

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

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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

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

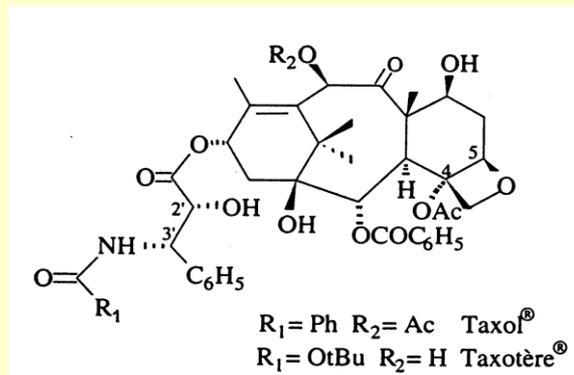


## 2. Some important concepts and limits

Plants that are not concerned:

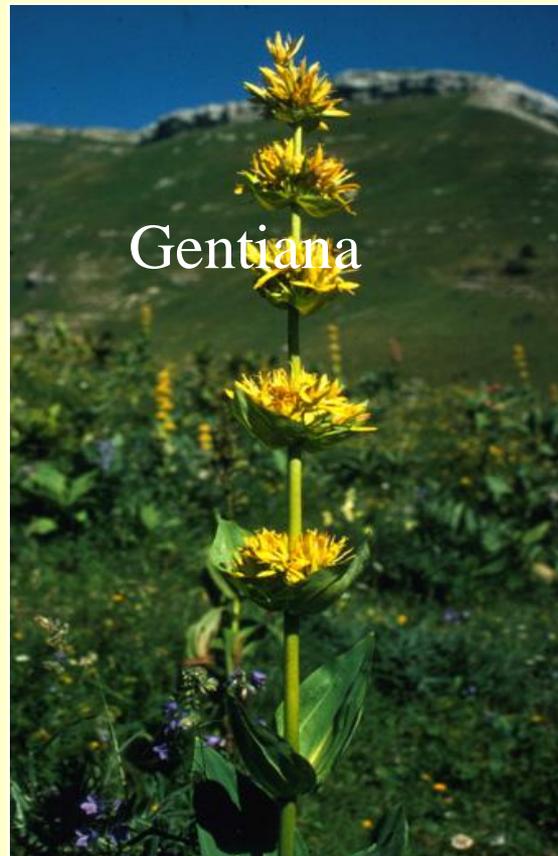
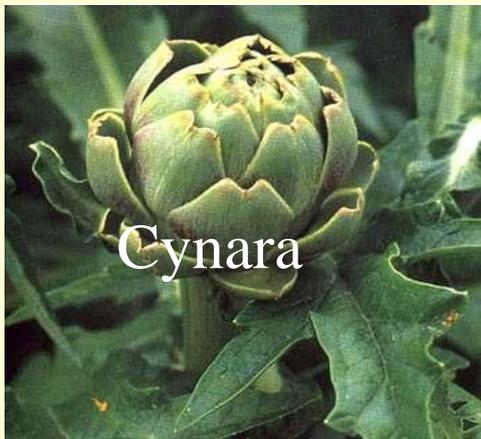
1. Primary metabolites: proteins, lipids, polysaccharides
2. Secondary metabolites: extraction for ethical drugs or toxic constituents:

*Belladonna* (atropine), *Catharanthus* (vinblastine), *Colchicum* (colchicine), *Digitalis* (digoxine), *Ephedra* (ephedrine), *Ipeca* (emetine), *Papaver* (morphine, codeine)... *Taxus baccata* (taxol)



