

Learning goals and rationale

Course philosophy:

The fields of nutrition and toxicology both elicit strong feelings in the popular press and in the general public. People with little expertise express strong viewpoints on nutrition and toxicology, and the spread of misinformation is enabled by the internet.

This course is designed to provide students with some fact-based knowledge, but also the tools to assess common forms of research in the fields of nutrition and toxicology, and to make critical judgements and accurate interpretations of research results.

Learning Outcomes:

By the end of this course students will learn:

- 1) the principle concepts of nutritional sciences and toxicology, and the ways that these two disciplines interact
- 2) that nutritional status may alter the absorption, metabolism and excretion of xenobiotic compounds. This discussion will center on acetaminophen toxicity.
- 3) that xenobiotic and drug exposure may impact on nutritional status. This discussion will be centered on the effects of ethanol consumption.
- 4) to assess the diet as a vector for the delivery of natural and synthetic xenobiotics
- 5) to assess the relationships between diet and the risk of various cancers
- 6) to recognize different forms of research models, and to characterize their strengths and weaknesses
- 7) problem solving and critical thinking skills
- 8) to effectively communicate ideas and arguments in graphic and written form
- 9) interpret data in class, in homework assignments and on exams
- 10) to work in a group environment to produce an integrated research critique

Course Resources

The course outline, a tentative lecture schedule, readings and handouts for specific lectures can be found at the CourseLink site for the course, where students can also submit questions on the course discussion board, and Danyelle Liddle or Dr. Kirkland will provide guidance.

Course Textbook: There is no required textbook for this course. All assigned readings will be available on the CourseLink site for the course, including the book chapter listed below.

Required reading: Kirkland, J.B. Phytochemicals, xenobiotic metabolism and carcinogenesis. In: Nutrient Drug Interactions (K.A. Meckling, Ed.), Marcel Dekker, NY, pp 63-94, 2007.

Useful Report: Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective

(<http://wcrf.org/sites/default/files/english.pdf>)

This report, prepared by the AICR and the World Cancer Research Fund, may be obtained in book form, or viewed on the web. It is very useful for background information on understanding cancer in general, and lifestyle influences on cancer.

Course Concepts:

There are 3 main concepts that summarize the interaction between nutrition and toxicology. These include:

1) The role of the diet as a source ("vector") of natural or man-made toxins.

While most people are aware, and perhaps worried, about the occurrence of toxic substances in foods, there are a number of misconceptions about the source of these risks. The greatest fears of the general public are of artificial or imposed risks, like pesticide residues and genetically modified foods. In reality, the bulk of toxic substances in our diet are natural plant or animal products, or are formed during the cooking of foods. Plants raised for pest resistance and grown without artificial pesticides may produce high levels of natural products that pose risk, or benefits, to consumers. Even essential nutrients may act as xenobiotics if consumed unwisely. The expanding and poorly regulated nutraceutical and herbal industries are creating new opportunities for diet-related poisonings.

2) The effect of nutritional status on toxin metabolism and pathology.

Our ability to metabolise dietary xenobiotics is often dependent on our nutritional status, and our exposure to other dietary compounds. Diets high in fruits and vegetables are known to decrease cancer risk, and much attention has been focused on nutrients like vitamin C and beta-carotene. Current knowledge, however, is pointing towards non-nutrient phytochemicals as the most potent anti-carcinogenic components of fruits and vegetables. While many plant products that appear to decrease the risk of cancer or CVD are marketed as “antioxidants”, we find that the phytochemicals are likely functioning through modulation of xenobiotic metabolism.

3) The effect of toxin exposure on nutritional status.

Chronic exposure to xenobiotics such as ethanol, or other drugs, will also have a direct effect on nutritional status. This creates a very complex interaction between the nutrients and toxins that are present in our diet and impact on our short and long term health.

