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## Artículo Especial

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# The manufacture of gelatine capsules in the XIX century based on Aleksander Karwacki's publication dating from 1859

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**RESUMEN**

La primera patente para la elaboración de cápsulas gelatinosas fue emitida en Francia en el año 1834. La publicación titulada "*Torebki albo kapsułki galaretowe, capsulae gelatinosae oraz torebki otwierające się, envelopes medicamentecises sposób robienia i użyteczność tychże*" ["Cápsulas o cápsulas gelatinosas, *capsulae gelatinosae* y cápsulas con apertura, *envelopes medicamentecises,* forma de elaboración y su utilidad"] de Aleksander Karwacki (1825-1871) fue publicada veinticinco años después de dicho acontecimiento y contiene información sobre la fabricación de cápsulas gelatinosas y su aplicación.

**PALABRAS CLAVE:** cápsulas, método de elaboración de cápsulas orales, Aleksander Karwacki, historia de la farmacia

**ABSTRACT**

The first patent regarding the preparation of gelatine capsules was granted in France in 1834. The publication entitled "*Torebki albo kapsułki galaretowe, capsulae gelatinosae oraz torebki otwierające się, envelopes medicamentecises sposób robienia i użyteczność tychże*" ["Gelatine shells or capsules, *capsulae gelatinosae*, and shells that can be opened, *envelopes medicamentecises,* the way of manufacturing and usefulness thereof"] by Aleksander Karwacki (1825–1871) was published 25 years after this event. It contains information regarding the manufacture of gelatine capsules and their application.

**KEY WORDS:** capsules, method of obtaining oral capsules, Aleksander Karwcki, history of pharmacy

## INTRODUCTION

The publication entitled "Torebki albo kapsułki galaretowe, capsulae gelatinosae oraz torebki otwierające się, envelopes medicamentecises sposób robienia i użyteczność tychże" ["Gelatine shells or capsules, *capsulae gelatinosae*, and shells that can be opened, *envelopes medicamentecises,* the way of manufacturing and usefulness thereof"] by Aleksander Karwacki (1825–1871) was published by Edward Kołakowski's printing house in Kielce in 1859. It consists of several pages and it is devoted both to single-piece and two-piece capsules. The former are nowadays referred to as soft gel capsules, whereas the latter – as hard gel capsules. The publication also contains drawings showing the equipment used in manufacturing this form of medication.

The Author of the work, A. Karwacki, studied medicine in Cracow and then worked as a doctor in the Austrian army. He also practised medicine in Kielce where he was a doctor in the county hospital, as well as in Solec and in Warsaw[1]. A. Karwacki published works which included a study on procedures in the event of Santonin poisoning in "Tygodnik Lekarski" ["Physician's Weekly"] journal. A. Karwacki was also interested in botanics, plant cultivation and pomology and wrote books on these topics.

The purpose of this article is to present the abovementioned publication, which is dedicated entirely to one form of medicinal product that is unique in Polish literature as far as the technology of dosage forms in the mid-nineteenth century is concerned. In the Polish language, capsules were in those times referred to as: shells, gelatine shells, glue shells[2]. They were introduced into medicine in order to mask the unpleasant taste and odour of medicinal substances. The intention of the author of the publication was "*for every person to become familiar with and to provide the most accurate method of making the above mentioned gelatinosae shells, particularly not involving significant outlays, being recommended to the Public through their cheap price, for those that cannot stand unpleasant medicinal substances"*[3].

It should be noted, however, that an extensive amount of interesting information on the history of capsules was included in the book of Brian E Jons[4].

