

# Reviving Ancient Remedies: Botanical Knowledge and Medical Practices Across Cultures in the Age of Discovery

Dr. Zahra Mohammadi<sup>1</sup>, Dr. Mehdi Karimi<sup>2</sup>

<sup>1</sup>School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

<sup>2</sup>Faculty of Pharmaceutical Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

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## Abstract

*This research paper will cover the revolutionary era in the history of medicinal botany between the time Columbus first voyaged in 1492, and the middle of the seventeenth century. It follows the changing knowledge of therapeutic plants in Europe, influenced by the rediscovery of classical Greek works, the re-evaluation of Arabic and mediaeval pharmaceutical tradition and the addition of newcomers' flowers of the Americas. The article notes the transformation of textual philology to empirical botanical determination and institutionalizing botanical gardens as teaching institutions. It also looks at how well New World plant knowledge was absorbed or repelled by European medical systems, providing anWARE.*

**Keywords:** Botanical therapeutics; medicinal plants; New World medicine; pharmacognosy; herbalism; early modern science; Dioscorides; colonial botany; medical humanism; pharmacology history.

## 1. Introduction

A sea change in the therapeutic systems of the Old World occurred in the early modern period, especially in the late 15<sup>th</sup> through the 17<sup>th</sup> centuries. The period, roughly spanning the fall of Constantinople (1453), the renaissance humanist revival of learning, and the emerging empirical science, provoked a reassessment of ancient medical traditions. At the heart of this change was the increasing suspicion of Arabic and medieval texts on pharmaceuticals, which had held sway in European therapy since the 11<sup>th</sup> century. Translated into Latin at places like Salerno, Toledo, and Montpellier, these texts were full of terminological inconsistencies. Technical and botanical terms were frequently transliterated directly from Arabic, which sowed ambiguity and resulting in substantial misidentification of both ingredients and prescriptions. Confusion was further added by the complex nature of the compounded medicines whose pharmacodynamics were not well known and they were sometimes explained more based on theoretical considerations than clinical observations.

This seeded an intellectual breakthrough in the early 16<sup>th</sup> century, when humanist scholars, led by men such as Nicolaus Leoniceo, started questioning the authority of Arabic and medieval sources. Comparative studies of Arabic, Latin and Greek medical texts by Leoniceo made him state that numerous works considered sacred, such as the *Historia Naturalis* of Pliny, were full of errors that had propagated due to wrong interpretations of the Greek original texts. In his polemic 1492 work *De Plinii aliorumque in medicina erroribus* Leoniceo advocated a radical going back to the Greek texts of therapeutics, condemning the many centuries of commentary that had accumulated as deceptive and even hazardous(1).

This intellectual rebellion led to what is now called by historians "medical humanism" a movement that not only initiated the recovery of Greek texts, especially the *De Materia Medica* of Dioscorides, but attempted to base pharmacological knowledge on botanical reality. By the early 16<sup>th</sup> century, the Greek text of Dioscorides had been reprinted several times, and translated into Latin and the vernaculars. Learned men like Jean Ruelle and Pietro Andrea Mattioli laboured to interpret and comment on the botanical lexicon of Dioscorides, and to increase the area of its coverage. The commentaries successively written by Mattioli served to bring closer the textual scholarship and the field-based botany and promote the identification of the ancient plants within modern ecosystems.

The resulting intellectual ferment saw the emerging stricter practices in the preparing of medicines. The *Ricettario Fiorentino* of 1498, the first pharmacopoeia in the modern sense, tried to rationalize the production of medicinals, by providing a tested list of safe compounds. A student of Leoniceo, Antonius Musa Brasavola, extended this program by rigorous analyses of the pharmaceutical products of the day, classifying them according to their methods of preparation, syrups, pills, powders, and evaluating how well they corresponded to classical prescriptions.

