

REVERSE PHARMACOLOGY AND REGISTRATION OF AYURVEDIC DRUGS



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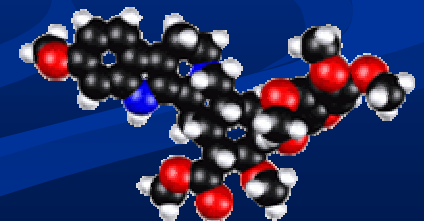
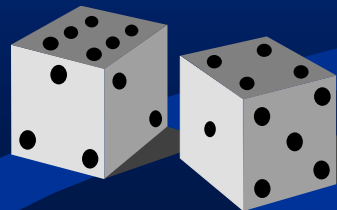
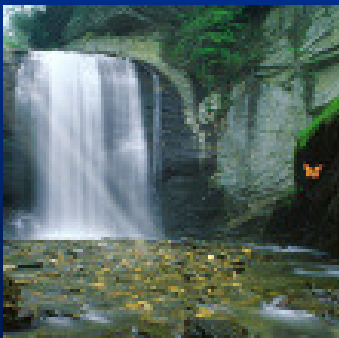
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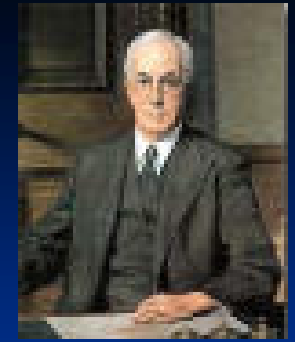
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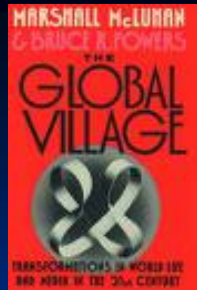


PRESENTATION DOMAINS

- Ancient and live heritage of Ayurvedic drugs
- Trans-cultural differences in regulatory milieu
- Strategize Ayurvedic drug registrations: Horizons
- Re-education of regulatory bodies on Ayurveda
- Reverse Pharmacology Path and clinical trials
- Future scope and direction for Ayurvedic drugs

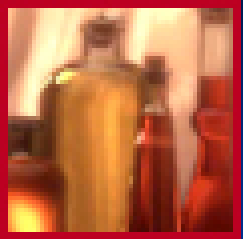


AYRVEDIC DRUGS: ANCIENT LIVE HERITAGE



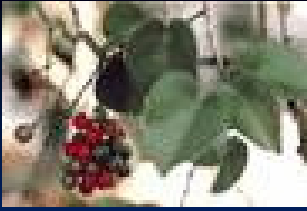
- Pluralistic Health Care: World Leader
- Majority of the population use Ayurvedic drugs
- Generally regarded as safe (GRAS)
- Ayurvedic plants: Mother of therapeutics
- Observational Therapeutics and Documentation
- Reverse Pharmacology and Ayurvedic Biology

INDIAN HEALTH SYSTEM



- World's largest democracy > 1 billion people
- Reliance on indigenous systems = 70%
- Pluralistic health care (A.Y.U.S.H.)
- AYUSH colleges (UG = 450; PG = 99)
- Number of practitioners: Regd. = 717860
- Manufacturing units of AYUSH = 9493





G.R.A.S. AYURVEDIC DRUGS

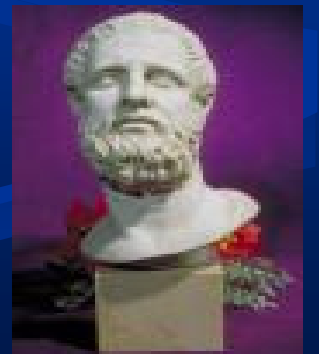
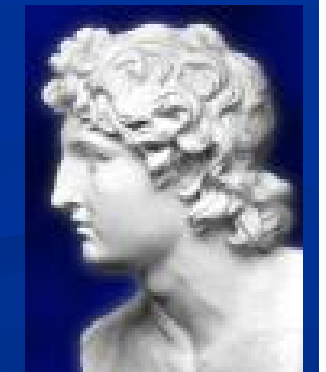
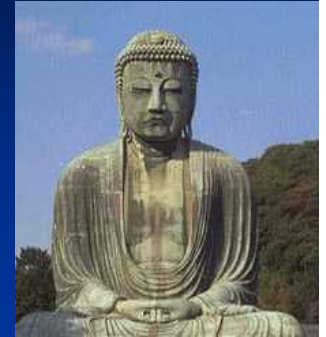


