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Review Article

Fractals in pharmacognosy: Linking morphology, metabolites, and pharmacological relevance

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Abstract

Fractals are self-similar and hierarchically organized patterns found throughout nature that can offer a framework to describe complexity in both plants and humans. Fractal architectures are evident in many aspects of plant structures, such as roots, leaves and venation networks, suggesting adaptive strategies for efficient resource acquisition and resilience to environmental stress. In addition to providing a quantitative measure for distinguishing taxa and monitoring plant health, fractal dimension can help outline the pattern of secondary metabolite biosynthetic pathways and chemical fingerprints, supporting chemometric analyses and quality control. In this context, fractalomics, a proposed discipline analogous to genomics or metabolomics, may extend fractal principles across biological systems and could be applied to pharmacognosy by linking plant morphology, metabolite networks, and systemic functions. Under a holistic view, it is possible to suggest a hypothesis-generating concept of "fractal resonance" between medicinal plants and human systems, inviting a modern reinterpretation of the historical "theory of signatures". Integrating fractal analysis with machine learning and high-throughput techniques may not only advance predictive phytochemistry and personalized phytotherapy but also promote a more sustainable use of medicinal resources by bridging ethnopharmacological knowledge with contemporary systems biology.

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1. Introduction

1.1. Fractals, complexity, and medicine

The natural world presents an intricate interplay of order and variability where organisms, from single cells to complex ecosystems, exhibit self-organization, hierarchical structures, and interactions that defy simple linear descriptions. One of the most powerful mathematical frameworks for explaining this complexity is fractal geometry, which was pioneered by Benoit Mandelbrot in *The Fractal Geometry of Nature* [1]. To join a wide range of irregular, fragmented, and self-similar objects under a single concept, Mandelbrot introduced the neologism *fractal*, derived from the Latin adjective *fractus*, meaning "broken" or "irregular," rooted in the verb *frangere*, meaning "to break". This etymology captures the essence of fractals: structures that may seem discontinuous or irregular but reveal striking patterns at different scales. In biological systems, such self-similar architectures are not merely mathematical abstractions but reflect the fundamental principles of organization and efficiency observed in living organisms, from branching vasculature and neuronal networks to the distribution of metabolites in plants, as discussed herein.

Central to this context is the fractal dimension (FD), which quantifies the complexity and scaling behaviour of living systems. Unlike integer Euclidean dimensions, FD often takes non-integer values that express how completely a structure fills the space. Values between 1 and 2 correspond to patterns that partially occupy a plane, lying between lines and surfaces, whereas values between 2 and 3 indicate intricate, surface-like structures within a three-dimensional space. This non-integer scaling is a feature of fractal geometry [1, 2]. Its theoretical foundation lies in the Hausdorff–Besicovitch dimension [2-4], which quantifies how "space-filling" a structure is by capturing its complexity across scales, and provides a rigorous definition of dimension for highly irregular sets. However, accurate estimation of the Hausdorff–Besicovitch dimension is often impractical for empirical biological data, as noted by Stewart in his discussion of numerical methods for fractal dimension analysis [5]. One commonly used approach for estimating the FD is the *box-counting dimension* [2, 6-13], also known as the *Minkowski–Bouligand dimension.* This method provides a practical way to approximate how an object fills space as the observation scale changes. This involves covering the object with a grid of boxes of side length ϵ (the scaling factor) and counting the number of boxes, N(ϵ), that contain at least a part of the object (Fig. 1). The process is then repeated for progressively smaller box sizes. For a fractal, the relationship between the number of filled boxes and the box size follows a power law, which reveals its scaling behaviour:

$$N(\epsilon) \propto \epsilon^{-D_B}$$

where D_B (the "B" stands for "Boxes") is the FD estimated by the box-counting method. The fractal dimension D_B can be formally defined as the following limit:

$$D_B = \lim_{\epsilon \to 0} \frac{\log N(\epsilon)}{\log(1/\epsilon)}$$

This corresponds to the slope of the log–log plot of N(ϵ) versus $1/\epsilon$ *(Fig. 1 and Supplementary material Annex 1).* This approach has been widely applied to biological images and signals, offering a rigorous metric for quantifying complexity in systems in which traditional linear descriptors are insufficient [7, 10, 11, 13]. By describing how biological forms fill space and self-organize, fractal analysis provides a conceptual bridge between structure and function, a perspective that underpins its growing importance in physiology, pathology, and pharmacognosy.

The role of fractals in medical science has been well recognized, as schematically illustrated in Fig. 2. Human physiology itself demonstrates fractal organization: heartbeat intervals, respiratory rhythms, neuronal firing patterns, neuroanatomy, and vascular or lung branching all exhibit scale-invariant dynamics [15-27]. Organ systems, such as the gastrointestinal tract, display fractal morphologies that optimize surface area and function [28]. Pathological states often involve breakdowns or alterations of fractal patterns [29-33], as observed in cardiac arrhythmias, chronic obstructive pulmonary diseases, cancer growth, and neurodegeneration [34-36]. Interestingly, fractal geometry has been suggested as a possible, valuable diagnostic and prognostic tool, offering insights into both the health and disease condition in medical decision making [37]. At the biochemical molecular level, proteins exhibit fractal symmetry in their interiors [38, 39]. Fractal architectures are also evident in chemical structures such as dendrimers, where Tomalia and colleagues demonstrated self-similar branching patterns that mirror fractal organization [40-42]. In pharmaceutical sciences, fractal concepts have been employed to describe drug dissolution, release, and absorption kinetics, processes that frequently deviate from linear models and instead follow fractal time–dependent scaling [43-48]. The application of fractal concepts in pharmacology has a long-standing foundation. Early studies in the 1990s suggested that drug–receptor interactions and pharmacodynamic responses often follow nonlinear dynamics that can be described using fractal models rather than strictly linear frameworks [49, 50]. This approach resonates with the broader concept of fractal reaction kinetics, introduced by Kopelman [51], who demonstrated that chemical reaction rates in constrained or heterogeneous environments deviate from classical laws and obey fractal-like scaling. Fractal theory has also been introduced for the evaluation of pharmaco-

