Drivers from Indian perspective

GOLDEN TRIANGLE APPROACH

Traditional Knowledge
Modern Science
Modern Medicine
Drug Discovery and Development Process

Expensive, time consuming, numerous bottlenecks

Target Identification
Lead Identification
Lead Optimization
Preclinical Studies
Clinical Trials

Drug to Market

Economical, time sparing, least bottlenecks

Reverse Pharmacology

Phase IV
Relevant Science
Animal Pharmacology
Drug Development
Clinical Trials Phase III & I

Safety Study

Drug to Global Market

Drug to Market
# New Botanicals under Clinical trials using Reverse Pharmacology approach

<table>
<thead>
<tr>
<th>Drug</th>
<th>Clinical Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>M-97 (live 1)</td>
<td>Hepato-protective</td>
</tr>
<tr>
<td>NMHPT</td>
<td>Viral Hepatitis-curative</td>
</tr>
<tr>
<td>RRLJCD-SFE</td>
<td>Anti-Psoriasis</td>
</tr>
<tr>
<td>NMITLI-DM-FN</td>
<td>Type II Diabetes</td>
</tr>
<tr>
<td>NMITLI-OA-JP</td>
<td>Osteo-arthritis</td>
</tr>
<tr>
<td>RRLJ0125-F09</td>
<td>Anti-Hepatocellular carcinoma</td>
</tr>
<tr>
<td>AP9CD</td>
<td>Breast Cancer</td>
</tr>
<tr>
<td>RJMActeo</td>
<td>Anti-oxidant</td>
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</tr>
</tbody>
</table>
## NMITLI Programme

### Deliverables: 3 New Botanicals

### Targets

<table>
<thead>
<tr>
<th>Diabetes mellitus</th>
<th>Hepatitis</th>
<th>Arthritis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Insulin sensitisation</td>
<td>• Cytoprotective</td>
<td>• Pain relief</td>
</tr>
<tr>
<td>• Dyslipidemia</td>
<td>• Hydrocholeretic</td>
<td>• Anti-inflammatory</td>
</tr>
<tr>
<td>• Complications</td>
<td>• Antifibrotic</td>
<td>• Chondroprotective</td>
</tr>
<tr>
<td>• P.C.O.S.</td>
<td>• Immunomodulation</td>
<td>• TNF - α</td>
</tr>
<tr>
<td>• Oxidant damage</td>
<td>• N.A.S.H.</td>
<td>• Sarcopenia</td>
</tr>
<tr>
<td>• New leads</td>
<td>• Antiviral</td>
<td>• Q.O.L.</td>
</tr>
</tbody>
</table>
Ayurveda

• The traditional approach is to prescribe formulations with frequent and consistent repetition of certain herbals individually or as a group for a variety of diseases.

• The rationality of this kind of therapy was investigated scientifically and systematically by a team of scientists at RRL, Jammu.
The ancient wisdom of Ayurveda which is embedded in the art of multi-component therapy has been scientifically revealed.

It could be the ability of specific plants(s) to synergise each other for enhanced action profile.

(Biological Response Modifiers)
• One of the foremost of such group of herbals which has been documented very frequently as an essential part of about 70% prescriptions is `Trikatu’ which contains three herbs in equal proportions: 
  Piper longum
  Piper nigrum
  Zingiber officinalis
• Studies conducted at RRL, Jammu, have revealed the important role of `Trikatu’ as a drug bioavailability/bioefficacy enhancer.

• During the last 20 years a new approach of enhancement of drug bioavailability using drugs in combination with plant based substances as an adjunct was conceptualized and developed at RRL, Jammu
BIOENHANCER
AN AGENT CAPABLE OF ENHANCING
- BIOAVAILABILITY
- BIOEFFICACY
OF SPECIFIC DRUG WITH WHICH IT IS COMBINED WITHOUT ANY TYPICAL PHARMACOLOGICAL ACTIVITY OF ITS OWN AT THE DOSE USED
Effect of PIP + Rif against Mtb infection (mice) [in vivo]
Comparison of plasma levels of rifampicin in volunteers dosed with 200 & 450 mg of the drug with and without pip

Rif plasma levels (ug/ml)

Time in hrs

Rif 200mg
Rif 450mg
Rif 200 mg+ Pip
Rif 450 + Pip
New concept based on TK (Ayurveda)

New Drug formulations

Anti-infective
Anti-cancer
Anti-hypertensives

Bioenhancers

Dose Reduction by 50 – 80 %

Reduction in:
- Dose related toxicity
- Cost

Final approval of DCG (I) for marketing permission

Transformed into a Product (Anti TB drug formulation)
Herbal Therapeutics
Expected Deliverable:

