

HISTORY OF PHARMACY SIG

Pharmacy Chronicles: Past, Present, and Future

WELCOME MESSAGE FROM THE CHAIR, HISTORY OF PHARMACY SPECIAL INTEREST GROUP

As I wind down my term as chair of the History of Pharmacy SIG, I'd like to remind you of a few business and networking opportunities for the group. First, we have our virtual business meeting, on Monday June 24 (12-1 EST). Advance meeting registration is required for participants to receive the Zoom meeting link, and so we can track attendance. We'll spend some time going over our activities from the past year and will swear in the new officers. Registration link: https://us02web.zoom.us/meeting/register/tZ0pcO2tqTMqG9FUfLtPzq4l-NA_G9fxIuC8

At the annual meeting, we'll have two chances to meet, both on Monday, July 22. First, join Michael Hegener and Essie Samuel for their presentation "Making History Inno-

vative: Using Pharmacy History Activities to Support Content in a Variety of Courses" (10:30-11 am EST). At noon, join us for an informal networking session, and be sure to bring ideas for the next year with you. The SIG is always on the lookout for new webinar and annual meeting presentation ideas.

A few closing thoughts. Some of you may have attended this year's American Pharmacists Association annual meeting. If so, hopefully you were able to attend the keynote address by Ryan Leek. Leek talked about his "Bread Crumb" exercise, in which we were encouraged to visualize a bread crumb trail working backwards from where we are today. Who were the people and events that

put us where we are now? They are our bread crumbs.

I lost one of my bread crumb people this week. He was the reason I am in this role as SIG chair, because without him, I wouldn't be teaching History of Pharmacy. Some of you may have known Avery Spunt, either from his time with University of Illinois or Midwestern University, or his years at NABP. Others may have known him from professional organizations like this one, or APhA. Still others may not have known him at all. But he had a huge impact on countless pharmacy students and colleagues. A coworker reminded me this week of his advice to students heading out on rotations: "Show Up, show up on time, show up prepared." It is timeless advice. And only a small portion of what I and so many others learned from Avery.

One thing in particular that I learned from him was to remember where we came from as a profession. That's obviously a major part of teaching any kind of history course, but field-specific ones need it for additional reasons. Not only do we learn about the timelines, but the people, and what the profession

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Meet the Editors

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Thank you ...

The Editors would like to thank the volunteers who performed the peer reviews and editing for this issue.

*Robert Cisneros
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Message from the Editors

Welcome

WELCOME! We are pleased to present the 16th issue in our 11th year of publishing, of the History of Pharmacy SIG Newsletter *Pharmacy Chronicles: Past, Present, and Future*. This is first issue for this year, and our fifth year of providing two issues per year thanks to the interest of our read-

ers and to the authors who labor to provide us with outstanding articles. A big Thank You to our peer reviewers who respond quickly and with constructive comments to the authors, resulting in a higher quality publication. We always welcome volunteers to be peer reviewers; we appreciate your efforts and the

burden is light.

Of course, our peer-reviewers must have something to read, so we also gratefully acknowledge the authors who have taken the time to provide insightful and interesting stories to better illuminate our professional history. In that vein, we encourage our readers to enlist the aid of your stu-

dents to add to our pages. A number of our articles have both teacher and student authors and they do a great job! Also, as many of our readers are teachers of pharmacy in so many disciplines, please take a moment as you organize your courses and lectures to incorporate some historical facts or context for drugs

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ANNOUNCEMENTS

Chair's Message, continued from pg 1.

looked like from a practical standpoint. It really struck students when they realized that not only was mandatory patient counseling a relatively new development (one that happened in my lifetime, and probably many of yours), but it wasn't all that long ago that we were forbidden from doing it. Hearing such facts from someone that remembered those days showed the strides pharmacy has taken.

I was extremely lucky to have worked with Avery, and especially blessed to have been able to teach with him. His desire to focus our history course on the "heroes" of the profession (based on Dennis Worthen's article series in JAPhA, later compiled into a book) really made me focus more on those people that came before me, to continue to point them out to my students, and to constantly search for new and currently practicing pharmacists to add into that category. Some of those heroes are too distantly removed to fall into the bread crumb category I mentioned above. For me, Avery qualified as both. Hopefully, everyone reading this has had an Avery in their lives.

Sincerely,
Karen Nagel-Edwards, SIG Chair

References:

Leek R. Level Up: 12 Questions to Elevate Your Personal and Professional Development.

Editor's Notes, continued from pg. 2.

or diseases. One never knows where that spirit of inspiration will well up.

Our issue this spring focuses on two very diverse topics. One article is a study of student attitudes relative to preparing herbal products, harking back to ancient origins. The second article is more recent, on dextromethorphan, synthesized in the late 1940's but has had an active history in its brief time on the scene.

Another item of significance is the book announcement for, *We Remember Them: Pharmacy's Fallen*, that recounts the pharmacists who died in active military service during World War II. It is available free through the American Institute of the History of Pharmacy's website.

