

Ayurveda

Global opportunities & challenges

Dr.H.S.Palep

Dr.Palep's Medical Research Foundation

Pharmexcil LAC Hyd. 28/6/07

New Drug Approval

- Single target centre approach
- 1996 decline in NDA
- Only Botanicals
- Potent molecules
- Disease: Multi component complex system
- Partial result
- No cure
- Severe side effects

Commercial Botanicals

- Colchicum, Colchicine, betulinic acid, Camptothecin, topotecan (Hycamtin®), CPT-11 (irinotecan, Camptosar®), 9-aminocamptothecin, delta-9-tetrahydrocannabinol (dronabinol, Marinol®), beta lapachone, lapachol, Podophyllotoxin, etoposide, podophyllinic acid, vinblastine (Velban®), vincristine (leurocristine, Oncovin®), vindesine (Eldisine®, Fildesin®), vinorelbine (Navelbine®), docetaxel (Taxotere®), paclitaxel (Taxol®), Tubocurarine, Pilocarpine, Scopolamine etc.

- Time present and time past are both perhaps present in time future and time future is contained in time past. -T.S.Eliot
- Time – Circular --- Orient
- Linear ----- Occident

“Your traditional knowledge base appears to me to be the most valuable resource that India has. If you look at the knowledge contained in Ayurveda and other vedic traditions, you will find a whole system that has been greatly undervalued at this point of time and this body of knowledge, I feel, has the potential to transform India and the world.”

