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THE STUDY OF PHARMACOPOEIAS USED IN THE ROMANIAN AREA IN XVIII-XXTH CENTURIES: EVOLUTION OF PROPORTIONS FOR DRUG SUBSTANCES AND PHARMACEUTICAL PREPARATIONS

EMILIA STANCU, ANA CARATA, ADRIANA-ELENA TĂEREL*, VALENTINA SOROCEANU

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Abstract

The main function of Pharmacopoeias is to officially regulate the quality of medicines. Indirectly, Pharmacopoeias allow also the reestablishment of the pharmacological picture for the period they were in force, medicinal substances and pharmaceutical preparations used in therapy being included as individual monographs. Depending on the progress and needs in therapeutic practice, successive editions of the Pharmacopoeia recorded changes. Relating to the introduction of new monographs or removing those outdated and change in percentage of representation for various categories of medicinal substances (herbal, animal and mineral or obtained by chemical synthesis). According to the Pharmacopoeias used on the current Romanian territory from 1780 to present, there were decreases for herbal (63.96%), animal (7.64%) derived drugs and pharmaceutical forms (33.02%) and a growth for mineral remedies / synthetic drug substances (71.60%).

Rezumat

Principalul rol al Farmacopeilor este acela de a reglementa oficial calitatea medicamentelor. Indirect, Farmacopeile permit însă și refacerea tabloului farmacologic al perioadei pe care o reglementează, substanțele medicamentoase și preparatele farmaceutice utilizate în terapie fiind înscrise ca monografii individuale. În funcție de progresele și necesitățile din practica terapeutică, edițiile succesive ale Farmacopeilor înregistrează modificări care constau atât în introducerea monografiilor noi și eliminarea celor depășite, cât și în modificarea procentului de reprezentare al diferitelor categorii de substanțe medicamentoase (de origine vegetală, animală și minerală sau de sinteză chimică). Conform Farmacopeilor utilizate pe teritoriul României actuale între anul 1780 până în prezent, s-au constatat scăderi în ponderea substanțelor medicamentoase de origine vegetală (63,96%), animală (7,64%) și a preparatele farmaceutice (33,02%) și o creștere de 71,60% pentru remediile de origine minerală / substanțele medicamentoase de sinteză.

Keywords: Pharmacopoeias, drug substances, pharmaceutical preparations.

Introduction

In the past, obtaining drugs was often an art known only by the pharmacists. In time, it was required the desecretization and regulation of therapeutic practice, Pharmacopoeias being the main pharmacists' guidelines. In the Romanian Principalities, that were dependent on foreign powers, it was possible to develop a national pharmacopoeia only in 1862, by that time being used the Austrian Pharmacopoeia [1, 3].

Materials and Methods

During the study, there were used:

- Pharmacopoea Austriaco-Provincialis (1780) and Romanian Pharmacopoeia (11 editions): F.R. I (1862); F.R.II (1874); F.R. III (1893); F.R. S. (1915); F.R. IV (1926); F.R. V (1943); F.R. VI (1948); F.R. VII (1956); F.R. VIII (1965); F. R. IX (1976); F.R. X (1993).
- Analytical study of each Pharmacopoeia and grouping monographs according to pharmaceutical preparations and medical substances (herbal, mineral /chemical and animal).
- Comparative analysis of Pharmacopoeias and monitoring the evolution of proportions for drug substances (herbal, mineral/chemical, animals) and pharmaceutical preparations.

Results and Discussion

Pharmacopoea Austriaco-Provincialis (Ph.A-P), IVth Ed. [18], was published in Vienna, in 1780, and was applied in the provinces of Habsburg Empire. Responsibility for issuing the work belonged to Anton von Storck, the doctor of Empress Maria Theresa. Ph. A-P is written in Latin, the language used traditionally by the intellectual elite.