The first patent regarding the single-piece capsules which constitute the form that we know today was granted on 25 March 1834 to two Frenchmen – François Achille Barnabé Mothes and Gérard Auguste Dublanc[5]. The next patent was granted to Mothes himself on 4 December 1834[6]. Initially, the single-piece capsules were made with the use of moulds in the form of small round pouches made of soft leather. The single-piece form was attached to a small long-necked metal funnel. The moulds were filled with mercury to make them firm. The capsules were made by dipping the mould in an appropriate solution, after which the mercury was removed and the capsules were take off the moulds and left to dry. With time, the production of the capsules was further developed and improved with the use of solid brass moulds. Mothes produced capsules filled with Copaiba balsam as well as empty capsules that could be bought from the pharmacy.

The idea of producing capsules quickly obtained approval and rapidly spread throughout France and outside its borders. There were many attempts at producing them by manufacturers. In 1835, capsules were not only widely known throughout Europe but also in the United States. For example, in 1836 in New York, capsules were being produced by Hermanus Planten – a Dutchman who emigrated to the United States of America. He used gelatine that was imported from France to produce them.

Returning to the history of capsules in Europe, it has been confirmed that capsules were being produced in Germany in 1837, while in Great Britain; they started to be produced in in the 1940s. In 1843, information entitled "On the formation of gelatinous capsules of Copaiba balsam" was published in the "Pharmaceutical Journal" in the "Extracted Articles" section which was based on the work of Adolph Steege, a pharmacist from Bucharest[7]. The information also included drawings of examples of capsule making equipment. Furthermore, Steege also pointed out that the capsules could be made to be more flexible by adding Saccharose to the Gelatine mixture and more transparent by using Caruc instead of Gelatine.

Capsules were produced in Italy in 1844 by moulding them in forms and not through immersion. Brass moulds with special capsule-shaped openings were used for this purpose. A similar method of production was used by the physician Jean Lavalle as well as the pharmacist Charles Honoré Théveont in France in 1846. The shape of the capsules produced in this way was more regular than Mothes' capsules and they were referred to as pearls (*perles*).

The capsules were quickly accepted in medicine as a comfortable form of administering unpleasantly tasting medicinal substances, particularly Copaiba balsam. The need existed for the equipment that was necessary to mass produce capsules to be constructed. The patent for such apparatus was obtained by Mothes, Lamouroux & Company in 1846. The patent was for a rotational machine that passed gelatine foil sheets through two rollers. Mothes soon obtained a new patent for the production of capsules

using the immersion method (in 1850). Many patents for the production of capsules were obtained, which testifies to how popular this form of medicinal product was at the time.

Another Frenchman, Jules César Lehuby, on 20 October 1846, was granted a patent for two-part capsules termed as *enveloppes médicamementeuses*[8]. Lehuby used silver plated metal cylinder moulds to produce them and he recommended Carragheen as the main component of the solution used in producing the capsule. Some studies mention James Murdoch from London as the inventor of the two-part capsules, who obtained a patent in 1847[9-10]. There are many similarities between the patents of Lehuby and Murdoch. Nevertheless, in the introduction to Murdoch's patent it is stated that he based his work on findings from abroad, which would suggest that Lehuby should be considered as the inventor of two-part capsule.