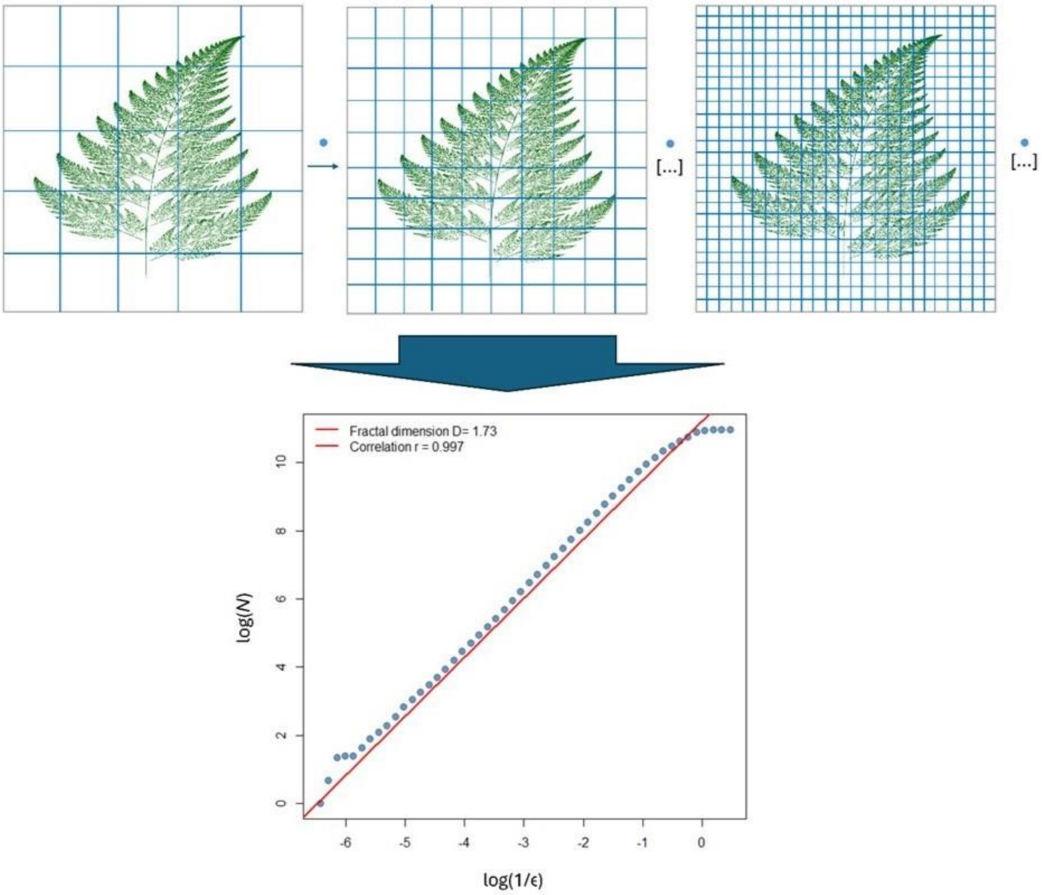

Figure 1. Example of the box-counting method for estimating the fractal dimension (D_B) on a generated fractal image, based on the Barnsley fern model [6]. The figure shows the Barnsley fern with overlaid grids of boxes with side length ϵ (scaling factor). The number of boxes, N(ϵ), containing at least one part of the object was counted. Below, the log–log plot of N(ϵ) versus the inverse of the box size 1/ε is shown, where the slope corresponds to the estimated fractal dimension D_B. This approach, also known as the Minkowski–Bouligand dimension, quantifies how the apparent detail of a structure changes with scale, capturing its self-similar properties. The fern image was generated using a custom R script, and box-counting analysis was performed using the *Rdimtools* package [14]. See Supplementary Material - Annex 1, for details.

kinetic parameters [52-54]. These studies collectively introduced the idea that FD could serve as a quantitative descriptor of pharmacological complexity, suggesting a new representation of dose–response relationships, variability among patients, and emergent biological effects.

Fractal geometry may offer a practical model for pharmacognosy, where both plant structures and chemical compositions exhibit hierarchical and self-similar patterns. By quantifying these patterns through the FD, it is possible to capture the multiscale complexity of morphology and phytochemical organization in a single, scale-invariant measure. Building upon this foundation, the present review examines how fractal concepts can be further integrated into pharmacognosy, with a particular focus on plants of possible interest, their metabolites, and their pharmacological relevance.

2. Materials and methods

This review was conducted as a narrative synthesis to examine the integration of fractal concepts into pharmacognosy research. A narrative approach was deemed most appropriate given the interdisciplinary and heterogeneous nature of the available literature, which spans theoretical mathematics, plant physio-