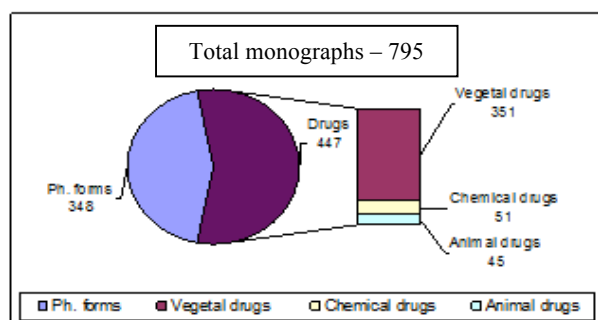


Figure 1.

Monographs in Pharmacopoea Austriaco-Provincialis (1780)

Romanian Pharmacopoeias: in the second half of the 19th century, in many European countries it was published national Pharmacopoeias. Pharmacists from United Principalities of Moldavia and Wallachia followed this trend and draw up three editions of the Romanian Pharmacopoeia in 1862, 1874 and 1893 [2, 4-7].

The first Romanian Pharmacopoeia appeared in 1862 [7, 19], during the reign of Al. I. Cuza, in a period of great political changes. Although, the metric system was imposed since 1860, it continued to be used the old Romanian measures and weights from Austria and Nüremberg. Therefore it was required the standardization of pharmaceutical activities throughout the United Principalities. To establish a local academic terminology, the work was drawn up in Latin and Romanian in six subcommittees, coordinated by Constantin Hepites who was a leading figure of physicians and pharmacists.

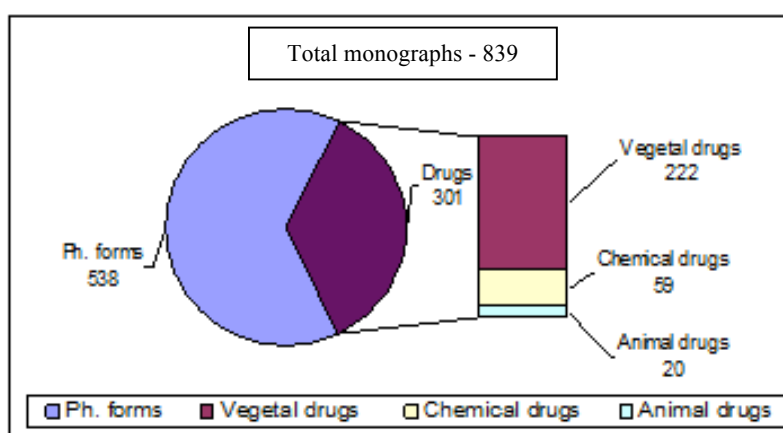


Figure 2.

Monographs in the first Romanian Pharmacopoeia (1862)

The IInd Edition of Romanian Pharmacopoeia (1874) [20] contained less information compared to the first one. In “Foreword” it was mentioned that there were selected only substances and pharmaceutical preparations with certain action. Characteristic for this edition is the simple drawing and reduction of monographs’ number. These are arranged alphabetically and are not written in Latin, fact that proves acquiring own terminology in Romanian language [20].

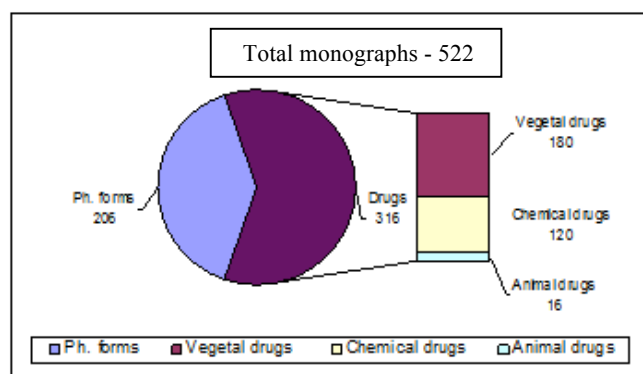


Figure 3.
Monographs in the second Romanian Pharmacopoeia (1874)

Third edition (1893) of the Romanian Pharmacopoeia [2, 9] appeared as a result of increasingly wide use of synthetic medicines. Thus, synthetic or semisynthetic herbal substances become officinal: atropine, caffeine, quinine, pilocarpine, strychnine and just as the chemical ones: acetanilide, phenacetin, antipyrin. The paper was structured into three parts: the first and the second comprised monographs of drug substances and galenic preparations for human use and the third formalized, for the first time, a series of veterinary preparations.

