

# 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.



# EUROPEAN PHARMACOPOEIA

## 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).
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# 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

WHO/PSM/QSM/2006.2  
page 2

### 1. NATIONAL

COUNTRY	TITLE	1. PHARMACOPOEIA COMMISSIONS 2. PUBLISHER/DISTRIBUTOR 3. WEBSITE 4. FREQUENCY OF PUBLICATION	EDITION	YEAR	LANGUAGE
Romania		1. Romanian Pharmacopoeia Commission National Medicines Agency Aviator Sanatescu 48, R-71324 Bucuresti			
	Farmacopeea Romana	2. Editura Medicala- Bucuresti	A X-A Supplement Supplement Supplement	1993 2000 2001 2004	Romanian Romanian Romanian Romanian
		3. National Medicines Agency <a href="http://www.anm.ro/home.html">http://www.anm.ro/home.html</a>			Romanian English

*[http://www.who.int/medicines/publications/pharmacopoeia/WHO\\_PSMQSM2006\\_2\\_IndexPharmacopoeiasUpdated.pdf](http://www.who.int/medicines/publications/pharmacopoeia/WHO_PSMQSM2006_2_IndexPharmacopoeiasUpdated.pdf)*



# Romanian Pharmacopoeia

*ROMANIAN PHARMACOPOEIA FROM THE FIRST TO THE LAST EDITION*, Valentina SOROCEANU, UMF “Carol Davila” Bucharest,  
<http://www.revistafarmacia.ro/20113/art17.besciu.farmacia3.2011.447-452.pdf>

# 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.



- o **vegetal products:** *Matricaria chamomilia*, *Hypericum perforatum*, *Artemisia absinthium*, *Arnica montana*, *Chelidonium majus* etc.
- o **animal origin drugs:** Jecoris aselli, Cetaceum, Cera, Cantharide, Fel bovinum.etc.
- o **inorganic substances** - substances which could be purchased commercially: Sulfas magnesiae, Argentum foliatum, Acidum chlorhidricum.
- o **organic substances:** camphor oil, indigo, vinegar, creosote and sodium soap.

# THE FIRST EDITION OF ROMANIAN PHARMACOPOEIA



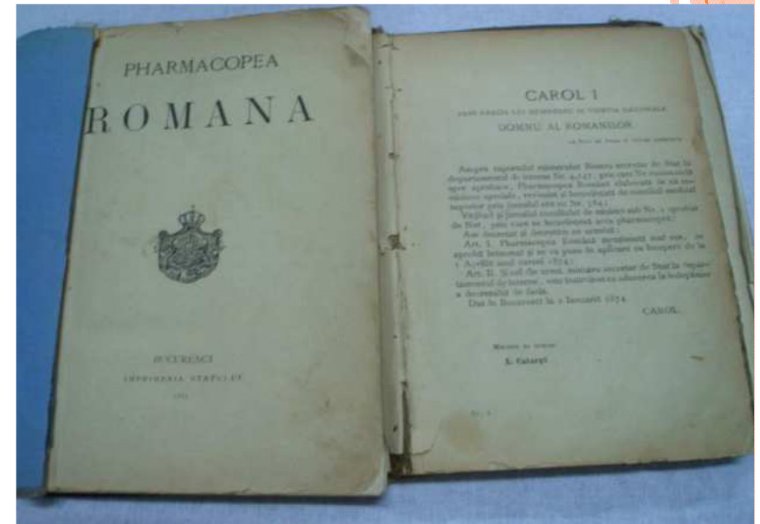
## 2. *Preparata Pharmaceutica*

- 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 drugs
- 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%





# SPECIAL EDITION OF ROMANIAN PHARMACOPOEIA

*“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

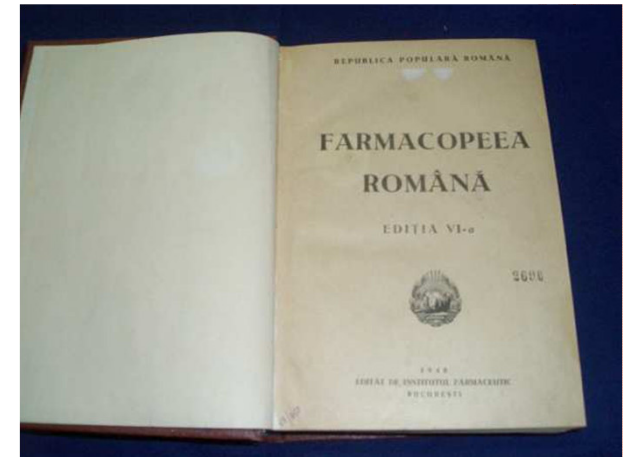
→ edited in **1943**





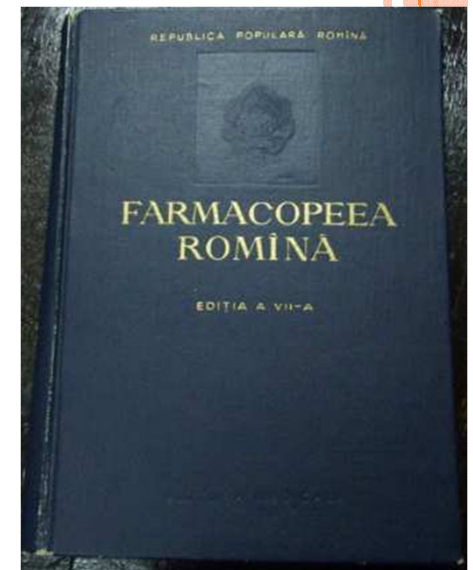
## SIXTH EDITION OF ROMANIAN PHARMACOPOEIA