Please note that we welcome a short, newsy piece of trivia or a full article for peer review (1500-2000 words). Pictures are always good! To volunteer, contribute as author or peer reviewer or just have a question or suggestion, please feel free to contact either Megan Undeberg or Bernie Olin. We are always happy to hear from you.

*—Bernie Olin, PharmD,
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DON'T FORGET!

**History of Pharmacy SIG
Business Meeting**

**Monday, June 24, 2024
12-1 pm EST**

REGISTRATION AT:
<https://us02web.zoom.us/meeting/register/>

RECOGNIZE YOUR STUDENTS FOR THEIR ACTIVITIES RELATING TO THE HISTORY OF PHARMACY!

The American Institute of the History of Pharmacy offers certificates to students to recognize their achievements in the area of History of Pharmacy. Nominate deserving students at the link below. The certificates could be sent directly to the students or to the schools for presentation at an awards ceremony.

Link: [#AIHP/ Student recognition certificate](#)



DISPATCH FROM THE AMERICAN INSTITUTE OF THE HISTORY OF PHARMACY

The AIHP has some exciting news to share in a few areas.

First, AIHP has focused on "Community Pharmacy" for its Spring Kreminar – named after Edward Kremers and a seminar – and an upcoming issue of *History of Pharmacy and Pharmaceuticals*. The many historical facets of community pharmacy have *not* been examined and the Kreminar in 2024 is a launch pad, as is the Special Issue of HoPP, which should be published in 2025-2026.

Second, AIHP is slowly developing new educational materials for its members and the wider public. The short webinars will help viewers better understand how to do basic searches in pharmacy history, Archives 101, and Artifacts 101, among other topics. Please stay tuned and in touch about these resources.

Third, AIHP Executive Director Lucas Richert is traveling to England in June to continue with his consulting work for the Boots-Walgreens digitization initiative and as a member of the advisory group for the AHRC-funded project to understand the role of British pharmacy in Empire-building. In September, Richert and former AIHP Director Gregory Higby will be traveling to the International Society for the History of Pharmacy meeting in Belgrade, Serbia to give out the George Urdang Medal.

Besides bringing in new personnel and trying to connect with broader audiences, the AIHP is in the midst of a gift giving campaign and membership renewal drive. The Institute has always carried out its mission to advance the history of pharmacy and medicines through the generosity its members, sponsors, and friends. In 2023, the gift giving campaign has focused exclusively on [protecting and bolstering our historical collections](#). I hope you can help.

Fourth, AIHP needs your support and advice. In an effort to grow the AIHP as well as live up to the long and strong tradition of pharmacy history in the United States, the organization will embark on a campaign to grow its membership and raise funds in 2024-2028. The aim is to develop a brighter future for the field and better connect pharmacy history with more people. Please stay in touch if you wish to be part of this effort.

Lucas Richert, PhD

Professor & George Urdang Chair in Pharmacy History, UW-Madison

*Executive Director, [American Institute of the History of Pharmacy](#)
[Transdisciplinary Center for Research on Psychoactive Substances](#)*

Editor at [Social History of Alc & Drugs](#) / [History of Pharmacy & Pharmaceuticals](#)



Clinical Pearl – Teaching the History of Pharmacy

STUDENT PHARMACISTS' ATTITUDES TOWARDS PREPARATION OF HERBAL HOME REMEDIES

**BY TRACEY L. MERSFELDER
FERRIS STATE UNIVERSITY**

Introduction:

Student pharmacists have limited exposure to herbal products in the pharmacy curriculum. While over 89% of student pharmacists report wanting more education in this area, only 34% of pharmacists reported receiving training in herbal supplements/natural products during their pharmacy education.¹ These results are similar to an earlier study where a majority of pharmacy programs reported inclusion of complementary/alternative medicine content in the curriculum, but most of the instruction is offered in elective courses.² With over 17% of patients in the United States reporting that they used an alternative medicine in 2012, there is a need for enhanced instruction in this area.³ In addition, the use of alternative medicines is expected to increase as the country continues to face unprecedented drug shortages.⁴ While the current literature focuses on the limited training student pharmacists receive regarding the use of herbal remedies and alternative therapies, none mention education on preparing herbal remedies as was done before modern manufacturing advancements.

Objective:

The purposes of this study were to determine if students participating in an activity that required them to provide detailed instructions for making herbal home remedies changed their views of patients taking home remedies and if they gained knowledge required for making medicinal products from plants.

Methods:

Student pharmacists who were enrolled in the history of pharmacy elective course at one college of pharmacy were included in this study. As part of the two-credit hour, on-line elective course, students were given an assignment on home herbal remedy preparation. The assignment was to select a plant that could be grown in the same state where the college of pharmacy was located and to research how to prepare the plant for medicinal use. Students were provided with a list of plants to select for the assignment, or they could choose their own. Examples of these plants included: elderberry, yarrow, violet, rosemary, and oregano. Students were required to list the specific steps needed to prepare the herbal remedy and create a YouTube video that highlighted their product for the class to view. The preparation was determined by the student; however, a few examples were provided on the grading rubric.