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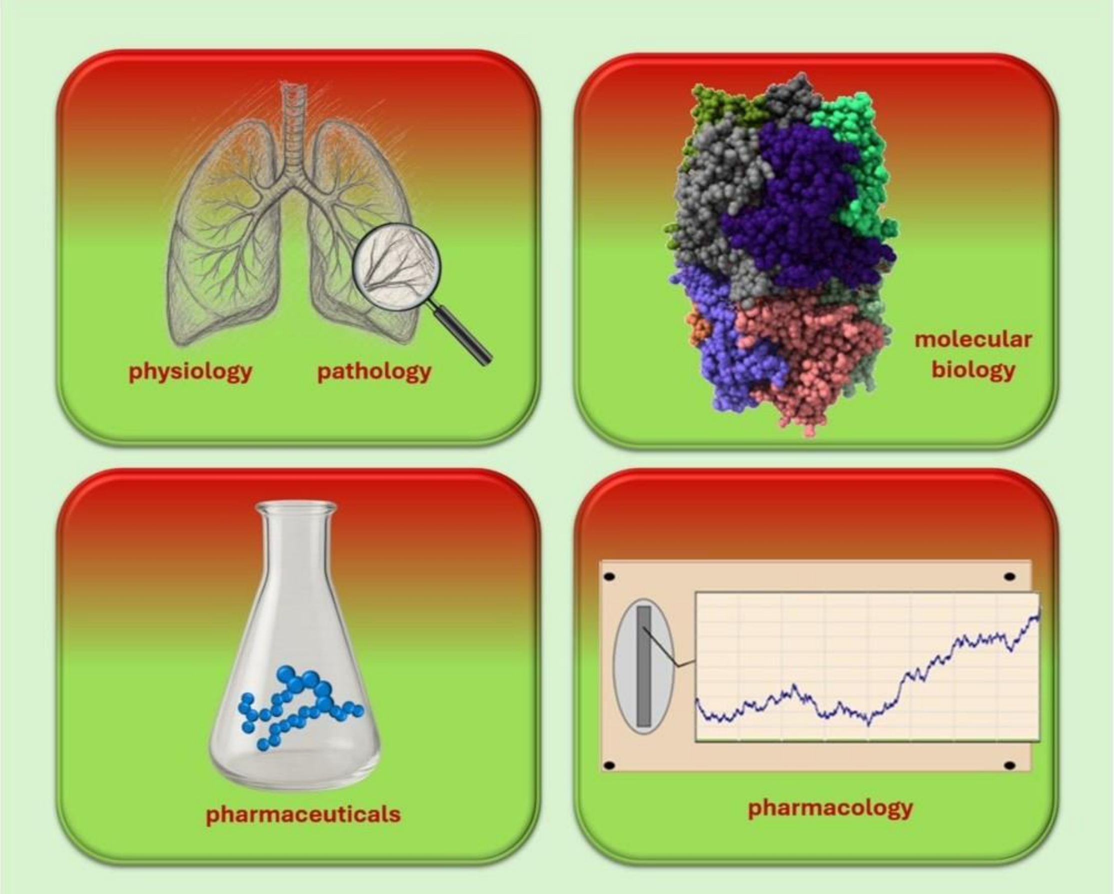

Figure 2. The scheme illustrates the applications of fractals in medical science across multiple scales. Human physiology shows fractal organization, while pathological states often involve fractal alterations. At the molecular level, proteins and chemical structures, such as dendrimers, exhibit self-similar patterns. In pharmaceutical sciences, fractal models can describe drug dissolution and release; in pharmacology, fractals can capture drug–receptor interactions and pharmacodynamic responses, offering novel perspectives on dose–response relationships.

logy, phytochemistry, and pharmacological sciences. Relevant publications were identified through searches on PubMed, Scopus, and Google Scholar in August 2025, using Boolean combinations of keywords such as “plant AND fractals,” “plant AND metabolites AND fractals,” “fractal AND pharmacognosy,” and “fractals AND herbal”. Additional sources were identified by screening the reference lists of the key articles. In total, approximately 1384 records were retrieved (PubMed: 441; Scopus: 783; Google Scholar: 160), from which 55 studies were considered eligible for inclusion based on the following criteria: i) studies applying fractal theory to plants with biological, chemical, or pharmacognostic relevance and ii) both foundational (1990s–2000s) and recent applied studies in pharmacognosy and related disciplines. No temporal restrictions were applied. The exclusion criteria were as follows: i) studies focused exclusively on mathematical modeling without biological or pharmacognostic application and ii) articles outside the scope of plant-based pharmacology and chemistry (e.g., general fractal theory without biological context). General articles on fractals were considered for the introductory section of the study.

Notably, many foundational studies on fractal applications in pharmacognosy, pharmacokinetics, and phytochemistry were conducted during the 1990s and the early 2000s, reflecting the period when fractal theory was first introduced in these fields. Because the present review focuses specifically on fractal models and their integration into plant-based pharmacology

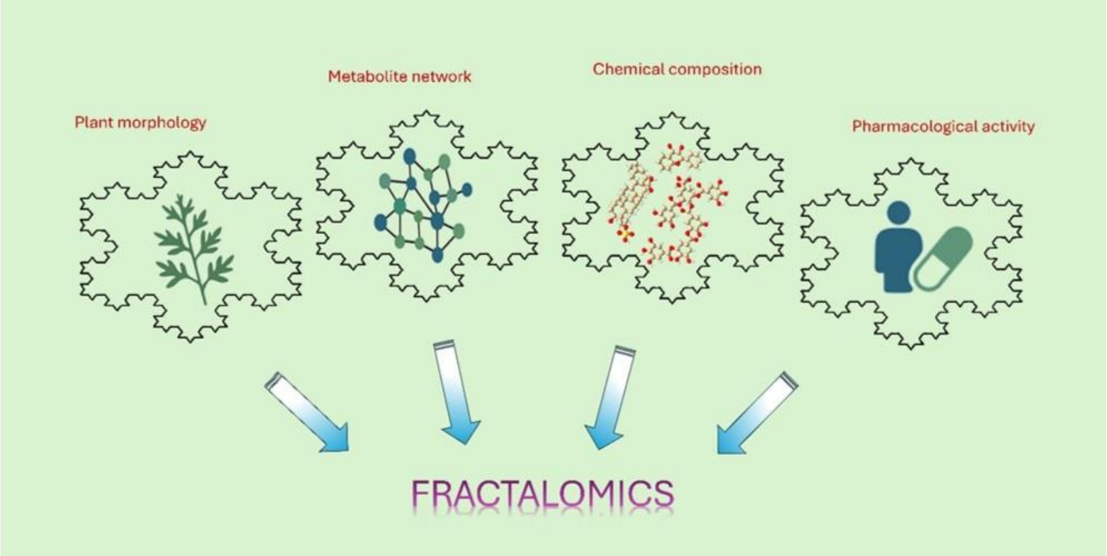

Figure 3. The conceptual scheme of *fractalomics*, originally proposed by Losa [55], is applied to pharmacognosy to illustrate how the hierarchical, self-similar organization of living systems can inform this field. The figure highlights how fractal principles can integrate the structural, chemical, and functional aspects of plants, linking morphology, metabolites, and biological activity within a unified, self-similar framework.

and chemistry, priority was given to this core body of literature. Although recent advances in metabolomics, imaging, and AI-based chemometrics are relevant to plant science, they generally do not directly employ fractal formalisms and are therefore considered beyond the scope of this review. Data from eligible sources were examined qualitatively, with particular attention to how fractal analysis has been applied to describe structural complexity in plants, elucidate metabolite organization, and inform therapeutic or historical interpretations in pharmacognosy. To facilitate synthesis, the literature was organized into four thematic domains: (i) fractals in plant pathophysiology and pharmacognosy, (ii) fractal perspectives on secondary metabolites and phytochemical diversity, (iii) therapeutic and historical dimensions of fractal thinking, and (iv) future directions in pharmacognosy.

