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HISTORY OF ANALYTICAL CHEMISTRY

Contributions from N.A. Izmailov and M.S. Schraiber to the Development of Thin-Layer Chromatography (On the 70th Anniversary of the Publication of the First Paper on Thin-Layer Chromatography)

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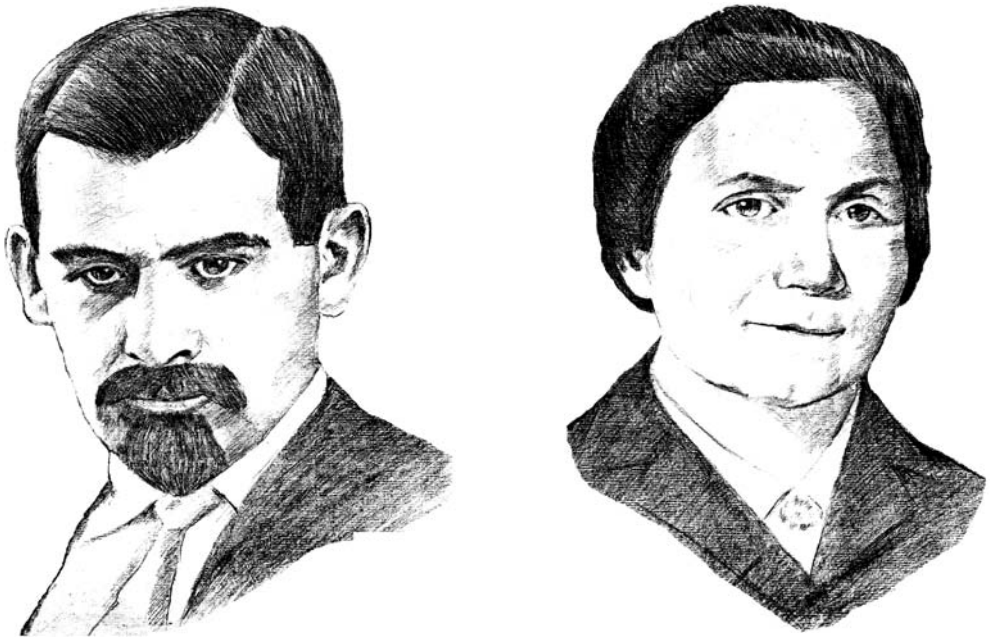
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Abstract—It is well known that N.A. Izmailov and M.S. Schraiber are the authors of the first paper in thin-layer chromatography (TLC). The detailed analysis of this publication has shown that Izmailov and Schraiber have also proposed the following TLC versions: (i) circular chromatography (this was earlier outlined by F. Geiss), (ii) frontal TLC, (iii) elution TLC, and (iv) frontal elution TLC. The last named version is of interest as a preconcentration method.

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Thin-layer chromatography (TLC) has been actively used for many decades all over the world. This method was proposed by Izmailov and Schraiber, whose paper published in the journal *Farmatsiya* in 1938 [1] covered the fundamentals of TLC and its application to pharmacology. Corresponding Member of the Academy of Sciences Nikolai Arkad'evich Izmailov (1907–1961) (Fig. 1) was an outstanding physical chemist; he made a significant contribution to electrochemistry, the theory of solutions, and other branches of physical chemistry. Among his most widely used applied achievements in chromatography is, probably, thin-layer chromatography, a new physical and chemical research method he proposed in collaboration with his



Nikolai Arkad'evich Izmailov

Maria Semenovna Schraiber

Fig. 1. Nikolai Arkad'evich Izmailov (June 22, 1907–October 2, 1961) and Maria Semenovna Schraiber (September 11, 1904–August 29, 1992), the authors of thin-layer chromatography.

colleague, Mariya Semenovna Schraiber (1904–1992), Candidate of Pharmacology (Fig. 1). This important micropreparative physical and chemical method of analysis is very simple, highly economic, and versatile. Thin-layer chromatography has long been used in science, industry, medicine, pharmacology, environmental analysis, etc.

Many outstanding researchers have repeatedly paid attention to the its scientific importance: "The method is more important than a discovery, because the correct method will lead to a new, even more outstanding discovery" (L.D. Landau, Nobel Prize Winner); "The method nears the fate of a study in its hands" (I.P. Pavlov, Nobel Prize Winner); "An essential condition of any fruitful study is an adequate technique. Any scientific progress is the progress of a method" (M.S. Tswett).

Chromatography was proposed by Russian scientist Tswett [2, 3] at the beginning of the 20th century in Warsaw. Today, it is the most widely used analytical method all over the world and also a preparative separation method.