During this period, systematic botany also emerged, e.g. in the work of Otto Brunfels and Leonhart Fuchs. Their depicted herbals tried to equate Dioscoridean species with local plants and moved the field of study with written

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interpretation to a more empirical study. In Pisa (1542) and Padua (1543) botanical gardens were created not only as sources of medicine, but as laboratory schools. Medical students could learn and test non-native plants that were both fresh and acclimated in these gardens, further medical botany and botanic medicine became firmly established(2). At the end of the 16th century Northern European cities like Leiden and Basel had taken over the Italian tradition and made botanical instruction a center of their activities.

Thus the early modern tradition of therapeutics in the Old World shifted its reliance on blurred, synthetic texts to a more empirical, more botanical science. It was a change-over that was engineered by a combination of textual criticism and institutional innovation and which set the pattern towards subsequent colonial appropriations of universal medicinal knowledge.

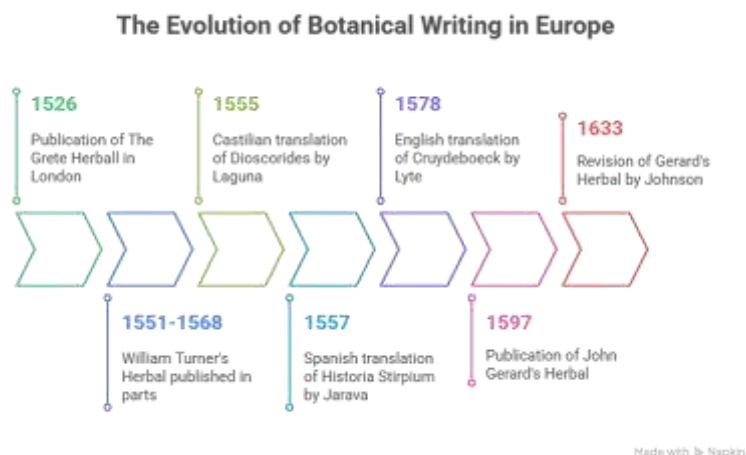
## **2.Cultural Crossroads in Print: The Rise of Vernacular Herbals in Spain and England**

The sixteenth and the seventeenth century saw a truly marvelous distribution of botanical writing in the European vernaculars, especially in Spain and in England. This transition has been a turning point in the democratization of medical knowledge since the ancient and scholarly tradition, previously available only to the Latin-reading elites, was modified and adjusted to the local audiences. The reintroduction of the Greek texts of medicine via the humanist study in both Iberia and England gave the framework to this new literature, yet each cultural environment gave rise to its own botanical persona. Luxuriously illustrated, usually experimental in spirit, and frequently bound up with empirical observations, these herbals were the foundation stone of early modern popular medicine and also important agents of the transmission of therapeutic knowledge during the initial stages of European colonial expansion.

The most basic text in the Spanish-speaking world was without a doubt the Castilian translation of Dioscorides *De materia medica* by Andrés de Laguna. Laguna had made not a translation but a commentary in which he took account of his own observations, of current practice, and of the adaptation to the Spanish pharmacopoeia, the work was first printed at Antwerp in 1555, and was reprinted many times in Spain up to the end of the 18th century. Laguna, a personal physician to Emperor Charles V, combined a degree of scholarly rigour in the work with making it understandable and relevant to daily practice. His commentary gave specific directions on how to identify and prepare medicinal plants hence filling the gap between classical antiquity and modern usefulness(3). The translation was monumental in the uniformity of pharmaceutical practice in Spain and the colonies. its authority and utility may be noted by the fact of its longevity of influence, with editions printing as late as 1783.

The works of such men as Juan Jarava (who translated the *Historia Stirpium* by Leonhart Fuchs into Spanish in 1557) further enriched this movement. The translation provided Iberian readers with entry into Northern European tradition of botany, its abundant illustration and empirical tradition of identification. By introducing the work of Fuchs to the Spanish realm, Jarava was able to facilitate a pan-European botanical dialogue where plant knowledge was not subject to borders, but instead Germanic methods of empiricism mixed with the Mediterranean tradition of pharmacology. Through these translations, the introduction of new American species into the European botanical canon was also made easier. When Spanish botanists began to encounter unknown plants in the New World, they typically tried to place them within schemes based on Dioscorides and other classical authors, a project which was advanced by vernacular texts such as that by Laguna.

