Why different criteria between botanical food supplements and herbal medicinal products for health claims?

Robert ANTON

Emeritus Professor of the University of Strasbourg
Member of national Academies of Pharmacy and Medicine

robert.anton@unistra.fr

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Summary

I. A short analysis of the current situation
II. Some important concepts and limits
III. What are differences between herbal drugs and botanical FS?
IV. Are there some convergences?
V. What questions to be solved?
VI. Are there any solutions?
1. A short analysis of the current situation

1. The understandable attitude of EFSA
2. The Traditional Herbal Medicinal Products Directive (THMPD)
3. Consequence: a locked situation
2. Some important concepts and limits

Plants that are not concerned:

1. Primary metabolites: proteins, lipids, polysaccharides
2. Secondary metabolites: extraction for ethical drugs or toxic constituents:

   - *Belladonna* (atropine), *Catharanthus* (vinblastine),
2. Some important concepts and limits

Plants of concerned: ambivalent or borderline botanicals

- Cynara
- Gentiana
- Ficaria
- Passiflora
- Melilotus
2. Some important concepts and limits: a proof of efficacy: history and modern science

XVI e century: clinical trial of aerial parts of spirea (*Spirea ulmaria*, Rosaceae) antipyretic

↓

salicylic aldehyde glycoside

Hippocrates 500 b.c. (*Salix alba*, *Salicaceae*), bark antalgic

salicylic alcohol glycoside
2. Some important concepts and limits: a proof of efficacy: history and modern science

- Gerhardt: acetylation of salicylic acid (1853)
- Anti-inflammatory-antirheumatic (prostagladines) (1971)
- Platelets aggregation inhibition (1985)
- Colon cancer prevention (1997)

Salicylic acid \(\text{HOOC-C(\text{O})-H}_2\text{C-O-CH}_3\) and Acetylsalicylic acid (Aspirin)
2. Some important concepts and limits

1. Plants with active constituents: anthraquinone derivatives: laxative and purgative

2. Plants with defined chemical group of constituents: naphtoquinone derivatives anti depressant

3. Plants with an active « totum »: essential oil, more or less polar constituents

<table>
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<tr>
<th>Senna</th>
<th>Hypericum</th>
<th>Valeriana</th>
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3. What are the differences between herbal drugs and botanical supplements?

1. Definitions:

- **Herbal drug**: prevention and treatment of human disease—modify, restoring, correcting, modifying physiological functions—pharmacological, immunological, metabolic activities—therapeutical indication

- **Botanical supplement**: maintain of homeostasis state—well-being—physiological impact—health claim
3. What are the differences between herbal drugs and botanical supplements?

2. For herbal drug:

**EMA:** two levels of labelling for therapeutical indications, marketing authorisation and plants with a therapeutical aim

- « *traditional use* » (history of use, traditional mode of preparation)
- « *well-established use* » (bibliography: pharmacoclinical data available)

3. For botanical food supplements:

- proof of efficacy with clinical trials on healthy subjects.
- No traditional claims delivered by EFSA
3. What are the differences between herbal drugs and botanical supplements?

- **AFSSA**: « Framework for the evaluation of the safety, the effect and the claim foodstuff, made from plants for the human diet » (02. 2003)

- **COUNCIL OF EUROPE**: 
  - Guidelines on the quality, safety and marketing of plant-based food supplements (06.2005)
  - Populations possibly at risk (11. 2006)
  - Homeostasis, a practical tool to distinguish between food supplements and medicines (11.2006)
4. What are the convergences between herbal drugs and botanical supplements?

Some imperative criteria must be present as for traditional herbal drugs

1. Same plant species (The Plant list…)
2. Same part of plant
3. Same traditional uses
4. Same safety: history of use: 30 years minimum
5. Same type of traditional preparation
6. Same quality criteria
7. Same type of population
4. What are the convergences between herbal drugs and botanical supplements? The novel food
5. What questions have to be solved?

1. Herbal drug against disease and botanical supplement for homeostasis: why an incomprehensible and separate judgment for the same plant preparation?

2. An important european market and a problem for the future of manufacturers?

3. How to demonstrate the clinical efficacy on an healthy person? Which biological or physiological criteria? Which kind of clinical tests? Which published specific guideline for plant extracts?
6. Any solutions for botanical supplements claims?

- Tradition: a key word in all the world
- An important ancestral, empirical observation on human or animal effect and now confirmed with new concrete scientific data
6. Any solutions for botanical supplements claims?