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



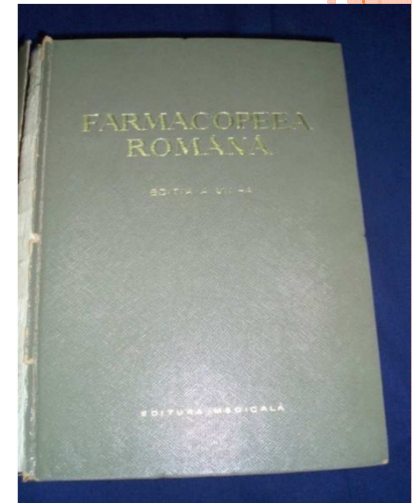
## SEVENTH EDITION OF ROMANIAN PHARMACOPOEIA

Review work began in 1952 and ended in **1956**.



## EIGHT EDITION OF ROMANIAN PHARMACOPOEIA

- was made in 1965

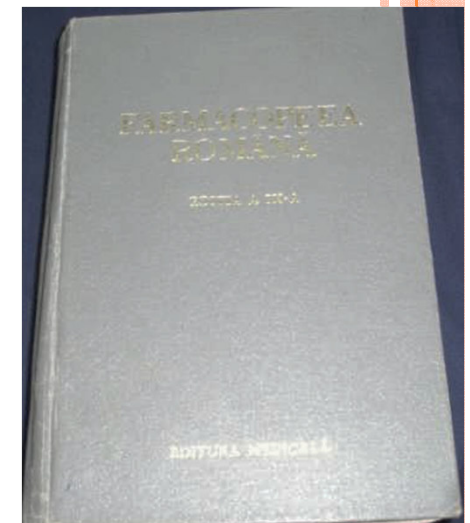


## SUPPLEMENTS OF THE 8TH PHARMACOPOEIA

- were made in 1968-1970

## NINTH EDITION OF ROMANIAN PHARMACOPOEIA

- published in 1976

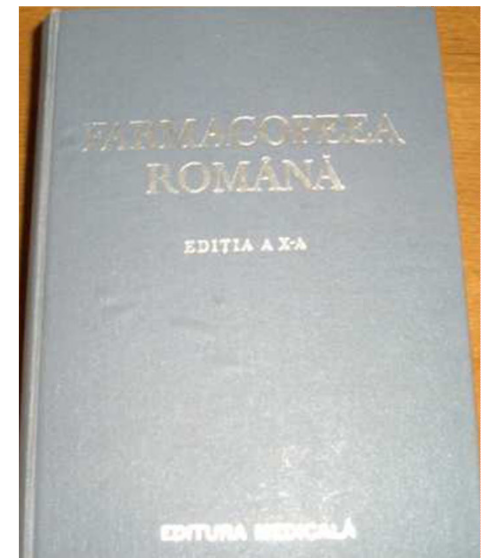


# TENTH EDITION OF ROMANIAN PHARMACOPOEIA

- 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.

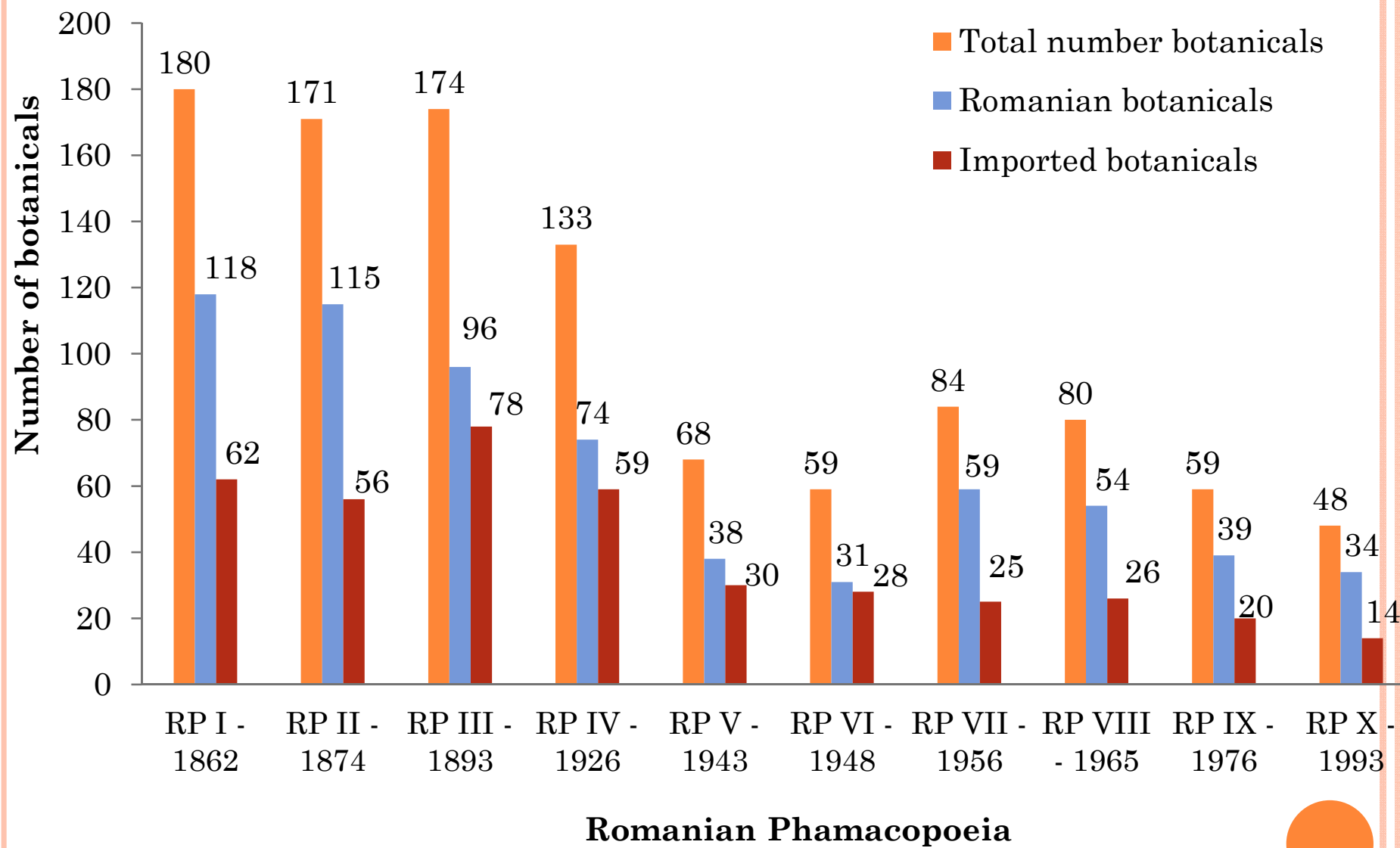
## **2004 - the 2nd Supplement for RP X**