In England, meanwhile, the arte of medicinal botany took a somewhat different path, but with similar driving forces: to render plant-based medicine practicable, convenient and locally customisable. The Grete Herball, a translation of a French vernacular work, and itself published in London in 1526, was the first important English herbal, and was founded on the medieval *Herbarius*. It was mainly derivative and absence of critical analysis would become characteristic of later works, but it provided the foundation of the expansion of English-language botanical writings. The real breakthrough was with the herbal of William Turner, which appeared in parts between 1551 and 1568. Having studied in Italy and imbibed continental humanist techniques, Turner applied a scientific rigour and approach to English botany. It was the initial original English-language herbal not founded on translation, but on personal botanical observation(4). *Turner's Herball* was a synthesis of the learning of Dioscorides, Galen, and the German fathers of botany, with a comprehensive commentary on the identification, location, and (where relevant) use of plants in the British Isles.



**FIGURE 1** The Evolution of Botanical Writing in Europe

Continental influence was still to be felt in English botanical culture, notably in the work of Henry Lyte, who in 1578 translated the Cruydeboeck of Rembert Dodoens into English as *A Niewe Herball*. Dodoens, a Flemish botanist, had assembled one of the richest herbals of the era, grouping plants not in the traditional alphabetical order, but according to their therapeutic effects. This structure was carried forward in the translation by Lyte, thus bringing a more systematic, clinical classification of plant medicine, to the English-speaking world. His was not a passive copy, but an interpretative work, as had been that of Laguna in Spain, an adaptation of a foreign text to English landscape and pharmacological requirements.

It was also during this period that interest in New World medicinal plants exploded, many of which entered Europe via Iberian trade routes and trickled into English herbals via secondary sources. John Frampton, *Joyful News Out of the Newfound World* (1577) was a translation of the works of the Spanish physician Nicolais Monardes about American botanical products including tobacco, sassafras and guaiacum. The work, although scientifically unsound, contributed to popularize exotic substances in England, and to form popular ideas about the therapeutic riches of the Americas. Frampton translation showed how English writers in the early periods depended on Spanish sources to gain knowledge of the botanical world of the New World, thus showing how the European colonial and intellectual circles were interdependent.

Arguably the most representative English herbal of this period was that of John Gerard, whose Herball had first appeared in 1597. Gerard, with much dependence upon Dodoens, Fuchs, and other continental writers, endeavoured to compose a compendium of the vegetable kingdom as familiar to the English reader. Despite the numerous inaccuracies of which it has been accused (some inserted by Gerard himself, and some carried over from faulty sources) it was very popular and influential. A major attempt at correction was the 1633 revision of the work by Thomas Johnson, showing a botanical practice that had begun to mature, and which now featured peer review and field checking. Johnson, aided by apothecary John Goodyer, also started a complete English translation of Dioscorides, showing the still-dominant role of ancient sources in early modern botanical thinking(5).

In Spain as well as in England, in other words, the emergence of vernacular herbals involved more than a change in language: it was an epistemological breakthrough. Through these texts the infrastructure of popular medical literacy was created and botanical knowledge entered the homes, monasteries and apothecaries of Europe and its colonies. Whereas Spain was more likely to stay close to classical authority and hierarchical medical organisation, English herbalism was to become more pragmatic and eclectic, embracing folklore, trial and error testing, and commercial imperative. What it does show, in both instances, is that vernacular botanical texts were a source of colonial bioprospecting, colonial public health practice, and the larger scientific revolution.

### 3.Medicines of Empire: Encountering and Exploiting the Therapeutic Resources of the New World

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The post-1492 European discovery and colonization of the Americas brought about a botanical revolution that radically increased the pharmacological horizons of Western medicine. The New World lands were not just the treasuries of valuable metals and economic potential- they were also overfilled with vegetation that was previously unheard of to the European eyes. Most of these plants had vivid and usually powerful medicinal uses and immediately attracted the attention of imperial physicians, merchants, and natural historians. Nevertheless, however deeply promising this new pharmacological archive would prove to be, the fact of the integration of indigenous botanical knowledge into European medicine was spotty, selective, and often occurred through the existing Greco-Roman filters. It is this dynamic of encounter, appropriation, and in many cases suppression of indigenous medical traditions that sheds light on the colonial dynamics of globalization of therapeutic knowledge that took place in the early modern period (6).

