

---

# Solubility and extractability in the Pharmaceutical Sciences: A practical exercise with pure compounds

Hossein Taouba, Jean-Luc Hayen, Jean-François Liégeois\*

University of Liège, Department of Pharmacy, avenue Hippocrate 15, 4000 Liège, Belgium

## 5 ABSTRACT

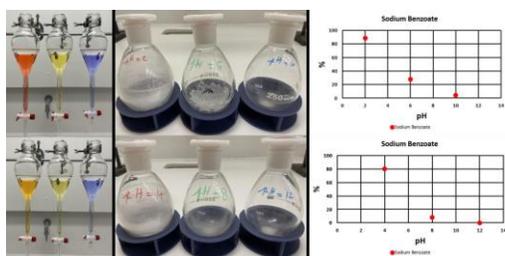
The extractability of pure organic compounds is a ubiquitous concept in the pharmaceutical field.

During this laboratory session, each student receives one vial containing an unknown compound. For this sample, they will determine its solubility in an organic solvent, in water, and then its extractability profile by three liquid-liquid extractions at different pH values followed by the evaporation of the

10 organic phase and the quantification of the residue by gravimetric analysis. The data obtained will allow students to draw a curve representing the acid/base and the hydro- and lipophilic character of their given compound. Once the first part of the session is finished, the students who have tested the same compound share the results obtained. These pooled results will show that the sigmoidal-like curve of the lipophilic acid and its conjugate base or the lipophilic base and its conjugate acid have the

15 same shape, although the solubility in organic solvent and water is different. Lipophilic amphoteric and neutral compounds are also tested in the same laboratory session. This exercise with pure compounds will allow students to identify the physicochemical characteristics of organic compounds and anticipate the separation of such compounds in a mixture.

## 20 GRAPHICAL ABSTRACT



## KEYWORDS

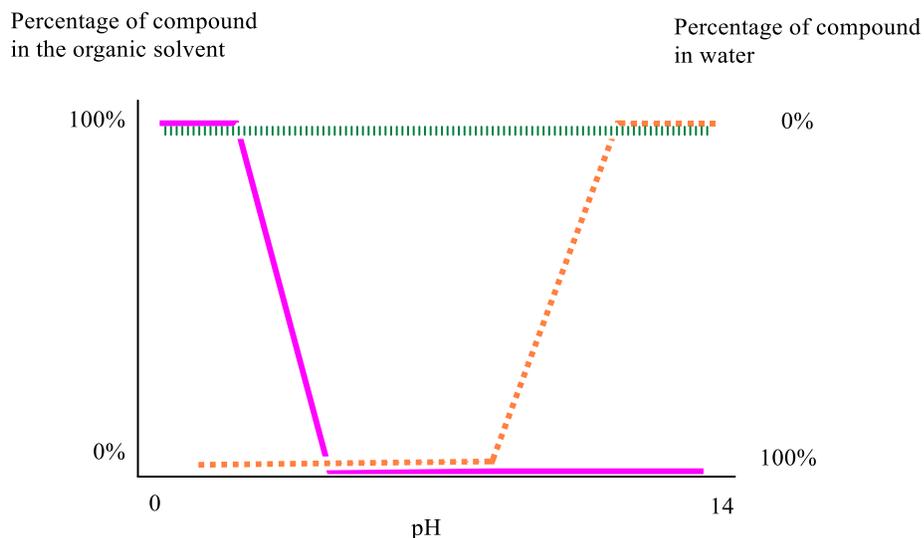
Second-Year Undergraduate, Organic Chemistry, Hands-On Learning/Manipulations, Acids/Bases, Organic compounds, pKa, Extractions

---

## INTRODUCTION

Understanding the physicochemical properties of pure organic compounds, such as their acid/base character and their hydro/lipophilic character, is an essential prerequisite in the training of pharmacy students. It will help students to improve their understanding of certain key concepts, such as chemical reactivity, isolation procedure, solubility, pharmacokinetics, pharmacology, formulation, and quality control of drugs, throughout their formation. The impact of the physicochemical properties of pure organic compounds on their behavior will be demonstrated by students in this laboratory session in which they will study the solubility and the extractability of these substances by using liquid-liquid extraction.

Before this laboratory session, a live demonstration on solubility and extractability is organized.<sup>1</sup> During this activity, different extractability curves of representative compounds are presented while the theoretical ones are extensively used during the course and the examinations (Figure 1).



40

**Figure 1.** Theoretical extractability curves for the acidic compound and its conjugate base (full line) and the basic compound and its conjugate acid (dashed line). The curves can be shifted to the left or right depending on the strength of the acid or the base. The hashed line shows the curve of a lipophilic neutral compound.

---

---

45 In relation to this demonstration, a new practical session has been designed. During this session, students will individually perform solubility tests and three liquid-liquid extractions of a pure compound at different values of pH.

These pure compounds can be acidic, basic, neutral, or amphoteric. For the latter, an acid and a basic group are simultaneously present in the molecule. In addition to the demonstration, the  
50 corresponding salts, namely, the conjugate acid for an amine and the conjugate base for a carboxylic acid, which are the ionized form of the corresponding base and acid, are also tested.

As mentioned in previous articles published in this journal, liquid-liquid extractions are challenging for students and have been the topic of many papers for a while.<sup>2-13</sup> This is especially the case in the early stages of their formation, as they must integrate many basic chemistry concepts,  
55 such as the acid-base theory, polarity, solubility, and compound structure. The educational literature for laboratory experiments or demonstrations reports frequently the use of dyes with their own physicochemical properties to explain the concept of extractability.<sup>2-4,6-7,10-13</sup> In this laboratory experiment, to facilitate the liquid-liquid extraction, the students will be provided with buffers containing a water-soluble dye that will be used as a pH indicator (see Figure S1). This will greatly  
60 improve the distinction between the aqueous phase and the organic phase. Subsequently, to allow students to visualize and quantify the extraction process, the supervisors will evaporate, after each extraction, the organic solvent that may contain the compound. Students will then weigh the remaining residue and calculate the extraction yield for each experiment. Some papers report different analytical quantification procedures<sup>14-18</sup> of compounds after extraction, but using gravimetric analysis  
65 remains the simplest method as it is accurate and does not require expensive equipment.

With their own three data points, students will draw an extractability curve for the pure compound they received. Once all the data obtained by students with the same compound are gathered into one graph (see Figure S2), they will have a complete and representative curve for the acid (and its conjugate base), the base (and its conjugate acid), the neutral compound, and the amphoteric  
70 compound. These curves will also be used for the theoretical part of the course and must be known for the examinations.

