

# *DRUGS FROM INDIAN MEDICINAL PLANTS*

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# Allopathics

- PLUSES:
- Normally single molecules.
  - Well defined, purity as well as impurity profiles known.
  - Structures optimized.
  - Rigorously tested in vitro as well as in vivo.
  - Proven through clinical trials.
  - Mechanisms known for many drugs.
- MINUSES:
- Adverse reactions: 4<sup>th</sup> to 6<sup>th</sup> largest cause of death in US Hospitals (J.Am.Med.Assoc.,98)
  - Considered unsafe. Psychological disadvantage.

# Herbals

- MINUSES:
- Poorly defined: contain many molecules.
  - Detailed composition known approximately.
  - Active molecules not always known.
  - Seldom proven through in vitro, in vivo and clinical trials.
  - Mechanisms involved generally not known. Interactions among molecules may have adverse effects.

- PLUSES:
- Used over centuries. Considered safe.
  - General impression that they are good for degenerative diseases.

~ 40% of allopathics based on leads from natural sources.

# Pre-requisite for Herbals to be better

- IF:**
- a herb has a single active molecule, and other molecules are inert
- THEN:**
- this herb offers no advantage over an allopathic drug using the same molecule.
  - the optimized single molecule may be more effective, and less toxic.
- THEREFORE:**
- for a herbal to be preferred to single molecule, it needs to be polyfunctional involving many molecules at low concentrations.

# Synergism through multiple mechanisms

- A number of active molecules.
- Each molecule inhibits a different pathway, or a different target on the same pathway.
- For multifactorial diseases, different molecules may cover different factors.
- Active molecules present in low concentrations work in consonance.
- Hence less toxic.

# Bioenhancers: The efficacy improvers

- Frequent use of Trikatu in Ayurvedic products.
- Piperine is a molecule in Trikatu.
- It enhances effect of rifampicin against tuberculosis.
- Works through increased absorption, slower degradation, increased inhibition, & improved immune response.
- Other mechanisms are also possible.
- New bioenhancers have been discovered for other drugs.
- Makes molecules effective at lower concentrations.
- Apart from herbals, they are valid for single molecules too.

# Additional Functionalities

Some specific herbs may provide additional features such as:

- Metabolic activation.
- Protection against toxic effects.
- Immuno-balancing.
- Antioxidants.
- Rejuvenation & toning.

Most TSM products are polyherbal and possibly depend on polyfunctionality.

# Starting materials

- Preparations of ISM
  - Herbal preparations from Ayurveda, Siddha and Unani systems.
- Minero-herbal and mineral preparations from ISM.
- Preparations from
  - Tibetan system.
  - Chinese system.
- Preparations specially designed through TSM.
- Single plants based on in vitro, in vivo and mechanism elucidation tests.

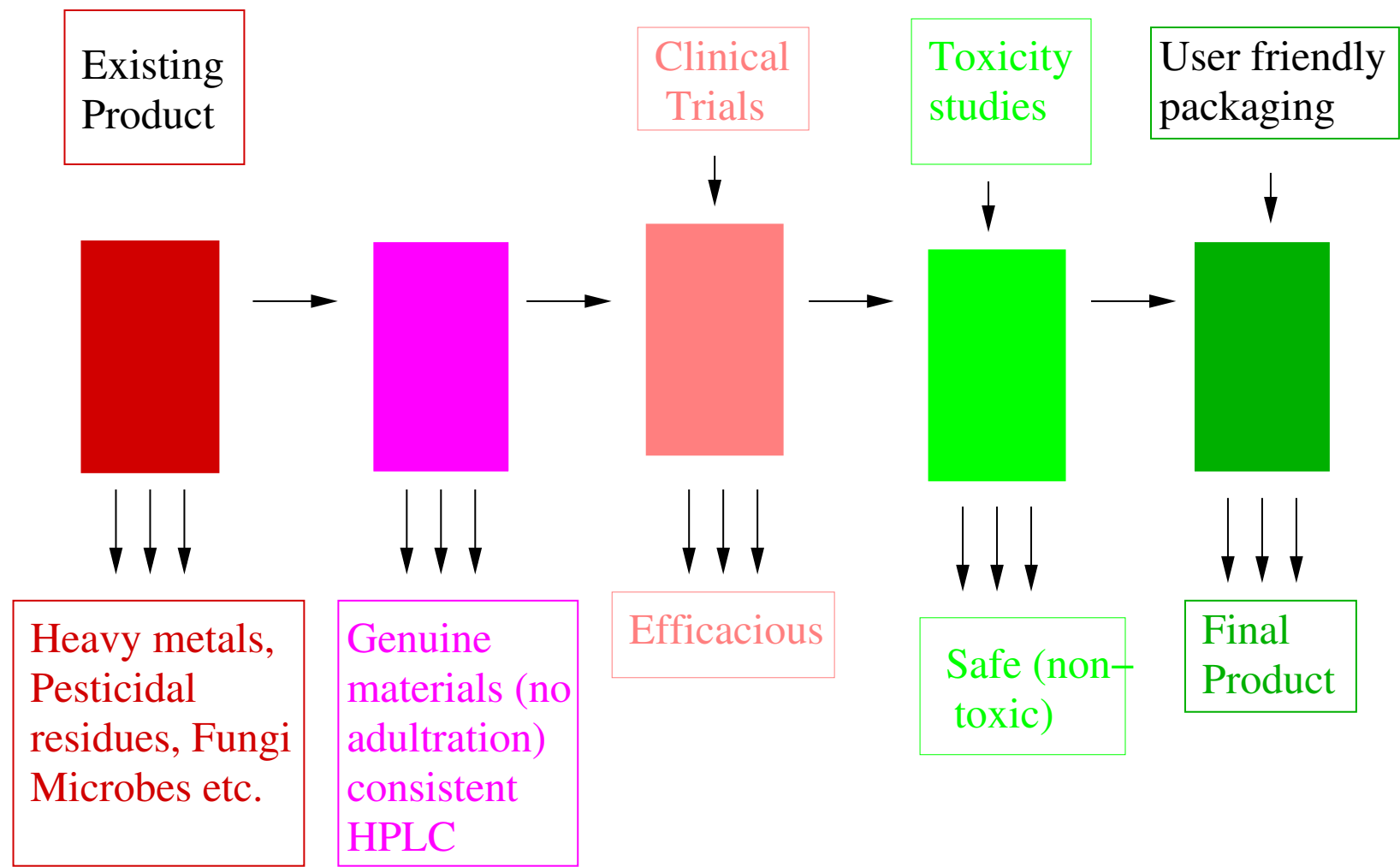
# Contributions from contemporary science