Thin-layer chromatography is an implementation of the chromatographic process under the conditions when the stationary phase is a flat layer. A characteristic feature of TLC is the simplicity of the technical solution. This allows the chromatographic method to be used not only in scientific laboratories and industry, but also at home, in schools, at first-aid stations, etc. Therefore, thin-layer chromatography (TLC) can be considered as a version of an actually popular chromatography [4]. The method was developed in 1937–1938 at the Physicochemical Laboratory of the Ukrainian Institute of Experimental Pharmacy in Kharkov. Thus, the age of thin-layer chromatography is about 70 years. However, TLC is a living method; it is being developed in all of the main directions, as scientific fundamentals and as new versions and practical applications.

The conclusions to the first article on TLC actually contained the definition of thin-layer chromatography: "the separation of substances as zones is observed in a thin adsorbent layer" [1]; in other words, thin-layer chromatography is a version of chromatography in which substance separation as zones is observed in a thin adsorbent layer. This definition virtually coincides with the IUPAC definition [5].

An important characteristic in evaluating any principally important scientific work is not only its priority, but also the public opinion about its priority, which should evidently be correlated with the known facts. (Unfortunately, as was noted by Norbert Wiener, the recognition of one or another scientific work by the scientific community depends not only on its value, but on its contents as well.) Today, the priority of Izmailov and Schraiber in discovering thin-layer chromatography is recognized by almost all researchers working in this area all over the world. As an example, below I present statements of some well-known foreign scientists about the authors of TLC.

"Dr. Schraiber, together with Professor N.A. Izmailov, developed thin-layer chromatography. Their first publication on the technique appeared in 1938" [6].

"Following column chromatography came the development through the 1940s of paper chromatography as described by two Russian workers Izmailov and Schraiber in 1939" [7].

"The first thin layer chromatogram ever was developed in 1938 by Izmailov and Schraiber in the circular mode" [8].

"Bei der Suche nach Trenomoglichkeiten im Nicromaßtab fuhrten 1938 die beiden Russishen Wissenschaftler Izmailov und Schraiber die ersten versuche auf einer 'offenen Saule' also auf einer dunnen Schicht, durch" [9].

"The technique of TLC was first used in 1937–1938 at the Institute of Experimental Pharmacy in Kharkov (Ukraine) by Nikolai A. Izmailov (1907–1961) and Maria Schraiber (1904–1992), his graduate student" [10].

"I delicate my book to Prof. N. Izmailov and M. Schraiber, pioneers of thin-layer chromatography" (E. Stahl, inscription on the book E. Stahl, *Dunnschicht–Chromatographie*, Berlin: Springer, 1962, presented by Shtal to Izmailov and Schraiber [11].

Izmailov and Schraiber have actually proposed not only thin-layer chromatography, but also a number of its versions, which is evident from the more careful analysis in [1]. Table 1 contains the analysis of methods used by Izmailov and Schraiber in their first publication on TLC. This analysis allows us to more comprehensively characterize the contribution of these scientists to chromatography. Izmailov and Schraiber are also the authors of the following important TLC versions: (i) frontal circular TLC, (ii) eluant circular TLC, and (iii) frontal elution circular TLC. The last named version seems to be appropriate in present-day thin-layer chromatography, because, in frontal chromatography at the first stage, not only substances are separated, but also impurities present in the test mixture are noticeably preconcentrated.

In [1], circular TLC was described for the first time (Fig. 2). After the first preliminary frontal separation of samples of alcohol tinctures of medical plants, Izmailov and Schreiber performed their more fine separation, additionally using elution circular chromatography.

Figure 2 taken from [1] presents the chromatograms of *Atropa belladonna* tinctures obtained by the classical Tswett method of column chromatography (I) and by TLC (II). The eluant was ethanol, and then adsorbent, aluminum oxide. At the first stage of separation in column and thin-layer chromatography, they used frontal

Table 1. Chromatographic versions described in the first paper by Izmailov and Schreiber [1]