- 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**

- 'Introduction to the European Pharmacopoeia, 5th edition',
- new analytical methods,
- pharmacotechnical methods,
- alcoholmetric tables,
- tables of physical characteristics of radionuclides in EP.
- homeopathic preparations
- updated standard Romanian terms.

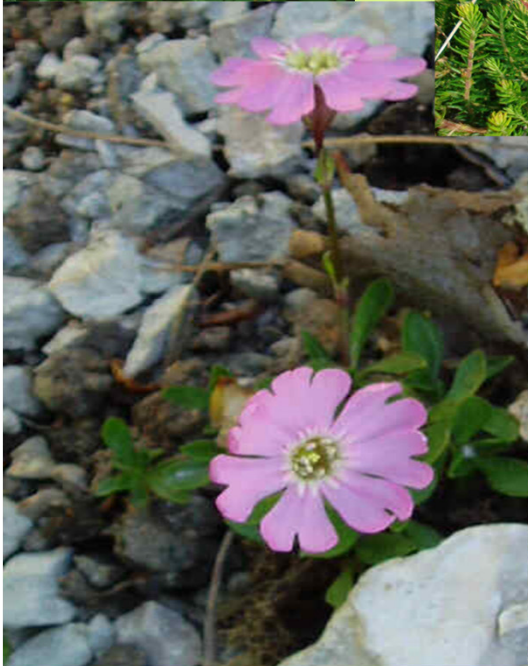






**Romanian specialists have extensive studies on medicinal plants** (spontaneous flora) found in large quantities in various parts of the country (eg *Hippophae rhamnoides*, *Ruscus aculeatus*, *Hedera helix*, *Clematis vitalba*, *Aristolochia clematitis*, *Meadowsweet* etc.)

*Flore spontané – plantes endémiques*



*Hepatica transilvanica*  
*Primula auricula*  
*Lychnis nivalis*  
*Carduus carduelis*  
*Leucanthemum waldsteinii*  
*Brukentalia spiculifolia*  
*Thymus comosus*  
*Anthemis carpatica* –  
*subspecia pyrethriformis*



# BOTANICAL - PLANT FOOD SUPPLEMENTS

- 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*



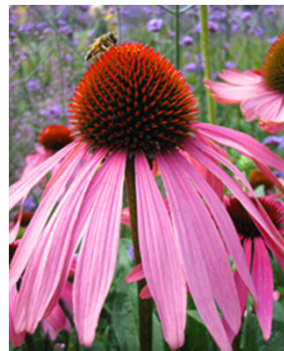
*Thymus serpyllum*



*Chrysanthemum balsamita*  
*var. balsamita*



*E. pallida*



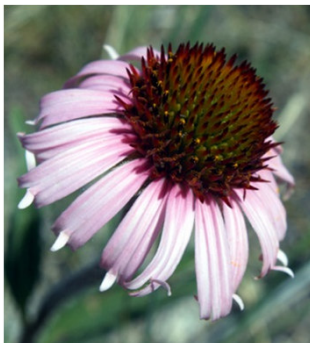
*E. purpurea*



*Plantago*  
*major*



*Plantago*  
*media*



*Echinacea angustifolia*



*Vaccinium vitis idaea*



*Plantago lanceolata*





# TRADITIONAL ROMANIAN PHARMACOPOEIA - priority objective Romanian Society of Ethnopharmacology

*Angela Mărculescu*

*Universitatea Transilvania Braşov*

*Societatea Română de Etnofarmacologie*

- 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





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

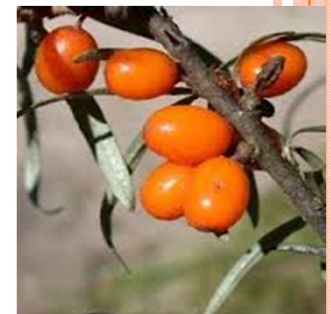


- Seabuckthorn plantations on Romanian territory were originally used to showcase the hillside that was subject to degradation.
- Then underbrush was used in a fruit growing area
- In Central Asia, underbrush has the most beneficial development conditions
- In Romania, the largest expansion has in the South (Muntenia, Dobrogea) and in the East, the riverbeds. Sea buckthorn also lies in the Danube Delta region