**-John Fagan, Chief Scientific Officer
IDNA (licensing Authority for GMO Testing &
Certification)**

2nd Feb 2002- Times of India

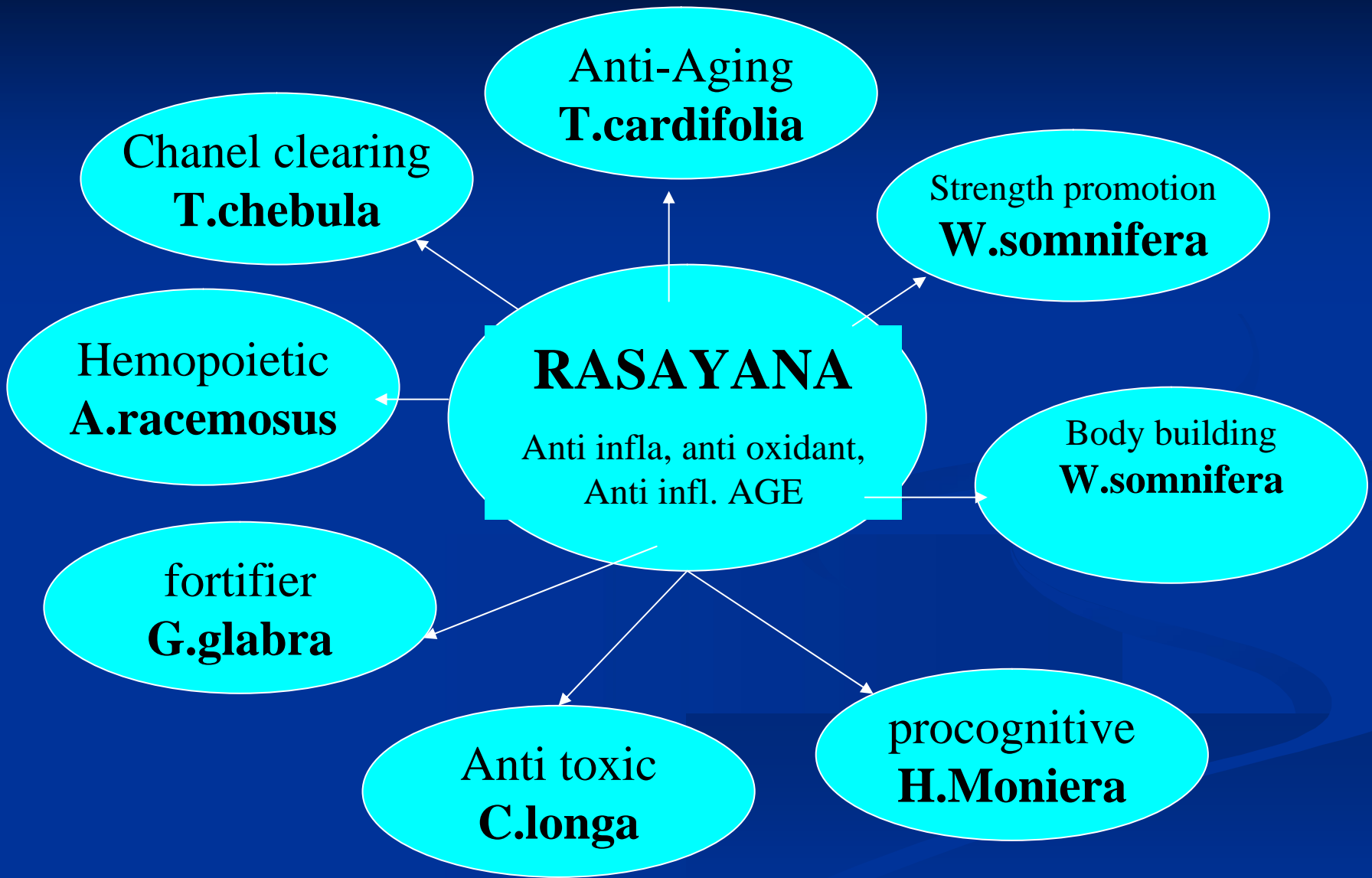
Ayurveda

- 4000 years of living tradition
- Most complex system consisting of about 20,000 basic Rules (Sutras) described in Ayurvedic Classics:
 - Charak Samhita,
 - Sushrut Samhita,
 - Vagbhat,
 - Madhav Nidan

Indian Contribution to World

700 Herbs / Resource for new Novel Molecules

- Aloe vera
 - Cassia angustafolia
 - Boswelia serrata
 - Glycerrhiza glabra
 - Picrorrhiza kurroa
 - Zingiber officianale
- Atropa belladonna
- Curcuma longa
- Commiphora mukul
- Mucuna pruriens
- Rauwolfia serpentina

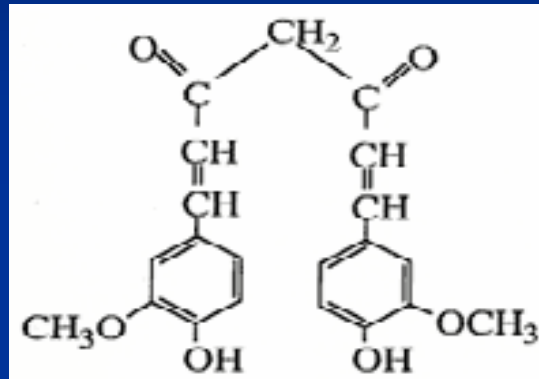


“Human condition has been enhanced considerably by those biochemists and pharmacologists, who have applied scientific method to prove ancient myths and legends . For example , mystical power of snake root plant of India, either ignored or ridiculed by scientists for decades were dispelled with the isolation and identification its active alkaloid”

Richard E. Davis

Curcuma longa

- Ayurvedic description
- Lead molecule: Curcumin



हरिद्रा

मेहेषु घात्री निशा (अष्टांगहृदय)

हरिद्रा विषण्ण कुशुब्ध कंठूष्ण (चरकसंहिता)

हरिद्रा कटुका तिक्ता रूक्षोष्णा कफपित्तनुत् ।

वर्ष्या त्वग्दोषमेहासशोथ पांडुव्रणामहा ॥

(शावप्रकाशनिघंटु)

- Biological targets: Aryl hydrocarbon receptor, Cytochrome P450 enzymes, Glutathione S-transferase, kinases, COX, iNOS, MMP
- Therapeutic class: Cancer, Inflammation, **Diabetes** and **Chemo prevention**

Chen HW. Anti-invasive gene expression profile of curcumin in lung adenocarcinoma based on a high throughput microarray analysis. *Mol Pharmacol.* 2004 Jan; 65(1): 99-110.

Limtrakul P, Modulation of human multidrug-resistance MDR-1 gene by natural curcuminoids. *BMC Cancer.* 2004 Apr 17; 4(1): 13.