- Techniques for characterization, bioevaluation, mechanism elucidation and optimization.
- – Separation and chemical characterization of complex mixtures
  - Chemical analysis at ppm, ppb levels of heavy metals, pesticides etc.
- Bioevaluation: in vitro, in vivo, toxicology, pharmacokinetics, clinical trials, mechanisms.
- Optimization: Design of experiments, statistical analysis of data.

# Likely products of confluence

- Based on existing products
  - made more acceptable
  - optimized
  - truncated
- New products
  - novel design
  - protected IPR
  - transnational ingredients
  - rigorously proven
  - universal acceptance
- Products for combo-therapy
- Bhasmas & Minero-herbals

# Based on existing products: Standardized



# Optimized products

- Which herbs in an existing product really contribute?
- Number of ingredients for antidiabetic Ayurvedic products vary by an order of magnitude.
- Deletion experiments can identify contributing herbs.
- Fractional factorial design of experiments can yield optimum preparations as well as interaction among herbs.

# Ingredients in a few antidiabetics

● Diabecon	33	● Diabetab H	6
● Diacont	7	● Diabetex Strong	9
● Glucomap	9	● Dia Care	8
● Tribangashile	5	● Diabin Cap	8
● A.D. Powder	11	● Diatus	4
● Carbomet	11	● Diawin	10
● Diabecure	5	● Episulin	9
● Glucolev	7	● Glycem	10

In all, around 60 Ayurvedic preparations are available

# Truncated products

- A product may contain active components, detoxifiers, fillers, toxins, components having undesirable activities like immuno-suppressants, depressants, contributing to malodour, unpleasant taste, fungal or bacterial growth.
- Fractionation to remove undesirables will yield truncated products.
- These products will be
  - trimmer,
  - better defined,
  - less toxic,
  - with lower bulk,
  - more acceptable.

# New products: Special Design Features

- Synergism of many molecules working at low concentrations
- Mechanism based, incorporating multiple factors of disease
- May incorporate metabolic activation
- Exploit bioenhancing
- Incorporate international ingredients
- Fraction based
- Optimized
- Rigorous testing of toxicity, efficacy
- Acceptable clinical trials
- More universal in nature