Among the first therapeutic discoveries to be made on behalf of American plants was that of guaiacum bark (*Guaiacum officinale* L.), a resin-yielding tree indigenous to the Caribbean and northern South America. This plant was discovered by Spanish conquistadors and samples of it were taken back to Europe where it quickly gained a reputation as a cure of syphilis which had only just started to devastate Europe itself. The bark began to appear in European medicine through the court physician Paulus Riccius in 1518, and the German physician Ulrich von Hutten extolled its virtues in his 1519 treatise *De guaiaci medicina et morbo gallico*. Although the real-world utility of guaiacum is nowadays somewhat dubious according to current standards, its sensational reception illustrated the marketability of new, exotic remedies in a medical marketplace desperate to believe in hope and progress.

Tobacco (*Nicotiana tabacum*) was another plant of transformation: Columbus and his successors witnessed its ceremonial and medicinal use among the locals on the first expeditions. First appearing in the discourse of therapy, as a means to heal everything from headaches to wounds and skin imperfections, tobacco rapidly entered into the European pharmacopeia and was being grown by settlers in the Caribbean by the 1530s. Its skyrocketing success, though, was also an expression of a confluence of medicinal interest and financial desire. Tobacco was being exported to Portugal by the mid-sixteenth century, and in 1561 Jean Nicot, the French ambassador to Lisbon, brought it to the French court. The plant American seed catalogue

Nobody perhaps, embodies the early attempt at a systematic assessment of American medicinal plants as much as the person of Nicolas Monardes, a Spanish physician in Seville. As Spain positioned itself at the receiving end of its colonial trade lines, Monardes had an advantageous access to the botanical material returning to Spain after discovery in the Americas. His *Dos libros...* (1565) was a pioneer work of classifying and rating these substances in the context of Dioscoridean and Galenic medicine. Monardes discussed a remarkable range of plants, such as sassafras, mechoacan, tobacco and the bezoar stone, evaluating their qualities on the basis of observation and experiment, yet in all cases in relation to classical paradigms. His approach was characteristic of a wider European approach: instead of taking on local epistemologies, scholars forced new plants through the old paradigms, frequently misunderstanding native uses in the process. Nevertheless, the work of Monardes was much translated, including into English by John Frampton in 1577 as *Joyful News Out of the Newfound Worlde*, which would be influential on English ideas about American therapeutics for generations(7).

still another important event in the fomentation of American botanical knowledge was the *Libellus de Medicinalibus Indorum Herbis*, or Badianus Manuscript. Produced in 1552 by two learned Aztec writers - Martín de la Cruz and Juan Badiano - this bilingual Latin-Nahuatl treatise listed 204 medicinal plants employed in Aztec medicine, with illustrations and comments on their application. The manuscript was commissioned by Spanish ecclesiastical officials and forwarded to King Charles V as a gesture of native medical espionage. But although of astonishing detail and revelation of the native therapeutic systems, the manuscript received little attention on the part of Spanish officials. Based on indigenous cosmologies and symptomatology, its content also never meshed with the existing European medical orthodoxies still wedded to Greco-Roman models.

The failure to do this would be replicated in the figure of Francisco Hernández, who was perhaps the most ambitious of all scientific emissaries of early Spanish imperialism. Hernández was sent by King Philip II in 1570 to catalogue the botanical riches of New Spain (modern-day Mexico), and spent three years making a careful field survey aided by local Indigenous informants and artists. The result of his efforts was the multi-volume *Historia de las Plantas de Nueva España*, a giant botanical encyclopedia with illustrations, vernacular names, and Medicinal use description. Bureaucratic inertia and the subsequent loss of much of his archive in the fire at El Escorial in 1671 meant, however, that the findings of Hernández did not have great immediate impact. An abridged form, edited by Antonio Recchi,

and subsequently published in Mexico in 1615 by Francisco Ximenez, presented but but a glimpse of the immense body of material which had been collected.