Zingiber officinale

- Ayurvedic description
- Lead molecule: Gingerols

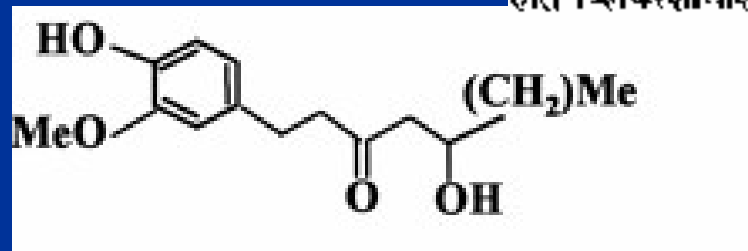
शुंठी

शूलप्रशमन दीपहीय तृप्तीघ्नानि (चरकसंहिता)

शुंठी रुच्यामवाहनी पाचनी कटुका लघु । स्निग्धोष्णा मधुरा पाके
कफनातनिबन्धनत् ।

कृष्यास्वर्या वमिकासशूलश्वास हृदाम्थान ।

हृति श्लिफशोथार्श आनहोदरमारुतान् ॥ (भावप्रकाशनिघंटु)



- Biological targets: Vanilloid receptors
- Therapeutic class: Antipyretic, analgesic, antitussive, cardiotonic, and sedative

Dedov VN. Gingerols: a novel class of vanilloid receptor (VR1) agonists. *Br J Pharmacol*. 2002 Nov; 137(6): 793-8.

Ohizumi et al. Stimulation of sarcoplasmic reticulum Ca (2+)-ATPase by gingerol analogues. *Biol Pharm Bull*. 1996 Oct; 19(10): 1377-9.

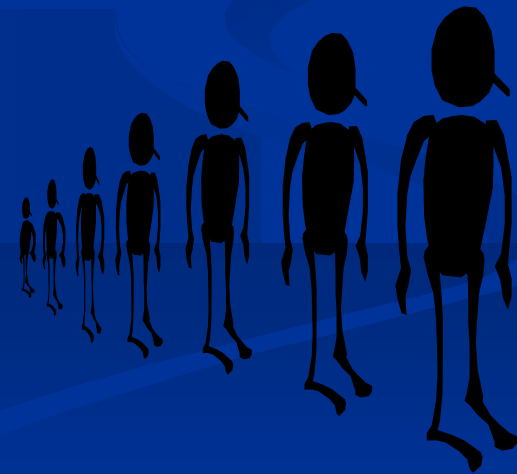
Pharmaco-genetics

- For years physicians have noted these differences but had no way to predict them. Pharmaco-genetics promises to give scientific answers.

- David L. Cooper, Editor-in-Chief, Molecular Diagnostics

Populations and Polymorphisms

- The human race is believed to have originated in Africa.
- We are 98% genetically same as of Chimps
- Generally speaking, humans are classified into three major groups:
 - The Negroid, Mongoloid, and Caucasoid.
 - Genetically all are 99.9% same
 - Rest 0.1 differences are SNPs



Ayurveda: Prakruti

- Relationship between Panchamahabhuta and Prakruti
- Ayurveda classifies the human race into Prakruti based on TriDoshas:
 - Kapha,
 - Pitta
 - Vata

Vata, Pitta, Kapha Metabolites-Molecular Mech.

- Genes, regulation factors, receptors, cytokines
- Short perturbations Mol. level
- Acute & Chr. disease processes
- Physical signs for identification of Mol. Mch
- Life style, Dietary & Drug interventions with 4 millennia of experiential Wisdom.

Syndromes..Not just Disease: Cancer, RA, Asthma....

- Breast cancer has three subclasses based on gene expression resulting in over five fold difference in life expectancy.
- RA is an oligogenic disease and it has been estimated that up to 30% of genetic component may be accounted for by HLA.
- Asthma may be driven by circulating IgE or inflammatory cells or neurogenic.
- Therapeutic approaches are bound to be different

Systems Biology

Body fluids

cell, tissue, organ & organism

- Genomics ---- DNA
- Transcriptomics ----- mRNA
- Proteomics ---- Proteins
- Functional proteomics– Protein complex
- Metabolomics----- Metabolites

Combinatorial and Holistic Approach: The Most Modern View

Multi-targeted drugs: The end of the 'one-target-one disease philosophy?

- The preparation of dual- or multiple-ligands on an almost rational basis is now conceivable and it can be expected that many of these molecules will yield drugs of superior clinical value compared with mono-target formulations.