It was not required for the students to prepare the product due to the uncertain availability of obtaining the herb. A quiz based on the information in the video clip was developed by the instructor. A grading rubric/table was developed for the assignment that detailed how the students would be graded on their submission. After completing the project, students were administered an 11-question rating survey with one open-ended question regarding their impression of the assignment. Many of the questions were before and after assignment statements focusing on knowledge, comfort and attitude regarding plant based herbal remedies including:

- How knowledgeable were you before/after the herbal/plant activity regarding medicinal use of plants that can be grown in this state? (Very-4, Somewhat-3, Not very-2, No knowledge-1)
- How comfortable were you before/after the herbal/plant activity regarding the process of making plant into a product? (Very-4, Somewhat-3, Not very-2, No comfort-1)
- What was your attitude to-

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Herbal Remedies . . .

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wards people that make their own herbal remedies before/after the herbal/plant activity? (Fully support-4, Support-3, Do not support-2, Against-1)

- Before/After this herbal/plant activity, would you ever recommend any of the herbal remedies we covered? (Yes, and I have, Yes, I would, No, I would not, No, and I would recommend against it)

Mean scores or percentages were calculated for responses. Wilcoxon signed-rank test was used to compare paired scores and McNemar's chi-square test for paired frequency responses. Analysis was done using Stata 18, StataCorp LLC, College Station, Texas 77845. This study was classified by the Institutional Review Board as exempt.

Results:

A total of 30 students were enrolled in the history of pharmacy elective course. After completing the assignment, 37% of the student pharmacists thought that there may be a time when pharmacists will again be more involved with making herbal remedies for patient care. The majority (77%) of student pharmacists were inspired to grow the plants that were used to make their herbal remedies. All but one student (3%) felt that this assignment should remain as an activity for this elective. The free text responses were mainly positive regarding the assignment. The student pharmacists stated that they liked learning about the herbal remedies and plants and having the ability for freedom in their learning. Some did not like using YouTube for creating their video and would like to write their own quiz questions. Two examples of the YouTube video are as follows: https://youtu.be/a_Q39OLV7cU and <https://www.youtube.com/watch?v=Lj9HBnRAvyQ>.

Students self-rating of knowledge about, comfort with preparing, and attitude toward people's use of herbal products improved following the activity as compared to prior ($p < 0.001$, see Table 1). In addition, the percent of student who would make recommendations regarding herbal remedies also increased ($p = 0.0005$, see Table 1).

Table 1: Student pharmacist responses before and after herbal activity			
	Time Period		
	Before activity	After activity	p-value*
	(N=30)	(N=30)	
Knowledgeable (4-Very to 1-None) Mean (SD)	1.83 (0.75)	3.43 (0.57)	<0.0001
Comfortable (4-Very to 1-None) Mean (SD)	1.63 (0.85)	3.20 (0.55)	<0.0001
Attitude (4-Fully Support to 1-Against) Mean (SD)	2.67 (0.71)	3.07 (0.58)	0.0005
Recommend			
No, I would not, or I would recommend against	21 (70.0%)	9 (30.0%)	0.0005
Yes, and I have previously or would in future	9 (30.0%)	21 (70.0%)	

* Knowledge, Comfortable and Attitude from Wilcoxon signed-rank test, Recommend from McNemar's chi-square test.

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HISTORY OF DEXTROMETHORPHAN

BY SABRINA ZHENG, JEFFRY W. DU, HARRY S. PATEL, AND JANE E. KRAUSE

Discovery of Dextromethorphan and its Mechanism of Action

Dextromethorphan (3-methoxy-N-methylmorphinan), also known as DXM, is a synthetically produced cough suppressant (antitussive) currently found in more than 120 over-the-counter cough and cold medications, either alone or in combination with other agents such as analgesics, antihistamines, decongestants, and/or expectorants.^{1,2,3} In November 1949, Hoffmann-La Roche Inc., a Swiss pharmaceutical company, applied for a patent on dextromethorphan, a synthetic analog of codeine.^{4,5} This discovery was a result of research focused on modifying the chemical structure of opioids (e.g., codeine) to create a cough suppressant that retained the antitussive properties of opioids but with fewer adverse effects (e.g., drowsiness) including a reduced abuse potential.⁶ Dextromethorphan was patented in April 1954 and was approved by the United States Food and Drug Administration (FDA) as an over-the-counter antitussive in 1958.^{5,7} Dextromethorphan is not a controlled substance and is not a regulated chemical under the Controlled Substances Act.²

During the 1960s and 1970s, dextromethorphan became available in an over-the-counter tablet form (10 mg/tab) and syrup form (10 mg/4 ml) by the brand name, RomilarTM (Figure 1).^{5,8} RomilarTM was introduced as a replacement for cough medications containing codeine in an effort to decrease abuse.⁵ However, in 1973, RomilarTM was removed from the market after an increase of recreational use of dextromethorphan was noted. In