---

---

## DESIGN OF THE EXPERIMENT

75

The compounds selected in these experiments are commonly used in the pharmaceutical field. They were also chosen based on several criteria such as their availability, safety, solubility, and extractability. A preselection of the compounds was carried out by choosing those which were, in their nonionized form, lipophilic and soluble in an organic solvent like diethyl ether. It is important to test acid and base salts when they are available. The counterion is as small as possible to limit its impact in the quantification process. Once the preselection was complete, the solubility and the extractability of these compounds were systematically tested using the same protocol as the one provided for students. Only the compounds that had their extractability and solubility profiles that corresponded to what would be expected in theory were selected. For each extractability assay, 250 mg of each compound is used (~ 1 g distributed for each student).

For these experiments to be successful, the compounds must be lipophilic in their nonionized form and should give a residue following the evaporation of the solvent if the compound is extracted. It is understood that by using very polar or volatile compounds (ethanol, glycerol, glucose, acetic acid, formaldehyde, etc.) the students will have a difficult time acquiring conclusive results as there will be no residue after the extraction.

The products distributed to students are the following: for the compounds containing hydroxyl groups and related (Table 1), benzoic acid (and sodium benzoate), salicylic acid (and sodium salicylate), *O*-acetylsalicylic acid, *para*-nitrobenzoic acid, *para*-hydroxybenzaldehyde, vanillin, menthol and thymol (Figure 2). From a chemical point of view, these are all acidic compounds as they have mobile hydrogen. These compounds were chosen for teaching purposes in order to illustrate the impact of the electronic environment of the hydrocarbon part or the substituents on the strength of an acid or a base of the functional group. These compounds are lipophilic in their nonionized form. Most of them possess various hydroxyl functional groups for which the electronic environment has an impact in terms of acidity (Table 1).

100

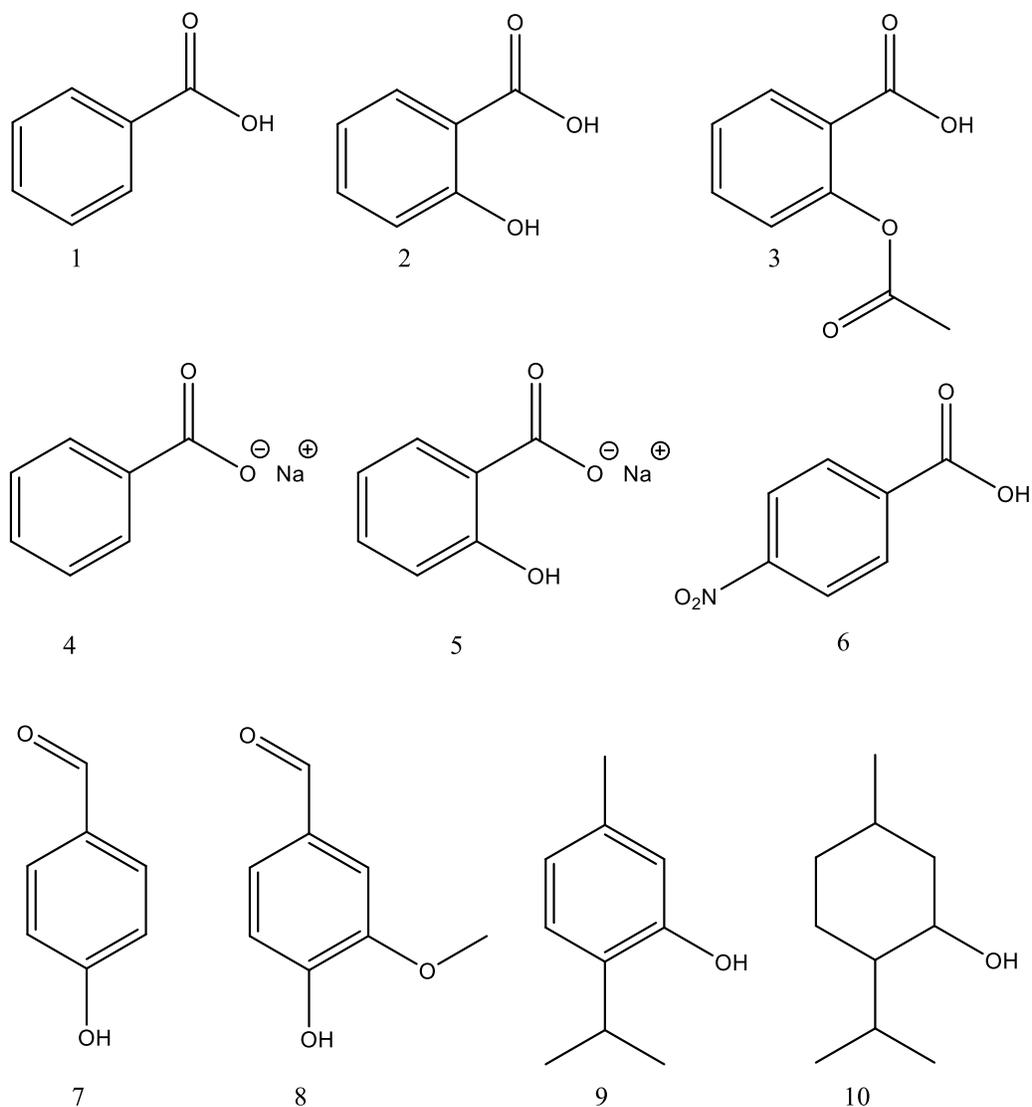
---

**Table 1.** Characteristics of hydroxyl functional groups and related ones present in the selected compounds

Functional group	Hydrocarbon environment (R)	Function (pKa)	Electron-withdrawing effect of the hydrocarbon chain	Presence of electron-withdrawing (or -releasing) substituent	Example of selected compound
R-O-H	Cyclic or acyclic aliphatic	Alcohol (15-18)	No	No	Menthol
	Aromatic	Phenol (10-11)	Yes	Yes	Vanillin, Thymol,...
R-CO-O-H	Aliphatic	Carboxylic acid (4-6)	No	/	Not tested
	Aromatic	Carboxylic acid (4-6)	Yes	Yes	Benzoic acid (and sodium benzoate), ...
H-O-H*	/	(15,74)	/	/	

\* water is a crucial component in the acid or base character of compounds tested

By hydroxyl group, we mean an oxygen linked to a hydrogen atom which is found in an alcohol (aliphatic hydroxyl), a phenol (aromatic hydroxyl), or a carboxyl (this group is the association of a hydroxyl group and a carbonyl, a group with an electron-withdrawing property). Amines are also present (aliphatic or aromatic).