3. Results and discussion

3.1. Fractals in plant pathophysiology and pharmacognosy

As a global concept, the hierarchical, self-similar organization of living systems, from cells to organs, can be gathered under the new field of *fractalomics*, originally introduced by Losa [55]. Analogously to genomics or metabolomics, this "omics" research topic, referring to a concept of wholeness, can encompass diverse biological structures and processes displaying spatial or temporal self-similarity.

Fig. 3 schematically illustrates how fractalomics can be applied to pharmacognosy, highlighting how plant morphology, metabolite networks, chemical composition, and pharmacological activity can be integrated under a unified, fractal-based approach. Plants inherently exhibit fractal characteristics: their roots, leaves, venation networks, and branching patterns adhere to fractal principles [11, 55-60], and in some cases, such structures have been linked to underlying gene activity [61, 62]. Even plant distribution patterns across an ecosystem may reflect the underlying fractal characteristics of the soil [63]. Fractal analysis of leaf contours and venation enables plant identification by quantifying self-similar geometric patterns through FD [64, 65]. Beyond morphology, plant chemical organization, from biosynthetic pathways to metabolite aggregates, also demonstrates self-similarity, as discussed herein, further supporting the application of fractalomics in pharmacognosy. To illustrate this, Table 1 summarizes representative studies that have applied FD analysis to plant systems, encompassing morpho-

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Table 1. Representative studies applying fractal dimension (FD) to plant systems, highlighting morphology, metabolites, and pharmacognostic relevance.

Species/ System	**Method (FD)**	**Focus (Morphological/ Metabolic)**	**Key findings**	**Ref.**
Rice leaves (bacterial stress)	Spectral FD Index (SFDI) on hyperspectral curves	Morphology/ physiology	SFDI strongly correlated with chlorophyll content; predicted better than traditional vegetation indices.	[66]
Quercus spp. leaves	Box-counting (ImageJ) on leaf outlines	Morphology/ taxonomy	FD discriminated functional groups (sclerophyll vs. deciduous); supported taxonomic resolution.	[67]
Tree crowns	FD on canopy silhouettes	Morphology/ health status	Crown FD tracked structural decline, transparency; correlated with tree health indicators.	[68]
Wheat roots (hydroponic)	Box-counting, RCI (Relative Complexity Index)	Morphology/ stress physiology	FD/RCI detected heavy-metal effects earlier than biomass; Cd/Cu reduced complexity, Zn increased it.	[69]
Brachiaria spp. leaves	Multi-scale FD descriptors	Morphology/ taxonomy	Multi-scale FD effectively classified species; captured ecologically relevant variations.	[70]
Vitis vinifera leaves from different genotypes and environments	Box-counting on leaf images	Morphology	FD use for ampelography.	[58]
General plant metabolism	Conceptual fractal framework	Metabolites/ systems biology	Argued metabolic networks (incl. flavonoids) show fractal properties; FD as systems-level descriptor.	[71]
Dihydroquercetin (Taxifolin)	FD of fractal aggregates post-lyophilization	Metabolites/ solid-state flavonoid	FD described flavonoid aggregation/porosity; experimental validation of fractal metrics.	[72]
Herbal mixtures	Box-counting on ESI-MS spectra	Metabolites (phytocomplexes)	FD reproducibly characterized extracts; batch clustering and stability monitoring.	[73, 74]
Herbal chromatograms /spectra	FD descriptors (including Higuchi FD) in spectral/ chemical data	Metabolites	FD improved discrimination of chromatographic/mass spectral fingerprints.	[75-78]
Chromatographic wine data	FD discriminates among wine varieties	Wine sample constituents	FD permitted discrimination of wines based on HPLC-DAD data.	[79]
Herbal extract	FD of pore structure change of *Radix Scutellariae* by wine processing	Parameters of pore structure by mercury intrusion method	Correlation between the dissolution and the FD of pore structure parameters.	[80]
Herbal extract & *in vivo* study	FD of pore structure of *Scutellaria baicalensis* extract (wine-extract vs raw)	Total flavonoids + five major flavones (baicalein, baicalin, scutellarin, wogonin, wogonoside)	Positive correlation was observed between FD and dissolution.	[81]
Herbal extract	FD of pore structure in wine-processing of *Radix Clematidis*	Triterpenoid saponins	FD and microporosity of *Radix Clematidis* enhanced saponin extraction yield.	[82]
Tannins	FD of aggregation / porosity	Metabolites (condensed tannins)	FD captured fractal aggregation patterns; relevant for material/biological interactions.	[83]

Entries are presented in the order discussed in the main text.

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logy, metabolites, and pharmacognostic relevance.

In the context of plant pathophysiology, Cao et al. [66] explored how the spectral fractal dimension index (SFDI), derived from hyperspectral data, could be used to predict the chlorophyll content in rice affected by bacterial (*Xanthomonas oryzae* pv. *oryzae*) blight disease. Unlike traditional vegetation indices that rely on a few wavelengths, the SFDI captures the overall structural complexity of the spectral curves. This approach showed a stronger and more consistent correlation with the chlorophyll levels. Interestingly, the combination of SFDI with machine learning models further improved the predictive accuracy. Consequently, fractal-based analyses are not only robust but also practical for the non-destructive monitoring of plant health under disease stress, thereby providing a possible new additional method for ensuring quality control in the field of herbal products.