Figure 1: RomilarTM advertisement sent by direct mail to physicians.⁸

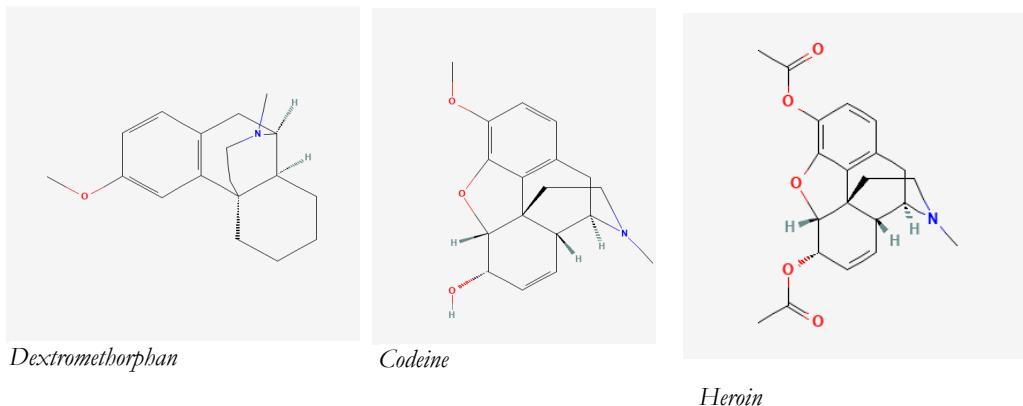
1977, cough syrups containing dextromethorphan with an unpleasant taste were introduced; however, the same manufacturers soon began producing cough syrups with a better flavor. Internet access during the 1990s allowed users to rapidly disseminate information about dextromethorphan causing online discussion groups to form around using and acquiring dextromethorphan.⁹ As early as 1996, dextromethorphan hydrobromide powder could be purchased in bulk from online retailers, allowing users to avoid consuming dextromethorphan in syrup preparations.⁹

Despite being structurally similar to opioids (Figure 2), dextromethorphan acts through a different mechanism that effectively suppresses cough and reduces analgesia and addiction potential.⁶ Unlike opioids, dextromethorphan does not act through mu-opioid receptors in the brain. At therapeutic doses, dextromethorphan

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Figure 2: Chemical Structures of Dextromethorphan, Codeine, and Heroin^{10,11,12}



interacts with various receptors in the central nervous system, such as N-methyl-D-aspartate (NMDA) receptors and sigma-1 receptors in the medullary cough center.¹³ Dextromethorphan and its metabolite, dextrorphan, function as a non-competitive antagonist at NMDA receptors.¹⁴ By blocking NMDA receptors, dextromethorphan reduces the transmission of pain signals in the brain.¹⁵ Dextromethorphan also acts as a sigma-1 receptor agonist, influencing calcium signaling, neurotransmitter release, and neuronal excitability.¹⁶ The effects on sigma-1 receptors can affect mood, cognition, and other neurological functions. Activation of the sigma-1 receptor is responsible for dextromethorphan's antitussive effects and potential antidepressant action.⁶

Following oral administration, dextromethorphan is rapidly absorbed from the gastrointestinal tract, where it enters the bloodstream and crosses the blood-brain barrier.¹⁷ Dextromethorphan is converted into the active metabolite, dextrorphan, in the liver by the cytochrome P450 enzyme CYP2D6.⁷ The usual adult dose necessary for effective antitussive therapy (immediate release formulation) is 10-30 mg every 4 hours.^{7,17} Dextromethorphan has a median half-life of approximately 2.4 hours in individuals with an extensive metabolizer phenotype (majority of the population); this is increased to approximately 13 hours when dextromethorphan is given in combination with quinidine.⁷

Earlier Cough Suppressants

Before the introduction of dextromethorphan, other substances, including codeine, heroin, and diphenhydramine were used for their cough suppressant properties, each with their own set of advantages and limitations.^{18,19,20,21,22} For example, codeine, an opioid alkaloid derivative from opium, was discovered in 1832 by a French chemist named Pierre Jean Robiquet.^{18,23} At the time of introduction, codeine was considered the safest of all opiate analgesics which led to its use as a cough suppressant.²³ Although it was effective in suppressing cough, it also carried the high

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risk of dependence, respiratory depression, and other opioid-related side effects.²⁴ Increasing concerns of dependence and respiratory depression have made codeine a prescription-only drug.²⁵

Heroin was used as a cough suppressant during the late 19th to early 20th centuries.²⁰ Heroin, a synthetic opioid, was originally synthesized in 1874 by Charles Romley Alder Wright for Bayer Pharmaceuticals, and was marketed as a cough suppressant and pain reliever.^{19,20} At the time of discovery, opioids and their addictive properties were not yet fully researched and evaluated, thus heroin was believed to be a safer alternative to morphine.²⁶ However, it was soon learned that heroin was a dangerous drug and after the 1920s, strict regulations on the production and consumption of heroin occurred.²⁰ The Controlled Substance Act classifies heroin as a Schedule 1 controlled substance, making the drug inappropriate for any medical purpose.²⁷

