

FROM THE HISTORY OF DRUGS: *OLEUM JECORIS ASELLI*, A LONG TIME USED REMEDY

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Abstract

Since ancient times, fish oil (*Oleum Jecoris Aselli*, *Cod Liver Oil*, *Oleum morrhuae*) has been used in Northern peoples' diet. At the end of 18th century, it began to be used as a remedy, the physician Thomas Percival indicating it in chronic rheumatism and women's bone demineralization treatment. Later, the indications for this product were extended to other diseases such as tuberculosis, rickets, scrofula, psoriasis and keratosis. Chemical studies, undertaken simultaneously with the development of clinical use, have established the correlation between composition and therapeutic indications. The remedy was used as it is, both externally and internally, but because its unpleasant smell and taste, oral administration was difficult. To overcome this disadvantage, various formulations, particularly emulsions, were prepared. *Oleum Jecoris Aselli* is used even today, a Cod Liver Oil monograph appearing both in the European Pharmacopoeia 8.0 and the USP 35. The product has been used in Romanian Principalities, evidence in this regard being the reference to it in the Pharmacopoeias, in copy registers, in specialized periodicals such as the "Journal of Pharmacy" and on storage vessels labels.

Rezumat

Încă din timpuri ancestrale, uleiul de pește (*Oleum jecoris aselli*, *Cod Liver Oil*, *Oleum morrhuae*) era prezent în dieta popoarelor nordice. La sfârșitul secolului al XVIII-lea a început să fie folosit și ca remediu, medicul Thomas Percival menționând utilizarea sa în tratarea reumatismului cronic și a demineralizării osoase la femei. Ulterior indicațiile acestui produs s-au extins și asupra altor afecțiuni: tuberculoză, rahitism, psoriazis, keratoze. Studiile chimice întreprinse în paralel cu dezvoltarea utilizării clinice au stabilit corelația între compoziția sa și indicațiile terapeutice. Remediu se folosea ca atare, atât extern cât și intern, însă din cauza mirosului și gustului neplăcut, administrarea orală era dificilă. Pentru remedierea acestui dezavantaj se recurgea la prepararea unor forme farmaceutice, în special emulsii. *Oleum jecoris aselli* continuă să se folosească și în prezent, monografia *Cod Liver Oil* figurând atât în European Pharmacopoeia 8.0 cât și în USP 35. Produsul era utilizat și în Principatele Române, dovezi în acest sens fiind menționarea sa în Farmacopei, în registrele de copiere a rețetelor, în periodicul de specialitate „Revista Farmaciei” și pe etichetele vaselor de păstrare.

Keywords: *Oleum Jecoris Aselli*, Pharmacopoeia, Museum Collection, "Journal of Pharmacy"

Introduction

As it is defined by monographs, the remedy named *Oleum Jecoris* (fish oil, fish lard) [22], *Cod Liver Oil* (Type A) [9], and *Cod Liver Oil* [10] is obtained from the fresh livers of *Gadus morrhua* L.

or other species of *Gadidae* family. Specific for the recent pharmaceutical regulatory standards is imposing maximum and minimum levels for A and D liposoluble vitamins (Table I).

Table I

Levels imposed on A and D vitamins in some recent Pharmacopoeias

Pharmacopoeia	A Vitamin		D Vitamin	
	minimum	maximum	minimum	maximum
Romanian Pharmacopoeia (IX, 1976)	850 I.U./g	-	-	-
European Pharmacopoeia (7.5, 2012)	180 µg (600 I.U.)	750 µg (2500 I.U.)	1.5 µg (60 I.U.)	6.25 µg (250 I.U.)
U. S. Pharmacopoeia (35, 2012)	180 µg (600 U.S.P. Units)	750 µg (2500 U.S.P. Units)	1.5 µg (60 U.S.P. Units)	6.25 µg (250 U.S.P. Units)

Materials and Methods

This paper was carried out by researching old items, articles and treaties, from the period between the last decade of the 18th century to the third decade of the 20th century.

Documentation regarding the therapeutic use of the product *Oleum jecoris aselli* in contemporary period involved the study of:

- European Pharmacopoeia 8.0 (2013);
- United States Pharmacopoeia 35 (2012);
- National Catalogue of Human Medicines (2013).