Complementing this functional perspective, Musarella et al. [67] applied FD analysis to the leaves of several *Quercus* species, showing that distinct fractal signatures could differentiate marcescent-deciduous from sclerophyllous forms and clarify the affinities of a hybrid species in agreement with molecular data. Extending these insights to a broader ecological scale, Murray et al. [68] developed a hemispherical imaging methodology to quantify the tree crown structure through FD analysis. Unlike traditional visual assessments, which rely on subjective categorization and overlook intra-category variability, this approach translates canopy features such as transparency, vitality, and structural integrity into a continuous, quantitative scale. The studies indeed suggest greater precision and repeatability of the approach, allowing more objective evaluation of tree conditions and the potential to inform arboricultural, ecological, and forest management practices, as well as studies in pharmacognosy aimed at assessing medicinal plant morphology and quality. Although additional refinement is required to define interspecific thresholds and test acquisition sensitivity, these investigations demonstrate how fractal-based metrics can provide transferable and scalable tools for characterizing the structure of a tree across diverse contexts.

On a similar approach, Li et al. [69] applied fractal geometry to characterize the complexity of the root system morphology of wheat plants under the exposure of heavy metals, namely cadmium, copper, and zinc, which are also of concern in the cultivation and safety assessment of medicinal plants due to their potential to contaminate plant tissues and affect phytochemical quality, or even expose to toxicological risks. The authors proposed a measure, called the relative complexity index (RCI), based on FD, before and after exposure to heavy metals. FDs were calculated by the box-counting method using digitized and skeletonized images of the roots of wheat plants cultivated in a hydroponic system and under different concentrations of the investigated metals. Specifically, RCI decreased under Cd and Cu stress, whereas it increased under Zn exposure, underscoring its potential as a reliable indicator of root system complexity under metal stress. These results imply that RCI can be an effective measure of both negative and positive effects of heavy metals on root system development. By extension, such fractal-based metrics could be applied in medicinal plants to monitor root system health, assess heavy metal contamination, and potentially predict the impact on bioactive compound distribution.

Fractal analysis has proven to be a versatile tool in agriculture, botany, and ampelography. Specifically, Florindo et al. [70] demonstrated that leaf images of *Brachiaria* species, analyzed using fractal descriptors and classified with a support vector machine, could be discriminated with an accuracy of over 93%. This finding highlights the method's potential for varietal identification, seed purity testing, and breeding programs, while also providing a non-destructive approach for taxonomic verification in natural product research, including herbal products. Likewise, Mancuso [58] applied the box-counting algorithm to grapevine leaves, showing that FD could reliably distinguish most Sangiovese-related genotypes and remained consistent across diverse environments. Therefore, FD can serve as a scale-invariant, environment-independent morphological parameter, making it particularly valuable for ampelographic and taxonomic research.

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Taken together, these studies illustrate that FD, integrated into fractalomics, is both a conceptual and practical tool. By capturing complexity across scales, fractal analysis provides a consistent quantitative descriptor that links morphological, physiological, and ecological domains, offering a promising avenue for the characterization of bioactivity profiles in natural product research.

3.2. Fractals in secondary metabolite systems

Fractal analysis provides a unifying tool for understanding and managing the intrinsic complexity of plant-derived metabolites across biosynthetic, analytical, and pharmaceutical scales. For instance, Ivanov et al. [71] demonstrated that flavonoid biosynthesis in plants is not governed by simple linear relationships with environmental factors but reflects stochastic fractal dynamics. The flavonoid biosynthesis pathway can be considered as a fractal system characterized by self-similar metabolic networks in which precursor flows and regulatory thresholds generate predictable patterns of flavonoid formation across multiple scales [71]. Such findings emphasize that secondary metabolism operates per se through non-linear, self-similar regulatory processes, where biochemical or ecological perturbations may lead to differences in metabolite outcomes.

Still linked to the flavonoid field, while Ivanov et al. [71] focused on the native biosynthetic scale, Terekov et al. [72] extended the application of fractal principles into the pharmaceutical domain by investigating taxifolin (dihydroquercetin, DHQ), a bioactive flavonoid of industrial and therapeutic relevance. Lyophilized co-crystals of DHQ with different coformers spontaneously organized into fractal structures, with the measured FD strongly correlated with water solubility (r = 0.94). These findings demonstrate that fractal analysis can be used not only as a theoretical descriptor of metabolite variability in plants, but also as a predictive tool for the physicochemical properties of phyto-derivatives, enabling non-destructive, automated assessment of solubility and bioavailability. In particular, this study illustrates how fractal principles bridge biological self-organization with pharmaceutical performance, providing a practical method for standardizing plant-derived active pharmaceutical ingredients.

Prior to the work of Ivanov et al. [71] and Terekov et al. [72], Mattoli et al. [73, 74] laid the groundwork for analytical applications of fractal analysis in pharmacognosy, introducing the concept of FD as a quantitative descriptor of phytochemical complexity. In their 2012 study [73], they demonstrated that the intricate ion intensity distributions obtained from electrospray ionization (ESI) mass spectra of herbal extracts displayed self-similar properties that could be captured through FD analysis. This approach enabled a quantitative assessment of spectral heterogeneity, effectively condensing the multidimensional information of the phytocomplexes into a single fractal parameter. Unlike conventional peak-by-peak interpretation, which focuses on specific marker compounds, fractal analysis provides an integrative view of the overall organization and complexity of the extract, thus reflecting its holistic chemical identity. A subsequent study by the same group [74] expanded the fractal-based metrics to compare ESI mass spectra from different botanical preparations, showing that FD values could discriminate among herbal species, extract types, and even production batches of the same product. These results highlighted the potential of fractal descriptors as objective, and reproducible tools for phytochemical profiling and quality assessment. The method proved particularly valuable in cases where conventional chemical fingerprinting yielded ambiguous results, as the fractal metrics captured subtle differences in the global spectral organization. In a pharmacognostic context, this pioneering study suggests that fractal analysis can serve as a non-targeted, scale-invariant approach for the characterization and standardization of complex botanical matrices. By providing a numerical measure of extract complexity, FD may complement existing analytical techniques in quality control, offering a new level of objectivity and comparability among herbal products, and allowing correlations between chemical complexity, pharmacological activity, and potential therapeutic efficacy.

A fractal approach has also been applied to chromatographic and colorimetric profiles, further broadening the scope of fractal-based chemometrics in pharmacognosy and food analyses. Yiyu et al. [75] introduced the concept of fractal fingerprinting of

HPLC chromatographic profiles through wavelet decomposition, calculating fractal dimensions at different resolution levels. This method generated stable chemical fingerprints that were more robust than raw chromatographic data, particularly with respect to variations in peak retention times. Applied to *Angelica sinensis*, fractal fingerprints enabled quality grade discrimination with remarkable accuracy: clustering analyses distinguished samples by pharmacological quality, while artificial neural network models achieved near-perfect identification, surpassing conventional profile-based evaluation.

