Nutraceuticals in the Work of Scribonius Largus, a Pioneer of Clinical Pharmacy in Ancient Rome

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ABSTRACT: The therapeutic potential of nutraceuticals has been recognized by several ancient civilizations. The majority of physicians would use them in their practice and transmit their experience to their disciples. Nonetheless, few physicians have contributed to the dissemination of this knowledge further and its integration into the standard of care of their era. Scribonius Largus, a renowned physician and pharmacist in ancient Rome has summarized the existing knowledge on nutraceuticals in his pharmacognosy and therapeutics textbook “Compositiones”. As a physician to the imperial court, he used his position and resources to advance the relevant knowledge, educate erudite and lay physicians across the Roman Empire, and establish ethical practices in the field. Revisiting his contributions provides valuable lessons for contemporary researchers and practitioners. © 2022 iGlobal Research and Publishing Foundation. All rights reserved.


INTRODUCTION
Nutraceuticals constitute types of food or nutrients beneficial for health. They include but are not limited to non-processed foods containing antioxidants, dietary supplements, fortified dairy products, citrus fruits, vitamins, minerals, herbs, milk, and cereals. To date, there is no universally accepted definition of nutraceuticals [1]. However, their potential in preventing, mitigating, or even healing medical conditions has been well known since ancient Greek antiquity [2].

Hippocrates, the so-called father of scientific medicine, used to advise his disciples and patients to let food become their medicine, and their medicine become their food. This statement not only recognizes the importance of healthy nutrition but highlights food as a short of medication capable of preventing diseases or enhancing the treatment of known medical conditions [3]. Numerous ancient physicians across the world would use nutraceuticals to treat conditions ranging from chronic pain and headaches to infections.

Due to the lack of established biomedical research and medical education practices, this knowledge used to be transferred from mouth to ear [4]. Each physician would modify this knowledge based on their observations, experience, and access to nutraceuticals. Those who would
leave an account of nutraceuticals in their practice would usually ghost-write their findings claiming Hippocrates, Galen or other prominent physicians to have authored their work [5]. Not only did this practice not allow them to receive proper credit and criticism, but it could also establish faulty theories as authentic, misinform physicians, and set patients at risk. Moreover, given that physicians did not have standard qualifications, several lay practitioners would face problems in accessing this information. In total, the dissemination of knowledge about nutraceuticals was precarious and there was little or no consensus on their proper use.

This problem became even more evident in the Roman Empire, a vast state occupying populations and regions from France to Egypt and Mesopotamia during the 1st century AD. Emperors and the nobility would employ the most capable physicians and pharmacists and provide them with the means to practice their treatment skills at either individual or population level. Nevertheless, health consisted of a priority of the state that relied on a vibrant population for its financial development, military campaigns, and security[6]. In this context, the safe integration of nutraceuticals in clinical practice could be addressed only by an influential physician capable of critically summarizing the existing knowledge and disseminating his findings in plain language. Scribonius Largus, an imperial physician, combined these competencies and made significant contributions towards nutraceuticals knowledge and use in his era.

**BIOGRAPHY AND HISTORICAL CONTEXT**

Scribonius Largus (ca 14 - 54 AD) was a physician of Greek origin who served in the court of Emperor Claudius. In 47 AD, he authored a textbook on pharmaceutical preparations in a clinical context covering the known disease spectrum of the period. Little is known about the whereabouts of Lagrus, his family background, his life events, or his death. Information about him derives from the writings of physicians, philosophers, or historians. Prominent Grecoroman physicians and authors, such as Galen, mention him in their works indicating his influence on medicine in ancient Rome. Being knowledgeable of the Greek language he was able to read the works of Hippocrates and his disciples. As an imperial physician, Largus was also able to interact with the most prominent doctors and scholars of his time and had ample resources for research and experimentation. His contribution to nutraceuticals is threefold: he provided a comprehensive overview of the existing knowledge, he contributed to the dissemination of this knowledge innovatively and he laid down a framework of ethics, which remains relevant until today[7,8].

**NUTRACEUTICALS IN ANCIENT ROME: CLINICAL PRACTICE AND IMPLICATIONS**

The basis of Largus's contribution to nutraceuticals is his book *De compositione medicamentorum liber* (Latin, Book of Medicinal Prescriptions). This consists of 271 prescriptions (compositions) attached to specific medical conditions, syndromes, or symptoms. The majority of them were developed or adapted by him, based on knowledge derived from the texts of eminent physicians and the teachings of his tutors and colleagues. He critically assessed the prescriptions he included in his book, with a focus on them making sense and preferably being supported by well-known physicians. Largus prioritized the rationality of a prescription, based on the medical knowledge of the era, and did not hesitate to include the prescriptions of practitioners who were considered barbarians, as long as they were reasonable[9,10].