Another commonly used cough suppressant before the introduction of dextromethorphan was diphenhydramine.²² Diphenhydramine was discovered in 1943 by George Rieveschl, a former professor at the University of Cincinnati and in 1946, it became the first prescription antihistamine approved by the FDA.²⁸ Diphenhydramine works by acting as an inverse agonist at the Histamine 1 (H1) receptor. In addition, diphenhydramine also readily crosses the blood-brain barrier and acts on the H1 central nervous system receptors directly resulting in drowsiness and suppression of the cough center. However, the efficacy of the drug in suppressing cough is still not well evaluated.²¹ Not only is the cough suppressant effect not well studied but diphenhydramine also has side effects such as drowsiness, dry mouth, central nervous system depression and significant drug interactions.²²

Misuse of Dextromethorphan

At usual doses, dextromethorphan is considered safe and effective; however, when misused, dextromethorphan can result in dose-related symptoms, ranging from mild stimulation to depersonalization, hallucinations, and loss of motor coordination.³ Reported cases of dextromethorphan abuse to poison control centers more than doubled nationwide between 2000 and 2003 (from 1623 to 3271).⁴ The vast majority of dextromethorphan abusers are teenagers or young adults who obtain the drug by buying it in over-the-counter medications. It is believed that the availability of dextromethorphan makes it an easy choice for drug abuse among teenagers who might feel uncomfortable buying illegal drugs. The increase of dextromethorphan abuse among teenagers sparked parent groups, legislators, and pharmacies to become active. For example, some national chain pharmacies have programmed their computer scanners to ask for an age identification before selling dextromethorphan products.⁴ Others restrict the number of packages a patient can buy.⁴ While other pharmacies have moved these medications from the main aisles into the pharmacy area, where the sale of these medications can be better monitored.⁴ By September 2004, several states were considering legislation that would prohibit anyone under the age of 18 from buying products containing dextromethorphan.⁴

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The DEA warns that high doses of dextromethorphan, particularly when used with alcohol or anti-depressants, can be deadly.³ The National Institute on Drug Abuse reports that long-term use can result in addiction (dextromethorphan use disorder). Street names for dextromethorphan include “triple C”, “skittles”, and “robo-tripping”.⁴ Long-term abuse of dextromethorphan is associated with psychological dependence.²⁹ The effects of dextromethorphan misuse are described in terms of dose-dependent “plateaus” (Table 1).² Most dextromethorphan abusers ingest the drug orally, although some snort the pure powdered form of the drug.²⁹ Treatment of acute dextromethorphan intoxication is mainly supportive.³⁰ The primary goal of acute management is control of agitation and psychotic symptoms with supportive psychological treatment. Short-acting benzodiazepines or low-dose antipsychotics have been suggested to be effective in published case reports.

Consumer Healthcare Products Association (CHPA)

In 2003, CHPA began to develop educational interventions against the abuse of dextromethorphan and in 2006, a question regarding the use of dextromethorphan first appeared in the Monitoring the Future survey for 8th, 10th, and 12th graders.^{30,31} In 2010, the DEA requested that the FDA evaluate whether dextromethorphan should be recommended for scheduling under the Controlled Substances Act. In September of that year (2010), the FDA opposed regulating it

**Table 1:
Dextromethorphan Dose Dependent “Plateaus”²**

Dose (mg)	Behavioral Effects
100 - 200	Mild stimulation
200 - 400	Euphoria and hallucinations
300 - 1500	Distorted visual perceptions Loss of motor coordination Out of body sensations

under the Controlled Substances Act and voted against requiring a prescription for dextromethorphan.³² It was decided that dextromethorphan should remain accessible to patients over-the-counter as controlled substance scheduling or prescription requirements would result in a reduction in the legitimate use of the drug. At this same time, CHPA formalized its abuse interventions through the development of an abuse mitigation plan with participation from over-the-counter companies in collaboration with misuse prevention experts. In identifying interventions, experts suggested to address key factors leading to abuse among teenagers, including low parental awareness, low teenager perception of risk, low perception of social disapproval, and ready availability. Digital and social media-based prevention initiatives targeting teenagers searching online for information on how to abuse dextromethorphan or chatting about abuse were launched.³³

Elements of the campaign included a website (whatisdxm.com), a mobile application (DXM Labworks), YouTube videos, and public service announcements.

Since 2006, annual prevalence of dextromethorphan abuse has decreased and during the period of 2010 –2015, reported abuse of dextromethorphan decreased by 35% (Table 2).^{31,34} It is believed that increased awareness of the issue

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Table 2: Prevalence of Abuse: Monitoring The Future (%) ^{31,34}										
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
8 th graders	4.2	4.0	3.6	3.8	3.2	2.7	3.0	2.9	2.0	1.6
10 th graders	5.3	5.4	5.3	6.0	5.1	5.5	4.7	4.3	3.7	3.3
12 th graders	6.9	5.8	5.5	5.9	6.6	5.3	5.6	5.0	4.1	4.6
Average	5.4	5.0	4.7	5.2	4.8	4.4	4.4	4.0	3.2	3.1

and the implementation of a targeted abuse mitigation plan contributed to the reduction in misuse.^{30,31} CHPA hopes this example of reducing substance abuse can provide learnings on effective approaches to help prevent substance abuse, especially with teenagers, in the future.³¹

Recent Dextromethorphan Indications

In 2010, the FDA approved the combination drug dextromethorphan/quinidine under the brand name