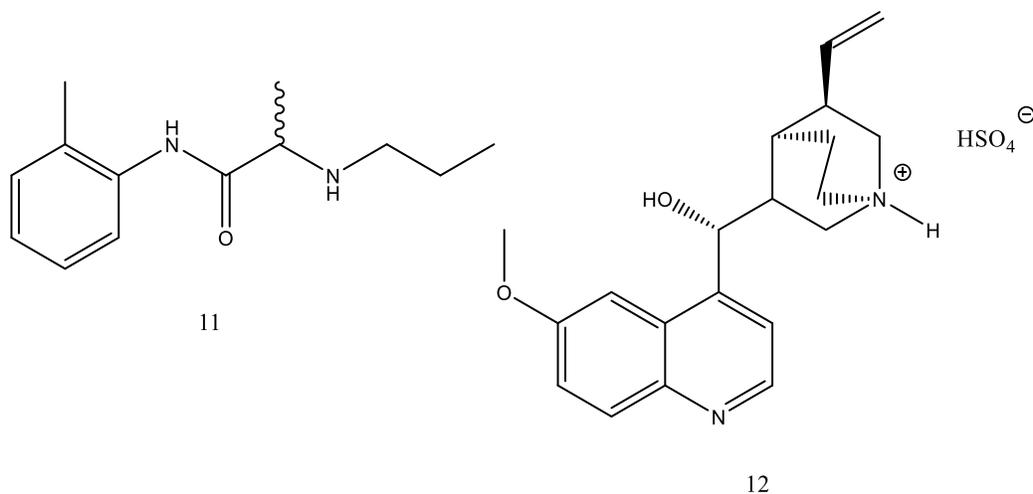


110

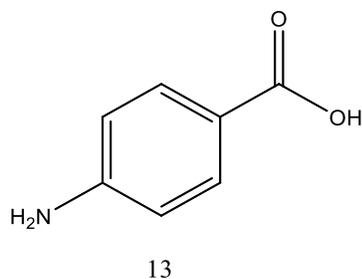
**Figure 2.** Chemical structures of compounds containing hydroxyl groups and related tested by students: (1) benzoic acid, (2) salicylic acid, (3) *O*-acetylsalicylic acid, (4) sodium benzoate, (5) sodium salicylate, (6) *para*-nitrobenzoic acid, (7) *para*-hydroxybenzaldehyde, (8) vanillin, (9) thymol, and (10) menthol.

115

For the basic compounds, the students will receive prilocaine and quinidine sulfate (Figure 3). The amphoteric compound will be *para*-aminobenzoic acid (Figure 4).



120 **Figure 3.** Chemical structures of basic compounds tested by students: (11) prilocaine and (12) quinidine sulfate (or hemisulfate).



**Figure 4.** Chemical structure of the amphoteric compound *para*-aminobenzoic acid (13) tested by students.

125

Most of the products used are expired in terms of the date of use and come from our laboratories and pharmacy. This will, in a way, allow us to give these products a second life. The other selected parameters are described in the Supporting Information.

130

## PRACTICAL SESSION

During this laboratory session, students will perform the liquid-liquid extraction of a pure compound, at different values of pH. The tested molecules are pure and frequently used in the pharmaceutical field. The compounds that the students will each receive are anonymized, and thus, they will be performing solubilities and extractions in blind conditions. An important point to consider

---

135 is the fact that these experiments will allow students to test on one hand the carboxylic acids and their corresponding salts, which are the ionized conjugate bases, and on the other hand the amines and their corresponding salts, which are the corresponding ionized conjugate acids.

The laboratory session is divided into four parts allowing students to assimilate important concepts (see Table 2) aiming to form a coherent whole. For this reason, it is important to respect the  
140 time dedicated to each part (see below).

**Table 2:** Learning outcomes of the laboratory experiment

Using laboratory equipment with precision: separatory funnel, balances, ...	Part II and III
Using tare flask to quantify the result of the experiments	Part III and IV
Understanding the differential behavior between an acid (or base) and their conjugate form in terms of solubility and of extractability	Part II, III, and IV
Understanding the behavior of drugs depending on their functional groups in various media	Part I-IV
Understanding the solubility of different ionization states of organic compounds with ionizable groups as a function of pH	Part I-IV
Clearly and accurately report scientific results	Part II, III, and IV
Preparing and understanding the separation of compounds in a mixture	Part I and III

Part I: Pre-lab explanations. Timing: 10 min.

Initially, the students will receive the laboratory's operating instructions, which they should read  
145 carefully before the session. It contains information on safety and theoretical reminders of the fundamentals: acid-base reactions, solubility, density, miscibility, and aqueous/organic phase.

Part II: Exploring solubility and acid-base characteristics. Timing: 20 min.

At the start of the laboratory session, students are given a laboratory report to use as a support  
150 tool throughout the session.

---

---

They are first asked to test the intrinsic solubility of the compounds in pure water and in the organic solvent. Thereafter, they measured the pH of the corresponding aqueous solution with a pH indicator paper. Once this has been done, they should note whether the compound has completely solubilized in the organic solvent or the water and indicate for the latter the value of the pH.