Usmanov et al. [76] demonstrated that HPLC chromatograms of *Chamaedaphne calyculata* leaf extracts exhibit stochastic fractal properties, where peak number, retention time, and intensity form self-similar patterns. This fractal organization reflects the dynamic and fluctuating nature of flavonoid biosynthesis, as evidenced by Ivanov et al. [71]. In addition, the multiple metabolic pathways appear to be influenced by microenvironmental factors, such as soil chemistry. By revealing both neutral (stochastic) and deterministic features of metabolite synthesis, fractal approaches provide deeper insights into the structural variability of phytochemical profiles and offer a basis for understanding how plants adaptively modulate secondary metabolite production under changing ecological conditions. This perspective may explain the chemical heterogeneity of medicinal plants, even under controlled cultivation, and highlights why attempts at standardization based solely on environmental or genetic determinants are often inadequate. From a pharmacognostic standpoint, recognizing such fractal organization highlights the value of chemometric analyses, fractal-based modeling, and artificial intelligence (AI)-driven pattern recognition in addressing plant metabolic complexity and supporting reliable quality control.

The above-mentioned investigations offer a methodological basis for standardizing plant-derived materials and supporting quality assessment. However, to the best of our knowledge, no studies have yet applied fractal analysis explicitly to the regulatory evaluation, clinical validation, or routine quality control of herbal drugs. This gap underscores the potential of fractal methodologies to provide quantitative, scale-invariant descriptors that can complement conventional pharmacognostic markers and guide future research in standardization and pharmacological assessment.

Extending the paradigm to food systems, Zheng et al. [77] combined fractal image analysis with RGB (red, green, and blue) intensity values to monitor biochemical changes in Chinese bayberry (*Myrica rubra* Sieb. & Zucc.) juice during storage. By integrating fractal descriptors with artificial neural networks and partial least-squares regression, the authors obtained highly accurate predictions of anthocyanins, ascorbic acid, and antioxidant activity, outperforming models based solely on classical spectral variables. It is possible to suggest that fractal analysis not only enhances the stability and discriminatory power of chromatographic and spectral fingerprints, but also provides a predictive tool for quality assessment in both herbal medicines and nutraceutical products.

An additional fractal approach in natural product research is represented by the Higuchi fractal dimension (HFD), a computational method used to quantify the fractal complexity of a signal, which is particularly effective for analyzing time series and spectral data [84]. Unlike traditional linear approaches, the HFD evaluates how a signal's apparent length changes at different scales, thus capturing hidden, self-similar patterns. Compared with other fractal tools, such as the box-counting dimension, or multifractal analysis, which characterizes a broader spectrum of scaling behaviors but requires large datasets and higher computational demand, HFD offers a balance of robustness, sensitivity, and computational efficiency for spectral chemometrics. Nanda et al. [78] demonstrated this by integrating HFD with near-infrared (NIR) spectroscopy and deep learning to predict the free fatty acid content in oil palm fruits, achieving high accuracy ($r^2 = 0.959$). In pharmacognosy, the significance lies in the potential application of HFD to spectral fingerprinting of medicinal plants and phytopharmaceuticals, where overlapping signals from diverse metabolites often complicate the analysis. By extracting scale-invariant features from spectral data, HFD can enhance the authentication, quality control, and standardization of herbal drugs. As regulatory frameworks emphasize reproducible and advanced analytical methods for botanicals, fractal-based descriptors, such as HFD, can provide a scientifically grounded way to embrace the inherent complexity of natural products.

Following these analytical advances, such approaches reflect the broader trajectory of plant metabolomics, which seeks to profile and interpret the large chemical diversity of secondary metabolites. Advances in LC–MS and GC–MS technologies have greatly expanded detection capacity, but challenges remain in managing false positives, annotating unknown metabolites, and integrating ultra-large datasets. As reviewed by Ma and Qi [85], new computational methods, such as multi-step filtering pipelines, QPMASS for high-throughput GC–MS, and MetDNA for automated annotation, have significantly improved data handling and interpretation. However, while these platforms generate exhaustive chemical inventories, they largely quantify metabolomes in terms of discrete molecular identities. In contrast, FD-based analysis provides a system level index of chemical complexity, condensing the scale-invariant heterogeneity of metabolite distributions into a single numerical descriptor. Rather than replacing metabolomics, FD can serve as a complementary layer of analysis that captures emergent organizational properties that conventional peak lists overlook.

Extending the investigation to complex natural product matrices, Pisano and Bortolato [79] applied FD analysis to principal components derived from the HPLC-DAD chromatographic data of six Argentine wine varietals. The fractal-based approach improved the discrimination between varietals compared with conventional linear methods, such as multivariate curve resolution-alternating least squares (MCR-ALS), and offered a simpler, more sustainable workflow aligned with Green Analytical Chemistry principles. It is to note that this study demonstrates how fractal analysis can capture subtle multiscale patterns in complex chemical mixtures, thereby enhancing classification, authentication, and quality assessment. For pharmacognosy, these findings emphasize the potential of fractal-based analytical methodologies to quantify, discriminate, and standardize complex phytochemical or natural product matrices, complementing insights from biosynthetic studies, pharmaceutical formulations, and mass spectrometric profiling.