In order to highlight the prolonged use of the remedy in Romanian and some aspects about pharmaceutical forms, prices and how the product was dispensed in our country, we searched:

- the periodical "Journal of Pharmacy";
- exhibits available in the patrimony of Museum Collection "Assoc. Prof. Zisi Fârșirotu, PhD" from the University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, Faculty of Pharmacy (the complete series of Romanian Pharmacopoeias and "Pharmaceutical fees" used in the period 1926-1985).

Results and Discussion

An important document for the history of this remedy was written in the late 18th century by the British physician Thomas Percival (1740-1804) [5]. It is about the introduction of Cod Liver Oil (CLO) (*Oleum Jecoris Aselli*, *Oleum morrhuae*) [1] in therapy. He also pointed out the traditional fish oil usage by Nordic peoples [5]. Due to a documentary source [2], nowadays producers of dietary supplements with CLO in their composition, declare frequently that the introduction of the remedy in British Pharmacopoeia from 1771 was made thanks to Percival. He mentioned the use of product for treatment of rheumatic disease and bone changes occurred in women after pregnancy, making references to the clinical experience of the surgeon and pharmacist Robert Darbey from Manchester [5]. Early moments of using the remedy *Oleum Jecoris Aselli* were recalled in the mid-nineteenth century by the physician W. S. Oke [4] who signed new therapeutic indications: various forms of tuberculosis and physical debility caused by malnutrition with weakness or atrophy of the body. At that time, the product became widely used to treat also gout, rickets, skin diseases, etc. [1].

The interest aroused by the intense use of the remedy has prompted the initiation of chemical research that revealed a complex chemical composition, dependent on several factors: the raw material used, the preparation process and the kind of *Oleum Jecoris Aselli* which was analysed.

Thus, the main species mentioned in the papers are: *Gadus morrhua* L. (*Asellus major*), *Molva molva* L. (syn. *Gadus molva*) (*Asellus longa*), *Gadus carbonarius* L. (*Asellus niger*), *Gadus merlangus* L. (*Asellus fibers*) distributed in North Atlantic [1, 3]. After collecting the raw materials, various methods of processing were applied, depending on the region and producer, to yield oils of different qualities. Fresh liver was laid down in wide tubes and exposed to the sun. Soon, it began to flow a clear oil which may be collected during eight days. After the raw material started the fermentation process, a new kind of oil was collected - light brown oil. The last oil fraction was obtained by

heating the residuum in a cast-iron pot, the product obtained in this moment being dark brown coloured [3]. Depending on their appearance, fish oils sold in the 19th century wore different names: *Oleum album*, *Oleum flavum*, *Oleum rubrum*, *Oleum fuscum*. The colourless or slightly coloured oils were transparent and had been used for medical purposes. Darkening was accompanied by the appearance of opalescence. These oils had no therapeutic indications and they were used only in the leather industry [1]. Based on the same criterion of classification, in the work of Dutch author L. J. Jonch are studied and presented comparatively three types of oil: *Oleum jecoris aselli fuscum*, *Oleum jecoris aselli subfuscum* and *Oleum jecoris aselli flavum sive album* [3].

In all these types of oil there were found organic compounds, mainly represented by a high percentage of free fatty acids (oleic, stearic - known at the time as margaric acid), glycerine, a brown substance (gaduin), volatile acids (butyric, acetic) and inorganic compounds (iodides, chlorides, elemental phosphorus) [3]. Subsequent studies have identified palmitic acid and a crystalline substance (morrhual), essential for the therapeutic action of CLO, in composition of which there are phosphorus, iodine, and bromine [8]. Gas chromatography analysis, imposed by current pharmaceutical standards, identified saturated fatty acids (myristic, palmitic, stearic), monounsaturated fatty acids (oleic, palmitoleic, gadoleic, gondoic, erucic), poly-unsaturated fatty acids (α linolenic, EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid) [9, 10]. As modern indications we mention: non-alcoholic steatosis, obesity, dyslipidaemia, cardiovascular diseases, etc. [6].