NuedextaTM, for the treatment of Pseudobulbar Affect (PBA) or uncontrollable laughing and/or crying episodes.³⁵ Dextromethorphan is the therapeutic agent in the combination, while quinidine serves to inhibit the enzyme CYP2D6 degradation of dextromethorphan causing an increase in concentrations.³⁶

Dextromethorphan affects NMDA receptors and sigma-1 receptors in the brain, which have been implicated in the pathophysiology of depression.³⁷ In 2022, the FDA approved the combination drug dextromethorphan/bupropion under the brand name AuvelityTM, a rapid acting antidepressant for patients with major depressive disorder (MDD).^{37,38} With this medication, bupropion, a CYP2D6 inhibitor, increases and prolongs plasma concentrations of dextromethorphan.

Epilogue

Today, dextromethorphan is one of the ten most commonly used over-the-counter medicines worldwide.³⁹ To continue to help prevent abuse of the drug, parents can

monitor over-the-counter medications containing dextromethorphan in the household.⁴⁰ In addition, parents and healthcare providers can be alert to physiological symptoms and/or behavioral changes in individuals, especially teenagers, that could indicate misuse and provide education on consequences of dextromethorphan misuse. Pharmacists can store over-the-counter products containing dextromethorphan in such a way to help discourage shoplifting and monitor inventory of dextromethorphan-containing products.

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References

1. Martinak B, Bolis RA, Black JR, Fargason RE, Birur B. Dextromethorphan in cough syrup: The poor man's psychosis. *Psychopharmacol Bull*. 2017 Sep 15;47(4):59-63. PMID: 28936010; PMCID: PMC5601090.
2. Department of Justice/Drug Enforcement Administration. DXM Drug Fact Sheet. Available at: <https://www.dea.gov/sites/default/files/2023-03/DXM%202022%20Drug%20Fact%20Sheet.pdf>. 2022 Oct; Accessed February 2024.
3. Kverno K. Dextromethorphan: From cough suppressant to antidepressant. *J Psychosoc Nurs Ment Health Serv*. 2022 Nov;60(11):9-11. doi: 10.3928/02793695-20221005-02. Epub 2022 Nov 1. PMID: 36317836.
4. Dextromethorphan. UXL Encyclopedia of Drugs and Addictive Substances. *Encyclopedia.com*. Available at: <https://www.encyclopedia.com>. Accessed February 2024.
5. ScienceDirect. The Vaults of EROWID. DXM Timeline. Available at: https://erowid.org/chemicals/dxm/dxm_timeline.php. Accessed February 2024.
6. Beard D. Dextromethorphan (DXM) guide: Effects, uses, legality, and safety. Reality Sandwich. April 6, 2021. <https://realitysandwich.com/dextromethorphan-dxm-guide-effects-uses-legality-and-safety/>. Accessed May 2023.
7. Oh S, Agrawal S, Sabir S, Taylor A. Dextromethorphan. 2022 May 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 30855804.
8. American Institute of the History of Pharmacy (AIHP). Romilar. Available at: <https://aihp.omeka.net/items/show/931>. Accessed February 2024.
9. Morris H. and Wallach J. From PCP to MXE: a comprehensive review of the non-medical use of dissociative drugs. *Drug Test. Analysis* 2014; 6: 614-632. <https://doi.org/10.1002/dta.1620>.
10. National Library of Medicine. Compound Summary. Dextromethorphan. Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/Dextromethorphan#section=Structures>. Accessed May 2023.
11. National Library of Medicine. Compound Summary. Codeine. Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/Codeine#section=Structures>. Accessed May 2023.
12. National Library of Medicine. Compound Summary. Heroin. Available at: <https://pubchem.ncbi.nlm.nih.gov/compound/Heroin#section=Structures>. Accessed April 2024.
13. Keam SJ. Dextromethorphan/Bupropion: First approval. *CNS Drugs*. 2022 Nov;36(11):1229-1238. doi: 10.1007/s40263-022-00968-4. PMID: 36301443
14. Wong EH, Kemp JA, Priestley T, et al. The antitussive action of dextromethorphan; a review. *Pulm Pharmacol*. 1993;6(3):189-207. doi:10.1006/pulp.1993.1022.
15. Zhou HY, Chen SR, Pan HL. Targeting N-methyl-D-aspartate receptors for treatment of neuropathic pain. *Expert Rev Clin Pharmacol*. 2011 May;4(3):379-88. doi: 10.1586/ecp.11.17. PMID: 21686074; PMCID: PMC3113704.
16. Su TP, Hayashi T, Maurice T, Buch S, Ruoho AE. The sigma-1 receptor chaperone as an inter-organelle signaling modulator. *Trends Pharmacol Sci*. 2010 Dec;31(12):557-66. doi: 10.1016/j.tips.2010.08.007. Epub 2010 Oct 1. PMID: 20869780; PMCID: PMC2993063.
17. Drugs.com. Dextromethorphan. Available at: <https://www.drugs.com/dextromethorphan.html>. Accessed February 2024.
18. Vora A, Nadkar MY. Codeine: A relook at the old antitussive. *J Assoc Physicians India*. 2015;63(4):80-85.
19. Woolf CR, Rosenberg A. The cough suppressant effect of heroin and codeine: a controlled clinical study. *Can Med Assoc J*. 1962;86(18):810-812.
20. From cough medicine to deadly addiction, a century of heroin and drug-abuse policy. Yale School of Medicine.