## 2. Some important concepts and limits

Plants of concerned: ambivalent or borderline botanicals



## 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.

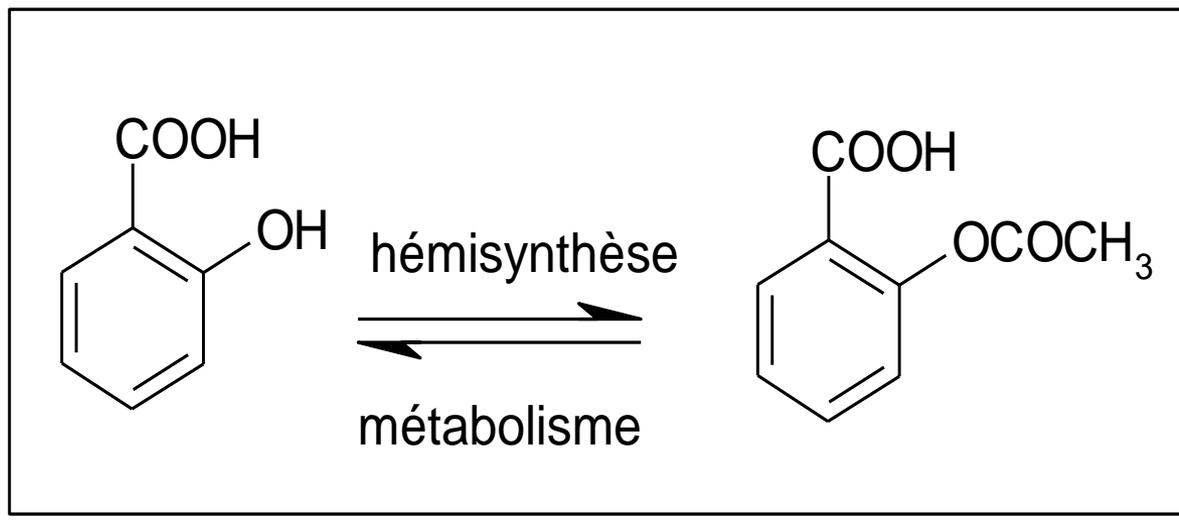
(*Salix alba*, *Salicaceae*), bark

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 (prostaglandines) (1971)
- **Platelets aggregation inhibition** (1985)
- **Colon cancer prevention** (1997)



salicylic acid

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

Senna



Hypericum



Valeriana



### 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?

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#### 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?

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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



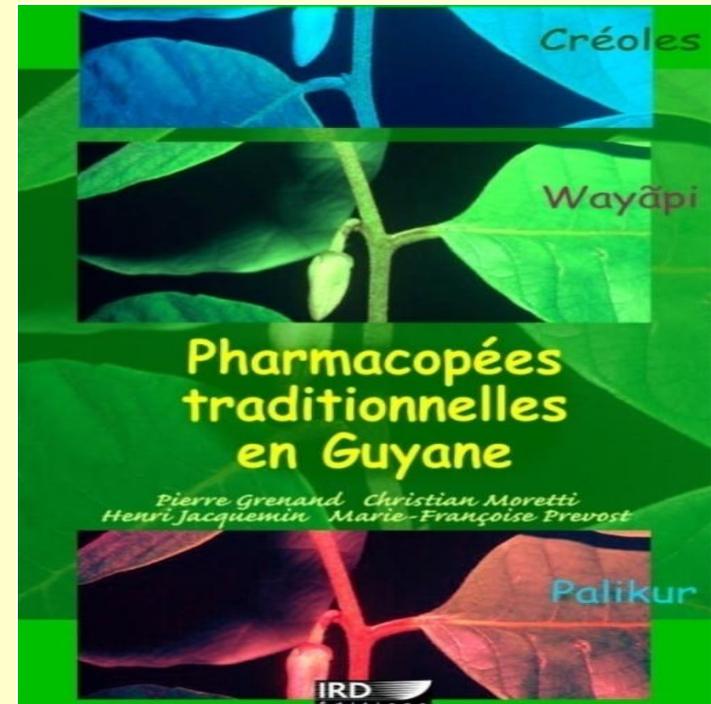
## 5. What questions have to be solved ?

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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?