In this collection, 56 prescriptions include herbal remedies solely or in combination with other treatment regimens. A number of the herbal preparations consist of edible plants and products, namely: raisins, honey, vinegar, oil, beet juice, pomegranates, myrrh, pepper, cucumber root, castoreum, galbanum, storax, pellitory, and a special variant of chicory called radichis Apollinaris, owing to the deity Appolon and saffron from the crocus. The main conditions for which these herbs are prescribed are epilepsy (honey), long-standing cough (myrrh, pepper, castoreum, galbanum, storax, chicory, saffron), bleeding (pomegranates, vinegar), swollen lymph nodes (cucumber root), labored breathing (vinaqar, asparagus root, honey). Largus's knowledge of nutraceuticals has been validated by experience, although there are no indications of his understanding of the underlying mechanisms. Given that the textbook has a rather practical format, there is no space for the development of theories linking nutraceuticals with the humorous pathology of the era[11].

Assessing these prescriptions with contemporary lenses, it is possible to confirm the efficacy of some of them. Nowadays, the anticonvulsive potential of honey has been recognized and its use as preventive measures for epilepsy in children is being discussed[12]. Honey has also yielded antinociceptive effects, which justifies its use to alleviate chronic, cough and labored breathing[13]. About bleeding, vinegar seems effective as a disinfectant due to its acidic acid content[14]. Nonetheless, the use of pomegranate against hemorrhage seems controversial due to its documented anticoagulant effects[15]. Black sea pepper seems to exaggerate chronic cough[16] instead of alleviating it, although Largus does not state which species of pepper he would use. The potential anticancer effect of black sea peper may justify its use against lymphadenopathy, however, this must have been masking the symptoms of neoplastic diseases rather than helping manage them[17].

Largus contribution to medical education was surely supported by his position in the imperial court. Not only did he access its resources, to collect information, but his position increased the credibility of his prescriptions and enabled them to be disseminated throughout the empire and improve pharmacotherapies of the time. An additional asset stemmed from his writing style, which is straightforward with extensive use of colloquialisms, making his knowledge accessible to physicians - pharmacists with the lesser erudite background. This has also been useful for memorization given the scarcity of textbooks and the practical difficulty of carrying them[18].
Combined, the aforementioned resemble an archaic open access model, with good practices disseminated beyond paywalls and language barriers.

Finally, yet importantly, Largus’s work shed light on professional ethics. Although the duties and roles of physicians and pharmacists were not distinct in his era, Largus illustrated the need for a common ground [18]. With his work on nutraceuticals, it became evident that a good command of pharmacology and nutrition is necessary for medical practitioners. Largus’s recommendations for disease-specific regimens consisted of a response to his colleagues that would downsize the contribution of pharmacotherapy and nutrition claiming that time and nature would eventually heal the patients [19, 20].

Nutraceuticals and natural products as a whole remain relevant nowadays. While several nutraceuticals such as Vitamin C and Vitamin D have an established – usually complementary - role in the management of health conditions ranging from respiratory infections to osteoporosis and anemia, a growing body of research is exploring the potential of known or novel nutraceuticals. The gradual integration of Vitamins C and D, Zinc and melatonin – based dietary supplements in the management of COVID-19 is a representative example of the above. Investigating the mechanisms of action of these compounds in immunity, inflammation and respiratory distress has helped elucidate part of the pathophysiological cascade of the disease. Nonetheless, nutraceuticals in COVID-19 have often been criticized due to the lack of homogeneous and large-scale studies. Therefore, research efforts in the field should become more consistent. Summarizing the existing knowledge and knowledge gaps, in a similar manner to the Compositiones of Largus, can be the starting point towards evidence based use of nutraceuticals [21].

Along the same lines, nutraceuticals and functional foods are gaining attention in the fields of oncology and cardiology, which represent the primary causes of morbidity and mortality in the Western world. Experience in this field has shown that whole foods containing a wide range of nutraceuticals may exert greater chemo-preventive action than dietary supplements based on isolated phytochemicals [22]. Apart from more effective drug design in the field, this also emphasized the need for health and healthy nutrition literacy. Supplements and preparations administered once or twice daily can achieve higher levels of compliance than healthy diet, which is frequently incompatible with the daily routine and the budget of individuals and households. Although individual efforts of healthcare professionals and science communicators are valuable, coordination with policymakers is necessary, in order to achieve favorable pricing of healthy ingredients and ensure that working routines do not collide with the time required for the preparation and consumption of healthy meals. The capacity of Largus to communicate his findings with high – end officials and receive their endorsement reflects the need of creating and maintaining channels of communication with regulators and stakeholders.

**CONCLUSION**

Overall, Largus’s contribution to the safe integration of nutraceuticals in clinical practice has set an example for contemporary clinical pharmacists and physicians. In his footsteps, these scientists need to contribute to the improvement of their field with ethically conducted scholarly work. It is also crucial to develop a good understanding of the power dynamics, in the publishing industry, in the media, and even in politics, to combat misinformation and malpractice in real-world settings.

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**AUTHOR CONTRIBUTION**

CT and AL conceptualized the article, wrote the first draft, and designed the figure(s). LM, ASP, DVM, and AL revised the first draft and wrote the second draft. AA and SP supervised the project and made the critical revision. All authors have agreed to publish the present article.

**ETHICS STATEMENT**

The authors have taken all the necessary permissions as per ethical guidelines wherever applicable. The authors will be responsible for all the technical content mentioned in the manuscript. Journal and Publisher will not be responsible for any copyright infringement and plagiarism issue.

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