**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's 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

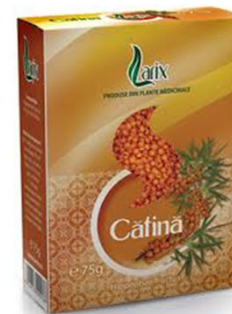
minerals (Ca,  
Mg, Fe, K, Na)

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)







# WHO AND WHEN CAN USE?



**children**



**adults**

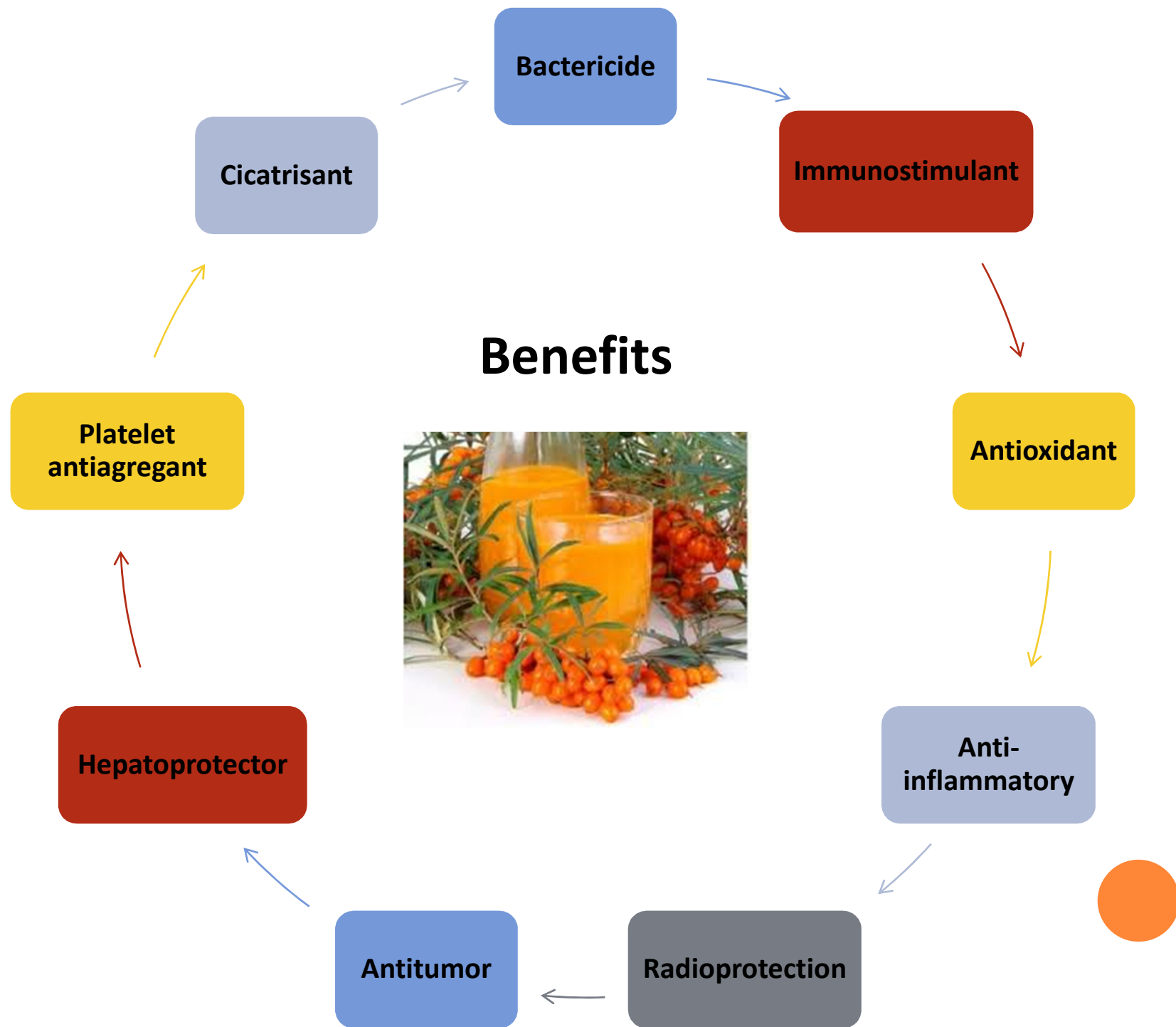


**breakfast**



**lunch / dinner**





## **Assessment (questionnaires)**

- the degree of public information about products containing sea buckthorn