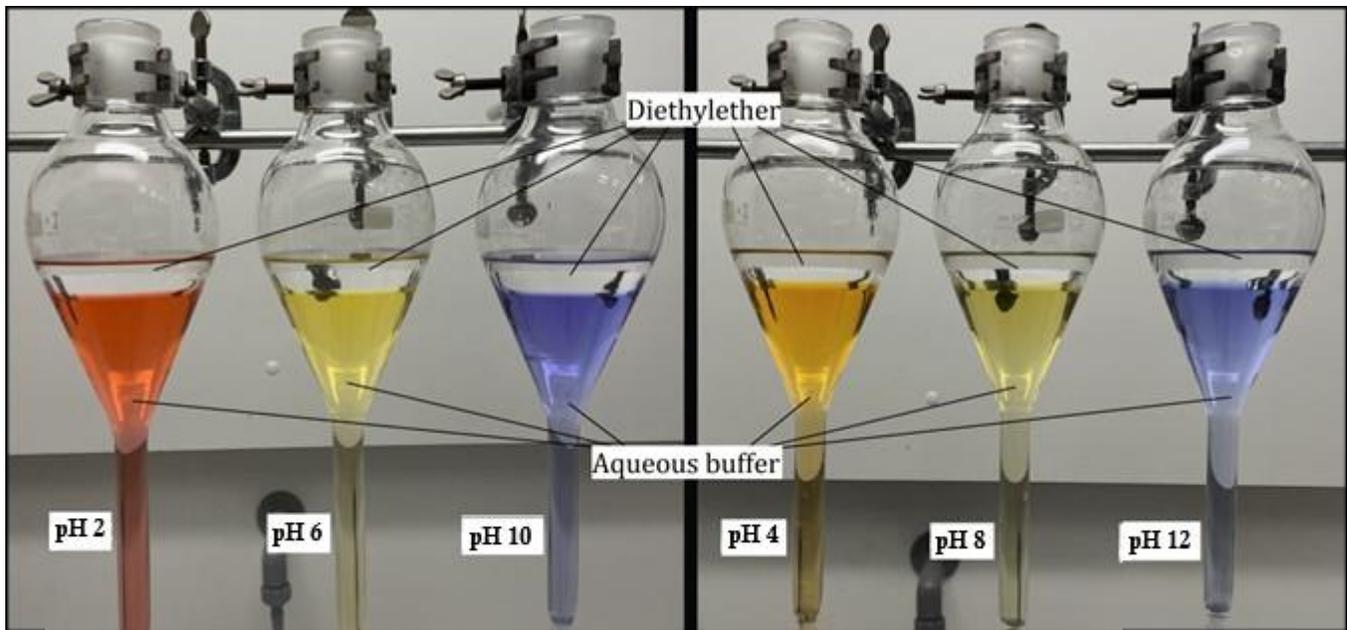
155 By testing the solubility of the compound in water as well as in the organic solvent, the students were able to characterize the hydro/lipophilic character of the compound. For water-soluble compounds, by measuring the pH of the aqueous solution, the students should be able to tell whether the compound is acidic or basic, meaning that it is a conjugate base or a conjugate acid.

160 Part III: pH-controlled Liquid-Liquid Extraction. Timing: 3 h.

To explore the physicochemical properties of the compounds in detail, students are asked to perform three liquid-liquid extractions between an organic phase and a buffered aqueous phase at three different pH values.

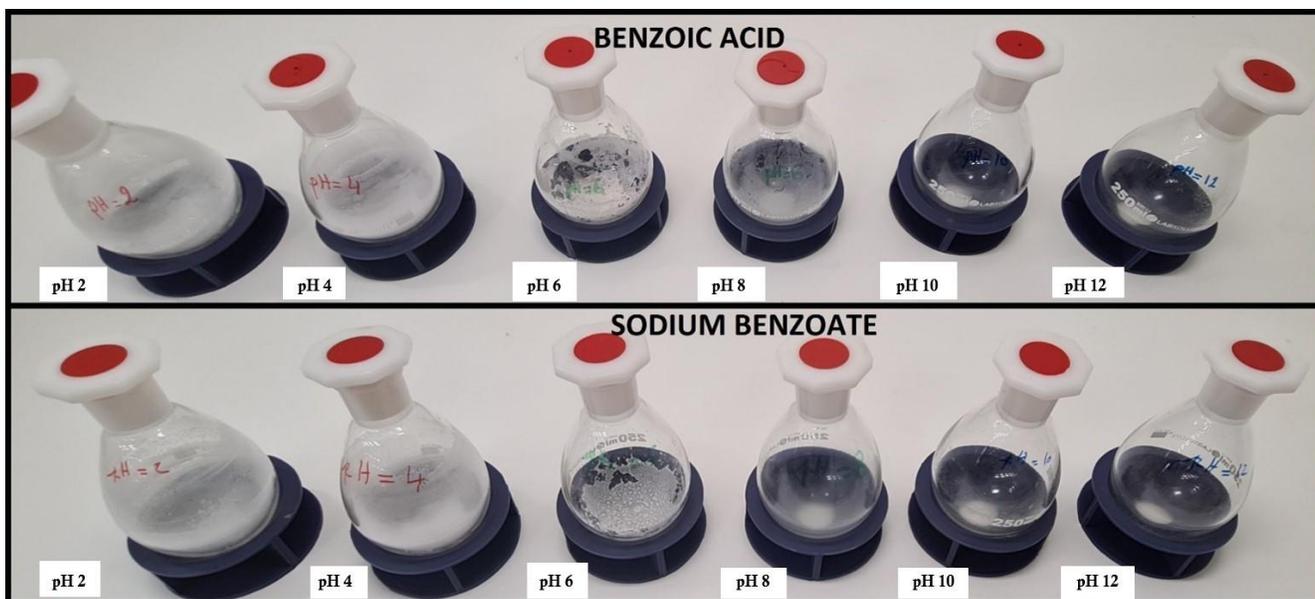
The first task is to weigh 250 mg of the sample to be tested. To perform their extractions, the  
165 students will have two sets of three solutions at different pH values. The first set includes solutions at pH = 2, 6, and 10, while the second set includes solutions at pH = 4, 8, and 12 (Figure 5). As the students are divided into two groups, the assistant provides one set for one room and the other set for the other. These buffer solutions contain water-soluble dye to make it easier for students to visually distinguish the aqueous phase from the organic phase. Buffers are colored differently depending on  
170 the pH (Figure 5).

---



**Figure 5.** Both sets of biphasic mixtures using three different buffer solutions. Due to its density, diethyl ether can be seen above each buffer.

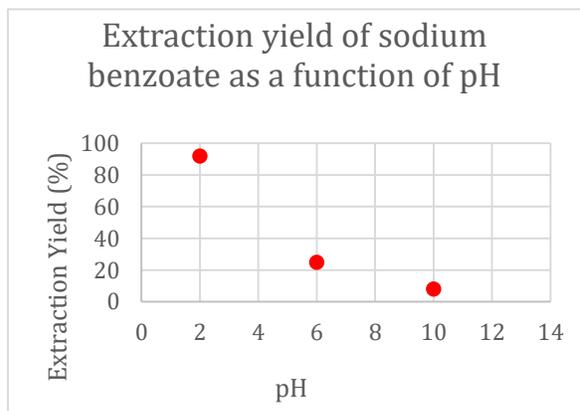
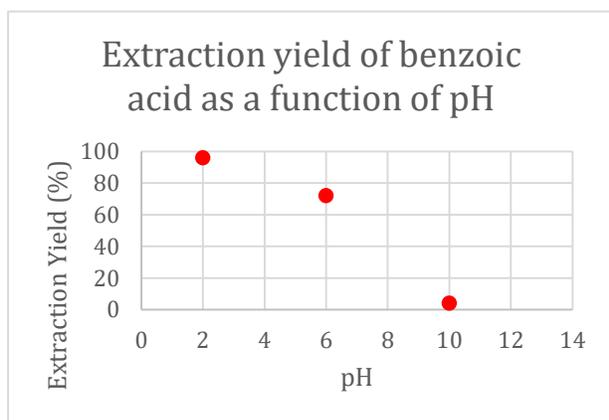
Before performing the liquid-liquid extraction, the students must tare their 250 mL flask into which they will evaporate the organic solvent after the liquid-liquid extraction. After evaporation, they will obtain a result that is both visual (powder at the bottom of the flask) and quantifiable (Figure 6).