Depending on the disease, the therapeutic use of the product *Oleum Jecoris Aselli* involved both external and internal administration. But fish smell and taste made it disagreeable for internal use. Thus, adherence to the remedy as such was reduced and practitioners of the time achieved some formulations that ameliorated its properties. In 1841, physician J. Bennett noted that the emulsions were the most commonly used. The main correctors were syrups (*Syrupus cortex aurantii*, *Syrupus flores aurantii*, *Syrupus menthae*), aromatic waters (*Anisi aqua*, *Foeniculi aqua*, *Aqua flores naphae*), oleosaccharum (*Elaeosachharum menthae piperitae*). Nevertheless, the author preferred his collaborator's simple recipes: the pharmacist Macfarlan in Edinburgh. He resorted to simple mixing of essential oils (lemon, mint, cinnamon or anisum) with fish oil in a proportion of 3-4 drops / ounce (oz) [1]. Information was preserved about how to obtain other formulations for internal or external use: pills, ointments, liniments. The recipe proposed by Deschamps allowed administration of

Oleum Jecoris Aselli as pills. Thus, fatty acids were saponified for obtaining pilular mass. Afterwards it was improved by addition of honey and then pills were coated with tragacanth powder. In Brefeld's ointment recipe a lead acetate solution was added to fish oil for its anti-inflammatory properties [3].

Like any medicine, the administration of *Oleum Jecoris Aselli* may lead to adverse reactions: cramps and diarrhoea (internal use) or rash (external use) [4, 7]. Moreover, not all patients responded satisfactory to treatment. Doses (0.5 ounce - 1.5 ounce 2 times a day) and duration of treatment (6 - 8 months) were decided depending on each case [4].

In terms of recent history it is worth mentioning the presence of *Oleum Jecoris Aselli* in the first edition

of International Pharmacopoeia (1954) [11]. Nowadays, although *Oleum Jecoris Aselli* is mainly used as dietary supplement [12, 13], it appears as monograph in the European Pharmacopoeia 7.5 (2012) and United States Pharmacopoeia 35 (2012) [9, 10]. In the National Catalogue of Human Medicines used in Romania (2013) it is recorded the parenteral emulsion "Omegaven" containing highly purified fish oil [14].

The remedy *Oleum Jecoris Aselli* has been constantly used for a long period of time in Romania. It was mentioned continuously in the Romanian Pharmacopoeia, from the first edition (1862) to the ninth (1976) [15 - 24] and in official pharmaceutical fees in years 1926, 1949, 1958, 1967, 1979 and 1985 [27 - 32].

Table II

The presence of monograph *Oleum Jecoris Aselli* in Romanian Pharmacopoeias

Monograph	Pharmacopoeia / publishing year										
	I 1862	II 1874	III 1893	S 1915	IV 1926	V 1943	VI 1948	VII 1956	VIII 1965	IX 1976	X 1993
<i>Oleum jecoris</i>	+	+	+	+	+	+	+	+	+	+	-

S = Special Pharmacopoeias (1915)

Some objects in the Museum Collection "Assoc. Prof. Zisi Fârșirotu, PhD" confirm the use of *Jecoris Oleum Aselli* in the Romanian pharmaceutical practice, both for capitalizing its therapeutic properties and to obtain other preparations. We present two recipes: one in which *Oleum Jecoris* was used for its likely action in treating rickets and another for obtaining, artificially *Axungia Leporis* (lard rabbit) employed only to incorporate medicinal substances.

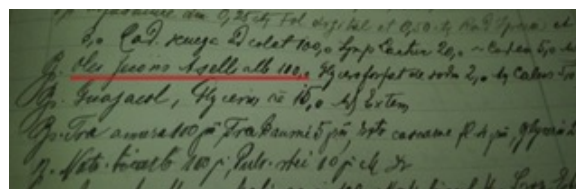


Figure 1.

Record sheet for recipe copying (period September 1900 - March 1902) from pharmacy "At Crown of Romania", Târgoviste, Romania, that contains a magistral formula with "*Oleum jecoris aselli*"

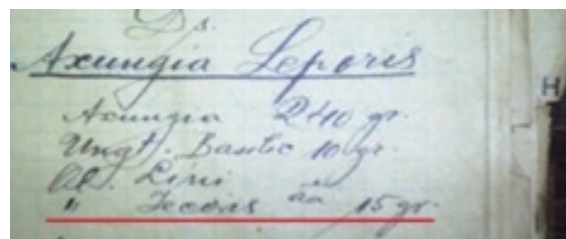


Figure 2.