Fractal theory has also been applied to understand how traditional herbal processing influences both the microstructure of the final products and their pharmacological efficacy. Zhang et al. [80] investigated the thermal effects of wine-processing on *Radix Scutellariae* (RS), the dried root of *Scutellaria baicalensis* Georgi, and demonstrated that higher processing temperatures increased the dissolution of total flavonoids and five major bioactive components. The study of the surface structures of samples by means of scanning electron microscope (SEM), together with the evaluation of the pore structure by mercury intrusion analysis, revealed that temperature-dependent increases in the total surface area, fractal dimension, and mesopore content were responsible for enhanced compound release. Drawing from these insights, Lu et al. [81] further demonstrated that wine-processing of RS not only modified pore structure and fractal parameters but also strengthened anti-migraine activity in nitroglycerin-induced rat models. In particular, the fractal dimension of the RS microstructure was positively correlated with the dissolution of flavonoids and major components such as baicalein, baicalin, scutellarin, wogonin, and wogonoside. RS stir-fried for 10 min exhibited optimal pore characteristics and therapeutic efficacy, highlighting how fractal-based structural analysis can link traditional processing methods to both compound bioavailability and pharmacological performance. Also Jiang et al. [82] observed that wine-processing of *Radix Clematidis* significantly increased the fractal dimension and surface area of the herb's pore structure, correlating with enhanced extraction yields of triterpenoid saponins, thereby suggesting the role of fractal parameters as reliable descriptors of processing-induced microstructural complexity in pharmacognosy.

Tannins, a large group of plant-derived polyphenols, are well known in pharmacognosy for their astringent, antioxidant, and antimicrobial properties [86], However, they also exhibit remarkable structural functions that align with fractal principles. As shown by Arzani et al. [83], using a surface fractal dimension based on the Frenkel-Halsey-Hill (FHH) model [87], tannins can act as porogenic agents in sol–gel processes, generating porous silica networks with self-similar, hierarchical morphologies. This property underscores how natural compounds are capable of guiding the emergence of fractal-like architectures, both in biological tissues and in engineered systems. In plants, the spatial distribution and polymeric complexity of tannins contribute to defense and resilience, reflecting a scale-invariant organization. Translating these features into pharmaceutical contexts, tannin-driven fractal porosity offers potential for novel drug delivery systems and bioactive surfaces, where fractal geometry enhances the surface area, molecular interactions, and controlled release. Thus, tannins exemplify how natural metabolites embody fractal organization and how this concept can be harnessed for pharmaceutical development.

Taken together, all these studies illustrate a multiscale paradigm in which fractal principles govern the generation, behavior, and characterization of plant-derived compounds. This approach can enhance the understanding of the inherent complexity of natural products, as well as support predictive, standardized, and reliable development of herbal medicines, taking into account ecological, molecular, pharmaceutical, analytical, and processing factors. Future research directions and testable hypotheses are summarized in the "Future Perspectives" box.

3.3. Healing and harmony: Fractals, theory of signatures, and human resonance

The presence of fractal patterns in both plant structures and metabolite networks naturally raises the question of their potential for more specific interactions with human biology. If fractals are fundamental descriptors of living complexity, the therapeutic effects of medicinal plants may, at least in part, be interpreted as a dialogue between two fractal systems, plants and humans, linking chemical and structural evidence to concepts of resonance and systemic harmony.

As noted above, human physiology exhibits fractal dynamics across multiple scales, from heartbeat variability and respiratory rhythms to vascular branching and neuronal networks [88]. Similarly, we have discussed how medicinal plants display fractal architectures in morphology and potentially, in metabolite organization. This parallel can motivate a hypothesis-generating concept of "fractal resonance", proposing that self-similar patterns in plant structures or chemical networks might conceptually align with human physiological fractals. It must be clearly emphasized that this idea remains speculative and is not intended to suggest a validated biological mechanism. Rather, it offers a conceptual scheme for exploring the possible correspondences between plant and human complexity.

Historically, this concept may show similarities with the Renaissance theory of signatures [89, 90], a notion discussed by herbalists such as Jakob Böhme (1575–1624) in *Signatura Rerum* (first English edition in 1651) [91] and Giambattista Della Porta (1535–1615) in *Phytognomonica* (first published in 1588) [92] *(Supplementary Material, Annex 2).* While this doctrine was largely symbolic, modern fractal analysis might provide a quantitative lens: plant forms, or more properly their metabolite distributions, can carry "fractal signatures" that conceptually mirror human patterns, as schematically represented in Fig. 4. For example, Della Porta [92] described ocular analogies using plants such as artemisia, anemone, argemone, scabiosa, iris, and acacia, highlighting structural features reminiscent of the human eye. From a contemporary perspective, branching venation in leaves parallels retinal vasculature, flower concentricity echoes iris patterns, and the microtextures of seeds reflect self-similar geometries observed in ocular microanatomy. Empirical examples may illustrate some (albeit fortuitous) associations between structure and potential activity. *Artemisia annua* exhibits antioxidant and anti-inflammatory effects relevant to ocular health [93]; species of *Anemone* retain ethnopharmacological applications in eye disorders [94]; and *Argemone*, whose Greek name references cataracts, highlights historical alignment between morphological "signs" and therapeutic relevance in some diseases of the eyes [95].