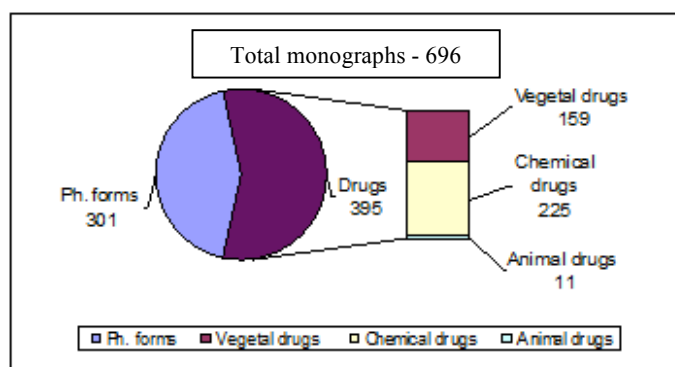


Figure 4.
Monographs in the third edition of the Romanian Pharmacopoeia (1893)

The special edition of the Romanian Pharmacopoeia (1915) [10], was published by the Society of Pharmacists due to Constantin Kollo's articles who militated for writing a Pharmacopoeia "to be a mirror of its time". Although this work was semiofficial, for 11 years (until 1926 when it was

published an official pharmacopoeia) all pharmacy activities were carried out in accordance with its stipulations. As reference material there were used the European Pharmacopoeia in force in that period, the list of "heroic" drugs drawn up by the International Commission of Pharmacopoeia (Brussels 1906) and American Pharmacopoeia. "Heroic" drugs were marked with the abbreviation P.I. (*Pharmacopoeia Internationalis*).

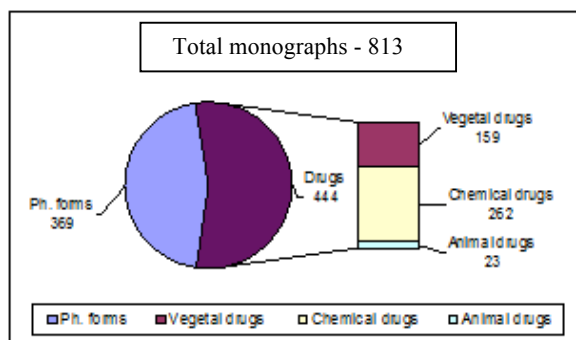


Figure 5.

Monographs in the special edition of the Romanian Pharmacopoeia (1915)

Drawing up the IVth edition of the Romanian Pharmacopoeia (1926) [11], was required because of the 33 years since the publication of the previous edition of the official Pharmacopoeia as well as due to political and geographical changes that resulted from the union of all Romanian Principalities. The Pharmacopoeia from 1926 contained a large number of synthetic organic substances, which brought a significant change in therapy of that time. For them, there are subtitles that indicate the name submitted by the patent.

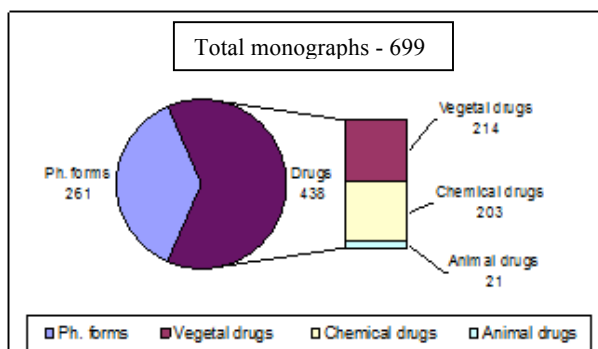


Figure 6.

Monographs in IVth edition of the Romanian Pharmacopoeia (1926)

The Vth edition of the Romanian Pharmacopoeia (1943) [12], reflected the development of the pharmaceutical industry, based mainly on organic synthesis. It published the first monograph for sulfonamides and the synthetic vitamins introduced into therapy. There were removed many "exotic" remedies which were outdated for therapy.

