Contemporary concepts in toxicology: a novel multi-instructor general education course to enhance green chemistry and biomedical curricula

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ABSTRACT
An undergraduate course in contemporary toxicology was developed by the Chemistry Department at Grand Valley State University (GVSU) with assistance and participation from the Dow Chemical Company Toxicology and Environment Research and Consulting department (DOW-TERC). It was designed as an overview of xenobiotic effects on human health and environment and focuses on new predictive approaches used early in sustainable product development. Planned as a hybrid, administrated by GVSU, with lectures by both GVSU and DOW-TERC scientists, the course included classical elements of dose/response, absorption, distribution, metabolism, excretion, and newer advances in predictive toxicology, bioprofiling, databases, and product stewardship. Student performance assessments on a series of scaffolded case study, journaling, and exams, indicated their emerging ability to think critically and to apply their growing toxicology knowledge in solving problems. Opinion surveys indicate students’ positive responsiveness to the multi-instructor format. This course can serve as a model for programs at other institutions.

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1. Introduction
There is increasing interest in the effects of both man-made and natural compounds on human health, and environmental quality. Over 100,000 compounds are in global circulation (1) and 700+ chemicals are introduced each year to the US market (2). One of the current global sustainability challenges is the design of compounds and applications with low risk and low environmental impact. Toxicology is a multidisciplinary science that combines chemistry, biology, physiology, informatics, and others
to determine whether substances we are exposed to can cause harmful health effects. Without an understanding of the basic principles of toxicology, one cannot make informed decisions about the benefits and risks associated with chemicals used in current and future products. As early as 1972 (3), toxicologists were looking for ways in which students might become more aware of xenobiotic-biological interactions, and therefore, became prepared to make informed judgments about chemicals. Toxicology is usually taught at the graduate level, however, programs in undergraduate education (4) are rare. Recognizing this need, the Society of Toxicology (SOT) recommended undergraduate and community college curricula to be considered as important venues for the development of toxicology education coursework. The newest guidelines from the American Chemical Society-Committee for Professional Training (ACS-CPT) for green chemistry inclusion in the curriculum (March 2018) speak of green chemistry as leveraging chemists’ ability to design new beneficial/sustainable substances (xenobiotics) while accounting for their interconnectedness with local and global systems. Guidelines include a series of conceptual topics stating the need for toxicology inclusion in chemical education. SOT is actively supporting ACS Green Chemistry Institute (ACS-GCI) efforts to promote educational activities that incorporate toxicology principles into the chemical design process. Rational design of new products should be based on the close relationships between molecular structure and predicted properties such as metabolism, rates of chemical or biodegradation, and their fate in the environment (5). A fundamental responsibility of chemists is to synthesize safe compounds utilizing available knowledge, including computational tools, and interacting with toxicologists in the very early stages of the design process. To fully integrate these critical parameters, a team approach is needed where chemists work side-by-side with toxicologists, life cycle assessment experts, and process designers.

Chemistry departments across the country have responded to this educational challenge by introducing elements of toxicology in existing chemistry courses and laboratories. There are few available models for stand-alone toxicology courses in undergraduate chemistry education, such as at Simmons College, South Dakota State University, and Wittenberg University (6). In concert with SOT and ACS-GCI, several other universities, green chemistry centers, and other organizations, have joined in the effort of producing educational materials the community so urgently needs. (7) However, among chemistry faculty, there are rarely experts in the topic and problems associated with the lack of training in teaching a new subject can be challenging. The main issue still remains: toxicology is rarely offered as a part of chemistry or general science curricula.

