More than Our Enemy: Making Space for the Microbiome in Pharmacy Education
Sarah P. Collier, PhD; Abby J. Weldon, PhD; Jessica L. Johnson, PharmD, BCPS

Abstract
The microbiome is the collection of commensal microorganisms along with their genomes inhabiting the human body. Despite the many known beneficial effects of these microbes on human health, the 2016 ACPE Standards for Doctor of Pharmacy curricula describe Medical Microbiology in Appendix 1 with a pathogen-centered focus. Over the last twenty years, evolving biotechnology has enabled a deeper understanding of the microbiome in the context of both wellness and disease. Retail stores are allocating increasing shelf space to commercial probiotic products, while the approach to PharmD training on the selection and use of these natural care products remains static, creating a disproportionate footprint between PharmD curricula and consumer markets. Looking to the future of patient care, we brief pharmacy educators on the current evidence and invite discussion around a proposed revision to the 2025 ACPE Standards that would add language recognizing the beneficial role of the commensal microbiota and expanding therapeutic applications of microbiome supplementation. We suggest a variety of opportunities within Doctor of Pharmacy curricula as leverage points for including relevant aspects of the microbiome in the training of future pharmacists.

Keywords: microbiome, pharmacomicrobiomics, curriculum, and microbiology

Friends + Enemies = Frenemies?
The Accreditation Council for Pharmacy Education’s (ACPE) Standards 2016 requires that candidates for a Doctor of Pharmacy degree study “Medical Microbiology: Structure, function, and properties of microorganisms (bacteria, viruses, parasites, and fungi) responsible for human disease, and rational approaches to their containment or eradication.” The wording of this ACPE Appendix 1 item fails to acknowledge the well-established beneficial effects of the human microbiota, unfairly demonizing microorganisms and portraying the role of the pharmacist as “The Exterminator.” Yet we wonder, isn’t there more to microbiology than just the collective list of human pathogens? Are we adequately preparing future pharmacists if we are only tackling microbiology in the context of antimicrobial therapies? Herein, we advocate for broadening the scope of medical microbiology education within pharmacy curricula in a manner that recognizes the positive contributions of the microbiota to human health and wellness. We present a variety of potential touchpoints within typical PharmD curricula that could be leveraged to explore an emerging understanding of the microbiome in the context of pharmaceutical sciences and clinical care.

The human body is colonized with commensal, or symbiotic, microorganisms of bacterial, viral, and fungal species in at least equal proportion to the number of human cells in the body. Together with their genome, commonly referred to as the ‘microbiome,’ these microorganisms occupy the interfaces between the body and the external environment, such as the skin and the gastrointestinal, respiratory, and genitourinary tracts. Each of these anatomical areas possesses its own regional biome that is influenced by local physical and chemical mediators. Beginning at birth, the depth and diversity of an individual’s microbiome is dynamically influenced by lifestyle factors, such as diet, environment, and, according to new scientific investigations, medication exposure.

It is well known that the species of microorganisms colonizing the body (collectively referred to as microbiota) play an important role in human health by aiding digestion, synthesizing essential vitamins, providing protection from pathogenic organisms, and influencing the development and regulation of the immune system. Microbiota catalyze and convert plant-based complex carbohydrates into short chain fatty acids that influence satiety, energy balance, and metabolism. In addition to vitamins B and K, gut microbiota produce gamma-aminobutyric acid (GABA), tryptophan precursors, serotonin, and catecholamines, suggesting that these organisms may influence neurological processes. Microbiota also defend against colonization by pathogenic microbes through the production of lactic acid and competition for resources.
Ignited by Genomics and Precision Medicine

Rapidly-expanding access to genetic sequencing technologies and bioinformatics is fueling the field of precision medicine and driving a growing body of evidence connecting the microbiome to human health and disease.\(^5\) Previously, understanding of the diversity and function of the microbiota was limited to organisms amenable to growth within a laboratory culture environment. Next-generation genetic sequencing technology has allowed for high throughput analysis of an increasing number and diversity of microbiota species at an exponentially decreasing cost, allowing scientists to quickly and easily identify the microbial species present and their relative abundance within an individual’s microbiome. Functional data useful for patient care decision-making can then be extrapolated from genomic data, for example, using the presence of antibiotic resistance genes to guide empiric antimicrobial selection.\(^10\) In response to a rapid expansion in gene sequencing technologies, the number of microbiome-related publications has exponentially increased since the year 2002 (Figure 1). These publications range in scope from descriptions of the species present in various anatomical regions to analysis of connections between microbial diversity and health.