TLC versions used in [1]	Definition of the chromatography version used (IUPAC Recommendations, 1993 [5])	Contributions by Izmailov and Schreiber to TLC
"...Using the chromatographic drop method of the analysis we developed, which consists in applying a drop of a test substance onto a flat adsorbent layer and the observation of substance distribution between the zones..."	*Thin-layer chromatography* is a separation method in which the stationary phase is a flat (thin) adsorbent layer. Planar chromatography is sometimes also named chromatography with an open adsorbent layer	1. It is generally recognized in the chromatographic literature that Izmailov and Schraiber are the authors thin-layer chromatography
"This gave concentric zones, which became visible through fluorescence under a mercury lamp; a so-called ultrachromatogram was obtained. This flat ultrachromatogram can be developed by applying several drops of a solvent, and zones are developed as in conventional chromatography"	*Circular chromatography* is a chromatography method in which zones are developed (mobile-phase moves) along the radius, from the plate center to its periphery	2. F. Geiss in [8] noted that Izmailov and Schraiber are the authors of circular (centrifugal) TLC
The first stage of chromatographic separation	*Frontal chromatography*	Izmailov and Schraiber are the authors of frontal circular TLC
"We put one drop of a test solutio on a prepared flat surface. This resulted in concentric circular zones, which became visible through fluorescence under the light of a mercury lamp; this gave a so-called ultrachromatogram"	Frontal chromatography is a chromatographic version in which the test sample is continuously introduced into the chromatographic system; frontal chromatography does not use any mobile phase	
The second stage of chromatographic separation	*Elution chromatography*	Izmailov and Schraiber are the authors of eluant circular TLC
"This flat ultrachromatogram can be developed by applying several solvent drops, and t zones are developed as in conventional chromatography"	Elution chromatography is a chromatography version in which the mobile phase continuously passes through (or along) the chromatographic column, and the sample to be separated is injected into the chromatographic as a zone of limited size	The zones preseparated by frontal chromatography are samples in the subsequent fine separation by elution chromatography. The authors of TLC have actually applied the combined circular frontal elution method of circular TLC. This method is advisable for use in present-day TLC

chromatography, and on the second stage, developed the initial frontal chromatogram. Izmailov and Schraiber noticed that the thin-layer and column chromatograms were completely identical. The authors of TLC had understood the practical value of their work and noted it in the conclusions: "The advantages of the drop chromatographic analytical method (this name was given by the authors to TLC, V.B.) consist in the possibility of working with one drop of a test solution, with a minute quantity of adsorbent, and within the shortest time." "The drop chromatographic method of analysis can be used in preliminary tests of adsorbent properties and color development methods," i.e., TLC can be used as a pilot method for column liquid chromatography in developing new separation methods.

It seems expedient to experimentally pass the same way as the authors of TLC; the way they described in the first publication.

Figure 3 presents the chromatograms of an *Artemisia gen.* tincture as an example of the results we obtained while separating herbal alcohol tinctures by TLC, both on plates with a nonfixed adsorbent layer we prepared manually and on standard plates from Merck with the fixed adsorbent layer [12].

One can admire the color pictures created by nature itself. The chromatogram obtained can be considered a form of abstract painting (one more nonanalytical application of TLC!).

The results of the first work on TLC and of our chromatographic study of the same tinctures of medicinal plants are qualitatively identical [12]. However, the use of modern plates with the fixed adsorbent layer allowed us to attain a better separation (Table 2). The results obtained are indicative of the great and successful way passed by thin-layer chromatography.

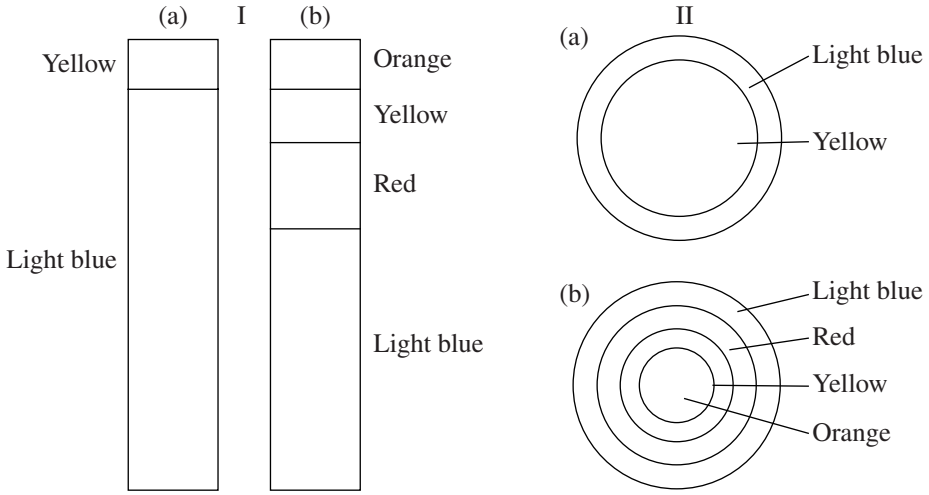


Fig. 2. Chromatograms of *Atropa belladonna* tincture [1], obtained by (I) column liquid chromatography (Tswett's method) and (II) thin-layer chromatography (Izmailov's method). Mobile phase, alcohol; adsorbent, alumina. (a) Frontal chromatogram of a test sample and (b) frontal elution chromatogram obtained as a result of the development (elution) of the initial frontal chromatogram.