GVSU proposes a model that is both sustainable, capable of coordination by faculty with varying expertise, and adaptive to remain relevant in a changing knowledge environment. This course was envisioned as an overview of contemporary toxicology concepts and is designed for students to connect the relevance of the science with their individual lives and the world. It focuses on the practical application of toxicology to relevant case studies of common compounds and materials, assessments, mechanisms, health effects, and strategies to reduce risk and exposure in everyday life. Models of applied toxicology introduce students to current modalities to protect human health through safety evaluation. GVSU was one of the first signing institutions of the Green Chemistry Commitment (GCC), which is a promise to provide opportunities for students to learn the principles of green chemistry including the basics of toxicology and the ability to apply these principles in their professional and personal lives. This course complements the Chemistry Department’s set of classes that cover green chemistry (5) by providing the necessary background in toxicology and the application competencies required by the GCC student learning objectives (SLO). The course was designed and prepared as a collaboration between GVSU professors Dalila Kovacs (GVSU-Chemistry) and Richard Rediske (GVSU-AWRI) and the DOW Toxicology and Environment Research and Consulting (TERC) team, led initially by Dr. Pam Spencer (currently at Angus Chemical Company) and completed under Dr. Sue Marty’s (DOW-TERC) leadership. This unique academia-industry collaboration brings experienced professionals in the classroom to interact directly with students and to present specific toxicology topics.

Inviting guest speakers with expertise in specific areas is a common practice, often encouraged and well received by audiences; however, it can be ineffective and sometimes, counterproductive for the students’ emotional comfort and ability to relate to the instructors (7). Using a multi-instructor pedagogical approach is challenging and there is a paucity of literature available to assist us in this area (8). We envisioned a GVSU instructor, with overall administration responsibilities, as the lead for course delivery and he/she would introduce students to the course, cover green chemistry principles, and the basic concepts of toxicology. The rest of the course would be presented by experts from the Dow-TERC team, supported by GVSU professors. Once the course was underway, a paper published by a Harvard group (9) discussed the advantages of guest-speaker format in a graduate chemistry
course. The authors found that themed guest lecturing yielded “tremendous benefits” and brought “significant value” to the process of achieving the course learning goals.

2. Course design

Contemporary Concepts in Toxicology is designed to provide a multidisciplinary overview of the toxic effects of xenobiotics on human health and environment, the role of public policies and their perception, and the development of safe and sustainable products through chemical design. It focuses on assessment methods, mechanisms, properties, health effects, and strategies to reduce risk and exposure in everyday life, across diverse societal groups.

2.1. General education program at GVSU

The course is offered in the General Education Program under the Health Issues theme, to attract Chemistry students and those majoring in Biochemistry, Biomedical Science, Biology, Allied Health, Nursing, Industrial Hygiene, and Environmental Studies. The course benefits science majors as it does not conflict with required or elective courses in any major. We selected collaboration, problem solving, and integration of knowledge for the students learning outcomes included in the General Education Program at GVSU. For collaboration, we assigned mixed work groups, containing different majors, to reflect the multidisciplinary nature of toxicology. The problem solving objective focused on addressing open-ended questions with multiple approaches possible, while knowledge integration required synthesis and application of information, experiences, and multiple perspectives in order to analyze new and complex situations. The syllabus was a collaborative effort between GVSU and DOW-TERC (supplement). Topics included: introduction to green chemistry and toxicology, hazard & risk, toxicokinetics, genetic toxicology, carcinogens, ecotoxicology, developmental and reproductive toxicology, risk and exposure, organophosphates, in-vitro and bioprofiling methods, Life Cycle Assessments (LCA), heavy metals, Flint water crisis, and others.

2.2. Hybrid format

A hybrid format was selected to foster the access to readily available, peer-reviewed, and validated education materials and to provide experiential learning opportunities in which students gain familiarity with accessing and evaluating information from worldwide databases. Such a format enables collaboration between faculty, professionals in government and industry, and students irrespective of time, classroom, and financial constraints. GVSU and DOW-TERC worked together to produce teaching materials, case studies, suggestions for student projects, and exam questions. All classes were videotaped and synched with PowerPoint slides for posting on the course management system site (Blackboard). DOW-TERC also provided biographical and contact information to encourage communication outside of the classroom. A site visit to the DOW-TERC laboratories served as a culminating experience and a networking opportunity for future research projects. While the specialists from Dow-TERC will continue to remain available for future collaboration, other professional collaborations may be added as needed.