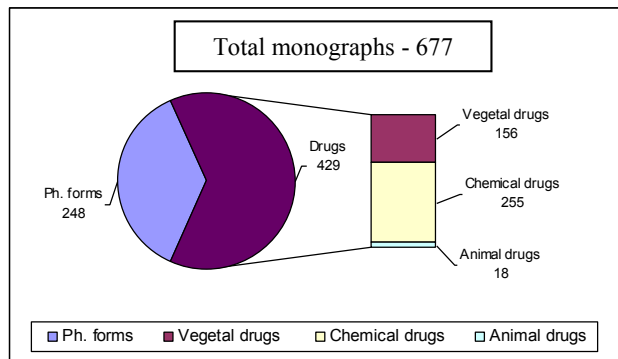


Figure 7.

Monographs in Vth edition of the Romanian Pharmacopoeia (1943)

The VIth edition of the Romanian Pharmacopoeia (1948) [13], was published only five years after the publication of the previous one and it was more a result of social and political changes in Central and Eastern Europe than of essential scientific modifications.

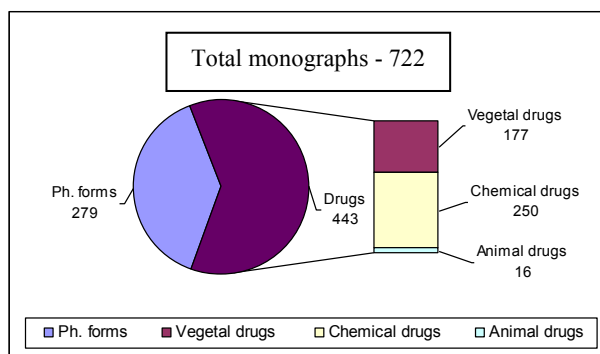


Figure 8.

Monographs in VIth edition of the Romanian Pharmacopoeia (1948)

The VIIth edition of the Romanian Pharmacopoeia (1956) [14], was developed by experts from the Institute for Pharmaceutical Research in Bucharest and Cluj (Romania) together with collaborators within the

Faculties of Pharmacy. The project was coordinated by Professor C.N. Ionescu, the Director of Institute for Pharmaceutical Research in Bucharest, Romania.

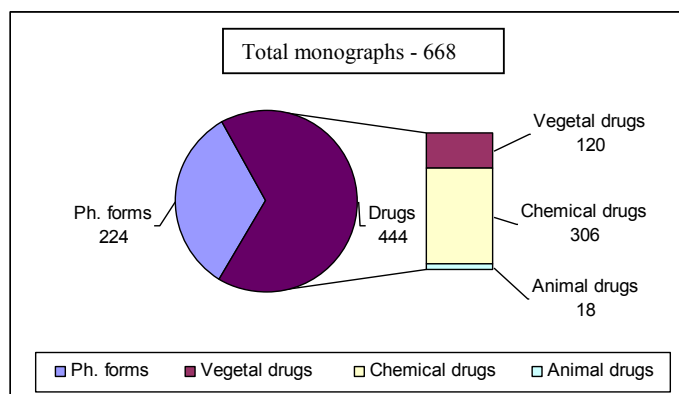


Figure 9.

Monographs in VIIth edition of the Romanian Pharmacopoeia (1956)

The VIIIth edition of the Romanian Pharmacopoeia (1965) [15], was carried out by nine committees of the Institute for State Control of Medicines and for Pharmaceutical Research (ISCMFR) that followed the lead of Professor P. Ionescu Stoian. This publication reflected the progress of local pharmaceutical industry and was the first edition benefiting of three supplements (1968, 1970 and 1972) that updated the scientific information.

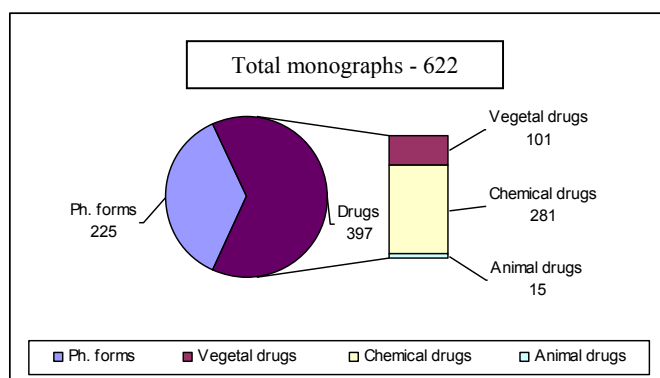


Figure 10.