- Triphala: *Terminalia chebula*, *T. belerica*, *Phyllanthus emblica*
- Trikatu: *Piper longum*, *Piper nigrum*, *Zingiber officinalis*
- Sitopaladi Churna: Cinnamon, cardamom, Vanshlochan
- Nisha-Amlki: *P. emblica* and *Curcuma longa*
- Samshamani Vati: *Tinospora cordifolia*, *Lobabhasma* etc.
- Chyavanprash: *Phyllanthus emblica* and multiple ingredients
- Hingwashtak Churna: *Ferula asafoetida*, trikatu, jeerak
- Khadiradivati: *Acacia catachu*, *Glycyrrhiza glabra*, Karpur, etc.



GLOBAL CONTRIBUTIONS TO THERAPEUTICS

- Panchkarma: emesis, laxation, enema, etc
- Ctesias of Cnidos : Charak Samhita
- Buddhist medicine → Tibet, China, Japan
- Universities : Nalanda and Takshashila
- Physicians / Surgeons to Greece
- Garcia da Orta : Indian Drugs
- Theory of Constitution : Prakriti



GARCIA DA ORTA (1490 – 1570 A.D.)

Acacia catechu

Acorus calamus

Aloe vera

Elletaria cardamomum

Azadirachta indica

Areca catechu

Piper longum

Zingiber officinalis

Semicarpus anacardium

Rauwolfia serpentina

Commiphora wightii

Curcuma longa

Dahira alba

Rheum emodi

Garcinia indica

Ipomoea turpethum

Cocos nucifera

Cinnamomum tamale

Holarrhena antidysenterica

Papaver somniferum

Piper nigrum

Piper betel

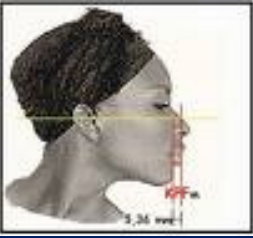
Alpinia galanga

Vitex negundo

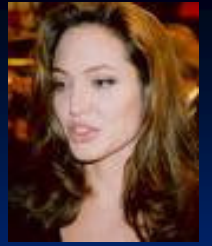
Cassia fistula

Cannabis indica





THE TRANS-CULTURAL DIFFERENCES



- US FDA, despite major flaws, flouted as ideal
- Dietary Supplements Act and Irresponsibility
- Human usage and safety be paramount
- Violence to animals for toxicity studies
- Amnesia regarding medicinal history
- Central Drug Authority of India
- Regional acceptance of Ayurvedic drugs

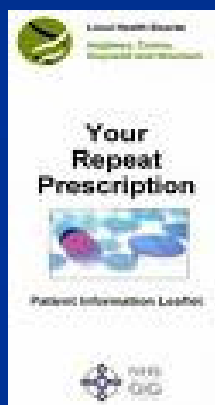




DIRECT REGISTRATIONS



- Usage data of last 15 years
- Standardization of the raw material
- Formulations: Quality and Shelf life
- Instructions for usage and precautions
- Drug safety monitoring cells
- Consensual validity of usage



STRATEGIC HORIZONS

Horizon One:

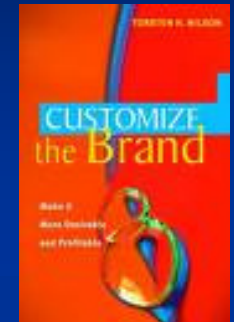
- GRAS Ayurvedic drugs: Global registration
- Direct registrations with minimum dossiers

Horizon Two:

- Reverse Pharmacology processed natural drugs
- Pharmacoepidemiologically safe drugs

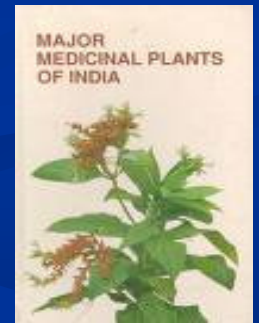
Horizon Three:

