ROMANIAN PHARMACOPEIAS – OVERVIEW OF 150 YEARS OF BOTANICAL USAGE. CASE STUDY OF HIPPOPHAE RHAMNOIDES

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AIM

- European Pharmacopoeia
- Romanian Pharmacopoeia – characteristics
- Case study - *Hippophae rhamnoides*
  - questionnaire study
  - general characteristics (ie. the content, format, benefits) of sea buckthorn products
European Pharmacopoeia
**EUROPEAN PHARMACOPOEIA**

- *Pharmacopoea Europaea (Ph. Eur.)*
- is a published collection of monographs that describe both the **individual and general quality standards** for
  - ingredients,
  - dosage forms
  - methods of analysis for medicines.
The objective

- to provide common quality standards throughout Europe to control the quality of medicines and substances used to manufacture them.

→ These standards apply to medicines for both human and veterinary use.
EUROPEAN PHARMACOPOEIA

- official reference to serve public health

- part of the regulatory requirements for obtaining a Marketing Authorisation Application (MAA) for a medicinal product.

- quality standards apply throughout the entire life-cycle of a product ➔ legally binding and mandatory on the same date in all 37 signatory states and the EU member states.
The 1st Edition - was published in 1969 and comprised 120 texts.

The 8th Edition
- published in July 2013 (currently in force)
- implementation date - January 1, 2014.
- contains more than 2220 monographs and 340 general chapters illustrated with diagrams or chromatograms and over 2500 descriptions of reagents.

Volume 1 contains introductory information, general chapters and reagents, as well as monographs grouped by theme (dosage forms, vaccines, plants, etc.).

Volume 2 contains all other monographs as well as an index of the entire contents of the Ph. Eur.

+ collection of eight non-cumulative supplements (8.1 to 8.8).
EUROPEAN PHARMACOPOEIA

- A new edition is published every three years.

- It is made available in **print** and **electronic** (online and USB stick) versions, in both **English** and **French** by the Council of Europe.

- The **online** version is also accessible from smartphones and tablet computers.

- *Translations into other languages* are published by the member states themselves e.g. a **German** version is jointly elaborated by Austria, Germany and Switzerland.
## INDEX OF PHARMACOPOEIAS

### 1. NATIONAL

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Romanian Pharmacopoeia

The First Edition of Romanian Pharmacopoeia

- The development was conducted by a group of professionals led by Prof dr. Carol Davila
  - 12 physicians and
  - 6 pharmacists.

- December 5, 1862 - the Medical Council approves the first edition of the Romanian Pharmacopoeia
  ➔ became applicable starting with January 1863.

- The volume represented a valuable work which corresponded entirely to the scientific requirements of that time.
  - comprising 790 pages divided into three parts,
  - the edition was written in two columns, both for Romanian and Latin language.
THE FIRST EDITION OF ROMANIAN PHARMACOPOEIA

1. *Materia pharmaceutica*

- 301 monographs
  - 207 were herbal drugs,
  - 23 were of animal origin,
  - 46 inorganic substances
  - 15 organic compounds.

- **vegetal products:** *Matricaria chamomilia, Hypericum perforatum, Artemisia absinthium, Arnica montana, Chelidonium majus etc.*

- **animal origin drugs:** Jecoris aselli, Cetaceum, Cera, Cantharide, Fel bovinum etc.

- **inorganic substances** - substances which could be purchased commercially: Sulfas magnesiae, Argentum foliatum, Acidum chlorhidricum.

- **organic substances** - camphor oil, indigo, vinegar, creosote and sodium soap.
2. *Preparata Pharmaceutica*
- contains 547 monographs of *galenic products and pharmaceutical formulations as well as organic and inorganic substances* which were developed in pharmacy (boric acid from borax, barium chloride from barium sulphate and so on).

3. *Reagentia et Tabulae Variae,*
- 52 tables and a list of foreign names and their popular synonyms of some of the most important drus
- instructions for the preparation of popular drugs.

- Tabula I. - Antidotes and some formulas for annihilating poisons.
- Tabula II. - Poisonous drugs and their conservation.
- Tabula III. - Highly active drugs.
SECOND EDITION OF ROMANIAN PHARMACOPOEIA

- is written in Romanian only
- comprises a total of 522 monographs
  - 316 pharmaceutical substances monographs
  - 206 pharmaceutical formulas.

Origin
- vegetable substances ~57%
- chemical substances ~38%
- animal origin ~5%
“Elaborated under the care of the Romanian Pharmacists Society Committee and edited by Speranta Institute of Graphic Arts in 1915”

Novelty

- mention **vials** in a separated chapter
  - the processes of vial filling, checking and sterilization.
- new ways of **sterilizing the substances used for hypodermics**
- the **molecular weights** calculated based on the last atomic weight (International Special Commission in 1913)

**Origin** of the medical substances

- chemical - 59%
- vegetable – 36%
- animal origin - 23%.
FOURTH EDITION OF ROMANIAN PHARMACOPOEIA

- The paper is approved by decree No. 1443, signed by King Ferdinand I on the 27th of March 1926.