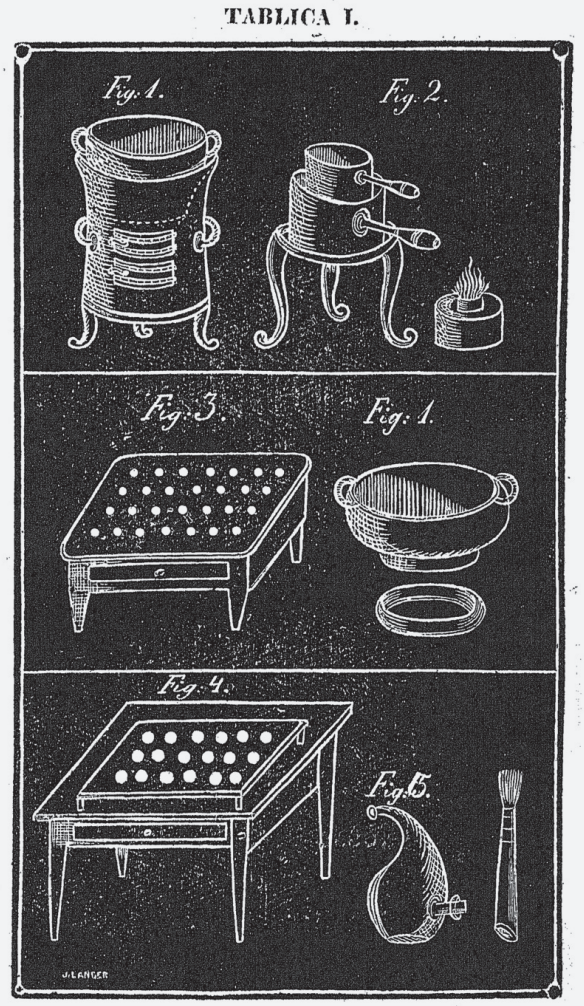
Large-scale production of two-part capsules took place in the mentioned company of H. Planten in New York. The production process of these two-part capsules was started up in this company in the early 1860s, however, they turned out not to be very durable and the production was soon interrupted.

The successful production of two-part capsules on a commercial scale was achieved by the pharmacist Frederick A. Hubel from Detroit. The capsules that he produced were hugely popular, particularly after he sold his company to Parke, Davis & Company in 1875. In 1924, Parke, Davis & Company commissioned the Arthur Colton Company to design improved apparatus and machinery for the production of capsules. The design they came up with was called 'C1' and it enabled the production of the constituent parts of the two-part capsule separately, and were multicoloured. In the 20th century, these two companies from the United States - Parke, Davis & Company and Eli Lilly & Company of Indianapolis, were pioneers in popularising the two-part capsules throughout the world. The first company produced capsules in 1875, while the second company started its production in 1897. Both companies produced the capsules on a large scale.

During the Partitions in Poland, gelatine capsules were produced in laboratories as well as next to pharmacies or in special workshops, for instance, in the Cracow workshop in 1869, in Warsaw in 1870, and in Lviv in 1881[11-12].

The publication of Karwacki, titled: "Torebki albo kapsułki galaretowe, capsulae gelatinosae oraz torebki otwierające się, envelopes medicamentecises sposób robienia i użyteczność tychże" ["Gelatine shells or capsules, *capsulae gelatinosae*, and shells that can be opened, envelopes medicamentecises, the way of manufacturing and usefulness thereof"] gives an insight into the capsule methods of production that were used in the middle of the 19th century.

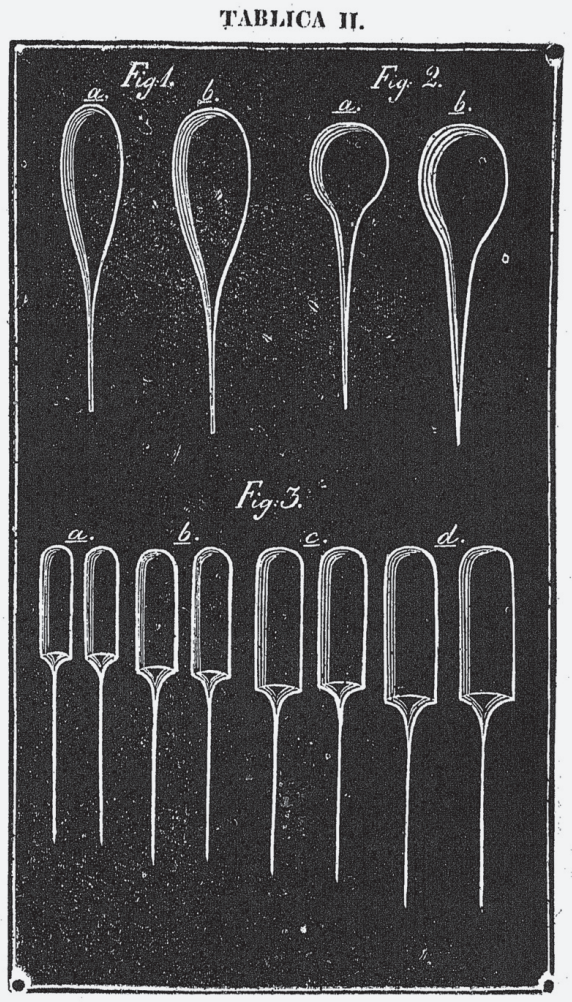
**Figure 1. Equipment used in the manufacture of capsules in the mid-nineteenth century [Fig. 1 – a porcelain evaporator and a sand bed, Fig. 2 – a cylindrical vessel, a boiling water bath and a spirit lamp, Fig. 3 – a wooden block, Fig. 4 – a cardboard rest with openings, Fig. 5 – a retort with a flat base and neck on its side and a paint brush].**