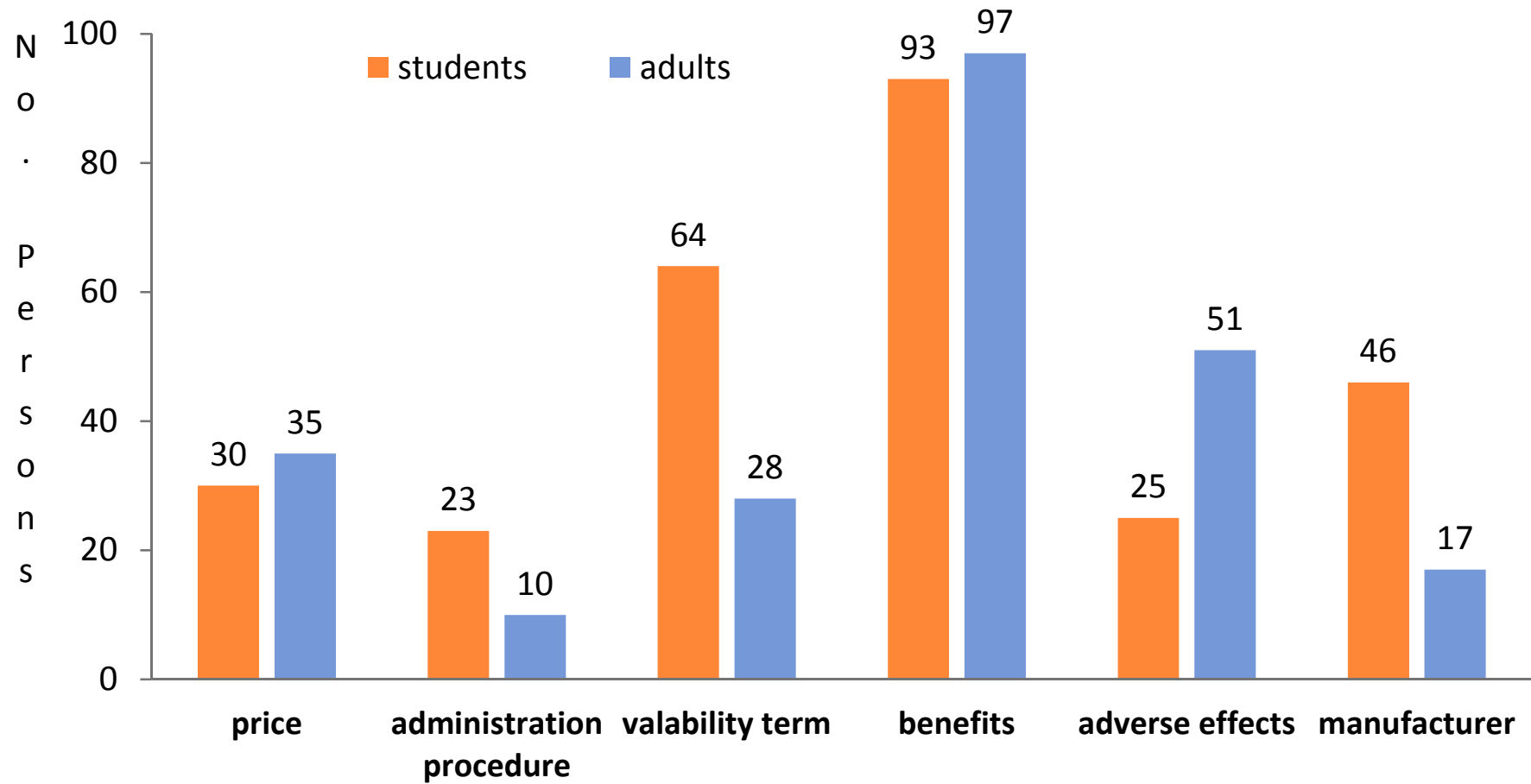




## Material and method

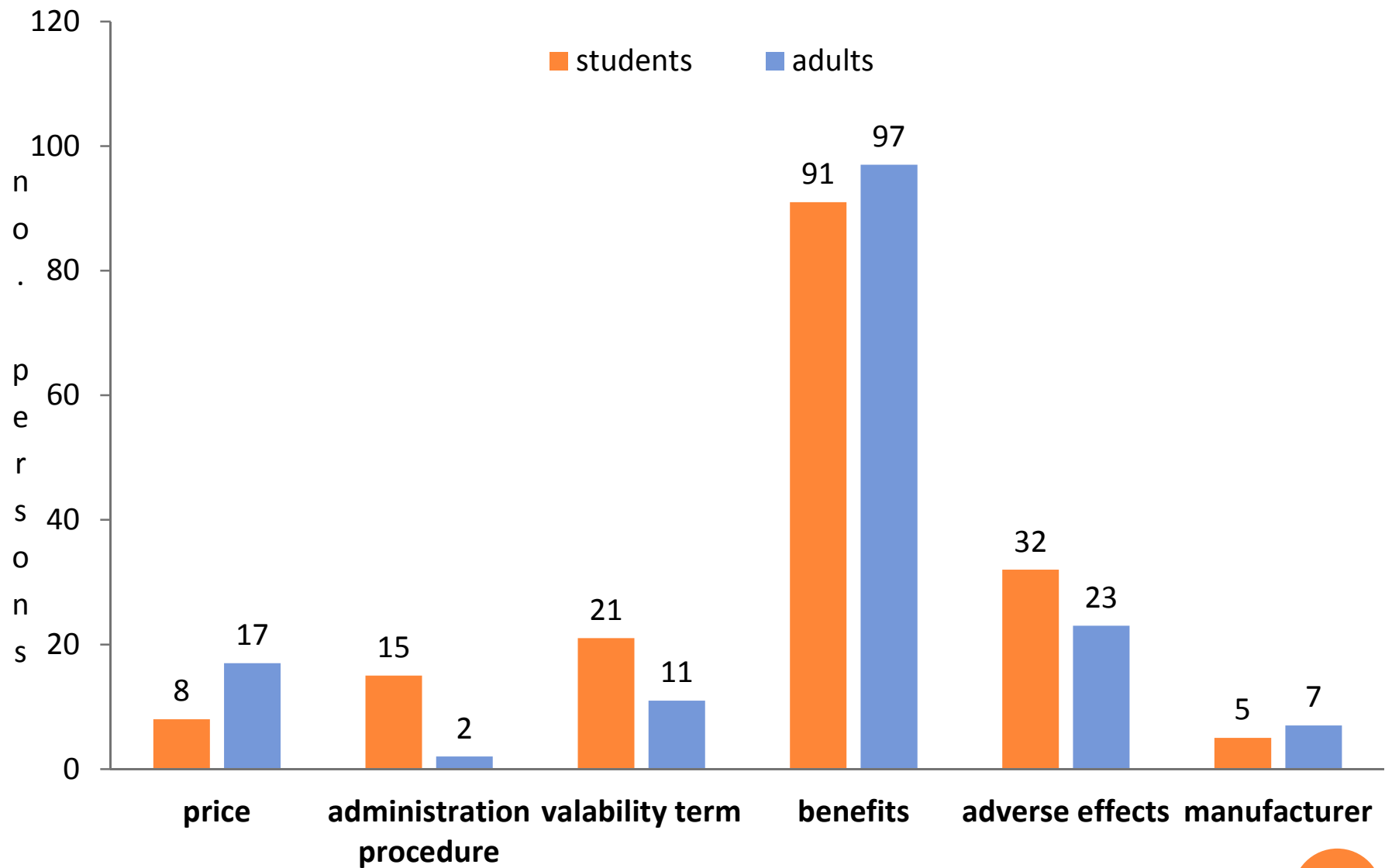
- Study conducted on two groups of population  
(students and adults aged 35-80 years)
- Analysis → extensive 20-item questionnaire with simple or multiple choice answer
- Obs – idea – PlantLIBRA questionnaire/survey
- A comparative study of the two target groups:
  - Their level of awareness of sea buckthorn products
  - The benefits and side effects thereof
- SPSS statistical analysis of the results (in work)