699 monographs

FIFTH EDITION OF ROMANIAN PHARMACOPOEIA

→ edited in 1943
SIXTH EDITION OF ROMANIAN PHARMACOPOEIA

- appears in 1948
- New vegetable drugs are formalized (*Radix Primulae*, *Folia Stramonii*, etc), both from the indigenous flora and imported.

SEVENTH EDITION OF ROMANIAN PHARMACOPOEIA

Review work began in 1952 and ended in 1956.
Eight Edition of Romanian Pharmacopoeia
- was made in 1965

Supplements of the 8th Pharmacopoeia
- were made in 1968-1970

Ninth Edition of Romanian Pharmacopoeia
- published in 1976
Tenth Edition of Romanian Pharmacopoeia

- applicable since 1993,
- consists of 1315 pages

Novelty

- Updating a large number of general monographs;
- Introduction of dissolution ‘in vitro’ test
- Completion of methods of analysis with:
  - Control of antimicrobial preservatives efficiency;
  - Pressurized liquids chromatography;
  - Disintegration, dissolving and dosage of tannins in vegetable products;
  - Atomic absorption spectrophotometry;
- 94 new monographs are introduced;
- 166 monographs are eliminated as well as 9 methods of analysis;
- The International System of Units (ISU) is adopted;
- Table with maximum therapeutic doses were completed with usual therapeutic doses.
2000 - Supplement I for RP X
- materials for containers for pharmaceutical usage,
- therapeutic usage recipients
- reagents and standard solutions.

2004 - the 2nd Supplement for RP X
- formalizes the International System of Units (ISU) used in the RP and other units.
- includes general chapters and individual and general monographs translated from the European Pharmacopoeia (EP), 4th edition.
- Standard Romanian terms and tables containing types of packaging, closure systems and administration information.

2006 - the 3rd Supplement for RP X
- new analytical methods,
- pharmacotechnical methods,
- alcholometric tables,
- tables of physical characteristics of radionuclides in EP.
- homeopathic preparations
- updated standard Romanian terms.
Romanian specialists have extensive studies on medicinal plants (spontaneous flora) found in large quantities in various parts of the country (e.g., Hippophae rhamnoides, Ruscus aculeatus, Hedera helix, Clematis vitalba, Aristolochia clematitis, Meadowsweet etc.).
With the scientific promotion of herbal food supplements it is observed a spectacular activity of rediscovery of plants traditionally used, many of which being not found in the monographs of the 10th editions of the Romanian Pharmacopoeias.

Manufacturers of herbal supplements have developed their own medicinal and aromatic crops, with specific concerns of BIO-crops.

Production companies have succeeded on the food supplements market, bringing out well-founded scientific arguments for usage of some traditional medicinal species (also endemic) ➔ SC Hofigal SA, SC Fares SA, SC PlantExtract SA, SC Dacia Plant SA, whose products are known in Romania and abroad.
Calendula officinalis

Thymus serpyllum

Chrisanthemum balsamita var. balsamita

E. pallida

E. purpurea

Echinacea angustifolia

Vaccinium vitis idaea

Plantago major

Plantago lanceolata
At the moment much of medicinal and aromatic plants used in nutritional supplements and pharmaceutical products are not formalized by a new edition of RF why we believe it is appropriate to formalize their inclusion to Traditional Romanian Pharmacopoeia.

We have information about traditional medicine in Romania:
- published works
- presentation brochure of production and research units
TRADITIONAL ROMANIAN PHARMACOPOEIA
- PROPOSAL

- framework structure of traditional pharmacopoeia monograph for discussion with professionals.
- relevant scientific information of a multidisciplinary team (botanists, agronomists, biochemists, ethnologists, pharmacists, doctors, engineers, technologists, chemists analysts)

It should contain:
- specific data and popular scientific name of the species - family,
- results of field surveys or information about (significant uses and precautions in use)
- geographical distribution in Romania,
- botanical description of the species
- popular names in different regions of the country and in Europe,
- chemical composition - biologically active substances (possibly significant content by origin),
- biological activity,
- toxicity,
- methods of use,
- citations/scientific references

To achieve this national target and to be able to access European funds
Case study
- *Hippophae rhamnoides*
The preliminary results

- **questionnaire** study concerning the perception on the use and benefits of products containing *Hippophae rhamnoides*

- exhaustive analysis of **packages of products** containing *Hippophae rhamnoides*

- Based on the scientifically-based results, botanical products for human usage could increase the health and safety of consumers.
CATINA

- „Hippophae rhamnoides”
- sea buckthorn

- "a pharmacy in a bush" - Prof. dr. Ion Brad

- "a miracle herb"
- “Romanian ginseng”
- “panacea of modern times”

- plant with a complex therapeutic potential and a wide range of applications
Seabuckthorn plantations on Romanian territory were originally used to showcase the hillside that was subject to degradation.