This rapidly-expanding body of literature frames the microbiome in new light. Alterations in the microbiota (i.e., dysbiosis) are increasingly associated with the metabolic and inflammatory pathologies associated with obesity, asthma, inflammatory bowel disease, vaginosis, hepatic encephalopathy, diabetes, and mental illness.\(^11-13\) If dysbiosis is a cause of disease, then microbial supplementation could perhaps be a treatment. Commercial probiotics have shown some beneficial effects that include the reduction of antibiotic-associated diarrhea, rotavirus diarrhea, travelers’ diarrhea, and chronic constipation, though the optimal dose and the matching of specific species to specific conditions is unknown.\(^12\) Increased marketing and use of probiotics is driving considerable interest in prebiotic, symbiotic, and nutritional/food-based approaches to microbiome modification/supplementation among public and scientific communities.

Perhaps the most striking example of microbiome research applied to therapeutics is the development and use of fecal microbiota transplantation (FMT) to regenerate a healthy microbiome. FMT, an investigational new drug, is currently used in the treatment of recurrent *Clostridioides difficile* infections (rCDI) refractory to standard therapies.\(^14\) FMT administration has transitioned from delivery by colonoscopy to capsules, which has the potential of expanding the pharmacist’s role in managing rCDIs.\(^15\)

Additionally, the diversity and composition of the gut microbiota influences the efficacy of certain medications and therapeutic outcomes. For instance, cancer patients with abundances of certain bacterial phyla display improved therapeutic responses to immune checkpoint blockage immunotherapies, reduced immunotherapy toxicity, and enhanced chemotherapeutic efficacy. Distinct bacterial phyla of the gut microbiome can also reduce graft-versus-host disease following hematopoietic stem cell transplant.\(^16\) These observations suggest that the interaction between a patient’s medications and microbiome (i.e., pharmacomicrobiomics) could be incorporated into therapeutic decision making and thereby add another tool to the field of personalized medicine.\(^16,17\)

Touchpoints across the Pharmacy Curriculum

Microbiome-related concepts are already being incorporated into teaching and research by some pharmacy educators. Presentations at annual meetings of the American Association of Colleges of Pharmacy (AACP) have described studies on how the gut microbiome influences bioavailability and intestinal metabolism of pharmacotherapeutics, as well as how genetically-modified microorganisms could potentially translate into treatment of enzyme deficiency disorders.\(^18,19\) Two authors of this commentary (Johnson, Weldon) previously described a microbiome elective course for pharmacy students.\(^20\) The microbiome and efficacy of probiotic therapies have also served as topics in active learning debate exercises within a pharmacotherapeutics course.\(^14\)

These examples reflect how topics relating to the microbiome are certainly finding a niche audience within pharmacy; however, a greater emphasis is needed for graduates to meet the growing expectations of the field. Studies increasingly suggest that pharmacists seek greater confidence and competence in counseling on complementary and alternative medicines or natural health topics.\(^22-24\) Patients also recognize probiotic foods and commercial supplements as some of the most commonly used complementary or natural remedies and rely on community pharmacists to provide specific and useful information about them.\(^22-24\) The evolving landscape of precision medicine research and its application in clinical practice necessitates a perspective shift involving the human microbiota. Although future treatment guidelines and standards of care are anticipated to consider the microbiome in patient care\(^25\) (similar to how pharmacogenomics is growing to guide therapeutic options), the current required elements of Doctor of Pharmacy curricula fail to encourage student pharmacist exposure to this therapeutic area.

The Accreditation Council for Pharmacy Education’s recent announcement of the planned “Standards 2025” offers an ideal opportunity to revise our approach to this topic within pharmacy curricula. The current wording of the ACPE Appendix 1 item “Medical Microbiology” reflects a narrow and biased caricature of microorganisms as the perpetual enemies of humanity. This perspective requires reframing to represent a broader and more inclusive view of the relationships between microbiota and their human hosts that affirms the positive contributions of microbiota to human health. Thus, we propose a modification (shown in bold, italics) of the wording of this

**Commentary**

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relevant required element to read “Medical Microbiology: Structure, function, and properties of microorganisms (bacteria, viruses, parasites, and fungi) responsible for human health and disease, and rational approaches to their modification, supplementation, containment or eradication.”