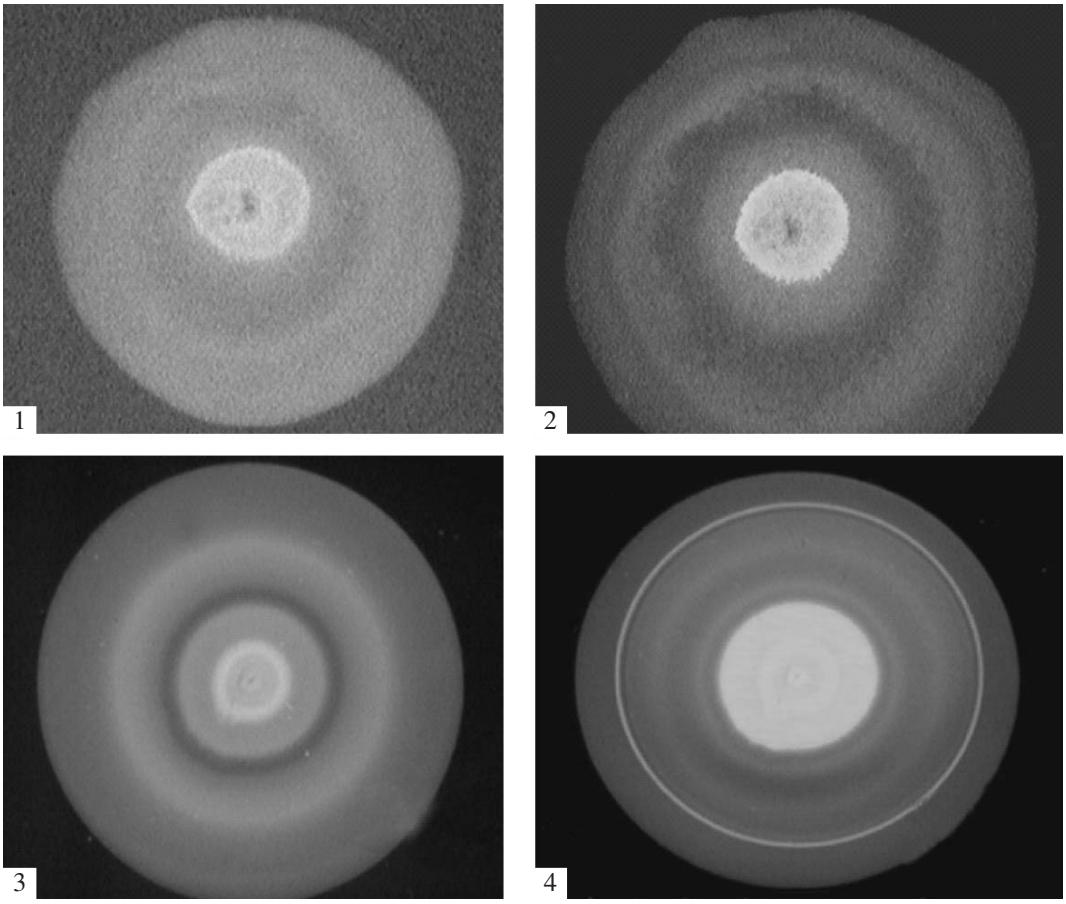


Fig. 3. Circular (1) frontal and (2) frontal elution chromatogram of *Artemisia gen.* tinctures under UV light obtained glass TLC plated prepared in the laboratory of chromatography of the Institute of Petrochemical Synthesis of the Russian Academy of Sciences with a nonfixed layer of alumina for chromatography (Photos 1 and 2) and (2) on glass TLC plates from Merck with a fixed layer of aluminum oxide (Photos 3 and 4).

Table 2. Total numbers of chromatographic zones separated in [1] and obtained today in studying the same tinctures of medical plants using standard plates from Merck with a fixed layer of aluminum oxide [12]

Data source	Tincture			
	Atropa belladonna	*Capsicum annuum*	*Valeriana*	*Mentha*
The first work on TLC	4	4	3	3
Reproduction of the first work on TLC using Merck plates [12]	14	13	5	6

Note that TLC today has also a lot of blind spots waiting for the researcher. Their development would significantly improve the analytical characteristics of present-day TLC and expand the area of its application.

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