Monographs in VIIIth edition of the Romanian Pharmacopoeia (1965)

Like the previous edition, *the IXth one (1976)* [8, 16], has been developed by specialists from ISCMFR under the coordination of Professor

P. Ionescu Stoian. The project was completed and updated through two supplements (1981, 1984).

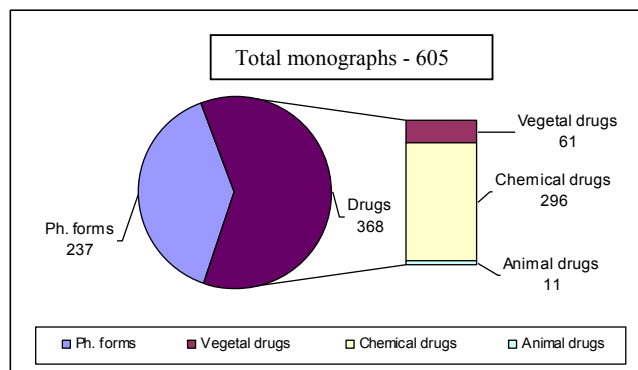


Figure 11.
Monographs in IXth edition of the Romanian Pharmacopoeia (1976)

The Xth edition of the Romanian Pharmacopoeia (1993) [1, 17], is currently in force being updated by Supplements in 2000, 2001, 2004 and 2006. Drafting was done during 1984-1992 by experts from ISCMFR, Institute of Chemical-Pharmaceutical Research in Bucharest, Faculties of Pharmacy from Bucharest, Cluj, Iasi, Târgu Mureş and also the production unit Sicomed.

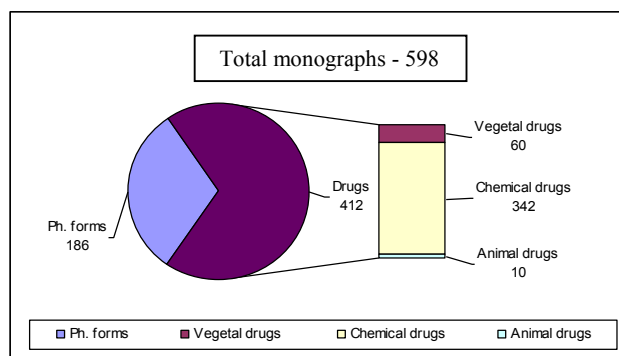


Figure 12.
Monographs in Xth edition of the Romanian Pharmacopoeia (1993)

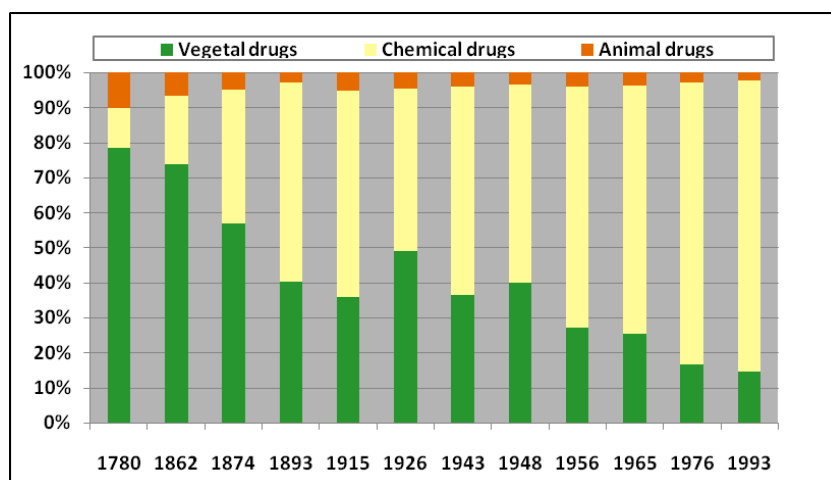
After the individual analysis of each Pharmacopoeia that governed Romanian pharmaceutical practice it also became possible their comparative study (Table II, Figures 13, 14).