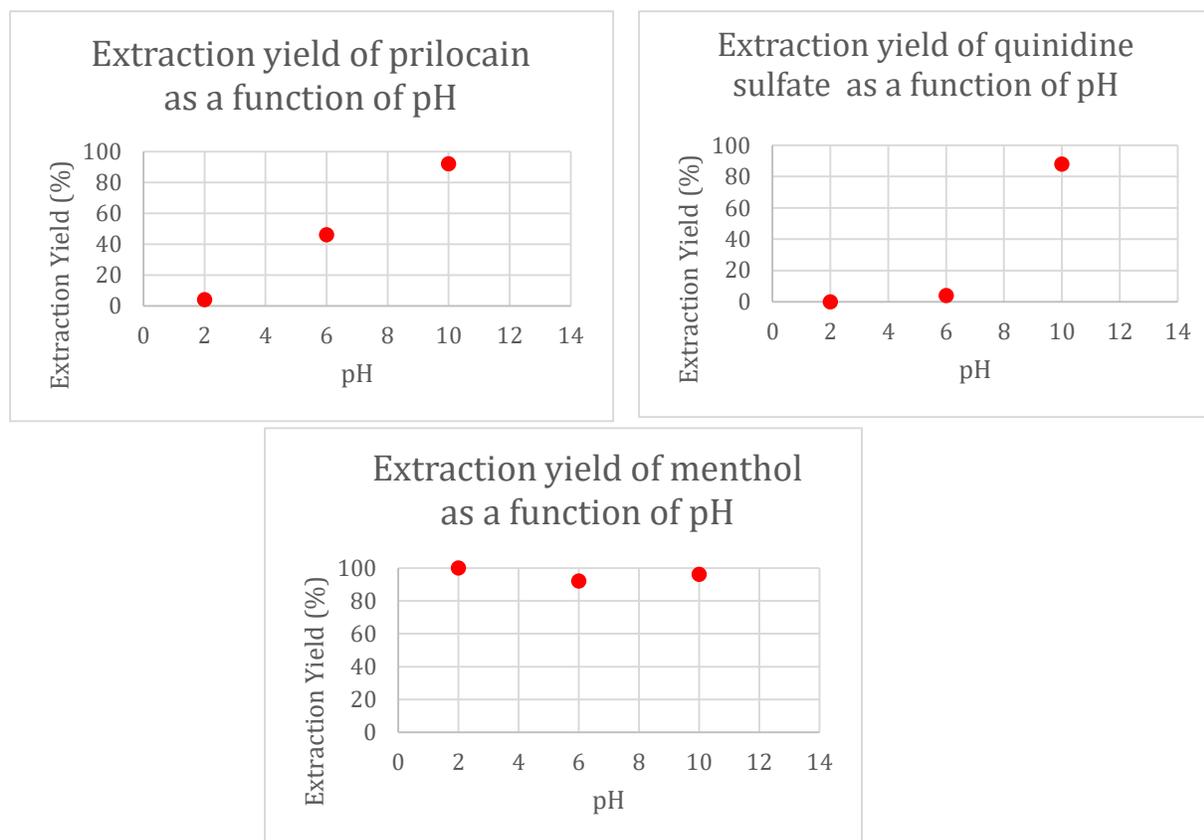


**Figure 6.** A set of flasks with (or without) a residue after evaporation

185 Students must note the weight of the residue obtained for each of the three extractions at different pH values and calculate the extraction yield as a percentage of the starting material. Thereafter, they will report in a graph these values to get a schematic representation in the form of a 3-point extractability curve (Figure 7).

190





**Figure 7.** An example of extractability curves for benzoic acid, sodium benzoate, menthol, prilocaine,  
205 and quinidine sulfate obtained by students individually.

As salts are also distributed, the loss of molecular mass linked to the counterion is not to be considered, bearing in mind that the most important thing is to have a correct extraction trend curve for the chemical species.

Part IV: Interpretation and pooling of the results. Timing: 1 h.

A 1 h session is then devoted to gathering the results obtained and discussing the data. As the concepts studied in this lab will follow students throughout their pharmacy course, it is essential that

all students understand the solubility of the different ionization states of organic compounds that have  
215 ionizable groups, depending on the pH.

## RESULTS AND DISCUSSION

During the last three academic years, we have collected a significant number of results using this  
extraction procedure. The experiments were successfully completed by almost three hundred students  
220 in a 4 h session (see details in Supporting Information section Table S1).

Thereafter, a 1 h exercise session is organized to pool all the results and to help the students  
understand all the concepts highlighted during this session. The results, which are expressed in  
percentage of the starting material, are represented in a global table in the laboratory and in the  
students' own laboratory report. A high percentage of success (ranging from 74.1% to 95.5%) has been  
225 obtained while displaying a low percentage of outliers (see details in Table S2 in the Supporting  
Information). The outlier values, which exceed the mean by 15%, are rejected and will not be used to  
draw the curves. In the tables, these values are not included in the mean and are highlighted  
(Supporting Information). The global results using the mean values for each pH are shown in Table 3.