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Available at: <https://medicine.yale.edu/news/yale-medicine-magazine/article/from-cough-medicine-to-deadly-addiction-a-century/>. Accessed May 2023.

21. Björnsdóttir I, Einarsdóttir TR, Gudmundsson LS, Einarsdóttir RA. Efficacy of diphenhydramine against cough in humans: a review. *Pharm World Sci.* 2007;29(6):577-583. doi:10.1007/s11096-007-9122-2.

22. Sicari V, Zabbo CP. Diphenhydramine - StatPearls - NCBI Bookshelf. Diphenhydramine - StatPearls - NCBI Bookshelf. Published July 11, 2022. Accessed May 2023.

23. History of Codeine. Narconon International. Available at: <https://www.narconon.org/drug-information/codeine-history.html>. Accessed May 2023.

24. Codeine | drug. Encyclopedia Britannica. Available at: <https://www.britannica.com/science/codeine>. Accessed May 2023.

25. Better Medicine. Codeine reclassified as a prescription-only medicine: a community pharmacy perspective. Available at: <https://bpac.org.nz/2020/codeine-rx.aspx>. Accessed February 2024.

26. Jones MR, Viswanath O, Peck J, Kaye AD, Gill JS, Simopoulos TT. A Brief History of the Opioid Epidemic and Strategies for Pain Medicine. *Pain Ther.* 2018;7(1):13-21. doi:10.1007/s40122-018-0097-6.

27. Ortiz NR, Preuss CV. Controlled Substance Act - StatPearls - NCBI Bookshelf. Controlled Substance Act - StatPearls - NCBI Bookshelf. Published September 21, 2022.

28. UC News. George Rieveschl, Inventor

of Benadryl, Dies. September 27, 2007. Available at: <https://www.uc.edu/news/articles/legacy/healthnews/2007/09/george-riebeschl-inventor-of-benadryl-dies.html>. Accessed April 2024.

29. US Department of Justice. Intelligence Bulletin. DXM (Dextromethorphan). October 2004. Available at: <https://www.justice.gov/archive/ndic/pubs11/11563/11563p.pdf>. Accessed February 2024.

30. Stanciu CN, Penders TM, Rouse EM. Recreational use of dextromethorphan, "Robotripping"-A brief review. *Am J Addict.* 2016 Aug;25(5):374-7. doi: 10.1111/ajad.12389. Epub 2016 Jun 11. PMID: 27288091.

31. Spangler DC, Loyd CM, Skor EE. Dextromethorphan: a case study on addressing abuse of a safe and effective drug. *Subst Abuse Treat Prev Policy.* 2016 Jun 23;11(1):22. doi: 10.1186/s13011-016-0067-0. PMID: 27333886; PMCID: PMC4918034.

32. ABC News. Over-the-Counter Cough Medicines Escape FDA Restrictions. Available at: <https://abcnews.go.com/Health/Wellness/dextromethorphan-ingredient-robutussin-cough-medicines-escapes-fda-restrictions/story?id=11638160#:~:text=%22Today's%20FDA%20advisory%20committee%20decision,group%20said%20in%20a%20statement>. Published September 14, 2010. Accessed April 2024.

33. Consumer Healthcare Products Association (CHPA). Preventing Dextromethorphan Abuse. Available at: <https://www.chpa.org/about-consumer-healthcare/activities-initiatives/preventing-dextromethorphan-abuse>. Accessed April 2024.

34. Miech RA, Johnston LD, Patrick ME, O'Malley PM, & Bachman JG. (2023). Monitoring the Future national survey results on drug use, 1975–2023: Secondary school students. Monitoring the Future Monograph Series 2023. Ann Arbor, MI: Institute for Social Research, University of Michigan. Available at: <https://monitoringthefuture.org/results/annual-reports/>. Accessed February 20.

35. Otsuka America Pharmaceutical, Inc. Nuedexta. Available at: <https://www.nuedexta.com/>. Accessed February 2024.

36. Horn JR, Hansten PD. Get to know an Enzyme: CYP2D6. *Pharmacy Times.* Available at: <https://www.pharmacytimes.com/view/2008-07-8624>. Accessed February 2024.

37. Middleton J. Meet the newest antidepressant: dextromethorphan/bupropion (Auvelity). *American Family Physician.* Available at: <https://www.aafp.org/pubs/afp/afp-community-blog/entry/meet-the-newest-antidepressant-dextromethorphan-bupropion-Auvelity.html#:~:text=While%20the%20combination%20of%20the,blood%20levels%20to%20allow%20for>. Accessed February 2024.

38. Axsome. Auvelity. Available at: <https://www.auvelity.com/?gclid=EAJaIQobChMLe2A08LthA>

Dextromethorphan...