Even though Spanish imperial projects generated a massive body of written work on New World plants, the integration of this information into European medical practice was frequently hampered by epistemological narrow-mindedness and political interests. Instead of replacing Old World cures, New World plants were often exoticized and sold as complements to known cures. This was especially true with French, Dutch and English colonial ventures that were later and more business than scientific in their ventures. Though the English colonists in Jamestown and Plymouth found abundant local plant life, their early practice of therapeutics was solidly rooted in the imported English herbals and medicinals. Indeed there was a school of thought among some European doctors that man must be dependent upon the plants of his native region and this may be seen in the works of Timothy Bright and others who asserted that English medicines were adequate even in foreign climes(8).

However, there was gradual acculturation. North American settlers started to steal indigenous herbal knowledge and use it without naming the indigenous people as the source of the knowledge by the seventeenth century. The process of knowledge sharing between colonists and Native American healers was informal and often covert, native cures creeping into settler pharmacopoeias. In spite of institutional opposed many of these plants such as echinacea, ginseng, and witch hazel eventually became mainstays of western herbal medicine. Nonetheless, the history of this knowledge was characterized by appropriation and erasure as opposed to equal collaboration.

To sum up, therapeutic resources of the New World had an extraordinary influence on European medicine, yet their adoption was refracted through the institutional forms of empire, trade and cultural hegemony. European scholars were not prepared to open themselves to the epistemological wealth of the indigenous medical systems but instead cherry-picked interpretations that could be incorporated into classical paradigms. that the history of New World botany is also the history of imperial taxonomy, of the commodification of knowledge, and of the frequent erasure of the medicinal knowledge of the Americas.

#### **4.Theories, Elements, and Essences: Philosophical Foundations of Early Modern Botanical Medicine**

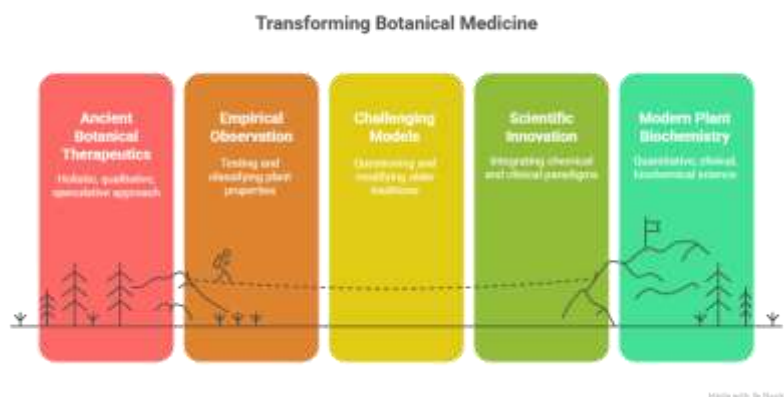
The early modern period in the long history of Western medicine marks both the flowering of the ancient schools of thought and a dawn of the proto-scientific thinking. This is nowhere more clear than in the theoretical systems which support botanical therapeutics. In the 16th and 17th centuries, physicians and naturalists attempted to describe the medicinal properties of plants not only based on empirical observation, but also on thoroughly ingrained cosmological and physiological systems. The key to this worldview was the theory of humoral balance, elemental theory, and, eventually, atomistic and materialist explanations of the action of drugs. The combination of these overlapping paradigms dictated how early modern practitioners thought about, viewed, and used botanical substances. The intellectual significance of botanical therapeutics during this era can hardly be estimated without entering into the tangled mass of theories which dominated medical thought, ranging on the one side over the holism of Hippocrates and Dioscorides to the composite systems propagated by Galen.