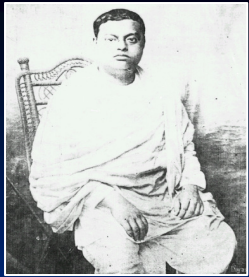
- Ayurvedic drugs with narrow therapeutic margins
- Innovative R & D based natural drugs and their derivatives



RE-EDUCATION OF DRUG REGULATORY BODIES

- Visits to regulatory bodies: Seminars on Ayurveda
- Ayurveda has 'different kind of evidence'
- Monographs on G.R.A.S. Ayurvedic drugs
- A new journal on Ayurvedic drug R & D
- Joint monographs of AP, IP and USP
- Exposure of regulatory leaders to Ayurveda





REVERSE PHARMACOLOGY: DEFINITION AND SCOPE



Definition:

Reverse pharmacology is the science of integrating documented clinical/experiential hits, into leads by transdisciplinary exploratory studies and further developing these into drug candidates by experimental and clinical research.

Scope:

The scope of reverse pharmacology is to understand the mechanisms of action at multiple levels of biological organization and to optimize safety, efficacy and acceptability of the leads in natural products, based on relevant science.

INITIATIVES IN REVERSE PHARMACOLOGY

- Medical Research Fund studies on plants
- ICMR-integrated research units and follow-up
- CIBA-GEIGY and Hoechst Research Centres
- CSIR institutes (IIM, CDRI) and NMITLI
- ICMR Advanced Centre in Reverse Pharmacology
- CCRAS and the Golden Triangle Approach



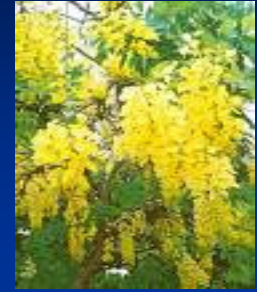
SUCCESS STORIES

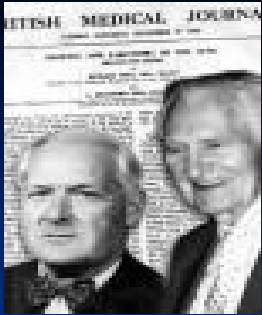
- *Rauwolfia serpentina* and amines watershed
- *Commiphora wightii* and inflammation
- *Picrorrhiza kurroa* and hepato-protective
- *Mucuna pruriens* and Parkinson's Disease
- *Tinospora cordifolia* and immuno-modulation
- AYUSH-64 and plants for malaria, filariasis
- *Pterocarpus marsupium* for Diabetes mellitus



THE WORLD OF MEDICINAL CHEMISTRY AND PLANTS

- *Cassia fistula* and sennosides
- *Atropa belladonna* and anti-cholinergics
- *Aloe vera* and derma-cosmetics
- *Zingiber officinalis* and antiemetics
- *Curcuma longa* and curcuminoides
- *Taxus baccata* and taxanes
- *Glycyrrhiza glabra* and glycyrrhizin



