Reverse Pharmacognosy: A Novel Strategy to Standardise ISM Drugs

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• Why-Novel Strategy?
• What is Reverse Pharmacognosy?
• How do it?
  – FRLHT’s Approach
Why A New Strategy?
ISM & Western Biomedicine are TWO DIFFERENT KNOWLEDGE-SYSTEMS THAT HAVE EVOLVED INDEPENDENTLY. 

....TWO DIFFERENT WAYS OF KNOWING
Epistemology: TK is Eco-system based

Level of Use & Familiarity helps in correlation of purpose & standard
Current QS of ISM Drugs…

• Parameters & Standards are Non-contextual to the culture from which it evolved

• Do not reflect safety & efficacy; but at best identity, purity

• While Traditionally identity, safety and efficacy were an integral part of Drug Property (Dravya guna)
Bacoside A (2.5 - 3 %), Bacoside B and other bacosides, Hersaponin, Betulic acid, Monnierin, Alkaloids - Brahmine (0.01-0.02 %) and Herpestine; Flavonoids; Saponin, D-mannitol, Nicotine, Saponins-Monierin. Sapogenins-Bacogenin A1-A4. Bacosine

Parallel Systems of Knowledge with no dialogue

Bacopa monnieri (Brahmi)

Modern

Ayurvedic

Rasa: Tikta Kasaya
Guna: Laghu, Sara
Virya: Sita
Vipaka: Madhura
Karma: V Kara, rasayana, medhya.

Varied Uses

Fever, Anaemia, Inflammation, Diabetes, Psychiatric disorders
Our approach in Standardisation today...
Some ‘Phytomedicines’ that have ‘failed’ in modern times
### Non-Contextual Usage

<table>
<thead>
<tr>
<th>Plant</th>
<th>Traditional Use</th>
<th>Recommendation</th>
<th>Modern use</th>
<th>Practice</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ephedra sinica</td>
<td>Asthma, cold</td>
<td>Under supervision, as a whole herb</td>
<td>Weight loss, Energiser</td>
<td>Isolated compounds, Synthetic compound, Large dose</td>
<td>Stroke, heart attack</td>
</tr>
<tr>
<td>Piper methysticum</td>
<td>Calming</td>
<td>Aqueous preparation</td>
<td>Anxiolytic effect</td>
<td>Acetone/Methanol extract</td>
<td>Hepatotoxicity</td>
</tr>
</tbody>
</table>
What is Reverse Pharmacognosy?

Pharmacognosy guided by Traditional Knowledge

Developing Contemporary Standards based on Traditional Advice, Parameters and tools
Factors Acknowledged by ISM

Identity of Ingredients

Collection

Processing & Storage

Diagnosis of the ailment

Administration of the Drug

Constitution of Patient

Efficacy

Quality Standards

(For What?.... The Purpose)

(What?)

(When? Where from)

(How? How long?)

Who to? How? How much? How long?
<table>
<thead>
<tr>
<th>Plant parts</th>
<th>Season of collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branches and leaves</td>
<td>Rainy (<em>Varsha</em>) and Spring (<em>Vasantha</em>)</td>
</tr>
<tr>
<td>Roots</td>
<td>Summer (<em>Greeshma</em>) or Late winter (<em>Shishira</em>)</td>
</tr>
<tr>
<td>Bark, Rhizome, Sap</td>
<td>Autumn (<em>Sharad</em>)</td>
</tr>
<tr>
<td>Heart wood</td>
<td>Early winter (<em>Hemantha</em>)</td>
</tr>
<tr>
<td>Flowers and fruits</td>
<td>As per Season</td>
</tr>
</tbody>
</table>
### Traditional Recommendations - Specific

<table>
<thead>
<tr>
<th>Factor</th>
<th>Plant</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity</td>
<td>Vidanga (<em>Embelia ribes</em>)</td>
<td>Chitra tandula, Kapaali</td>
</tr>
<tr>
<td>Collection</td>
<td>Haridra (<em>Curcuma longa</em>)</td>
<td>Collection at night</td>
</tr>
<tr>
<td>Processing</td>
<td>Pippali (<em>Piper longum</em>)</td>
<td>Should be boiled in milk (Kshirapaka)</td>
</tr>
<tr>
<td>Storage</td>
<td>Vidanga (<em>Embelia ribes</em>)</td>
<td>Should be used after storing for 1 year</td>
</tr>
</tbody>
</table>

**Abhava Pratinidhi Dravya**
Concept of Legitimate Drug Substitution
Yogadapi visham teekshnam uttamam bhashajam bhavet, bhashajam chapi duryuktam teekshnam sampadyate visham

(Cha. Su. 1.26)
Effect of Processing

- Rice - Uncooked - Very Heavy
- Cooked rice - Cooked with water - Comparatively light
- Kanji - Cooked with abundant water - light
- Puffed paddy - V. light

The changes in property of rice with cooking (Cha. Su.28. 271)
Tea Picking

- Picking early Spring & summer
- Hand pick only the top three leaves
- Put no pressure on the leaves in the basket
- Start processing promptly

Quality varies if long leaves are picked as opposed to young leaf buds
We should be investing similarly into each of the TM plants to study their variations, potencies and to state their USPs.
We need RELEVANT Parameters, Protocols & Standards that not only reflect Quality but also Safety & Efficacy…
Inter-cultural approach

1. Traditional recommendations?
2. Logic behind the recommendations?
3. Traditional quality parameters? How are they measured?
4. How do we make them contemporary and applicable to industry?
How do it?