The background of early botanical medicine was the classical theory of four elements of earth, air, fire, and water, each having its qualities (hot, cold, moist, dry). This cosmological model, which traverses the pre-Socratic philosophy and was subsequently formalized by Aristotle, was also strongly associated with the theory of the four humors: blood, phlegm, yellow bile, and black bile. These humors were considered as flowing through the human body and keeping it healthy in a delicate balance. In this paradigm, disease was caused by the disruption of this equilibrium. Therapeutics was thus directed to the restoration of harmony by the use of substances of opposite qualities--a doctrine which may be expressed by the maxim *contraria contrariis curantur*(9).

This structure organically stretched to pharmacological application of plants. A botanical reagent was not merely a chemical reactant but was invested with properties based upon its elemental constituents and history of exposure to the environment. A plant which had grown in warm, sunny regions, for instance, was supposed to imbibe heat and dryness--properties which would neutralise cold and wet tendencies in the human body, as phlegmatic conditions. This way of classifying plants by these qualities would form a foundation of early pharmacognosy, as medical recipes often directed the inclusion of particular herbs based on their classification. The 1st-century CE collection of

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medicinals *De materia medica* by Dioscorides was an example of this approach, in which not just the uses of plants are described, but also their qualities according to the humoral theory.



**FIGURE 2** Transforming Botanical Medicine

Although holistic conceptions of healing predominated in antiquity and throughout the Middle Ages, they were eventually supplemented - and in some cases challenged - by materialist and atomistic conceptions of how drugs work. The prolific 2nd-century Roman physician Galen tried to reconcile the different traditions into a more highly developed system. Galen developed the concept that therapeutic substances possessed a combination of opposites properties in his work *De simplicium medicamentorum temperamentis et facultatibus* (On the Mixtures and Properties of Simple Medicines); these substances were ranked in a scale of four degrees. accordingly, one plant might be rated as, say, hot in the second degree and dry in the third, reflecting a more sophisticated and quantitative appreciation of its actions. Significantly, Galen too speculated that the dynamic action of medical substances in the body was due to their “material qualities” i.e. to the physical shape and weight of the particles which they contained(10). This explanation was not yet atomism in the modern sense, but it was getting closer to a mechanical explanation of physiology.

This ambidextrous heritage of holism and materialism was still influencing medical theory as late as the Renaissance. Avicenna and Al-Razi Arabic scholars translated, preserved, and elaborated the teachings of Galen during the Islamic Golden Age. These writers applied Galenic reasoning to the study of compound medicines, and tried to determine the overall temperament of polyherbal prescriptions. Nonetheless, this endeavour was not without serious challenge: when the single ingredients ordained conflicting qualities, how was the ultimate character of a multi-component medicine to be known? This uncertainty prompted guesswork and ultimately prompted frustration among European doctors in the late medieval and early modern times.

Renaissance saw a new examination of these inherited systems. Humanist scholars such as Niccolò Leoniceno, although supportive of a revival of learning to classical Greek texts, were also highly critical of the ramified theorisation of Arabic medicine. Leoniceno and others advocated a return to empirical and textual purity, in the simple plant-based therapies of Dioscorides as opposed to the compound prescriptions of later times. Even these reformers, however, did not thrust humoral theory aside; instead they aimed to adjust it according to greater textual faithfulness and botanical classification. Field-based observation and botanical gardens, which began to appear in medical curricula (in Padua, Montpellier, and Leiden, among others), allowed a new generation of physicians to test, classify, and teach plant-based therapeutics more accurately.

Meanwhile, rivals scientific models started appearing. That authority was undermined by the rise of chemical medicine, advocated by Paracelsus in the early 16th century, which introduced alchemical and mineral medicines. Paracelsus stressed dosage, purification and the inner virtue or arcanum of substances. Even though he relied on older cosmological correspondences, his demand to test and personalize treatments anticipated modern pharmacology. The Paracelsian movement would in turn seed the Spagyrist and other chemical physicians who perceived plants as conveying chemical signatures, as opposed to elemental attributes. Nevertheless, classical models were entrenched in university instruction, royal medical practice, and apothecary texts well throughout the 17th century.