Undated recipe book manuscript that preserved the formula for obtaining artificially ointment *Axungia Leporis* (lard of rabbit)

Other testimonies existing in the Museum Collection are two storage vessels for *Oleum Jecoris Aselli*, and an advertisement type mock-up for Scott's emulsion.

Exhibits located in the Museum Collection "Assoc. Prof. Zisi Fârșirotu, PhD", Faculty of Pharmacy, Bucharest, Romania (Figures 1-5):



Figure 3.

Brown glass bottle (H = 22 cm, length of base = 9.5 cm, width of base = 8 cm) with flow device in which it was keep "*Oleum Jecoris*"



Figure 4.

Porcelain jar (H = 15 cm, base Ø = 8.5 cm, opening vessel Ø = 9.5 cm) for preserving Cod Liver Oil

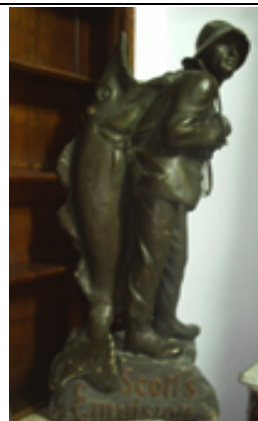


Figure 5.

Cardboard advertise mock-type (H = 90 cm, length of base = 40 cm, width of base = 20 cm) for "*Scott's Emulsion*"

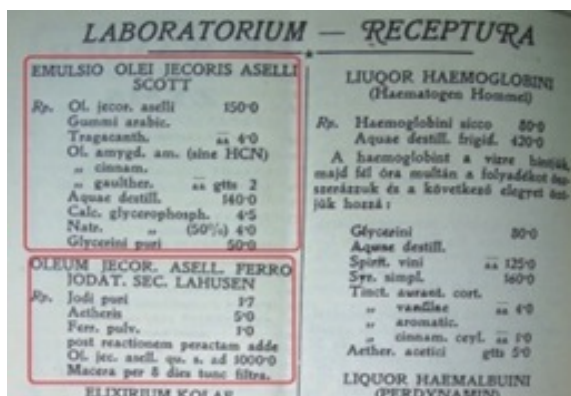


Figure 6.

The sheet in periodical "*Journal of Pharmacy*" allotted laboratory work in which there are two recipes with *Oleum Jecoris Aselli*: Scott's emulsion and Lahusen's preparation

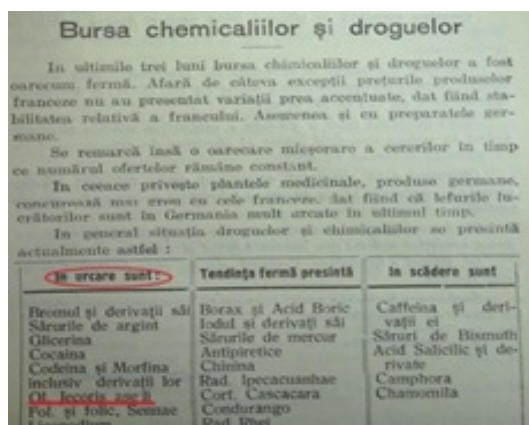


Figure 7.

The page in periodical "*Journal of Pharmacy*" that shows the trend of prices on some medicinal substances, of which *Oleum Jecoris Aselli*

Thanks to the Romanian periodical "*Journal of Pharmacy*" we could found Scott's emulsion

formula and some aspects about costs and how the product *Oleum Jecoris Aselli* was dispensed in the period between the two World Wars. According to the "Regulation selling bulk drug substances" available in 1921, *Oleum Jecoris Aselli* was classified in Table B, for remedies that were dispensed in limited quantities, 500g [25]. The article "Exchange of chemicals and drugs" written on October 15, 1924 by Eugen Solomonica, noted that at that time, the price of *Oleum Jecoris Aselli* was increasing [26].

Conclusions

The *Oleum Jecoris Aselli* constituents had been spontaneously used long before reporting its entry in therapy by physician Thomas Percival, at the end of 18th century.

The remedy has also been used for a good while in our country, being mentioned in various editions of the Romanian Pharmacopoeia and in official pharmaceutical fees.