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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

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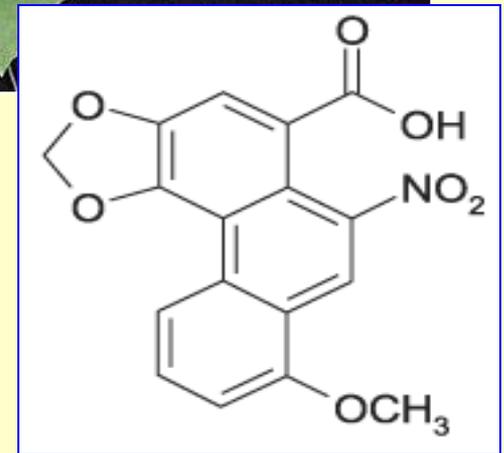
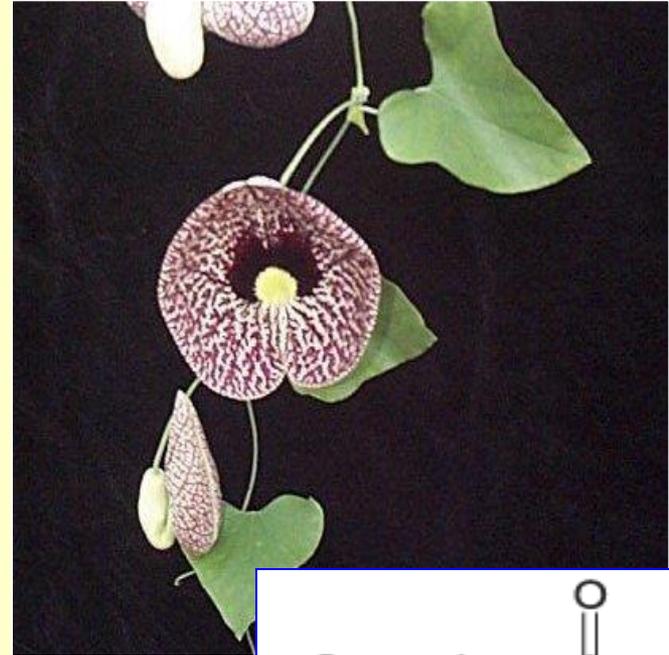
Because of the large variability of plant constituents

- ◆ Rigorous 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)