This change, if adopted into ACPE Standards 2025, would support and encourage faculty to actively incorporate the microbiome into their classrooms, which is achievable through several different contexts related to pharmacy education (Table 1). Currently, self-care pharmacotherapeutics courses provide general coverage of probiotics, but fail to address the effects that the microbiome may have on the pharmacological efficacy of a drug as seen with anti-cancer therapeutics. Table 1 provides a launchpad for identifying straightforward opportunities to incorporate the microbiome into the PharmD curriculum and clinical experiences. For example, traditional didactic courses like Microbiology or Immunology may include active learning or discussion investigating the role of commensal organisms in immune system development. In the Drug Information or Literature Evaluation classroom, students could undertake the critical examination of the growing body of microbiome literature. In Self-care (Over-the-Counter Medications) or Complementary Medicines (Natural Medicines) courses, students can practice communicating basic science concepts to a public, patient-facing audience seeking counsel on probiotic supplementation. An advanced pharmacy practice experience might include one or more of these suggested ideas into a real-world patient context.

In summary, the growing field of microbiome science advances steadily toward clinical application necessitating a change in health professions education. We invite pharmacy faculty to introduce student pharmacists to the microbiota from a perspective that is more inclusive and nurturing to commensal organisms in immune system development. In the Drug Information or Literature Evaluation classroom, students could undertake the critical examination of the growing body of microbiome literature. In Self-care (Over-the-Counter Medications) or Complementary Medicines (Natural Medicines) courses, students can practice communicating basic science concepts to a public, patient-facing audience seeking counsel on probiotic supplementation. An advanced pharmacy practice experience might include one or more of these suggested ideas into a real-world patient context.

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References


Figure 1. Trends in the number of microbiome publications per year indexed in Pubmed.gov.

Note: A search was conducted in January of 2022 for all publications with the keyword ‘microbiome’ in the Title/Abstract field from 2002 to 2021.
Table 1. Opportunities for Inclusion of Microbiome-Related Concepts into the Doctor of Pharmacy Curriculum

<table>
<thead>
<tr>
<th>Curricular Topic Area</th>
<th>Opportunities for Curricular Inclusion of Microbiome-Related Concepts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutics and Compounding</td>
<td>Compounding requirements for dosage forms containing live microorganisms (packets, capsules, gummies, topical creams). Storage considerations and product degradation over time, estimation of shelf life.</td>
</tr>
<tr>
<td>Calculations</td>
<td>Interpretation of colony-forming units (CFUs) in calculation of dose and cost of treatment.</td>
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<tr>
<td>Immunology</td>
<td>Microbes as an innate defense. Effect of microbial populations on immune effector cells and on synthesis of immune mediators.</td>
</tr>
<tr>
<td>Biotechnology</td>
<td>Development and use of genetically modified organisms.</td>
</tr>
<tr>
<td>Biostatistics and Drug Information</td>
<td>Interpretation of novel graphs and figures required to present a new class of data including three-dimensional graphics, such as Principal Coordinates Analysis (PCoA) or taxonomy and abundance graphs. Discussion of translational sciences and status of emerging therapies.</td>
</tr>
<tr>
<td>Anatomy and Physiology</td>
<td>Emphasis on commensal organisms and their benefit to the human host. Role of the microbiome in associated organ systems (primarily digestive, respiratory, reproductive, integumentary). Changes in microbiota across the lifespan.</td>
</tr>
<tr>
<td>Pharmacokinetics and Pharmacomicrobiomics</td>
<td>Effects of gut microbiota on drug therapy, including biotransformation and metabolism of orally administered medications.</td>
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<tr>
<td>Self-Care and Patient Communication</td>
<td>Evaluation of labeling and use of market available pre- and probiotic products. Patient-focused communication and patient education strategies.</td>
</tr>
<tr>
<td>Functional Foods and Nutrition</td>
<td>Microbiome contributions to digestion and vitamin synthesis. Links between microbial diversity and obesity. Mechanism and efficacy of prebiotic and synbiotic supplements. Cultural sensitivity in probiotic food or commercial product selection.</td>
</tr>
<tr>
<td>Pathophysiology and Therapeutics</td>
<td>Role of the microbiome in disease. Efficacy of probiotics in prevention and management of disease. Adverse effects of therapy including potential for iatrogenic infection.</td>
</tr>
<tr>
<td>Pharmacoeconomics</td>
<td>Cost-Benefit of treatment with probiotics to prevent serious disease.</td>
</tr>
<tr>
<td>Law</td>
<td>Marketing regulations for dietary supplements.</td>
</tr>
<tr>
<td>Integrative Health Care, Complementary and Natural Medicines</td>
<td>Non-conventional approaches to health including alternative, complementary, and integrative medicine practices.</td>
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</tbody>
</table>