**Characteristics followed in product acquisitions**





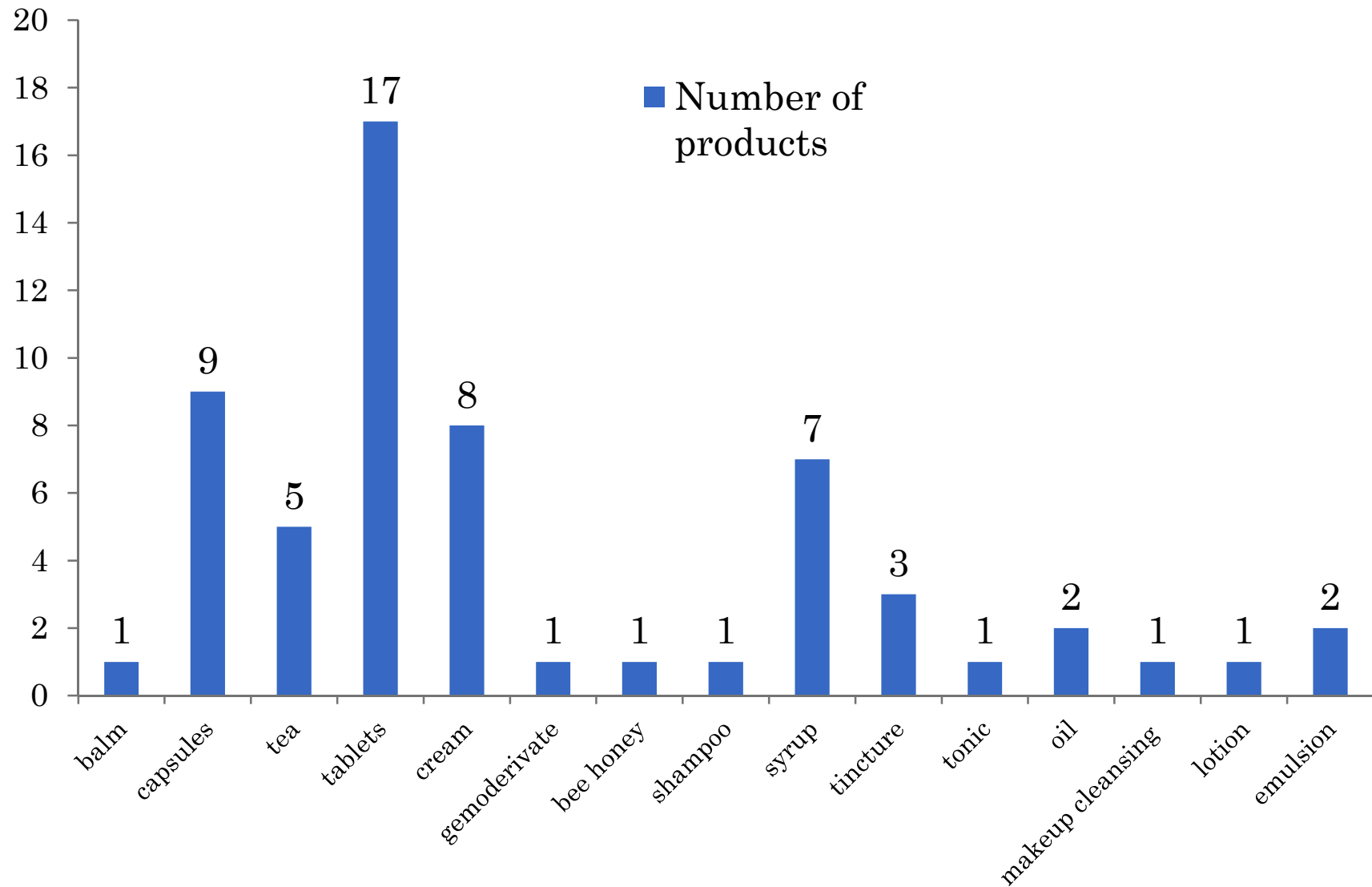
**The most important characteristic in aquisition**