Aristolochic acid

## 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

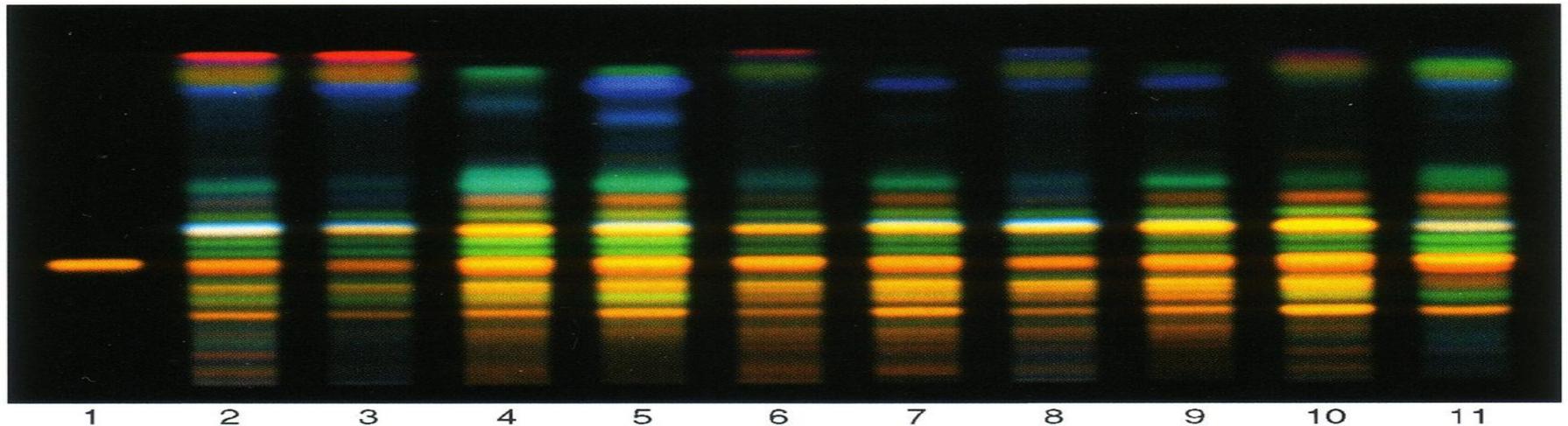
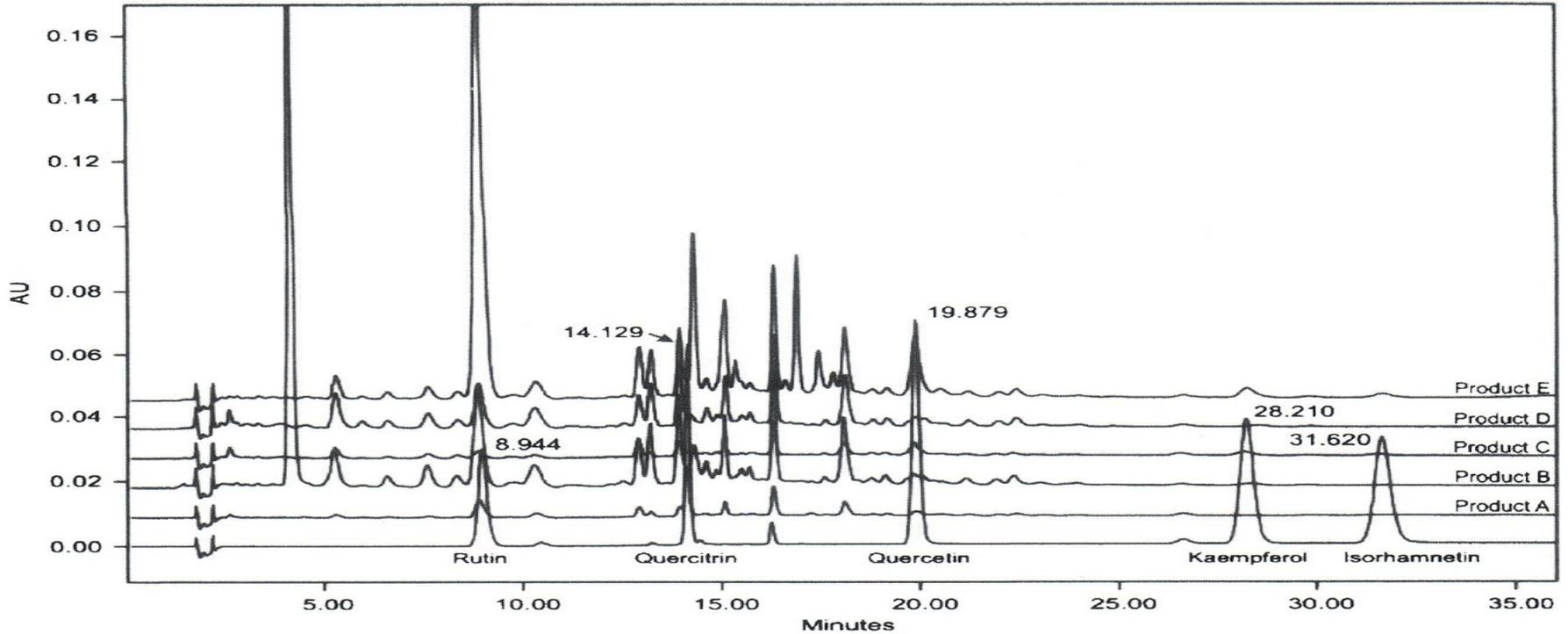
## 6.5. Traditional botanical preparations

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- ◆ **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

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- ◆ 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

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- 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

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- **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?

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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



# Additional data and recent bibliography

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- ◆ 1. Traditional knowledge for the assessment of the health effects for botanicals.

A framework for data collection:

R. Anton, L. Delmulle, M. Serafini

*Eur. Food and Feed Law*, 2, 74-80 (2012)

- 2. The role of traditional knowledge in the safety of botanical food supplements. Requirements for manufacturers

R. Anton, M. Serafini, L. Delmulle

*Eur. Food and Feed Law*, 5, 241-250 (2012)

- 3. Projet Belfrit: Harmonizing the use of plants in food supplements in the European Union: Belgium, France and Italy. A first step.

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

*Eur. Food and Feed Law*, 3, 187-196 (2013)

- 4. The substantiation of claims for botanical food supplements in relation to traditional use.

R. Anton, M. Serafini, L. Delmulle

*Eur. Food and Feed Law*, 8, 321-328, (2013)