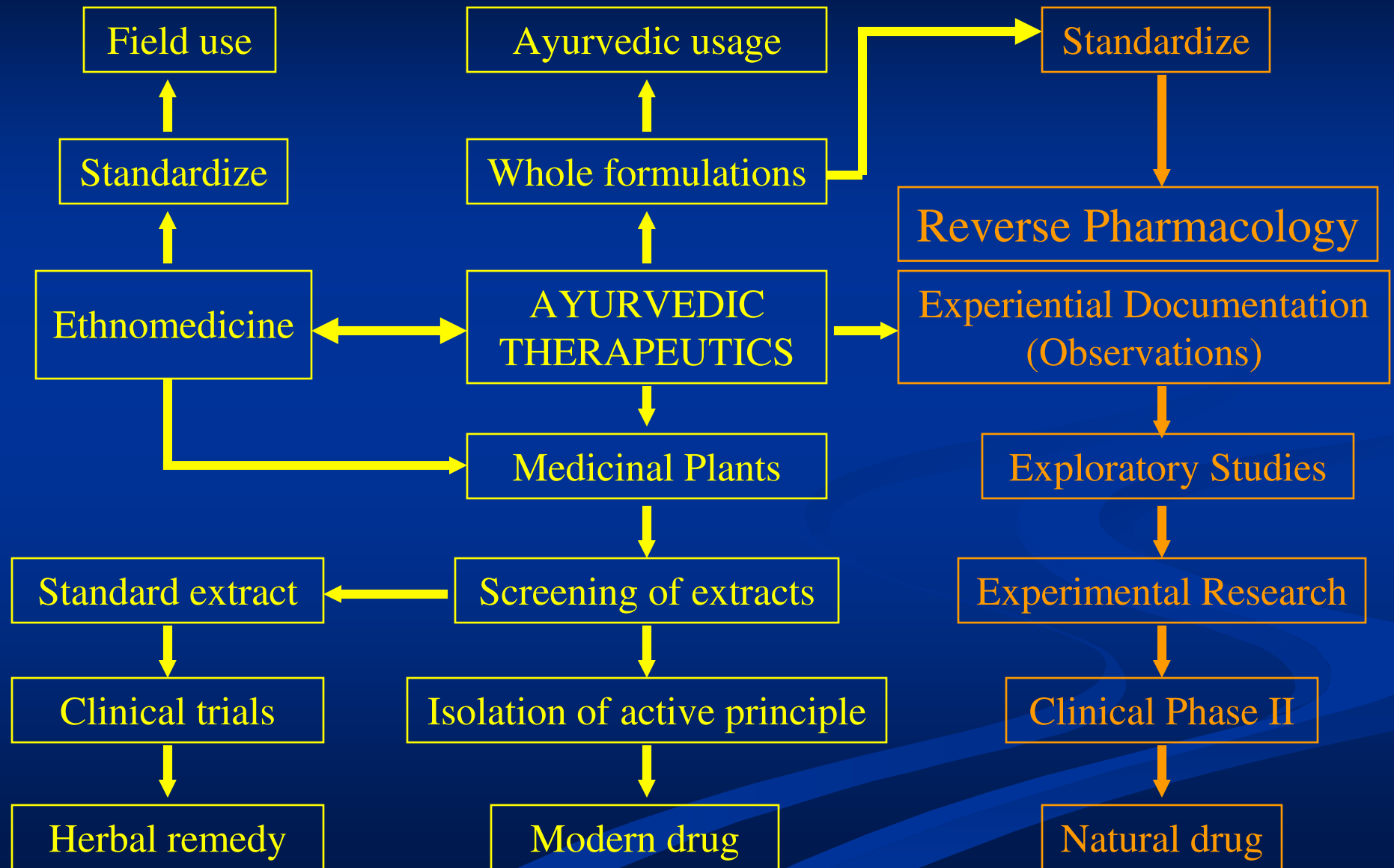


CLINICAL EXPERIENCE

“Such personal observations of a handful of patients, acutely made and accurately recorded by the masters of clinical medicine, have been and will continue to be, fundamental to the progress of medicine.... We were to use a new drug upon one proven case of acute leukemia and the patient made an immediate and indisputable recovery, should we not have a result of the most profound importance”.