230 **Table 3.** Mean of extraction efficiency (%) of the substances in the organic phase as a function of pH of  
the aqueous phase expressed in the percentage of the starting material.

pH	2	4	6	8	10	12	13	14
<b>Benzoic Acid</b>	93,7	94,2	68,0	9,1	3,0	0,7		
<b>Sodium benzoate</b>	80,7	90,0	28,6	8,0	2,7	3,2		
<b>Salicylic acid</b>	91,0	90,8	66,0	5,9	4,0	3,2		
<b>Sodium salicylate</b>	90,1	86,4	10,0	8,8	1,8	2,0		
<b>O-Acetylsalicylic acid</b>	86,7	83,0	64,5	1,9	2,7	1,8		
<b>p-Nitrobenzoic acid</b>	91,9	85,8	63,0	7,0	2,5	2,7		
<b>p-Aminobenzoic acid</b>	52,3	83,2	59,7	8,1	4,0	0,9		
<b>Vanillin</b>	90,6	89,5	88,6	70,6	11,9	2,7		
<b>p-Hydroxybenzaldehyde</b>	91,6	93,1	95,2	77,7	19,7	9,3		
<b>Thymol</b>	91,0	98,0	92,5	90,0	97,8	93,0	<b>71,5</b>	<b>68,5</b>
<b>Menthol</b>	95,5	91,5	93,2	89,5	91,2	96,0		
<b>Prilocaine</b>	3,3	6,6	48,3	88,6	90,4	87,4		

---

**Quinidine sulfate**

3,3

4,4

16,8

72,2

86,1

79,7

---

The acids and conjugate acids are written in **red**, the weaker acids are written in **orange**, the neutral product is written in **green**, and the bases and conjugate bases are written in **blue**. The amphoteric compound is written in **black**. For thymol, the data in bold have been obtained by the assistant. This color code is used in the following graphs (Figures 8-11 and also Figures S3-S15).

235

Then, these results are used to draw the corresponding extractability curves using the mean values (Figures S3-S15).

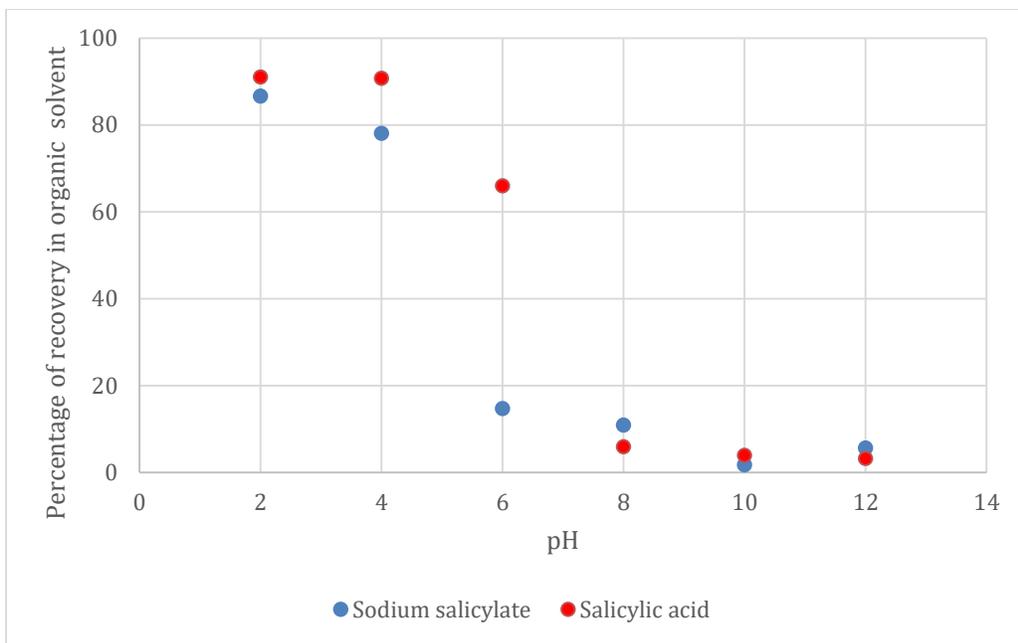
To compare the different chemical species, three main graphs are drawn representing the results obtained, one for a carboxylic acid and its corresponding salt, here salicylic acid (Figure 8; curves for other acidic compounds are reported separately in the Supporting Information), one for weak acids, here the phenolic compounds including the aliphatic and lipophilic alcohol menthol for comparison (Figure 9), and one for the basic molecule and the corresponding salt (Figure 10). The last graph presents the results for an amphoteric compound (Figure 11).

240

245

In Figure 8, one important message to keep in mind is that for the carboxylic acid and its salt (conjugate base) both curves have the same shape and can be superimposed. This similarity in shape is also seen with the curves of the basic compound prilocaine and the conjugate acid quinidine sulfate (Figure 10). This is illustrated in the demonstration's paper<sup>1</sup> with the cross relationship between the acid and base forms.

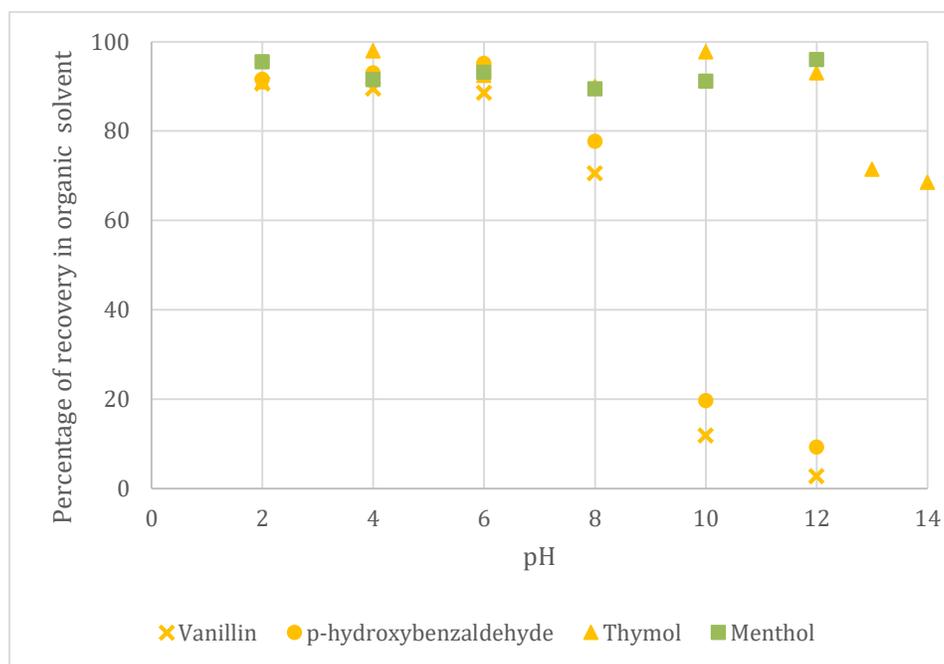
---



250

**Figure 8.** Extractability curves of an acidic compound and its conjugate base (here, sodium salt) obtained by students after gathering all the results.