## METHOD OF OBTAINING THE CAPSULES AS PROVIDED BY ALEKSANDER KARWACKI

In the preparation of capsules from animal gelatine, which was also referred to in the mentioned publications by the name of the glue, several pounds of white, clear and sliced raw material were required, which were then dissolved in distilled water. The solution was then heated in a porcelain evaporator on a sand bed until the right consistency was

**Figure 2. Moulds used in the manufacture of capsules in the form of rods or wires, which were round, oval or cylindrical in shape on one side.**




obtained (Tablica I - Fig. 1), after which one ounce of saccharin was added and dissolved. The liquid obtained was then transferred to a cylindrical vessel with a lid, which was placed in a boiling water bath heated by a spirit lamp (Tablica I – Fig. 2). Distilled water had to be added due to evaporation to ensure that the consistency of the liquid during the capsule preparation process remained the same. The metal moulds, which were referred to as machines, were then immersed in the solution.

The moulds were made from rods or wires which formed a round, oval or cylinder shape on one side. The round and oval moulds were used to make single-piece capsules, whereas cylindrically ended moulds were used to make long two-piece capsules. The set of moulds for making the latter capsules was comprised of two parts: a smaller and larger part, differing only slightly from each other in terms of their diameter. Once it turned into a solid, the smaller part was filled with the medicinal substance after which it was joined together with the larger part, which gave a closed, longitudinal container containing a single dose of the medicinal substance.

The round, oval and cylindrical moulds were available in a range of dimensions. Prior to them being used, the rods or wires had to be washed, polished, cooled and wiped with almond oil. The moulds for making the capsules were then immersed and rotated in the solution to ensure equal coverage, after which they were set aside to solidify, inserting the thin ends of the rods or wires into special wooden blocks (Tablica I – Fig. 3). Once they solidified, the empty capsules were removed and placed in a cardboard rest with openings and were then left for several hours to dry; thus prepared, they could be filled with the medicinal substances (Tablica I – Fig. 4).

The medicinal substances in liquid form were placed in the single-piece capsules using a vessel shaped like a retort with a flat base and neck on its side (Tablica I – Fig. 5). The capsules were not filled with aqueous solutions to prevent them from dissolving. The filled round or oval capsules were sealed with a warm solution prepared in the same manner as the capsules by transferring drops of the liquid with a paint brush onto its edge (Tablica I – Fig. 5). Particular attention had to be paid when preparing this form of medicine using oils. In order to facilitate the sealing of the said capsules special care had to be taken to ensure that the capsule edges did not to come into contact with the oils.

The two-piece capsules were filled with medicinal substances usually in solid form, depending on the needs. Both capsules filled with medicinal substances and empty capsules had to be stored in a dry place to prevent them from deforming.