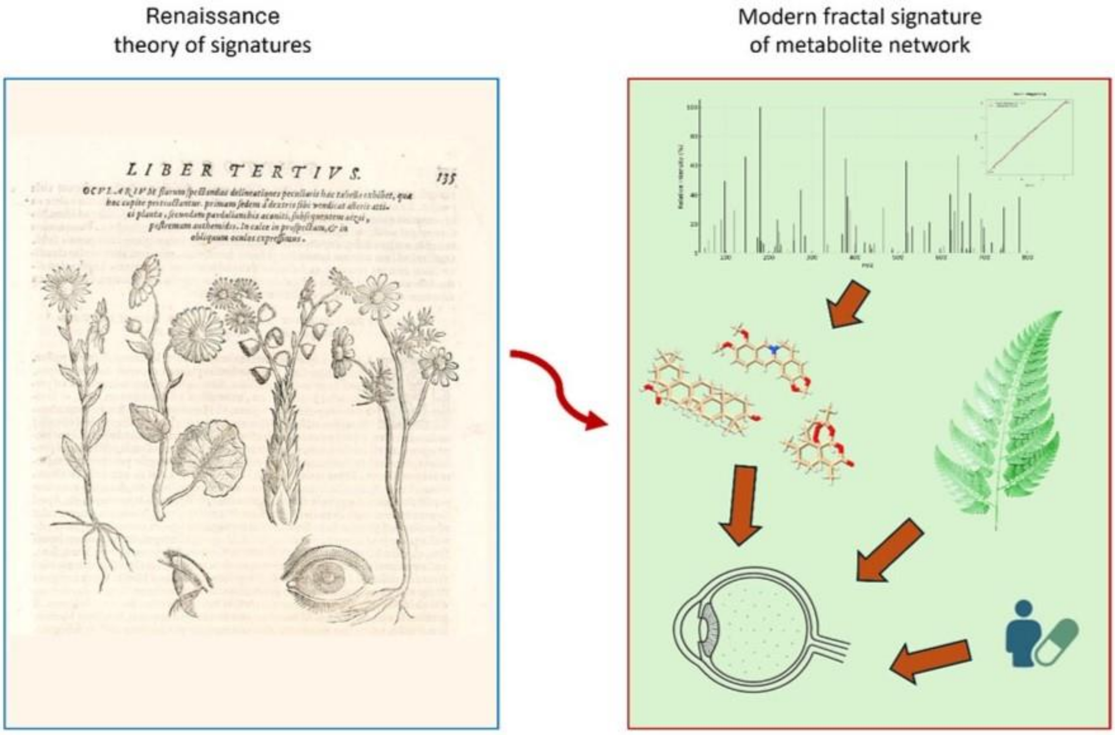

Figure 4. From historical doctrine to modern fractal analysis in pharmacognosy. Left panel: Illustration from Giovanni Battista Della Porta's *Phytognomonica* (1588) [92], representing the Renaissance *doctrine of signatures*, which proposed that plants resembling specific organs, such as eyes, could be used to treat diseases affecting those organs (see Supplementary Material – Annex 2 for further details). Right panel: Concept of "fractal signatures", as a modern, theoretical framework derived from fractal distributions in phytochemical spectra of herbal extracts, fractal patterns in plant morphology, and fractal scaling in pharmacodynamic responses. By quantifying self-similar structures and patterns in plants and their chemical constituents, fractal signatures aim to reveal the organization and distribution of bioactive compounds. This approach provides a potential method for linking plant morphology and chemistry to pharmacological activity, offering a quantitative and systems-level perspective.

Similarly, Satya-Murti [96] recently emphasized how mimetic analogies between plant and human structures have historically influenced medical terminology and conceptual thinking in the field of medicine. Such analogical reasoning, although symbolic, mirrors the broader idea of "fractal resonance," where self-similar patterns in plants and humans may conceptually align.

Beyond morphology, recent studies discussed in the previous sections reveal that secondary metabolites often exhibit fractal-like distributions within plant tissues; in particular, complex compounds, including sesquiterpenes, alkaloids, and flavonoids, follow scaling laws that reflect hierarchical organization [71]. It has been observed that pharmacological effects, such as dose-response relationships, receptor interactions, and network pharmacology dynamics, can show power-law as well as fractal behaviour [49, 50]. The convergence of fractal patterns in both plant metabolites and human physiological responses may provide a rationale for revisiting historical intuitions and bridging the field of morphology, chemistry, and physiology. By integrating these perspectives, pharmacognosy can move beyond individual bioactive compounds to explore the harmonies between complex biological systems, offering both a conceptual basis and practical tools for studying plant-human interactions while connecting modern scientific methods with traditional knowledge (Fig. 4). Future research could address the concept of fractal resonance through quantitative comparisons of fractal metrics between plant metabolites and human physiological systems, modelling potential correlations between scaling exponents and biological activity, or investigating whether shared fractal parameters influence pharmacological responses. Such studies could help determine whether the apparent parallels between plant and human fractal organization have measurable biological relevance or are coincidental.

4. Conclusion with future directions and applications

The integration of fractal analysis into pharmacognosy could open multiple avenues for both fundamental research and translational applications. In plant science, fractal descriptors can serve as high-resolution metrics to evaluate morphological plasticity, stress responses, and ecological function, complementing classical phenotyping approaches. In phytochemistry, fractal metrics enhance chemometric analyses, improve the classification of complex extracts, and provide quantitative indices for quality control and batch standardization. Coupling these descriptors with machine learning and high-throughput screening may enable more predictive and reproducible assessments of phytocomplexes, accelerating the discovery and optimization of bioactive formulations for various application.

Beyond laboratory applications, the use of a fractal approach, that is, reasoning within fractalomics, may offer a novel way to explore the systemic interplay between plant and human complexity. Viewing medicinal plants and human physiology as interacting fractal systems could allow the generation of testable hypotheses regarding therapeutic integrative interventions. This perspective may aid in the development of personalized phytotherapy, where plant formulations are selected not only for their chemical composition but also for their structural and dynamic compatibility with individual physiological patterns.

Recent conceptual work has highlighted that complexity management in medicine benefits from fractal thinking, with clinical decision-making often resembling a fractal tree in which each choice multiplies pathways of care, each with associated costs, risks, and outcomes. Analogously, evaluating phyto-complexes, polyherbal interactions, and patient-specific responses requires methods to navigate branching possibilities while preserving therapeutic efficacy.

Ultimately, the convergence of fractal theory, plant science, and human physiology positions pharmacognosy to move beyond the reductionist paradigms. By embracing fractalomics, researchers can uncover the underlying patterns governing both plant and human complexity and translate these insights into innovative strategies for health, medicine, and the sustainable use of botanical resources. Although some hypotheses, such as fractal resonance, remain exploratory, the framework provides concrete, testable directions for future research.

Future Perspectives

Fractal analysis may open new avenues in modern pharmacognosy. Future studies could:

- Apply fractal dimension (FD) as a spectral fingerprint for the authentication and quality control of herbal drugs.
- Integrate FD descriptors with machine learning to improve the classification and standardization of botanical extracts.
- Explore FD–bioactivity correlations to link chemical complexity with pharmacological activity.
- Extend fractal analysis to multi-omics data to support the emerging concept of fractalomics.

These directions may establish fractal geometry as a practical analytical and predictive tool in pharmacognosy and phytochemical research.

Supplementary materials

Annex 1 and Annex 2

Supplementary material related to this article can be found online at *https://leafletpub.com/images/articlesFile/supplementary.1760803340.pdf*

Authors' contributions

The author takes sole responsibility for all aspects of the article, including conception, literature review, analysis, and manuscript preparation.

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Availability of data and materials

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Conflicts of interest

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