# Assembled products

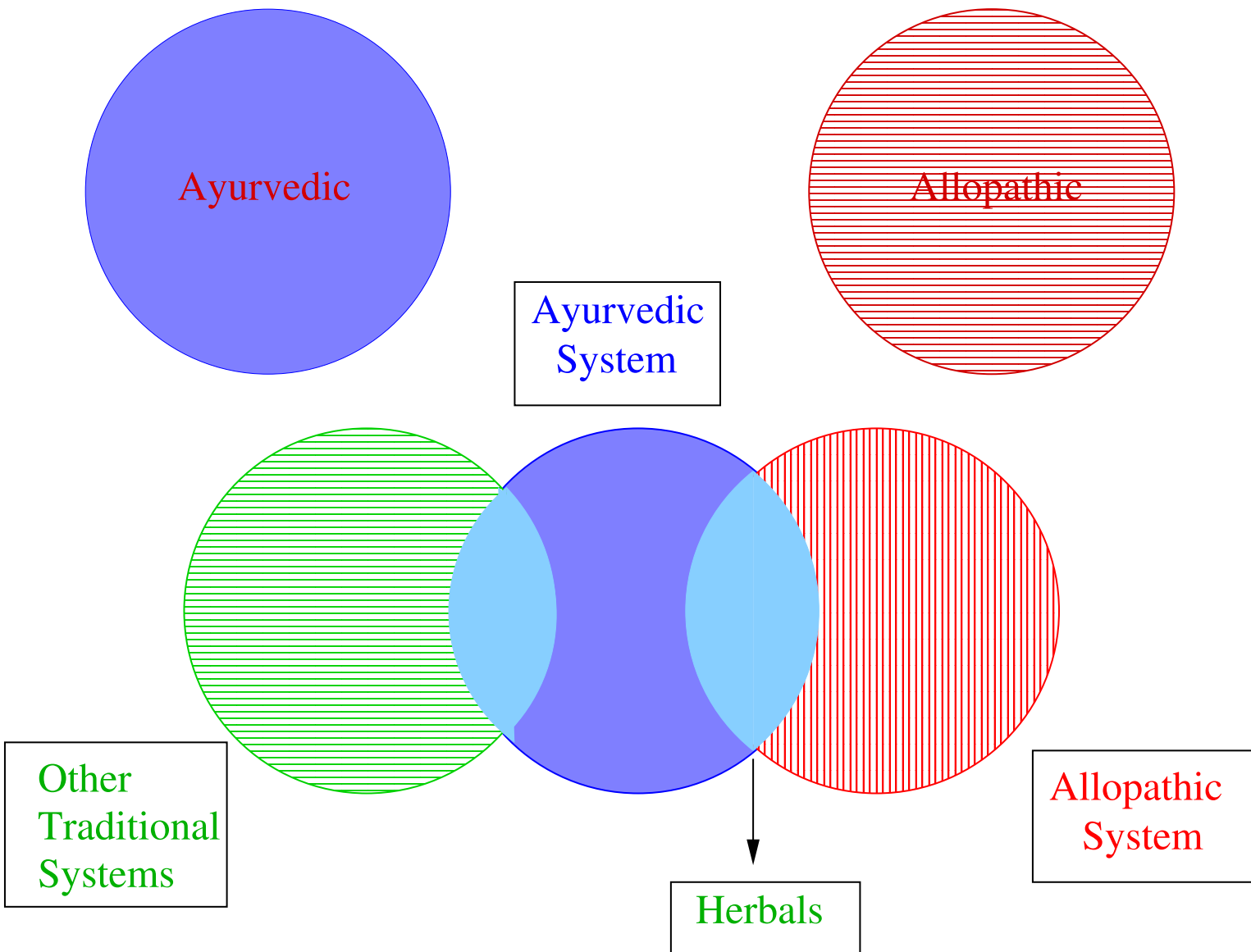
- When information about multiple factors for a disease available (say diabetes) –
- List herbs effective for each factor.
- Assemble various herbs, so that each contributes.
- Choice is possible in case of availability of excess herbs.
- Incorporate bioenhancers, after testing. (Piperine, Tinospora cordifolia etc.)
- Validate through vigorous protocols.

# For managing type II diabetes

- $\beta$  cell activation.
- $\beta$  cell protection from deterioration, regeneration.
- Lowering glucose absorption.
- Improving glucose uptake resistance to insulin.
- Stress reduction.
- Insulin mimicking.
- Modifying fat metabolism.
- Reduction of obesity.
- Protection from complications in eye, kidney etc.

Each many have many mechanisms. Some of the features are interdependent.

# Products through systems interaction



# Products for combo therapy

- Mop-up therapy.
- Detoxifiers (panch karma & purva karma based).
- Convalescence promoters.
- Toners and rejuvenators.
- Prophylactics.
- Functional foods.
- Benign Bhasmas.

All tested through rigorous protocols. Interaction with single molecule based drugs need thorough investigation.

# Bhasmas

- Use lead, tin, iron, arsenic, mercury, gold, sulfur, lime,  $\text{KNO}_3$  etc alone or in combination with herbs.
- Normally fast acting, but need toxicological support.
- May find use based on cost-benefit analysis on health

# Conclusions

- For efficacy and safety, herbals need be polyfunctional.
- Functions include multiple mechanisms: synergism, bioenhancing, metabolic activation, detoxification, toning, rejuvenation, and immuno-balancing.
- Existing formulations may be standardized, optimized, fortified, and truncated.
- New products may be assembled from single herb studies or designed through TSM and modified through sieve of polyfunctionality.
- Additional conditions for products of combo-therapy.
- Bhasmas to be used on health cost versus health benefit.
- Herbals with polyfunctionalities do have a good chance of contributing to world health care.