FRLHT Campus

FRLHT, 74/2, Jarakhabande Kaval, Attur Post, via Yelahanka, Bangalore 560 064
Tel: 080 28568017; www.frlht.org
Document Traditional Knowledge on Drugs (simple non-Instrumental measurements)

- Modern Stdsn. Methods

- Traditional & Biological Markers

- Physical, Chemical, & Biological Markers

- Standard Drug
TQS Informatics

Software to store, retrieve and analyse data
Develop Relevant Parameters, Methods and Standards

- Sensory Evaluation
- Morphology
- Microscopy
- Chemistry
- Molecular Markers
- Bioactivity

Bio-chemical Standards
Why Sensory Evaluation for Quality Control?

- Sensory Parameters were used to evaluate quality of *Dravya* (substance) particularly for on-line process control
- It is still the widely accepted, scientific technique for QC in Food & Beverage industries and Perfumeries
Uniqueness about Human perception

- All five senses-perceived & analysed by ONE instrument—the Human Body
- Cognition adds value—mental processor
- Sensitivity—more sensitive
  - Nose: 0.00025ppm; x1000 times better
- Correlation specific to requirement
  - E.g., unripe & ripe mango-purpose
- Measures characteristic differences
- Subjectivity..reduced by training panel
Sensory Analysis
An Important QC tool for ISM Drugs

MODERN ATTRIBUTES → PROFILING BY TRAINED PANEL → TESTING AND STATISTICAL ANALYSIS → SENSORY STANDARDS
TRADITIONAL ATTRIBUTES
Bio-Chemical Markers

Trade, Distribution information

Traditional Information & Botanical Authentication

Bioassay/ Phytochemical/ Microscopy/ Mol Bio studies

Identify unique profiles/chemical markers

Isolation/ Characterisation, Biological activity

Relevant Quality Parameters/Tests/Markers
Identity...?
Correct Botanical Correlation
Substitutes
Adulterants
Vidari
Etymological Analysis of Ayurvedic Synonyms

A. *Pueraria tuberosa*
B. *Palasha* (*Butea monosperma*)

*Triparni*: Three-leaved
*Palashparni*: Leaves similar to *Palasha*

White tubers of *Pueraria tuberosa* (*Shuklakanda, Sitha*)
TLC of *Pueraria tuberosa*

SCAR marker of *Pueraria tuberosa*

(CURRENT SCIENCE, VOL. 94, NO. 10, 25 MAY 2008)
Collection: Maturity

Ipomea mauritiana Jacq. (tuber)

Same Botanical identity but different stages of maturity

Comparision of bioactivity of Vidari-mature & immature tubers

ED 50 values (mg/ml)

Mature Immature

Bioactivity

Preliminary HPTLC of tubers @ 366 nm at different maturity stages

TLC @ 366 nm
Mature & Immature Tubers

Ipomea mauritiana Jacq.

HPLC

Ratio of peaks Vs girth
Compounds of interest

- At least 3 compounds identified that appear to be related to maturity
- Isolation has been completed
- Characterisation is ongoing in collaboration with IISC
- Scopoletin and B-sitosterol seem to be present in both mature & immature
- One compound, may be a plant sterol, significantly higher in mature
ANIMAL STUDIES

Mice model using colloidal Carbon

IMMUNOMODULATORY ACTIVITY OF VIDARI IS MORE THAN THAT IN CONTROL

BIOACTIVITY OF MATURE IS MORE THAN THAT OF IMMATURE TUBERS
Day & Night collection of *Curcuma longa* L.

Bioactivity of *C. longa*

Effect of collection time on bioactivity of *Curcuma longa* (roots)

LD50 value (mg/ml)

<table>
<thead>
<tr>
<th>Time of collection (hrs)</th>
<th>LD50 value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4:00</td>
<td>0.4</td>
</tr>
<tr>
<td>17:00</td>
<td>0.3</td>
</tr>
<tr>
<td>21:00</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Densitometric scans @ 254nm of *C. longa*
Bioactivity of *Piper longum* preparations

- **Bioactivity of water decoction & milk decoction**

- **Samples:** water decoction, milk decoction & standard Piperine (0.5 µg)

- **Piperine Extracted**
  - Milk Decoction: 0.17%
  - Water Decoction: 0.12%
In conclusion…
Conclusion

• Reverse Pharmacognosy is a contextual strategy to develop relevant standards
• Trans-disciplinary and inter-cultural objective parameters, protocols and standards need to be developed
• Research into TM principles, science and practice in order to understand the recommendations
Conclusion

Way forward

- Document TQS
- Select Top 100 traded drugs & their TQS
- R&D at 10 Research Partners
- Develop TK based objective methods & standards that not only reflect identity but activity as well, through modern tools
- Convert them to simple parameters & standards possibly non-instrumental
Challenges…

- Inter-cultural, Inter-disciplinary understanding
- Cost-effective QC Diagnostics for the industry
- Cost-effective Drugs for Consumers
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Thank You!