3. Results and discussion

3.1. Course offering

Fourteen students were enrolled in the initial cohort during the winter 2018 semester: 5 chemistry majors, 4 biomedical sciences, 4 microbiology, and 1 anthropology. In an introductory class survey, the students commented their interest in the main topic of toxicology and mentioned that enrolling in the course was driven by the consideration of the perceived advantage of receiving general education credit for a science-oriented course that did not conflict with requirements for their majors. Interest was raised by state-wide issues, such as the Flint water crisis (11) and the contamination of local aquifers with per- and polyfluoroalkyl substances (PFAs).7 The only prerequisite was one semester of chemistry and it was recognized that life science majors would have a better understanding of physiology while chemistry majors a stronger background in molecular structure and reactions. To mimic the real-life practice, we aimed to have students work on projects in multidisciplinary groups and learn to use information from complementary disciplines, a practice that mimics R&D teams in which students may one day participate. We focused on knowledge-transfer by assigning case study papers and take home exams. A mid-semester survey, administered in class and completed by all fourteen students (Figure 1) indicated that none of them found the chemistry prerequisite a factor that made the course difficult. However, 60% of the students found their background in chemistry important in succeeding in this class. For 54% of the students, the offering of the class by the Chemistry Department and counting as General Education credit were the most important factors in deciding to enroll in the course.
At the end-of-semester, the standard GVSU Laker Impressions of Faculty Teaching (LIFT) survey, and Students Assessment of Learning Goals (SALG) were used. SALG asked students to assess their accomplishments in understanding the content, in improving their skills, attitudes, and learning abilities. Students also assessed how assignments, recommended resources, class organization and lecture information contributed to achieving both the course and their personal goals. A separate section of the survey examined how much the presence and instruction delivered by the Dow specialists affected student accomplishments in the class. The answering options were compiled using a rating scale with no gain, a little gain, moderate gain, much gain, great gain, and not applicable options for answers. The SALG instrument provides graphical presentations of data and its own statistical analyses.

From all data collected, we focus here on student perception regarding their content mastering, personal skills gain, and the pedagogical effect of guest speakers (additional data in supplemental).

### 3.2. Assessment of student work

Student progress was assessed using a series of scaffolded case studies, a journal critique, and two written exams. Students made weekly journal entries contemplating on class materials. The journals provide feedback and encourage student reflection and critical thinking.

The first case-study was assigned after completion of the introductory unit. Teams of three students, including

![Figure 1](image_url)

Figure 1. Decision factors in student enrollment, mid-semester survey: (a) how important was the designation as an “issue course” (general education upper level) within the Chemistry department? (b) how important/adequate is your previous chemistry background with respect to fully understanding the content of this course?

![Figure 2](image_url)

Figure 2. SALG survey results (%): students’ perception of the role of class activities in supporting their own learning.
majors in chemistry, biomedical science, and microbiology, were asked to assess ethyl acrylate using the European Chemicals Agency Registration, Evaluation, Authorization and Restriction of Chemicals (ECHA-REACH) database and write a five-page report. Each student was asked to make specific contributions related to their majors. The paper should provide a review of physical/chemical properties and health effects of ethyl acrylate, exposure pathways, and safety considerations. For the second case study, the same groups focused on perfluorooctanesulfonic acid (PFOA) and started with a lecture-based discussion about local groundwater contamination that has affected over 1000 residential drinking water wells (see note 7). Student assignments included searching REACH, and using EpiSuite (a suite of Estimation Programs Interface – EpiSuite – based on physical and chemical properties and environmental fate estimation, developed by EPA and Syracuse Research Corp., available from EPA website) for toxicological and environmental data. The C8 Panel probable link reports and the EPA document “Drinking Water Health Advisory for Perfluorooctanoic Acid (PFOA)” were assigned as readings. Students were specifically asked to evaluate the safety factors associated with the EPA guideline of 70 ng/L PFOA in drinking water and how they would explain the science to a homeowner with a contaminated well. For the final case study, students chose a compound of interest and prepared, initially, a 2-page project proposal for conducting their research. Topics included NOx air pollutants, thimerosal, sucralose, DEET, acrylamide, phthalates, and tetrodotoxin. Students worked individually on a 20-min PowerPoint presentation and a 10–15 pages report that explains toxicological issues, scientific evidence, data analysis, and their own conclusions. In-class group peer-review sessions allowed for comments and feedback. These group activities increased the learning value of the assignment and lead to high quality products. The presentations and papers were of excellent quality and demonstrated that students acquired the ability to discuss toxicology outside of the area of their academic major.