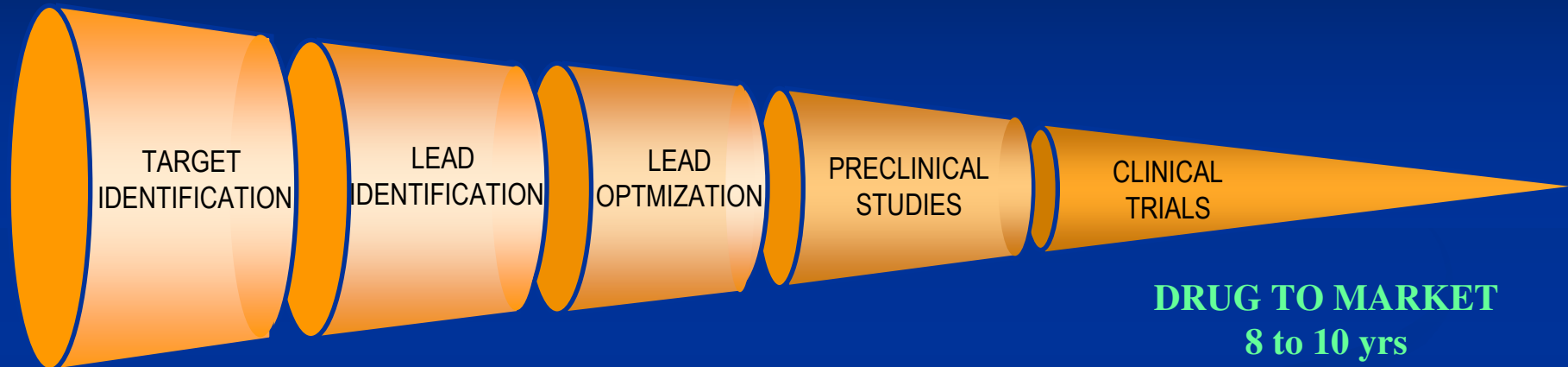
- Sir Austin Bradford Hill

R & D PATHS FOR MEDICINAL PLANTS



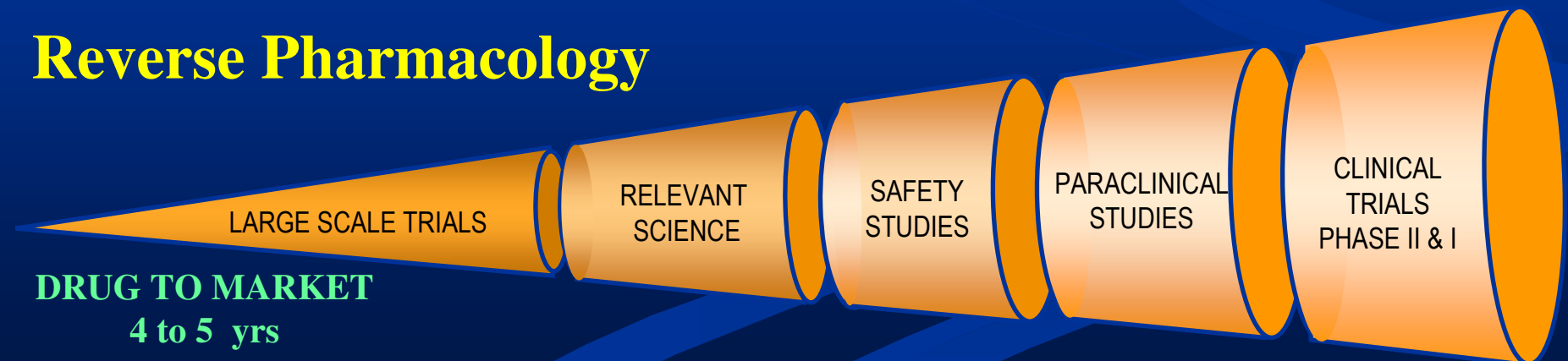
FAST-TRACK PATH OF REVERSE PHARMACOLOGY

Expensive, time consuming, numerous bottlenecks



Economical, time sparing, least bottlenecks

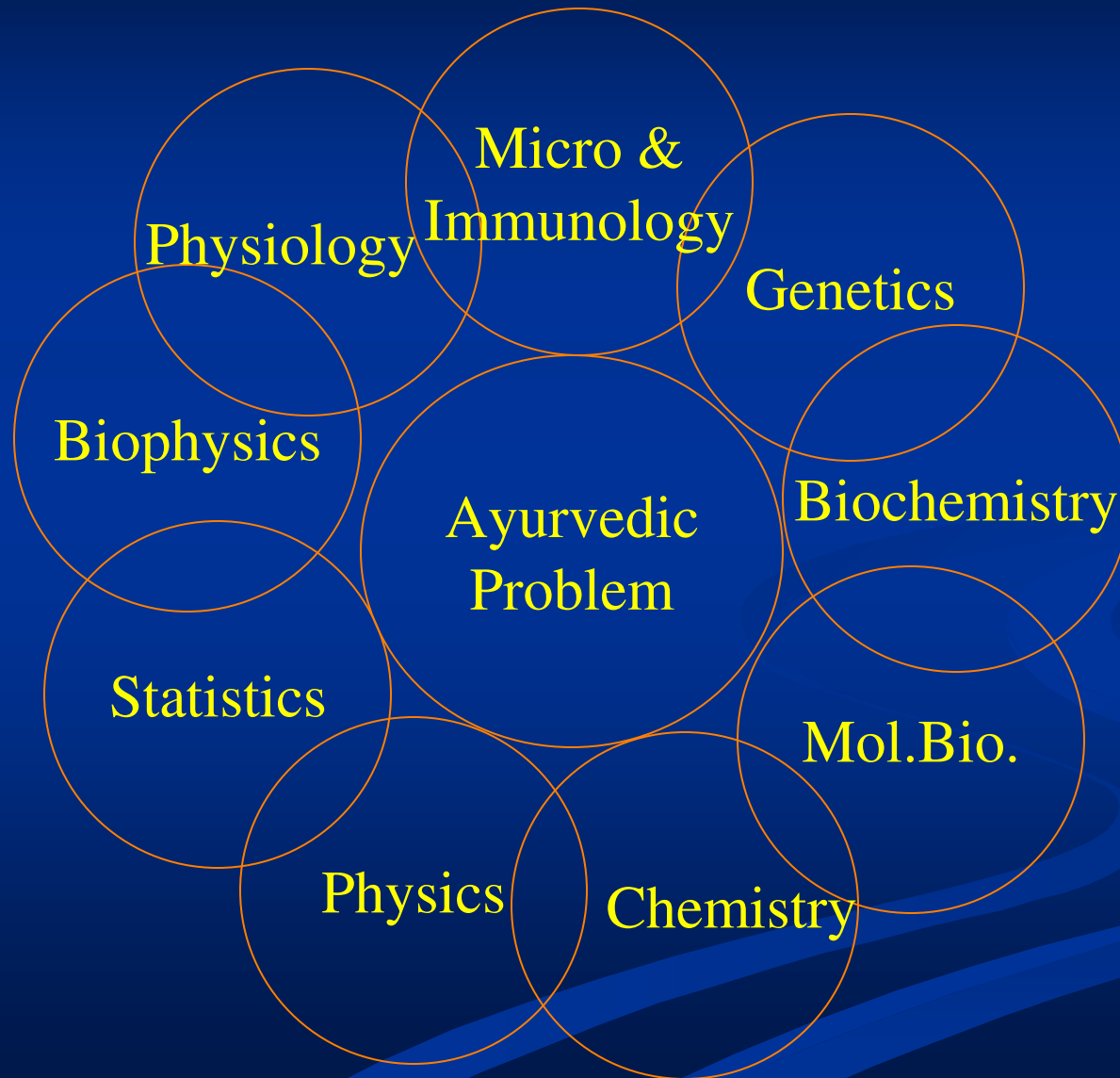
Reverse Pharmacology



International Arogya-2007

New Delhi

INTERDISCIPLINARY RESEARCH



CONCEPT TO PRODUCT

Kinetic marker ← Pharmaceuticals-Final dosage-form → Chronic Toxicity



Phase II (B) Dose-finding trial

- Diabetes mellitus
- PCOS with IRS
- Visceral obesity with IRS



Multi-centric Randomized Large Scale Trials

- Diabetes Mellitus
- Visceral obesity



Consolidate all data
Natural Drug Application Dossier



THE PRODUCT



FUTURE SCOPE

- Strategic horizons for registration accepted
- US botanicals regulation to cognise Ayurveda
- Indo-EU agreement on GRAS and Ayurvedic drugs
- Reverse Pharmacology section in CDRA
- Consensual validity meetings in South Asia
- Support for Ayurvedic Pharamcoepidemiology
- Industrial commitments for drug monitoring



DIRECTIONS

- Create an inter-research councils committee
- Industry-Academic collaboration in Ayurveda
- A journal for Ayurvedic drugs development
- Relevant R & D for IND and NDA
- National Medicinal Plants Board strengthening
- Focus on Golden Triangle Approach for strategy



"Over millions of years of evolution nature has created unique secondary metabolites which as a rule have protective and regulatory functions in biocenosis and are often active in minor and extra minor doses. This is virtually an inexhaustible source of ideas to draw upon in creating new generation pharmaceuticals and new drugs for the next Millennium." - Prof. Victor Kartsev