# **Analysis of the general characteristics** (ie. the content, format, benefits)

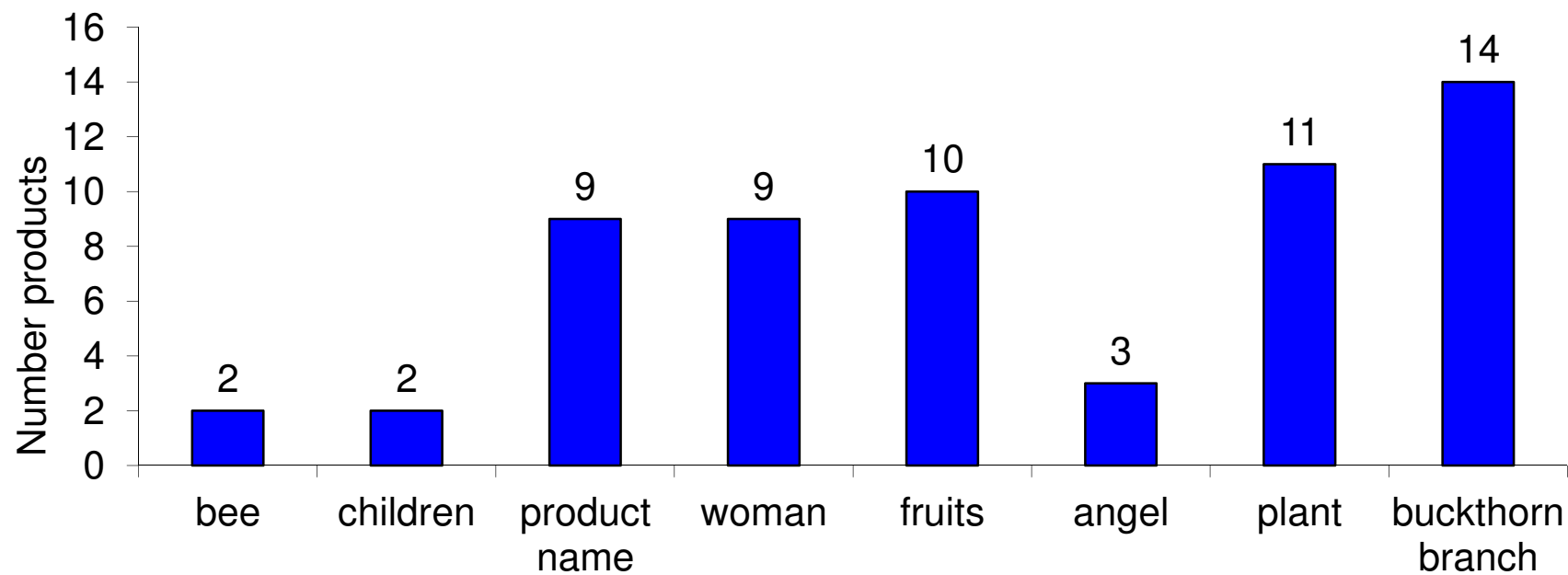
based on sea buckthorn products selected in herbal stores  
**products** containing sea buckthorn