Course Content

1. Nutrition and Xenobiotic Metabolism
 - (a) Physiology of Xenobiotic exposure
 - (b) Phase I and II detoxification processes
 - (c) Metabolic activation
 - (d) Conjugation and excretion
 - (e) Acetaminophen toxicity and nutritional status
2. Nutritional Status and Alcohol
 - (a) Alcohol metabolism
 - (b) Effects of alcohol on nutrient availability- e.g. vitamin A
3. Nutrients as Toxins
 - (a) Therapeutic Index
 - (b) Vitamin A, selenium, fluoride, pyridoxine
4. Natural Toxins in Plant Products
 - (a) Introduction to toxic substances in plant products
 - (b) Glucosinolates
 - rapeseed and canola
 - (c) Cyanogenic glucosides
 - almonds, cassava, lima beans
 - (d) Antinutrients; glucosinolates, trypsin inhibitors, phytate

5. Pesticides: Man Made and Natural
 - (a) Risk of toxicity from commercial pesticides
 - (b) Toxic potatoes and celery grown organically

6. Emerging areas of concern in toxicity of plant products
 - (a) Toxicity of nutraceutical and herbal products
 - (b) Toxicological concerns about genetically altered foods

7. Toxic Factors in Animal Products
 - (a) Seafood toxins: neural sodium gate inhibitors
 - puffer fish, ciguatera, paralytic shellfish poisoning
 - red tides
 - (b) Consumption of Ontario sport fish
 - bioaccumulation of mercury, PCBs
 - chronic health risks

8. Chemical Carcinogenesis and Diet
 - (a) Introduction to chemical carcinogenesis
 - initiation, promotion, progression
 - description of interactions with diet
 - (b) Pyroorganic toxicants
 - broiling, barbecuing
 - protection by fruits and vegetables
 - (c) Other carcinogenic products formed during cooking of foods
 - aromatic amines
 - browning reaction, Maillard reaction
 - (d) Nitrates, Nitrites, Nitrosamines
 - contaminated ground water, food processing
 - (e) Aflatoxin
 - mycotoxins are synthesized by molds during food storage
 - (f) Influence of nutrient status on carcinogenesis
 - oxidant defence and cancer? (vitamins C, E, selenium)
 - retinoids, differentiation and cancer
 - folate status, gene expression and DNA integrity

Methods of Assessment

Assessment				
Form of Assessment	Weight of Assessment	Due Date of Assessment	Course Content /Activity	Learning Outcome Addressed
MT Exam	25%	Oct 26	Lecture content, research interpretation.	1,2,3,6,7,8,9
Term Paper	30%	Nov 17	Independent literature research.	6,7,8,9,10
Final Exam	45%	Dec 13	Lecture content, research interpretation.	1,2,3,4,5,6,7,8,9

Midterm Exam Format: 15 Multiple choice plus 3 essay questions

Final Exam Format: will be similar to the midterm, with 20 multiple choice questions and 3 essay questions, covering the whole course. It will be weighted to the final half of the course, by about 30:70. One major essay question on the midterm and on the final will be based on a scientific abstract. The question will ask what the study type is, its strengths and weaknesses, what the properly worded conclusions should be, and what a logical next experiment would be. These 2 questions reflect our focus on learning to assess new knowledge in the emerging literature. These skills will be also be applied to the term paper, in which groups of 3 students research 3 full papers on a topic of their choice (described below).

Term Paper Instructions and Format:

The paper will address a topic that fits with one (or more) of the 3 concepts of this course, as described earlier this outline. Thus, the topic will address some interaction between diet and toxicology that may impact on human health. It is alright to just satisfy concept 1), where a toxic, or potentially toxic, component is present, or potentially present, in human foods. Notice the uncertainty that we accept when working at the front edge of the primary literature. Some topics will probe the interactions described in course concepts 2 and 3, but this is not essential. Some students think of a topic that lacks a toxicology aspect, or lacks a nutrition aspect; come to see me and I can often suggest a modification that will

make it work. Food borne bacterial or viral infections are also not suitable topics, as we will discuss in class. Some students are interested in companion animal health; that is an acceptable extension.

An ideal topic will have some level of uncertainty that requires interpretation by you as the authors of this paper. You will develop your argument/analysis around 3 main papers from the scientific literature (they should be listed on Pubmed). The uncertainty could involve conflicting results between different labs or methods of investigation, in which case you would need to assess the strengths and weaknesses of each approach, and decide which results you have more faith in. Another common approach is to look at cutting edge research that has uncertain application to human health. In this case, you may need to combine animal experiments, in vitro work and epidemiology data to arrive at an opinion. To accomplish this, you will need to look in detail at your 3 specific studies, and show that you understand how they were conducted and whether appropriate conclusions were drawn. You should avoid writing a general review. You will probably start with a broad topic, and as you research it, a more specific idea will emerge, your interest and curiosity will build, and you will have your topic!