Student evaluations of these assessment methods (SALG) were positive, with the exception of journaling (Figure 2). Good and great gains in knowledge were reported from lectures, case studies, class discussion, and the visit to Dow. While journaling was a valuable instrument for instructor’s assessment of its own teaching performance, taking the actual time for weekly reflection was not valued by most student, despite the lead instructor’s effort to provide timely individual feedback. To encourage additional reflective learning opportunities, the use of Wikis (12) will be evaluated in the future.

The students were assigned a recent paper (in Lancet, 13) on health effects of low level lead exposure and asked to write a three-page critique including one page of policy recommendations related to water and lead paint exposure. The critique paper had the second lowest ranking as perceived gain; two students had difficulty with policy recommendations.

The exams were assigned outside of class-time, to be completed in one-week; students could use lecture notes, scientific literature, and web-based materials. They consisted of six essay-questions (mid-term exam in Supplemental) designed to focus students’ critical thinking, where lecture material would be applied to real-world scenarios. Sample questions included:

- Prepare a simplified Life Cycle Assessment for coal. Would coal be approved as a new fuel today?
- Gulf War Syndrome was attributed to a variety of causes including the storing of diet soft drinks at temperatures >30°C. Use risk assessment to determine if this claim is realistic.

While most students were able to answer these questions, some had difficulty responding to a topic that was not discussed in class such, as the thermal degradation of aspartame, or struggled with how much detail to include in their answers. For future course offerings, more detailed rubrics and study problems, where students can practice answering similar questions, will be included.

Exams also contained an essay question where students had to reflect on the course influence on their thinking (selected responses in Supplemental). All students expressed their desire to use the knowledge gained to guide future decision-making about consumer products and environmental issues. Student responded that exam questions and cases studies were valuable in expanding their knowledge base (Figure 3). They felt the feedback on journals and assignments was constructive, although the journaling was not highly rated. There were several comments in LIFT related to the class being excessively writing oriented. Written reflection and commenting on the class material are important parts of the class learning objectives and this methodology will continue to be emphasized throughout the semester.

3.3. Student self-assessments

3.3.1. Content

We asked students to rate how much they gained as a result of their work in this class with respect to main concepts, and the relationship among main concepts (Figure 4). A separate set of questions asked them to
evaluate their gain in specific toxicology content areas (Figure 5). A majority of students indicated good or great gain for main concepts and the correlation among them, as well as in specific topics. Students expressed the greatest gain from the Predictive Toxicology topic, presented based on the current approaches used by DOW-TERC for evaluating chemical safety, approaches not covered in textbooks, available only from reviewing primary literature. Journal responses also showed this topic was of interest to students across all majors.

3.3.2. Skills
Students were asked to comment on the type of skills they have gained as a result of this class (Figure 6). Responses highlighted awareness of existing resources and databases, and mentioned the helpful practice on case studies and the journal critiques as being important. Among the acquired skills, students indicated the following:

- the ability to talk about toxicology-related issues
- they were better equipped to understand and communicate issue related with chemicals' toxicity
- the capability to use physical properties to estimate toxicity of a given compound and search effectively for literature on chemicals of concern
- the understanding of complex concepts such as hazard, risk, and exposure, and their interplay in assessing toxicity, and
- how to use several modeling tools and what to consider in determining the hazard/risk and overall toxicity.

Figure 3. SALG survey results (%): students’ perception of graded activities in assisting their learning.

Figure 4. SALG survey results (%): students’ perception of their overall content knowledge gain (1).
We feel that multidisciplinary teaching team, scaffolded case studies, group work assignments, and use of peer review, all lead to gain in knowledge. Exam scores showed the students’ increasing ability, regardless their major, to use toxicological principles. The SALG survey captured also students’ suggestions for including even more practice with databases and software.