255



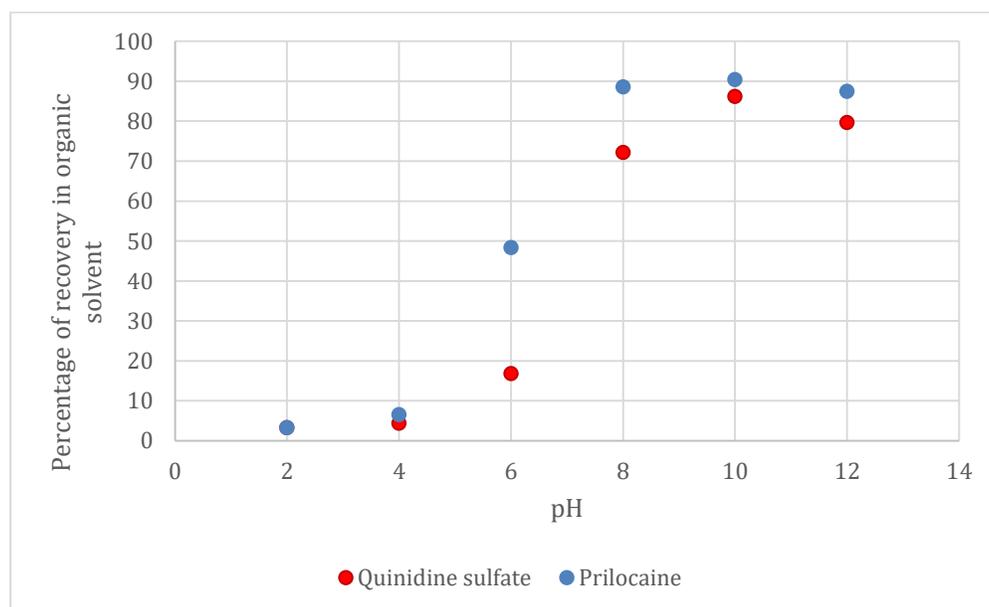
**Figure 9.** Extractability curves of weak acids and neutral compounds obtained by students after gathering all the results.

260

For weaker acids represented by phenolic compounds (Figure 9), the curves are shifted to the right in parallel to their pKa values. With these compounds, the impact of the presence of electron-withdrawing and electron-releasing substituents on this value is observed. Thymol has a higher pKa value in comparison with the two other phenolic compounds which possess electron-withdrawing substituents. It is only deprotonated at higher pH due to the influence of electron-releasing substituents. For the students, the curve resembles that of a neutral compound but the assays done by the assistant show the beginning of the deprotonation. Between thymol and menthol, the pKa of the aliphatic hydroxyl (menthol) is higher than that of the aromatic hydroxyl (thymol); therefore, the alcohol function is not acidic enough to be deprotonated in water, and thus, the compound is always protonated and lipophilic. With these results, it is shown clearly that, for hydroxyl-containing molecules, the electronic environment has a huge impact in terms of acidic character.

265

270



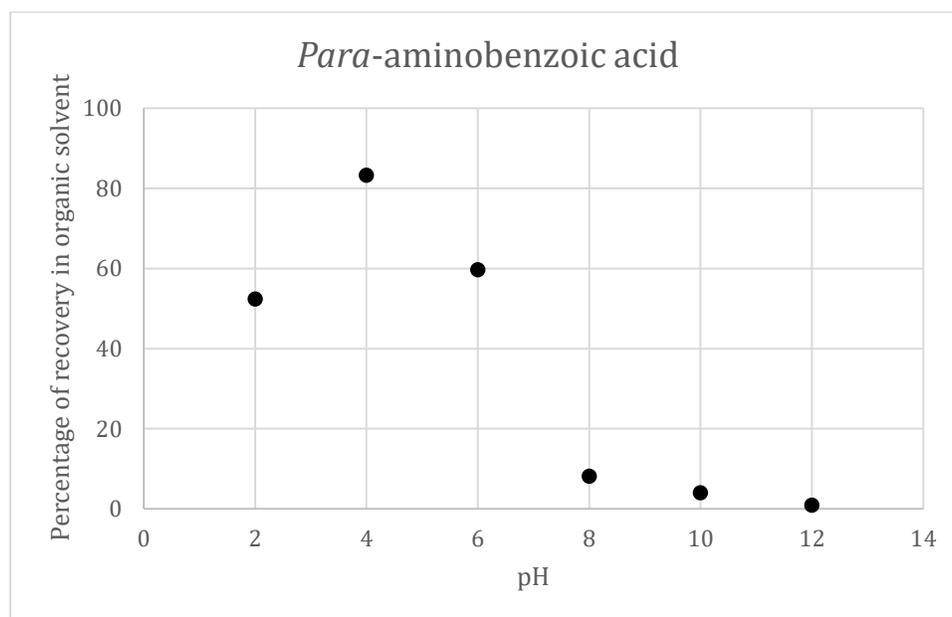
275

**Figure 10.** Extractability curves of a basic compound and a conjugate acid (here, sulfate salt) obtained by students after gathering all the results.

---

Another compound that may give rise to questions from the students is *para*-aminobenzoic acid. For this compound, depending on the set of buffers, individual students obtained a curve resembling that of an acid. Thus, it is necessary to gather the data of all of the students who tested this

280 compound. After that, a biphasic curve appears which results from the superimposition of the curve of the carboxylic acid on one hand and on the other hand those of the primary aromatic amine (Figure 11).



285 **Figure 11.** Extractability curve of *para*-aminobenzoic acid obtained by students after gathering all the results.

This indicates, on one hand, the ionization of the carboxylic acid at high pH and, on the other hand, the ionization of the weak base at low pH (Figure 11). Moreover, for this compound, the results observed can integrate the students' understanding of the isolation procedure which they had the

290 occasion to see when they recovered the corresponding *ortho* isomer (anthranilic acid) in a synthesis they performed during another practical session through a Hoffmann degradation with phthalimide to get the anthranilic acid. Although, in the case of the amphoteric compound, both the acid and basic poles can be ionized, as shown in Figure 11, at a low acid pH and at a higher pH, there remains a

---

---

295 range of pH where the lipophilic entity is present. This helps explain why the students crystallize such a compound by controlling the pH as was done during a previous practical session.

During the postlaboratory session, the discussion will consider the impact of the hydrocarbon environment (aliphatic or aromatic) and the presence of electron-withdrawing (aldehyde, nitro) or electron-releasing (alkyl, phenol, amine) substituents on the acid/base character of the compound.

300 These structural elements significantly influence the mobility of the proton in the corresponding functional groups. During this session, the precise structure of the compound tested is not revealed for practical reasons.