New Technologies

- Monoclonal Antibodies
- Peptides
- Anti-sense Oligo Nucleotides
- Optamers
- DNA Mapping
- Newer Imaging Techniques
- Mass Spectroscopy
- HPCL, GC-MS, NMR Spectroscopy
- Fourier Transformation Cyclotron Mass Spectroscopy
- Transgenic Mouse Models, e.g. in
- Alzheimer's, Metabolic Syndrome

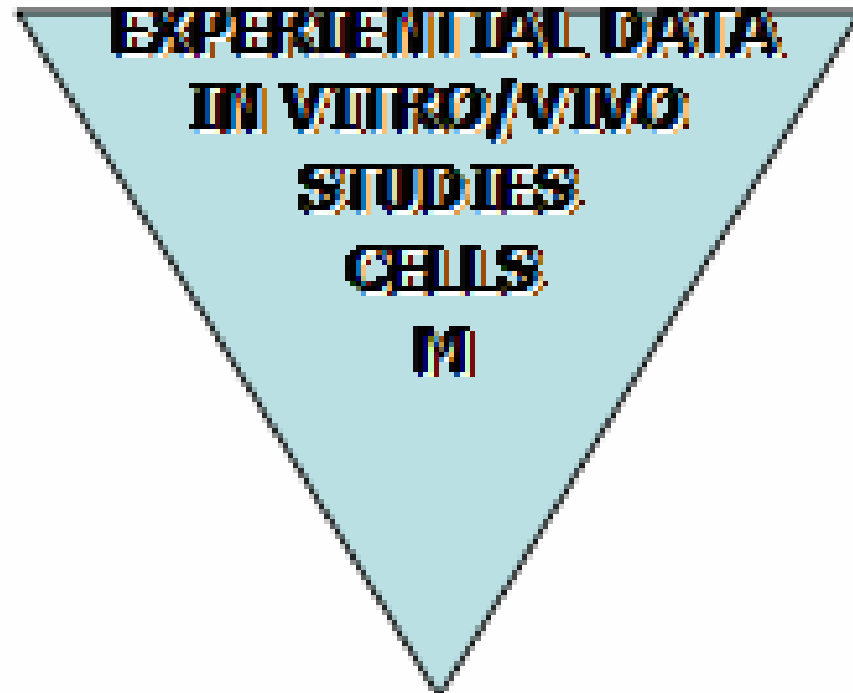
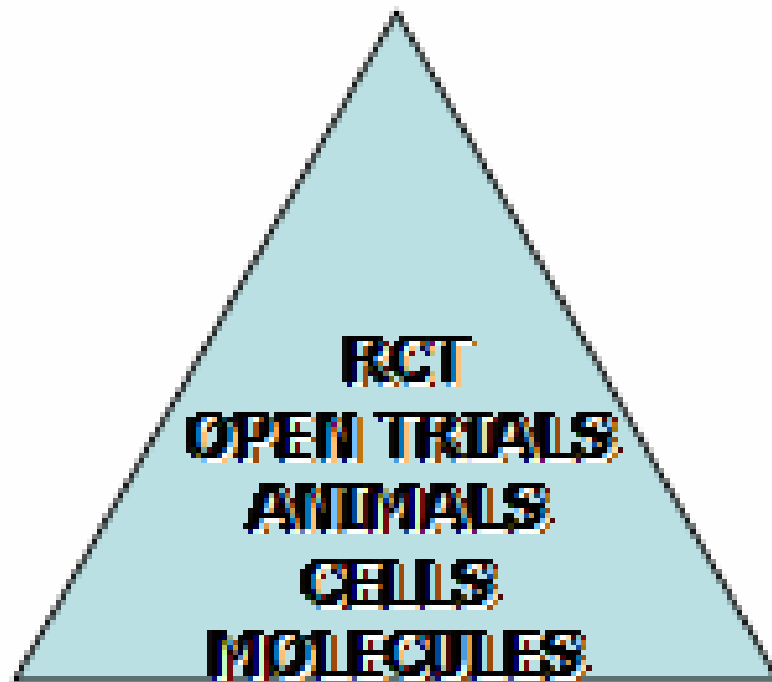
Testing Medhya Rasayanas (Cognition Enhancing drugs)

*Ashwa gandha, Brahmi, Bhringaraj Jyotishmati,
Manduka parni etc.*

In
Transgenic mouse

Levels of Evidence

- **Modern Medicine** **Ayurveda**



Challenges

- Proof of concept, efficacy & safety studies
- Mechanistic studies, dev. of Biomarkers & surrogate end points
- Finger printing of products to guide quality control
- Discovering and validating of new drug targets
- Discovery of new leads.

THANKS