Nowadays *Oleum Jecoris Aselli* appears in the European Pharmacopoeia 8.0 (2013), in the United States Pharmacopoeia 35 (2012) and in the National Catalogue of Human Medicines used in Romania (2013).

References.

1. Bennett J.H., Treatise on the *Oleum Jecoris Aselli*, or Cod Liver Oil as therapeutic agent in certain forms of gout, rheumatism and scrofula with cases. Edinburgh, 1841.
2. Guy R.A., The history of Cod Liver Oil as a remedy. *Am. J. Dis. Child.*, 1923; 26(2): 112-116.
3. Jonch L.J. The three kinds of Cod Liver Oil comparatively considered with reference to their chemical and therapeutic properties. Philadelphia, 1849.

4. Oke W.S., On the Primary Introduction of the *Oleum Jecoris Aselli* or Cod Liver Oil as an internal Remedy for Diseases. *Provincial Medical and Surgical Journal*, 1850; 93-95.
5. Percival T., Observations on the medicinal uses of Cod Liver Oil. Essays medical, philosophical and experimental, London, 1789; 354-362.
6. Popescu A.L., Vârgolici B., Păcurar D., Timnea O., Ranetti A.E., Orășeanu D., Zăgorean L., Beneficial effects of omega-3 fatty acids in nonalcoholic fatty liver diseases, in childhood obesity. *Farmacia*, 2013; 61(3): 598-608.
7. Rayner J., Cod Liver Oil: its used, administration (compiled from the best and latest authorities British and foreign), 1849; New York.
8. Sayre L.E., A Manual of Organic Materia Medica and Pharmacognosy, Philadelphia, 1917; *Oleum Morrhu*, Cod Liver Oil (monography 616).
9. *** Cod Liver Oil (Type A), *Iecoris Aselli Oleum A*, European Pharmacopoeia 8.0, vol II: 1950-1954.
10. *** Cod Liver Oil, USP 35, 2756.
11. *** Expert Committee on the International Pharmacopoeia, thirteenth Report, 26 August 1954.
12. *** Lista suplimentelor alimentare notificate în conformitate cu ordinul 244/2005.
13. *** Lista suplimentelor alimentare notificate în conformitate cu ordinul 1228/2005 / 224/6 3/2006.
14. *** Nomenclatorul medicamentelor de uz uman.
15. *** *Oleum jecoris*, Farmacopea Română, Bucuresci, Imprimeria Statului, 1893; 371.
16. *** *Oleum jecoris*, Farmacopea Română, București, Institutul de Arte Grafice „Speranța”, 1915; 441.
17. *** *Oleum jecoris*, Farmacopea Română, București, Atelierele Grafice „Socec&Co.”, 1926; 341-342.
18. *** *Oleum jecoris*, Farmacopea Română, București, Tiparul Românesc, 1943; 322.
19. *** *Oleum jecoris*, Farmacopea Română, București, Institutul Farmaceutic, 1948; 385-386.
20. *** *Oleum jecoris*, Farmacopea Română, București, Ed. Medicală, 1956; 451-452.
21. *** *Oleum jecoris*, Farmacopea Română, București, Ed. Medicală, 1965; 491-493.
22. *** *Oleum jecoris*, Farmacopea Română, București, Ed. Medicală, 1976, 518-519.
23. *** *Oleum jecoris*, Pharmacoepa Română, Bucuresci, 1862; XI.
24. *** *Oleum jecoris*, Pharmacoepa Română, Bucuresci, Imprimeria Statului, 1874; 102.
25. *** Revista Farmaciei, anul XXXII, aprilie 1921; 4: 123 (table B).
26. *** Revista Farmaciei, anul XXXV, oct-nov 1924; 10-11: 319-320 (Bursa chimicalelor).
27. *** „Taxa medicamentelor speciale” valabilă de la 1 aprilie 1926 pentru regiunile Ardeal și Banat.
28. *** „Taxa farmaceutică oficială”, iulie 1949.
29. *** „Taxa farmaceutică oficială”, ianuarie 1958.
30. *** „Taxa farmaceutică oficială”, 1967.
31. *** „Taxa farmaceutică oficială”, 1979.
32. *** „Taxa farmaceutică oficială”, 1985.