacytic stomata, two types of glandular trichomes, palisade and mesophyll
- **ASH CONTENT**
  Total ash; not more than 10%
- **EXTRACTIVE VALUES**
  Hot extraction: -water- not less than 15%; ethanol-not less than 10%. Cold extraction: -water-not less than 10%; ethanol-not less than 5%.
- **WATER CONTENT**
  By lost on drying-not more than 10%
- **HEAVY METAL AND MICROBIAL LIMIT**
  Must below permissible limit by regulatory authority.

### CHEMICAL FINGERPRINT
Exhibit characteristic fingerprint of:
1. Thin Layer Chromatography
   Mobile Phase: chloroform: ethyl acetate (6:4): reference compounds: Sinensetin (Rf: 0.4-0.5)
2. High Performance Liquid Chromatography
3. Fourier Transfer Infra Red

### CHEMICAL STANDARDIZATION
- Materials and products must contain four marker compounds by HPLC.
- Concentration of the marker compounds must distribute in order of RA>EUP>SN>TMF.

### BIOLOGICAL STANDARDIZATION
- Materials and products must exhibit significant levels of biological activities:
  1. Antioxidant activity by
     - DPPH assay (>69%)
     - B-carotene linoleic acid system (>60%)
     - Xanthine oxidase inhibition assay (>60%)
  2. *In vitro* study on inhibition of calcium oxalate crystal growth (Positive *I* value)
• Herbal products worldwide are registered in Malaysia.
• Currently only need to fulfil requirements related to safety and quality.
Cumulative Number of Traditional Herbal Products Registered by NPCB from 2001-2008
Total cumulative Number of Herbal Products registered by NPCB from 1985-2008
<table>
<thead>
<tr>
<th>S. No</th>
<th>Traditional Herbal Medicine</th>
<th>Part used</th>
<th>Individual Formulation</th>
<th>Mixed formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Eurycoma longifolia</em> (Tongkat Ali)</td>
<td>Roots</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>2</td>
<td><em>Labisia pumilla</em> (Kacip Fatimah)</td>
<td>Leaves</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td><em>Orthosiphon stamineus</em> (Misai Kuching)</td>
<td>Leaves</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>4</td>
<td><em>Centella asiatica</em> (Pagaga)</td>
<td>Leaves</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>5</td>
<td><em>Hibiscus sabdariffa</em> calyx (Roselle)</td>
<td>Calyx</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>6</td>
<td><em>Andrographis paniculata</em> (Hempedu Bumi)</td>
<td>Plant</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>7</td>
<td><em>Garcinia atroviridus</em> (Asam Gelugor)</td>
<td>Fruit</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td><em>Cosmos caudatus</em> (Ulam raja)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td><em>Serenoa repens</em> Saw palmetto (palm tree)</td>
<td>Fruit/Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td><em>Ficus deltoidea</em> (Mas Cotek)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td><em>Curcuma longa</em> (Kunyit)</td>
<td>Roots</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><em>Ginkgo biloba</em> (ginko)</td>
<td>Plant</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>13</td>
<td><em>Camellia sinensis</em> (green tea)</td>
<td>Leaves</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>14</td>
<td><em>Ocimum basilicum</em> (Selasih)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td><em>Zingiber officinalis</em> (Halia)</td>
<td>root</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td><em>Triticum aestivum</em> (wheat grass)</td>
<td>leaves</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>17</td>
<td><em>Phyllanthus niruri</em> (dukong anak)</td>
<td>Plant</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td><em>Tamarindus indica</em> (asam jawa)</td>
<td>fruit</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td><em>Polygonum minus</em> (Kesum)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td><em>Apium graveolens</em> (saderi)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td><em>Garcinia mangostana</em> (mangosteen)</td>
<td>Fruit</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>22</td>
<td><em>Carica papaya</em> (papaya)</td>
<td>Fruit</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>23</td>
<td><em>Piper betle</em> (sirih)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td><em>Morinda citrifolia</em> (Noni)</td>
<td>Fruit</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td><em>Spirulina platensis</em></td>
<td>Algae</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td><em>Sauropus androgynous</em> (cekor manis)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td><em>Malpighia emarginata</em> (acerola)</td>
<td>Fruit</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td><em>Piper nigrum</em></td>
<td>Seed</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td><em>Solanum nigrum</em> (terung meranti)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td><em>Murraya koenigii</em> (curry leaves)</td>
<td>Leaves</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>
High claims

- Must be evidence based
- Requires funding for R & D in preclinical studies involving safety, efficacy, quality and stability of the formulation.
- Followed by clinical studies on the standardised products.
REFERENCE MONOGRAPHS

- Scientific and technical reference data is formulated in monographs
- Indicates specifications for the individual plants
- To assure reproducibility of the samples.
- Malaysian Herbal Monographs Vol. 1 & 2 completed
- The basis for the development of the Malaysian Herbal Pharmacopoeia and Pharmacopoeia Commission.
- *Halalan Toyyiban* reference standards are crucial for global recognition and commercialisation of product.
CONCLUSION

• Halal Pharmaceuticals a niche brand
• Great potential for the industry
• Wide range of product for various categories looking for new and novel products worldwide.
• Highly regulated global healthcare sector
• Standards with *halalan toyyiban* features brings new challenges and opportunities