Continued from page 13

[MV8F1HAR3YWA7IEAYASAAEgKqjfD_BwE&gclsrc=aw.ds](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8811313/). Accessed February 2024.

39. Jacob D. RxList. Over-The-Counter (OTC) Medicines. Available at: https://www.rxlist.com/over-the-counter_otc_medicines/drugs-condition.htm. Accessed April 2024.

40. University at Buffalo. DXM (Cough Suppressant) Abuse. Clinical Research Institute on Addictions. Available at: https://www.buffalo.edu/cria/news_events/es/es7.html. Accessed April 2024.

Herbal Remedies...

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Discussion:

Overall, this activity received positive responses about herbal remedy education from the student pharmacists involved in this elective course. This is similar to an earlier study where the majority of student pharmacists reported wanting to learn more about herbal products.¹ Current pharmacy curricula may touch upon herbal products in over-the-counter medicine courses or alternative medicine elective courses, but these classes generally do not discuss the history of and processes for how herbal remedies were made.

This assignment increased the student pharmacists' knowledge, comfort, and attitude about medicinal plants and the process for making herbal remedies. In addition, the student pharmacists reported being open to individuals who choose to grow and make their own herbal remedies and may even recommend some of them as a result of this assignment. This positive change is supported by two previous studies where students in a required course on complementary and alternative medicine experienced changes in their attitudes.^{5,6}

One limitation of this study is that the student pharmacists were required to watch the Victorian Town Pharmacy BBC documentary series and complete an assignment using the Natural Medicines database to research herbal products used in the late 1800's. This may have influenced the results regarding the acceptance of using plant based medicinal products. No structured research was assigned on how to prepare the products selected by the students. Second, the structure of the elective administered online could have an impact on the results and how other programs may adopt the assignment. A third limitation is that this assignment was administered to students who selected a history of pharmacy elective. Results of this assignment should be generalized with caution to all pharmacy students. Lastly, the survey was administered only at the end of the assignment. This may have affected recall regarding their knowledge, skills, and attitudes prior to this activity.

Conclusion:

Through completion of this assignment in a history of pharmacy elective course, student pharmacists learned about plants and how to process them into herbal remedies. They gained some openness regarding those who grow and process their own remedies and reported being more willing to recommend them. The majority of the student pharmacists recommended continuing this assignment for the history of pharmacy elective course.

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References:

1. Stayduhar JM, Covvey JR, Schreiber JB, Witt-Enderby PA. Pharmacists and student knowledge and perceptions of herbal supplements and natural products. *Pharmacy*. 2023;11:96. doi:10/3390/pharmacy11030096.
2. Shields KM, McQueen CE, Bryant PJ. Natural product education in schools of pharmacy in the United States. *Am J Pharm Educ*. 2003;67:Article 10.
3. Clark TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002-2012. *Nation Health Statistics Reports*. 2015;79:1-15.
4. ASHP Drug Shortages Statistics. <https://www.ashp.org/drug-shortages/shortage-resources/drug-shortages-statistics?loginreturnUrl=SSOCHECKONLY>. Accessed December 13, 2023.
5. Evans E, Evans J. Changes in pharmacy students' attitudes and perceptions toward complementary and alternative medicine after completion of a required course. *Am J Pharm Educ*. 2006;70(5):Article 105. doi:10.5688/aj7005105.
6. Steenfeldt L, Hughes J. An evidence-based course in complementary medicines. *Am J Pharm Educ*. 2012;76(10):Article 200. doi:10.5688/ajpe7610200.



New Book Announcement!

We Remember Them: Pharmacy's Fallen Second Edition

2024

By Dennis Worthen, PhD

Dennis Worthen has spent decades identifying the pharmacists who died in World War II while serving in the military so as to tell their stories. The result was: *We Remember Them: Pharmacy's Fallen* in 2022. There is now a second edition, published this year that has filled in some gaps from the first edition and made a more complete record of 172 pharmacists.

The book is primarily a short biography of all of the pharmacists identified who lost their lives in service during World War II. It also includes a discussion of the environment of the times, numerous summary tables and explanatory material to help the reader navigate terminology.

You can find the book posted at the AIHP website at <https://aihp.org/wp-content/uploads/2024/04/Worthen-We-Remember-Pharmacy-Fallen-2e-print-2024-0227.pdf>

Pharmacy Chronicles

About the History of Pharmacy SIG

The academic year (2022 – 2023) marks the fifteenth year since the History of Pharmacy Special Interest Group (SIG) was formalized as an AACP SIG.

As an open academic forum, the SIG strives to facilitate the exchange of ideas and innovation among pharmacy faculty across disciplines; to serve broadly as an accurate information resource for teaching, learning, and scholarship pertaining to the evolution and history of the pharmacy profession; to develop and maintain historical collections of artifacts and school or college museums; and to ensure the lessons, the message, and the legacy of the pharmacy profession is preserved to educate future generations of pharmacy students.

The SIG's mission rests on the premise that the history and legacy of the pharmacy profession will always be relevant to all pharmacy practice areas, including current and future scopes of practice. The History of Pharmacy SIG is relevant to you too! Join the History of Pharmacy SIG!!

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