3.3.3. Learning directly from specialists

The specific instructional approach used in this course involved subject specialists who taught, provided specific reading materials, participated in discussions, and added personal stories about their career path and professional focus. Learning theory and pedagogy indicate both pros and cons regarding guest speakers (12, 13). Our survey results showed that guest speakers were not an important decision factor at enrollment, but that changed throughout the semester. Students became more open toward having multiple instructors as the class progressed and by the end of the course, all students appreciated the specialists’ presence in the classroom (Supplemental Information). To examine the students’ own perception of the impact of this approach, we asked them to assess how much they considered they gained from the Dow-TERC toxicologists’ professional expertise, ad-hoc examples, and presence in-person. More than 50% of the students indicated good to great gains (Figure 7) from all these aspects. The course’s culminating experience was the trip to the Dow-TERC facility, in Midland, MI. It included a tour of the facility and laboratories, meeting with specialists, and lectures on microplastics and product stewardship. The on-site visit was rated as providing good or great gain by 66% of the students who were able to participate. For work with databases and practice with software activities, we encountered several roadblocks, from difficulties with downloading software or even lack of experience with excel (for a couple of students), to database and software sites being updated precisely during the weeks when they were scheduled to be used. Despite these issues, students rated moderate-to-great gain in their ability to work with diverse databases and to practice with software (Figure 7). For the future, a serious review of the methodology used, a primer in Excel usage, and possible simplified versions of the exercises will be considered.

3.4. DOW-TERC’s experience

Dow’s goal for participating in the GVSU course on Contemporary Concepts in Toxicology was to support STEM (Science, Technology, Engineering, Math) education, a goal that is identified in Dow’s 2025 Sustainability Goals.14 To prepare for the course, DOW-TERC instructors met on several occasions to discuss strategies to cover a broad array of toxicology topics in a manner that was clearly understandable to undergraduate students with a variety of scientific backgrounds. For each class, instructors identified a few key learning points and developed sufficient background and case study information to illustrate these points. Each class also included a discussion of new alternative methods to assess toxicity and how these approaches can be used to assess safety more quickly and/or aid in chemical design. Database work was incorporated to illustrate how widely accepted models can be used (CONSEXPO, EpiSuite) and how to locate chemical-specific data to evaluate toxicity (REACH). Dow specialists spent numerous hours preparing for classes and, additionally, each donated a workday to travel to and from GVSU and present their
lectures, as scheduled, demonstrating DOW-TERC toxicologists’ full commitment for this course. DOW-TERC speakers thoroughly enjoyed interacting with the students at GVSU. Overall, they felt that students were engaged and asked relevant questions. The specialists also appreciated the opportunity to explain the importance of dose and exposure to toxicity and how hazard differs from risk, critical elements for students to accurately assess toxicology data in the future.

4. Conclusions and future work

ACS’ new CPT green chemistry guidelines speak of the need of toxicology elements to be implemented in undergraduate curricula (6). SOT identified a disconnect between student training and employer needs (5). The GVSU Contemporary Concepts in Toxicology course addresses the demands of both professional organizations by coordinating the curriculum with DOW-TERC. Sustainability is built in with the hybrid format, which is straightforward to update by including new guest speakers (14) and emerging topics. The course inclusion in the General Education Program instead of Chemistry or other academic departments allowed science students the ability to enroll without conflicting with required and recommended elective coursework. We are able to focus on multidisciplinary student teams and engage them in group activities that encourage using their knowledge base while working with other disciplines to analyze data and solve problems. Our use

![Figure 6. SALG survey results (%): students' perception of the skills they gained by the end of the course.](image1)

![Figure 7. SALG survey results (%): students' perception of the effect of Dow's toxicologists delivering lectures on specific aspects of their own learning.](image2)
of scaffolding assignments was successful in expanding multidisciplinary thinking, where students at the end of the course could integrate both life and physical science concepts to conduct a case study of their interest. By encouraging peer review at this stage, we hope to foster the need to seek input from others, inside and outside of this class, a typical scenario for a future R&D role. We believe the use of examples with databases was key for developing competency with data retrieval, analysis, and application. This competency was tested in the classroom and on the take home exams, where database usage was required to answer questions never discussed in class. We will continue to refine content and pedagogy based on student survey instruments and journals, while placing more emphasis on written expression earlier in the course. This model can be readily implemented in other undergraduate programs, by using expertise from local governmental or industrial organizations and consulting toxicologists. Building bridges between the professional practice and the academic curriculum and pedagogy of teaching is a way to strengthen and enrich undergraduate education and to prepare students for non-traditional careers fitting the current demands of global sustainability and human society development.15