You will not always notice uncertainty when you first look up your topic, but it will generally emerge as you choose 3 primary research papers and try to make a combined story from them. Embrace the uncertainty. All papers have strengths and shortcomings. A critique is not a "criticism"; it is an analysis of strengths and weaknesses with some form of conclusions and recognition of gaps in knowledge.

Understanding the gaps in knowledge allow you to finish your paper by suggesting the most important experiment that should be conducted next. This is the section that shows you understand how science works!

You should have 3 central references, with other more general references to cover your introduction and discussion. The total number of references should be around 10. Use the in text citation and referencing style found in "Environmental Health Perspectives". You can use numbers or author names in the body, just be consistent. Web references can be used to describe what is going on in the public sphere, but not for scientific points. Any figures used from papers or the web should be properly referenced. Sample figures may be added at the back as appendices, but are not required.

Structure of the Paper:

Your paper is a critique (not meaning “criticism”, but more a combined analysis of strengths and weaknesses), so it will not have the typical sections like Materials and Methods, Results, etc. You should start with a short Summary (half page, summarizing your overall findings), followed by an Introduction (background material setting up your specific area of interest, about 1.5 pages in length). The body of the paper will concentrate on your 3 major papers, describing and interpreting their findings. These sections can be named and subdivided as you see fit, and should be about 6 pages long. It is good to discuss your 3 papers individually first (about 3 pages) and then have an integrated discussion (about 3 pages), bringing out your ideas and interpretations, and leading up to your conclusions, including the gaps in knowledge that lead up to your future work. Finish your paper by suggesting the most important experiment that should be conducted next to improve the state of knowledge in your topic. Start by specifically stating what is missing from the published literature, make an objective (or hypothesis) and describe an experiment that effectively addresses your objective. This is the section that shows you understand how science works! This should be about 1 page in length. Once you let some of your sections run over, as they will tend to do, you now have about 10 pages (double spaced) of text, plus references. Include figures at the end if you choose, but fully reference them if they are not original. Double space, 12 point text, 2 cm margins. Do not exceed 10.5 pages of text. Do not tamper with line spacing and fonts to make your excessively worded paper fit onto 10 pages. These are the sorts of limitations that you will face in the real world. Hand in a HARD COPY in the box outside ANNU 335 on the specified date before the building locks up at 4:00.

Note: You may do quite a bit of work on a topic and end up feeling that there is no real toxicity threat to humans. Students usually get concerned at this point and come to see me about switching topics. You do not need to do this! As long as there was a reason to suspect toxicity when you started the topic, it is still a good topic. If you change topics, or worse, try to focus on selective information that makes your exposure seem more toxic, then you are participating in “publication bias”. We do not want any students to write papers in a biased fashion. It is critical that you make the proper conclusions of either safety or risk associated with a given exposure. You will not get a lower mark for claiming that your chosen exposure doesn’t appear to present risk.

Work on this assignment in groups of three, unless you have a good reason to do otherwise (cleared by me). Students should get their topic approved, at which point I can give advice for the best approach to a topic, although this is not essential. If you have trouble finding a partner, we will have a section in the CourseLink discussion board devoted to forming groups.

Sources of information:

Students sometimes struggle to come up with the idea for their paper; some items from the popular press are hopeless dead ends, as far as finding support in the proper scientific literature. However, many popular press items can be tracked back into Pubmed and be turned into good paper topics. I can help students with this process if they bring their ideas to me for discussion.

In addition to starting with an idea from the popular press, students can also go directly to the primary literature, or journal reviews or news items to get ideas for a topic. It is important to remember that the 3 major papers will all have to be primary publications (original work, not reviews) that appear on Pubmed.

Once you get an initial idea, put a couple terms of interest into Pubmed, which may generate as many as several thousand hits. The Pubmed hits will be in the order of most recent first, so you get an idea of what is happening currently in basic research. The papers will be extremely varied, and once you look through a few hundred, and you find one of interest, you can start modifying the search terms to find other more closely related papers. One useful tool is the series of windows on the right side of Pubmed, including "Related Citations", which help you branch away from a single article. Another tool is "Titles that include your search terms", which really focus down to more related articles if you have a large number of hits. In addition to Pubmed, you can look in specific journals, either online or in the library, including:

Science and Nature, including the news sections.