Antigastric ulcer IND (Botanical)

Ap76p (Batch 31)
- Six constituents
- All the constituents are necessary

Active against different models
- Cold restraint induced ulcer test
- Asprin induced ulcer
- Histamine induced ulcer
- Pyloric ligation
- Ethanol induced ulcer
- Active against H. pylori (in vitro)

✓ Equal or better than Omeprazole
✓ Acts by multiple mechanisms
✓ Only one drug is required
✓ Presently combination of three drugs are used in Allopathic
✓ Nontoxic (LD50 = >2200 mg/kg)
Anticancer (Colon, Cervix, Breast)

- AVS → AP9a → AP9cd (Mix 3 Compounds)
  - Active in vitro
  - Active in vivo
  - Non-toxic
  - US Patent (6649650 dt. 18.11.03)
  - PCT & Indian patent filed
  - Agreement with a Company for development

Human cancer cell lines
Liver Cancer

(Hepatocellular carcinoma)

RJM 0125 P04 A003 F009

(K001 & K002)

Model: Hepatitis B Virus

Disease causing gene

Breeding

HCC

HCC

NO HCC
BIO RESOURCES

PLANTS | HERBAL PREPs | BACTERIA & FUNGI

TRADITIONAL WISDOM

AYURVEDA (AVS) | UNANI (CCRUM) | SIDDHA (INCOPS)

MODERN SCIENCE & TECHNIQUES

CHEMISTRY | BIOLOGY | STATISTICS

NEW BIOENHANCERS

ANTICIPATED OUTPUTS

INVESTIGATIVE NEW DRUGS (IND)

ENTIRELY NEW HERBALS

SERVICES TO ISM

Resource Management
Standardization
Agrotechnologies
Automation
Product Safety
COORDINATED EXTRACTION AND ISOLATION ACTIVITY

PLANTS
(RRL, J) → CSMCRI → IICB → NBRI → RRL, Jt → RRL, Tvm

CSMCRI → CIMAP → IHBT → NCL → RRL(Bh) → RRL(Bi)

Fungi & Microbes
(IMTECH) → CIMAP → IHBT → RRL, Jm

NIO

Selection of NICHE AREAS
ISOLATION & EXTRACTION
CODING

DISTRIBUTION
BIOASSAY
LEAD IDENTIFICATION

BH
GND
GOA
BARODA
JAMMU
ANNA MALAI
DELHI
BIOLOGICAL SCREENING
DISEASE SELECTION

DEGENERATIVES
METABOLIC DISORDERS
CNS
TROPICAL
INFECTIVES
OTHERS

IN VITRO SCREENING

NBRI
CDRI
CIMAP
IICT
IICB
ITRC
RRL,J

ALZHEIMER
ATHEROSCLEROSIS
BACTERIAL
CANCER
DEPRESSION
DIABETICS
FILARIAISIS
FUNGAL
GASTRIC ULCER
HEPATITIS
HYPERTENSION
IMMUNOMODEFICIENCIES
INFLAMMATION
LEISHMAMIA
MALARIA
MEMORY REDUCTION
NEURO DISORDERS (3)
PARKINSONIAN
TRADITIONAL PREPARATIONS

SELECTION

CSIR - ISM IDENTIFIED

ISM DESIGNED

CSIR - ISM DESIGNED

AVS

IICT

CLRI

RRL,J

SIDDHA

CCRUM

IND

Lead optimisation

Activity evaluation At 12 centers

Processing

COUPLING

TRADITIONAL WISDOM WITH SCIENCE
**OBJECTIVES**

- Develop new formulations or NCEs
- Structure optimization
- Fast track screens
- Multidisciplinary
- Phytochemistry
- Syn.org. chemistry
- Modelling
- Pharmacology

**DISCOVERY GROUP FORMATION**

- TB (2)
- Anti-Cancer (10)
- Anti-Parkinson’s (6)
- Anti-Leishmanina (2)
- Hepato-protective (7)
- Anti-Gastric ulcer (6)
- Immuno stimulatory (6)
- Anti-Inflammation (5)
- Anti-Filaria (3)
- Anti-Malaria (2)
- Anti-Hyper tension (3)
- Memory enhancers (7)

59 Discovery Groups in 13 Institutes
CSIR Agenda

• New Drug discovery
• Cost effective generic drugs
• New 6 bioenhancer based formulations
• New standardized botanicals
• New standardized traditional knowledge based drugs
Thanks for your patience

Please visit us at
www.rrljammu.org
www.herbalnet.org
www.csir.res.in