Table I

Comparative data (absolute figures and percentage) of drug monographs (vegetal, chemical and animal) according to the studied Pharmacopoeia

The publishing year of Pharmacopoeia	Drugs (absolute figures and percentage)						
	Herbal drugs		Chemical drugs		Animal drugs		Total number of drugs
	AF	%	AF	%	AF	%	
1780	351	78.52	51	11.40	45	10.06	447
1862	222	73.75	59	19.60	20	6.64	301
1874	180	56.96	120	37.97	16	5.06	316
1893	159	40.25	225	56.96	11	11.57	395
1915	159	35.81	262	59.09	23	5.18	444
1926	214	48.85	203	46.37	21	4.79	438
1943	156	36.36	255	59.44	18	4.19	429
1948	177	39.95	250	56.43	16	3.61	443
1956	120	27.02	306	68.91	18	4.05	444
1965	101	25.44	281	70.78	15	3.77	397
1976	61	16.66	296	80.87	11	3.00	368
1993	60	14.56	342	83.00	10	2.42	412

AF = absolute figures

**Figure 13.**

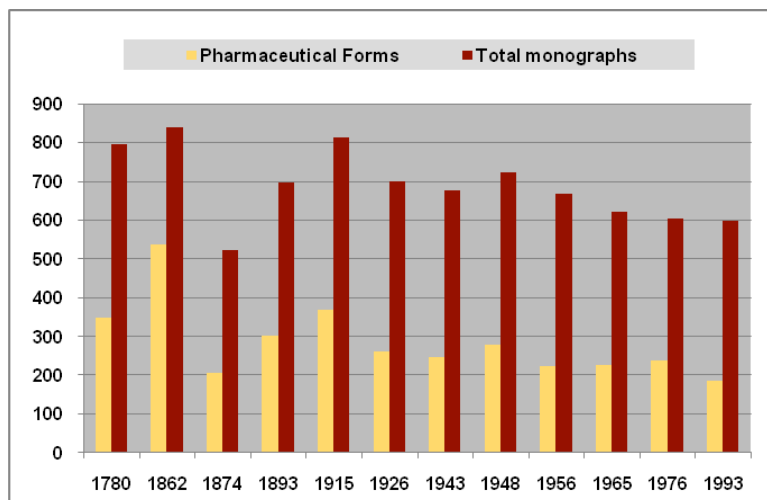
Evolution of proportion for drug substances (vegetal, chemical and animal) according to Pharmacopoeia used in Romanian area during XVIII-XXth centuries

Table II

Comparative data (absolute figures and percentage) of pharmaceutical preparations monographs according to Pharmacopoeias used in Romanian area during XVIII-XXth centuries

The publishing year of Pharmacopoeia	Pharmaceutical forms (Ph.F) (absolute figures and percentage)		Total (DS+Ph.F)
	AF	%	
1780	348	43.77	795
1862	538	64.12	839
1874	206	39.46	522
1893	301	43.24	696
1915	369	45.38	813
1926	261	37.33	699
1943	248	36.63	677
1948	279	38.64	722
1956	224	33.53	668
1965	225	36.17	622
1976	237	39.30	605
1993	186	31.10	598

DS = drug substances, Ph. F = pharmaceutical forms

**Figure 14.**

Evolution of proportion for pharmaceutical preparations according to Pharmacopoeia used in Romanian area during XVIII-XXth centuries

Conclusions

The comparative analyse of the pharmaceutical monographs according to Pharmacopoeias used in Romanian area during XVIII-XXth centuries, important conclusions can be outlined.

Herbal and animal remedies are in a general trend of decreasing percentage:

- herbal remedies - total decrease is 63.96%;
- animal remedies - total decrease is 7.64 %.

The proportion of mineral and chemical drugs is rising:

- mineral and synthetic chemical drugs record an overall increase of 71.60%.

The percentage of pharmaceutical preparations records:

- a peak (64.12 %) in the Ith FR (1862);
- a minimum (31.10 %) in the Xth FR (1993).

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