The empirical tradition of folk and local healers constituted an interesting contradiction to the elite theoretical systems. These healers were commonly females or villagers who employed herbal medicines that had been taught to them orally and by doing rather than by reading. Although most of their knowledge was marginal to the established medicine, it still played an important role in ensuring the continuity and development of herbal medicine. Meanwhile, an example of an 18th-century medical professional who made famous written record of a previously known use of a plant in medicine is the English physician William Withering, who noted the use of foxglove (*Digitalis purpurea*) in the treatment of dropsy after being told about it by a local healer. The systematic study of the effects of foxglove by Withering was thus a breakthrough, and represented the empirical testing and scientific recording that would become the hallmark of pharmacology in the modern sense.

Reflectively, the theoretical underpinnings of early modern botanical medicine indicate a complicated mixture of persistence and transformation. Although based on much older elemental and humoral traditions, practitioners were ever more questioning, modifying, and adding to these models in the face of novice botanical discoveries, cultural contacts, and scientific innovations. The slow reformulation of qualitative into quantitative thinking, of speculative theory into clinical experimentation, and of cosmological into chemical paradigms prepared the way to the transformation of medicine as an art of balance into a science of biochemistry. Yet these early modern constructions were not merely abandoned but re-worked and their trace is still with us today in the way we understand plant medicine, tradition, and healing.

## 5. Conclusion and Future work

The rise of botanical medicine in the early modern era was more than a tale of herbs and elixirs it was a wide-scale overlap of antiquity, transgressive wonder, imperial Project, and paradigm shift. The practice and study of medicinal plants was thus in a network of cultural, philosophical, and geopolitical factors across the Iberian Peninsula, Italy, Northern Europe, and later in the colonial cities of the New World. As will be seen in this survey, early therapeutic botany did not emerge in a vacuum; it was firmly rooted in the classical cosmologies, such as the humoral theory and the balance of elements, although it was also becoming progressively invested in the materialist reasoning of Galen and subsequent chemical traditions initiated by Paracelsus and his supporters. Whether in the Latin writings of Dioscorides and Galen, or in the profusely illustrated vernacular herbals of Turner, Gerard, Laguna, and Monardes, the medicinal efficacy of plants became the focus of a profound scholarly rediscovery, empirical listing, and cultural re-contextualization.

But this botanical renaissance was not merely scientific: it was imperial as well. The discovery of the New World created tremendous new pharmacological horizons, rich in new, unknown species and local medical traditions. European doctors, including Monardes and Hernandez, tried to categorize these resources in terms of classical paradigms, usually ignoring or displacing local epistemologies. Filtered and Europeanized interpretations were favored over the Badianus Manuscript and other contributions by natives. Such selective appropriation indicates that the colonial power did not only determine the usage of the plants but also the way in which such usages were signified and authorized. The imperial project thereby stretched to cover not just land and labour, but knowledge itself, with exotic plants becoming part of European systems whilst their cultural context was forgotten.

In spite of these shortcomings the early modern botanical project provided important foundations to the modern pharmaceutical sciences. The replacement of mystical and textual dependence by observation, experiment and classification marked a firm step towards empiricism. botanical gardens were turned into living laboratories, university curricula were reformed, and vernacular literature made sure that medical information could spread beyond the Latin-reading elites. In the background there were world trading systems that linked Seville with Goa, Jamestown with Antwerp, and along with the movement of goods, came cures, beliefs, and ideologies. The early modern world of therapy, in other words, was a local and global, ancient and novel, empirical and theoretical landscape.

Reflectively, early botanical therapeutics offers the example of how complicated transitional knowledge that is not utterly scientific or entirely premodern, but rather something liminal, produced in the furnace of cultural contact, textual rediscovery, and world encounter. The centuries have left behind not only an archive of useful plants, but a disputed history of how healing is defined, who owns it, and what it means to know nature. With the modern medicine returning once more to the use of plant-based medicines and native knowledge, the lessons of this history

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are once more urgent.

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### **Conflicts of interest**

The authors have no conflicts of interest to declare

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