Parameters to take into consideration about traditional information

- Long history of use (generally many centuries)
- Collection of all information on practical traditional use
- Existence of convergence of use in different continents without primitive contact
6.1. Summary of parameters to take into consideration on traditional information

Because of the large variability of plant constituents

- Rigourous botanical identification: scientific name
- Chemotaxonomic aspects
- Geographical origin and cultivation methods
- Part of the plant used
- Respect of the traditional type of preparation
- Identification of the type of population concerned
- Observation on eventual secondary effects
- Scientific confirmation with chemical profile in order to understand the pharmaco-clinical effects
6.2 Importance of the chemotaxonomy

- **Aristolochiaceae**: all species contain toxic aristolochic acid
- Other plant species from other botanical families also contain diverse aristolochic acids and aristolactames

Forbidden: severe renal and hepatotoxicity (oral route)
6.4. Importance of the part of the traditional plant used

- **Type of organs: differentiation concerning the same species**
  
  *Example of Cinnamomum zeylanicum*

- Bark of young stems
  - cinnamic aldehyde

- Leaves and young branches
  - eugenol
6.5. Traditional botanical preparations

- **Aqueous extraction** (hot water): infusion, decoction (root, seed), maceration (cold water for mucilages)

- **Dried aqueous forms**

- **Hydro-alcoholic extracts**: advantages: extraction of both lipophilic and hydrophilic constituents; presence of glycosides more physiologically active
6.6.. Numerous qualitative and quantitative available analytical techniques: Ginkgo extract: HPLC-TLC…
6.7. Monographs and reference standard texts

- European Pharmacopoeia
- French Pharmacopoeia = Pharmacopée française
- German Pharmacopoeia = Deutsches Arzneibuch (DAB)
- English Pharmacopoeia = British Pharmacopoeia (BP)
- US Pharmacopoeia = United States Pharmacopoeia (USP)
- WHO monographs and guidelines
- ESCOP = European Scientific Cooperation in Phytotherapy
- EMA (EMEA) : HMPWP (Herbal Medicinal Products Working Party)
- Other references: AFNOR (France), ISO, ICH….
- Data bank: COSING…
6.8. Positive contribution of the tradition for efficacy and safety

- 1° Most appropriate method of preparation and efficacy are confirmed by experience and scientific papers

  *Camellia sinensis*: solubility of caffeine only in hot water, not in cold

- 2° Identification and selection of the particular part of the plant for specific populations: mucilages of *Malva sylvestris* improve intestinal transit for children. Anthraquinones derivatives (*Cassia senna.*, *Rheum palmatum…*) are purgative for the same purpose in adults

- 3° Help to use botanical preparations in a safe way and eliminate potential risks: *Teucrium chamaedrys* (traditional aqueous infusion and toxic hepatitis powder)
6.8. Positive contribution of the tradition for efficacy and safety

- 4° Identification and selection of particular part for elimination of toxic components

*Borago officinalis*: seed: source of fatty acids (linoleic and gamma-linolenic); all the other parts contain strong hepatotoxic pyrrolizidinic alkaloids

*Manihot esculenta*: root traditional preparation (rasping, drying…): removal of toxic volatile cyanogenic compounds.
6.9. Numerous available bibliographical data

- Ancient books can be consulted: Hippocrates, Galen, Paracelsus…some pharmacological and clinical effects are confirmed
- Chronological ethnobotanical sources of information and references overview are available
- Numerous data bases e.g. pharmaco-toxicological papers give a justification of the traditional use and exposure estimation
- Important body of documentation during the last 25 years (minimum) is available
- Few clinical trials: limitation because: coast – no possible patent
6.10. Any solutions for botanical supplements claims?

1. EFSA Compendium: a guide for more safety
2. BELFRIT Project (Belgium – France – Italy): a future list of safe and active plants
3. A possible transfert of traditional plants from EMA?
4. A necessary dialog to convince the choice of option 2
5. An urgent european regulation harmonization
1. Traditional knowledge for the assessment of the health effects for botanicals. A framework for data collection:
R. Anton, L. Delmulle, M. Serafini

2. The role of traditional knowledge in the safety of botanical food supplements. Requirements for manufacturers
R. Anton, M. Serafini, L. Delmulle

Cousyn G., Dalfra S., Scarpa B., Geelen J., Anton R., Serafini M., Delmulle L.

4. The substantiation of claims for botanical food supplements in relation to traditional use.
R. Anton, M. Serafini, L. Delmulle