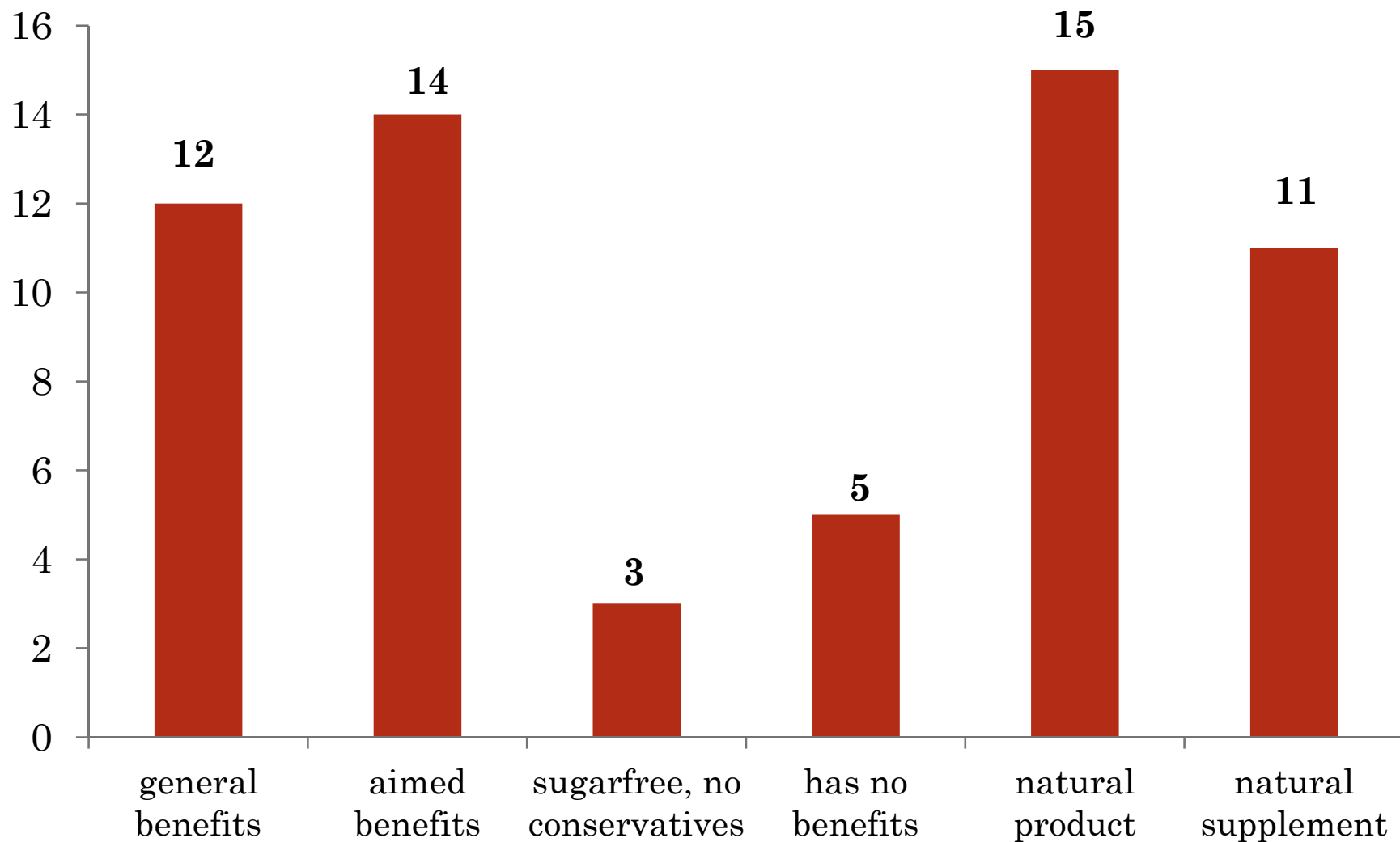
**Type of products – product format**





Image





**Distribution of the sea buckthorn products  
highlighting the benefits presented on the  
label/leaflets**



# 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 a extremely useful as therapeutic instrument.

- ROMANIAN PHARMACOPOEIA FROM THE FIRST TO THE LAST EDITION, Valentina SOROCEANU, UMF “Carol Davila” Bucharest,;  
<http://www.revistafarmacia.ro/20113/art17.besciu.farmacia3.2011.447-452.pdf>
- M. Cotrău- Medicamentul de-a lungul vremii. Ed. Apollonia – Iași 1995.
- V. Lipan – Istoria farmaciei române în date , Ed. Farmaceutică, 2009;
- J. Spielman, G.Baicu – Istoria științelor farmaceutice în România Ed. Medicală AMALTEA 1994;
- Farmacopea Română ediția I-a Ed. la Imprimeria statului, 1893- 790p
- Farmacopea Română ediția a II-a Imprimeria Statului, 1874-160 p;
- Farmacopea Română ediție a III-a Imprimeria statului, 1893 – 490 p;
- Farmacopeea Editie speciala, 1915, - 712 p
- Farmacopea Română ediția a IV-a; Atelierele grafice SOCEC &Co., Societate Anonima (Bucuresti) 1926.-570 p.
- Farmacopea Română ediția a V-a; Ed. Tiparul Românesc 1943.- 539 p.
- Farmacopea Română ediția a VI-a “Editată de Institutul Farmaceutic Bucuresti” 1948- 660 p;
- Farmacopea Română ediția a VII-a, Editura Medicală din Bucuresti 1956.944 p;
- Farmacopea Română ediția a VIII-a, Farmacopea Română ediția a VIII-a, 1965-946 p;
- Supliment I F.R. VIII., Editura Medicală din Bucuresti 1968 – 130 p;
- Supliment II F.R. VIII- Editura Medicală din Bucuresti,1970 – 71 p;
- Supliment III F.R. VIII- Editura Medicală din Bucuresti,1972- 155p ;
- Farmacopea Română ediția a IX-a, Editura Medicală din Bucuresti 1976 – 1005p;
- Supliment I F.R. IX., Editura Medicală din Bucuresti 1981;
- Farmacopea Română ediția a X-a, Editura Medicală din Bucuresti 1993 – 1315p;
- Supliment I F.R. X., Editura Medicală din Bucuresti 2000 – 158p;
- Supliment II F.R. X., Editura Medicală din Bucuresti 2004 – 310p;
- Supliment III F.R. X., Editura Medicală din Bucuresti 2006 – 370p
- Brad I. L., Brad I. Cătina și istoria ei (II). *Revista Hofigal*. 2006; 3; 10
- Manea Ș. *Cătina și uleiul de cătina*. Edit. Tridona. Oltenița. 2000; 4-20
- Pârnu C. Cătina – farmacia completă din grădină. *Revista Hofigal*. 2009; nr. 18; 20
- Mingyu X., Xiaoxuan S., Jinhua C. The medicinal research and development of seabuckthorn. *Journal Ethnopharmacology*. 2001;
- MARCULESCU A, LUPESCU I, HANGANU D, DRAGULESCU C., MARCULESCU I., Les plantes medicinales des differentes editions de la pharmacopee roumaine au cours du temps, *Ethnopharmacologia – Revue Ethnopharmacologia*, nr.33, mai. 2004, ISSN 1261-4572, pg. 26-43







**Thank you for your  
attention!**