Environmental Health Perspectives

- excellent web site (<http://ehp.niehs.nih.gov/>)
- look at reviews and mini-monographs for general topics
- read Correspondence, News, Forum and Focus sections for hot topics

Searching “toxicology” in the UoG ejournal window
(<http://sfx.scholarsportal.info/guelph/az>) gives 108 results, including;

Comments on Toxicology
Critical Reviews in Toxicology
Food and Chemical Toxicology
Food and Cosmetic Toxicology (but don't select a topic on cosmetics)

Other journals that have human cancer focus:

Nutrition and Cancer
Cancer Research
Carcinogenesis
Cancer Epidemiology Biomarkers & Prevention

Once you have an idea, pursue it using the references from your original papers and using PubMed.

Course and University Policies

When You Cannot Meet a Course Requirement

When you find yourself unable to meet an in-course requirement because of illness or compassionate reasons, please advise the course instructor (or designated person, such as a teaching assistant) in writing, with your name, id#, and e-mail contact. See the undergraduate calendar for information on regulations and procedures for [Academic Consideration](#).

Accessibility

The University of Guelph is committed to creating a barrier-free environment. Providing services for students is a shared responsibility among students, faculty and administrators. This relationship is based on respect of individual rights, the dignity of the individual and the University community's shared commitment to an open and supportive learning environment. Students requiring service or accommodation, whether due to an identified, ongoing disability or a short-term disability should contact Student Accessibility Services (formerly the Centre for Students with Disabilities) as soon as possible.

For more information, contact [Student Accessibility Services](#) at 519-824-4120 ext. 56208 or email csd@uoguelph.ca.

Academic Misconduct

The University of Guelph is committed to upholding the highest standards of academic integrity and it is the responsibility of all members of the University community – faculty, staff, and students – to be aware of what constitutes academic misconduct and to do as much as possible to prevent academic offences from occurring. University of Guelph students have the responsibility of abiding by the University's policy on academic misconduct regardless of their location of study; faculty, staff and students have the responsibility of supporting an environment that discourages misconduct. Students need to remain aware that instructors have access to and the right to use electronic and other means of detection.

Please note: Whether or not a student intended to commit academic misconduct is not relevant for a finding of guilt. Hurried or careless submission of assignments does not excuse students from responsibility for verifying the academic integrity of their work before submitting it. Students who are in any doubt as to whether an action on their part could be construed as an academic offence should consult with a faculty member or faculty advisor.

The [Academic Misconduct Policy](#) is detailed in the Undergraduate Calendar.

E-mail Communication: As per university regulations, all students are required to check their <uoguelph.ca> e-mail account regularly: e-mail is the official route of communication between the University and its students.

Drop Date: The last date to drop one-semester courses, without academic penalty, is the 40th class day. To confirm the actual date please see the schedule of dates in the Undergraduate Calendar. For regulations and procedures for Dropping Courses, see the [Undergraduate Calendar](#).

Copies of out-of-class assignments: Keep paper and/or other reliable back-up copies of all out-of-class assignments: you may be asked to resubmit work at any time.

Recording of Materials: Presentations which are made in relation to course work—including lectures—cannot be recorded or copied without the permission of the presenter, whether the instructor, a classmate or guest lecturer. Material recorded with permission is restricted to use for that course unless further permission is granted.

Grading: Indicate all course policies regarding in-semester tests and assignment submissions, including time and place for submission of assignments and explicit penalties for late submissions.

If you are concerned about any aspect of your academic program:

Make an appointment with a [Program Counsellor](#) in your degree program.

If you are struggling to succeed academically:

There are numerous academic resources offered by the [Learning Commons](#) including, Supported Learning Groups for a variety of courses, workshops related to time management, taking multiple choice exams, and general study skills. You can also set up individualized appointments with a learning specialist.

If you are struggling with personal or health issues:

[Counselling services](#) offers individualized appointments to help students work through personal struggles that may be impacting their academic performance.

[Student Health Services](#) is located on campus and is available to provide medical attention.

For support related to stress and anxiety, besides Health Services and Counselling Services, [Kathy Somers](#) runs training workshops and one-on-one sessions related to stress management and high performance situations.

If you have a documented disability or think you may have a disability:

[Student Accessibility Services](#) (SAS) formerly Centre for Students with Disabilities can provide services and support for students with a documented learning or physical disability. They can also provide information about how to be tested for a learning disability.