Notes

1. Eleven programs offer toxicology undergraduate degree in US; five of these are pharmacology and toxicology: Arizona State University-West, https://newcollege.asu.edu/pharmacology-and-toxicology; University of the Sciences, Philadelphia, https://www.ussciences.edu/philadelphia-college-of-pharmacy/pharmaceutical-sciences/pharmacology-toxicology-major/index.html; UC Berkeley: https://nature.berkeley.edu/advising/majors/molecular-toxicology; Ashland University: https://www.ashland.edu/cas/department-biology-toxicology/programs/toxicology; University of Buffalo, https://catalog.buffalo.edu/academicprograms/pharmacology__toxicology_bs.html (all accessed July 3, 2018).
2. https://www.acs.org/content/dam/acsorg/about/governance/committees/training/acsapproved/degreeprogram/green-chemistry-in-the-curriculum-supplement.pdf (accessed June 10, 2018).
3. For example Beyond Benign, https://www.beyondbenign.org/he-toxicology-for-chemists/; Molecular Design Research Network (MoDRN), https://modrn.yale.edu/; The Institute for Green Science, Carnegie Mellon, http://igs.chem.cmu.edu/index.php?option=com_content&view=article&id=355&Itemid=514 (all accessed July 3, 2018).
4. http://www.greenchemistrycommitment (accessed June 12, 2018).
5. Green chemistry at GVSU https://www.gvsu.edu/chem/green-chemistry-at-gvsu-175.htm (accessed May 28, 2018); CHM 111 Introduction to Green Chemistry; CHM 421 Green Chemistry for Sustainable Environment; CHM 427 Green and environmental Chemistry Laboratory; CHM 442 Synthetic Polymers: Life Cycle and Emerging Sustainable Technologies.
6. For example, the hybrid format allows discussions initiated in-class with peers and specialists may be continued on-line, asynchronous; in-class presentations, recorded/videotaped, could be accessed by students at any time, with the ability to pause and review, and ask questions in on-line forums; such records, testing materials, and others, known as reusable learning objects, may be utilized as class materials in the future. For an example of hybrid multidisciplinary science course in general education curricula, see Stubbs (10).
7. https://www.nytimes.com/2017/11/24/us/michigan-water-wolverine-contamination.html (accessed June 20, 2018).
8. Since 2016, Laker Impressions of Faculty Teaching (LIFT) is GVSU’s university-wide system for collecting student feedback about courses and instructors. https://www.gvsu.edu/lift/ (accessed May 12, 2018).
9. Students Assessment of Their Learning Goals (SALG), instrument # 81087, https://salgsite.net/instrument/81087 (accessed June 15, 2018). Our survey could be open-accessed as designed; it may be viewed, used, and modified, on SALG website.
10. https://salgsite.net/help/statistics SALG site reports: the mean, the mode, and the number of responses, and the sample standard deviation for ordinal results.
11. Databases and free downloadable programs:
   (a) REACH, a regulation of The European Chemicals Agency (ECHA) adopted to improve the protection of human health and the environment from the risks that can be posed by chemicals. It promotes alternative methods for the hazard assessment of substances in order to reduce the number of tests on animals. https://echa.europa.eu/search-for-chemicals (access Nov 22, 2018).
   (b) EPI Suite™ Estimation Program Interface, United States Environmental Protection Agency https://www.epa.gov/tsca-screening-tools/epi-suitem-estimation-program-interface (access November 22, 2018).
   (c) ConsExpo, a computer program that enables the estimation and assessment of exposure to substances from consumer products https://www.rivm.nl/en/conexpo developed by the Dutch National Institute for Public Health and the Environment. https://www.rivm.nl/en (access November 22, 2018).
12. http://www.c8sciepanel.org/prob_link.htm (accessed June 15, 2018).
13. https://www.epa.gov/sites/production/files/2016-05/documents/pfoa_health_advisory_final_508.pdf (accessed June 15, 2018).
14. https://www.dow.com/en-us/science-and-sustainability/2025-sustainability-goals (accessed July 1, 2018).
15. Global sustainability goals https://sdg-tracker.org/ (accessed July 4, 2018).

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