Then underbrush was used in a fruit growing area in Central Asia, underbrush has the most beneficial development conditions in Romania, the largest expansion has in the South (Muntenia, Dobrogea) and in the East, the riverbeds. Sea buckthorn also lies in the Danube Delta region.

**FAMILY ELEAGNACEAE**
**GENUS HIPPOPHAE**
**RHAMNOIDES SPECIES**

- Sea buckthorn flowers are of yellow-rust colour, grouped in globular inflorescence. It blooms in the period between March-May and is harvested between August and September, closely the seabuckthorn fruit appears orange.

- Sea buckthorn fruit is oval in shape, with a small size and a sour taste characteristic of this plant.
HISTORICAL USAGE

- The remarkable effects of sea buckthorn nutrients were known since Greek mythology ➔ Pegasus, the winged horse, ate it.

- The underbrush was used to feed horses participating in the equestrian competitions of the Olympics Hellas. The meaning of the word "hippophae" would be linked to the "hippos" meaning "horse" and "Phao" means "murder" because buckthorn fruit would have been used to eliminate worms that were in the intestines of horses.

- Sea buckthorn fruit consumption, and Theophraste Dioscoride indicated that horses' hair became brighter, shinier.

- The Gauls had also knowledge about sea buckthorn use in the treatment of various diseases such as liver disease, rheumatism, scurvy and many others.

- Using for the first time as buckthorn fruit medicine by the population of Tibet has been certified through historical documents, specifically due to medical book entitled "Sibu Yidian"
Digestive diseases and dermatological therapy was achieved in Central Asia by means of underbrush, according to Tibetan books "Rgyud BZI" since the reign of the Tang Dynasty (from the period between 619-907).

Called "Siberian pineapple" by the Russians, it was used sea buckthorn for its outstanding revival. Its protective role against cosmic radiation was considered, for which it was employed by the former Soviet Union astronauts, the current Russian Federation.

The introduction of sea buckthorn in Chinese Pharmacopoeia was conducted in 1977 and 1988.

Chinese athletes have used sea buckthorn beverages in the Olympics in Seoul, South Korea—general tonic.
CHEMICAL COMPOSITION

- fat-soluble vit. (vit. A, E)
- water-soluble vit. (vit. B1, B2, B6, B9, C)
- carotenoids (beta-carotene, lycopene), flavonoids
- minerals (Ca, Mg, Fe, K, Na)
- phytosterols, pectins

The sea buckthorn fruit - pH 2-3
Existing one-way membranes can retain vitamins, if not destroyed
➔ explain the paradox of "cohabitation" water-soluble vitamins (vit. B1, B2, B6, C) and the fat-soluble vitamins (vit. A, D, K, E)

Vătafu M. Hofimel S – formula 1. Revista Hofigal. 2008; 14; 30
WHO AND WHEN CAN USE?

- children
  - breakfast
- adults
  - lunch / dinner
Benefits

- Bactericide
- Immunostimulant
- Antioxidant
- Anti-inflammatory
- Radioprotection
- Antitumor
- Hepatoprotector
- Platelet antiagregant
- Cicatrisant
Assessment (questionnaires)
- the degree of public information about products containing sea buckthorn
Material and Method

- Study conducted on two groups of population
  - (students and adults aged 35-80 years)

- Analysis ➔ extensive 20-item questionnaire with simple or multiple choice answer

- Obs – idea – PlantLIBRA questionnaire/survey

- A comparative study of the two target groups:
  - Their level of awareness of sea buckthorn products
  - The benefits and side effects thereof

- SPSS statistical analysis of the results (in work)
Characteristics followed in product acquisitions
The most important characteristic in acquisition is benefits.
Analysis of the general characteristics
(ie. the content, format, benefits)
based on sea buckthorn products selected in herbal stores
products containing sea buckthorn
Type of products – product format
Distribution of the sea buckthorn products highlighting the benefits presented on the label/leaflets

- General benefits: 12
- Aimed benefits: 14
- Sugarfree, no conservatives: 3
- Has no benefits: 5
- Natural product: 15
- Natural supplement: 11
CONCLUSIONS

- Results of the studies show the complexity of the beneficial effects of sea buckthorn—a rigorous scientific research needs to be done to extend the use of seabuckthorn, using scientifically accurate facts.

- Correct and complete information concerning the product containing sea buckthorn could sustain the consumers to buy and to use these products, under advice of doctors.

- If the phytotherapy structure is done as a medical discipline based on botanic + pharmacology—it is extremely useful as therapeutic instrument.


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Thank you for your attention!