## APPLICATION AND USE OF CAPSULES

The oval, single-piece capsules could be filled with Copaiba balsam (*Balsamum Copaivae*), Castor oil (*Oleum Ricini*) or Cod liver oil (*Oleum Jecoris Aselli*). Copaiba balsam, no longer used medicinally in contemporary times, was used in the nineteenth century to treat Gonorrhoea or respiratory tract infections. This raw material was tapped from the trunks of various species of the genus *Copaifera* L. It came in the form of a thick, translucent liquid and its colour ranged from light yellow to golden pale brown; it had a balsamic, woody smell with a bitter and spicy taste[13]. It could have been administered in sugar, in black coffee, milk, aromatic water, yolk or gum emulsion, in boluses, pills with magnesia or lime, and most conveniently in shells (C*apsulae gelatinosae* containing in grains 18-20 Copaiba).

Castor oil was cold-pressed from the embryo of the Castorbean seed (*Ricinus communis* L.) and was transparent in colour. Administered orally both in the past as well as in contemporary times it works as a laxative, possesses a very peculiar taste and can be transparent or a pale yellow colour. The last raw material mentioned above – Cod liver oil, which is obtained mainly by melting the fresh livers of the North Sea Cod (*Gadus morehua* L.) – is used to this day for boosting the body's weakened immune system.

The book "Farmakologija wedle układu dra F. Oesterlena do podręcznego użytku" ["Pharmacology handbook according to Dr F. Oesterlen's system"] by Henryk Łuczkiewicz, which was published in 1860, mentions that three types of Cod liver oil were available at the time: browny red (*Oleum jecoris subfuscum)*, yellow (*Oleum jecoris flavum)* and brown (*Oleum jecoris fuscum)*. The last mentioned was very rarely used due to its unpleasant taste and repulsive odour.

The description of the action of the Cod liver is also interesting: *"hardly any difference can be found between Cod liver oil and other oils like, for example, Almond oil, or ordinary Olive oil with the only addition that the use of Cod liver oil surpasses the rest in terms of unpleasantness. Thus, when recommending it, we can often perceive the repulsion, disgust and even vomiting or diarrhoea of the ailing. Despite this, one cannot deny that after a lengthy time of taking Cod liver oil (if the ailing person is lucky enough to stand it), it improves appetite, helps a person put on weight, gives rise to sweating, and passing of urine is more profuse; (skin rashes may sometimes occur). In general, therefore (assuming the most pleasant effect), improvement in the eating habits of the ailing can be observed, which can also be caused by other oils"*[14].

The round capsules were recommended as packaging for Copaiba balsam with extract of the Cubeb fruit, obtained from Tailed pepper (*Piper cubeba* L.), characterised by a spicy and bitter taste. Two parts of extract from the Cubeb fruit combined with four parts of Copaiba balsam were used to treat Gonorrhoea. In long, two-part capsules and shells that could be opened it was possible to insert Quinine sulphate which has an antipaludian action, characterised by a very bitter taste, or iodine or mercury compounds which were used to treat Syphilis.

In his publication, Aleksander Karwacki also wrote about the usage of this form of medicine. Namely, prior to taking the capsules with the medicinal substance, it was required for it to be moistened with water and then becoming somewhat softened, it slips itself into the stomach and does not leave the slightest distaste in the mouth.

## CONCLUSION

Recapitulating, the publication entitled "Torebki albo kapsułki galaretowe, capsulae gelatinosae oraz torebki otwierające się, envelopes medicamentecises sposób robienia i użyteczność tychże" ["Gelatine shells or capsules, *capsulae gelatinosae,* and shells that can be opened, *envelopes medicamentecises*, the way of manufacturing and usefulness thereof"] is an interesting and exceptional text written in the Polish language that familiarises the reader with the various aspects involved in the production and usage of capsules in the nineteenth century. It can also be assumed that in writing the publication, the Author also used literature in the French language. The examples mentioned in this text are evidence of this, namely, when he mentions *Capsulae gélatineuses au baume de copachu*, that is, capsules with Copaiba balsam, as capsules that were already know at the time. A shortcoming of this unique nineteenth century publication is its lack of references.

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