### CONCLUSION

305 The new laboratory experiment has been successfully reproduced during three academic years, and the data are robust. All extractability curves are in accordance with those presented during the live demonstration<sup>1</sup> and fit with the theoretical ones (Figure 1) presented during the course. It is clearly shown that the acid and its conjugate base or the base and its conjugate acid, although having different intrinsic solubilities, have the same extractability curve. The variation in the acidic character

310 of the compounds is detectable between the carboxylic acid (or salt) and the phenol. Similarly, the aliphatic and aromatic amines are differentiated. The difference between two compounds having close pKa values is more difficult to detect. This could be solved by using other buffers with pH close to the pKa of the compound. This laboratory experiment permits students to examine the solubility and extractability of pure compounds in order to identify their physicochemical characteristics. In addition,

315 it allows them to be prepared for the next session about the separation of compounds in a mixture.

### HAZARDS, SAFETY and WASTES

Diethyl ether is used, during the practical sessions, as a solvent for extractions and is highly flammable. Thus, during this session, no flame is present in the laboratory and the use of

320 smartphones is prohibited. Most of the compounds to be extracted have limited toxicity (see the Supporting Information).

Students are asked to avoid skin contact with all organic solutions after extractions.

---

---

Regarding wastes, all buffer solutions are collected in one flask. The diethyl ether is recovered by the assistant in the rotavapor collector.

325 **ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available on the ACS Publications website at DOI:

10.1021/acs.jchemed.XXXXXXX. [ACS will fill this in.] It contains information on the material and reagents section, the composition of the buffer solutions, additional informations regarding hazards and safety, the organization of the session, the experimental protocols of solubility and extractability, the results for each compound (tables with crude values or without outliers and the corresponding graphs), an original student report along with a translation and some elements for assessment (PDF)

330 **AUTHOR INFORMATION**

Corresponding Author

335 \*E-mail: JF.Liegeois@uliege.be

**ACKNOWLEDGMENTS**

The undergraduate students (S. Al-Sadoon, G. Baudino, S. Habieb, C. Lhermerout) who performed the preliminary experiments on the extractions before introducing them as a new practical session are gratefully acknowledged. S. Counerotte is gratefully acknowledged for the technical assistance. Z. Taouba is gratefully acknowledged for the careful reading of the manuscript. JFL, HT, and JLH have a Master's degree in Pharmacy. HT was involved in the setting-up of this laboratory experiment, the preparation and the management of the practical sessions. JLH starts a PhD thesis as a Research Fellow of the F.R.S.-FNRS. JFL is a Research Director of the F.R.S.-FNRS and was the professor of the course CHIM0714 at the ULiège for more than two decades.

345 **REFERENCES**

- (1) Liégeois, J.-F.; Hayen, J.-L., Taouba, H. Solubility and extractability in the Pharmaceutical Sciences: A demonstration to address these essential concepts. *J. Chem. Educ.* **2024**, *101*, 5547-5555
  - (2) Hobbs, G.D.; Woodyard, J.D. A colorful extraction experiment. *J. Chem. Educ.* **1982**, *59*, 386.
  - 350 (3) Elder, J.W. Microscale acid-base extraction: A colorful introduction. *J. Chem. Educ.* **1990**, *67*, 266.
  - (4) Kelly, T.R. A simple, colorful demonstration of solubility and acid/base extractions using a separatory funnel. *J. Chem. Educ.* **1993**, *70*, 848-849.
-

- 
- (5) Love, B. Extraction of organic compounds from aqueous solutions. *J. Chem. Educ.* **1994**, *71*, 571-518.
- 355 (6) Raydo, M.L.; Church, M.S.; Taylor, Z.W.; Taylor, C.E.; Danowitz, A.M. A guided inquiry liquid/liquid extractions laboratory for introductory organic chemistry. *J. Chem. Educ.* **2015**, *92*, 139-142.
- (7) Shugrue, C.R.; Mentzen, H.H.; Linton, B.R. A colorful solubility exercise for organic chemistry. *J. Chem. Educ.* **2015**, *92*, 135-138.
- 360 (8) Celius, T.C.; Peterson, R.C.; Anderson-Wile, A.M., Kraweic, M. From Observation to Prediction to Application: A Guided Exercise for Liquid-Liquid Extraction. *J. Chem. Educ.* **2018**, *95*, 1626-1630.
- (9) McKnelly, K.J.; Howitz, W.J.; Lam, S.; Link, R.D. Extraction on paper activity: An active learning technique to facilitate student understanding of liquid-liquid extraction. *J. Chem. Educ.* **2020**,  
365 *97*, 1960-1965.
- (10) Grimminger, M.A.; Tracey, M.P.; Martinus, S.J. Colorful approach to teaching extraction using azo dyes and comparison of hands-on versus distance learning assessment. *J. Chem. Educ.* **2021**, *98*, 3509-3513.
- (11) Orzolek B.J.; Kozlowski M.C. Separation of Food Colorings via Liquid-Liquid Extraction: An At-  
370 Home Organic Chemistry Lab. *J. Chem. Educ.* **2021**, *98*, 951-957.
- (12) Luska, K.L. A multioutcome, guided inquiry-based liquid-liquid extraction laboratory for introductory organic chemistry. *J. Chem. Educ.* **2022**, *99*, 4124-4133.
- (13) Dobberpuhl, D.; Johnson, L.; Mattson, B. A colorful solvent extraction demonstration for teaching the concept of « like dissolves like ». *J. Chem. Educ.* **2022**, *99*, 3342-3345.
- 375 (14) Jones, M. M.; Champion, G. R. Simple liquid-liquid extraction experiment for freshmen. *J. Chem. Educ.* **1978**, *55*, 119.
- (15) Turner, D. E. An Experiment to Demonstrate the Effect of pH on Partition Coefficients in Liquid-Liquid Extraction. *J. Chem. Educ.* **1994**, *71*, 173.
- (16) Radford, S. A.; Hunter, R. E.; Barr, D. B.; Ryan, P. B. Liquid-Liquid Extraction of Insecticides  
380 from Juice: An Analytical Chemistry Laboratory Experiment. *J. Chem. Educ.* **2013**, *90*, 483-486.
- (17) Celius, T.C.; Peterson, R.C.; Anderson-Wile, A.M.; Kraweic-Thayer, M. From Observation to Prediction to Application: A Guided Exercise for Liquid-Liquid Extraction. *J. Chem. Educ.* **2018**, *95*, 1626-1630.
- (18) Bergamin, E.; Fabris, G.; Neffat, M.; Toaldo, P.B. ; De Luchi, D.; Bonomi, R. Multiple Solid-Liquid  
385 Extraction: Determination of Extraction Yield through UV-Vis Spectroscopy. *J. Chem. Educ.* **2023**, *100*, 875-879.
-