BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Revisión / Review

Exploring the potential of omics technologies in medicinal plant research: A review in Colombia

[Explorando el potencial de las tecnologías ómicas en la investigación de plantas medicinales: una revisión en Colombia]

Karen M. Cardona[1,2], **Paula A. Rugeles-Silva**[1,2], **Lina Tarazona-Pulido**[1,2], **Lucia A. Díaz-Ariza**[2], **Jaime E. Muñoz Florez**[1] **& Diana López-Alvarez**[1]

[1]Departamento de Ciencias Biológicas, Facultad de Ciencias Agropecuarias, Grupo de Investigación en Diversidad Biológica, Universidad Nacional de Colombia, Sede Palmira, Colombia
[2]Departamento de Biología, Grupo de investigación en Agricultura Biológica, Pontificia Universidad Javeriana, Sede Bogotá, Colombia.

Reviewed by:
Arnaldo Bandoni
Universidad de Buenos Aires
Argentina

José L. Martínez
Universidad de Santiago de Chile
Chile

Correspondence:
Diana LÓPEZ-ALVAREZ:
dilopezal@unal.edu.co

Section Review

Received: 6 June 2023
Accepted: 17 August 2023
Accepted corrected: 21 December 2023
Published: 30 July 2024

Citation:
Cardona KM, Rugeles-Silva PA, Tarazona-Pulido L, Díaz-Ariza LA, Muñoz Florez JE, López-Alvarez D
Exploring the potential of omics technologies in medicinal plant research: A review in Colombia
Bol Latinoam Caribe Plant Med Aromat
23 (4): 460 - 486 (2024).
https://doi.org/10.37360/blacpma.24.23.4.32

Abstract: This review presents advances in the implementation of high-throughput sequencing and its application to the knowledge of medicinal plants. We conducted a bibliographic search of papers published in PubMed, Science Direct, Google Scholar, Scopus, and Web of Science databases and analyzed the obtained data using VOSviewer (version 1.6.19). Given that medicinal plants are a source of specialized metabolites with immense therapeutic values and important pharmacological properties, plant researchers around the world have turned their attention toward them and have begun to examine them widely. Recent advances in sequencing technologies have reduced cost and time demands and accelerated medicinal plant research. Such research leverages full genome sequencing, as well as RNA (ribonucleic acid) sequencing and the analysis of the transcriptome, to identify molecular markers of species and functional genes that control key biological traits, as well as to understand the biosynthetic pathways of bioactive metabolites and regulatory mechanisms of environmental responses. As such, the omics (e.g., transcriptomics, metabolomics, proteomics, and genomics, among others) have been widely applied within the study of medicinal plants, although their usage in Colombia is still few and, in some areas, scarce. (185)

Keywords: Traditional medicine; Metabolomics; Phytocompounds; Multiomics; High-throughput sequencing.

Resumen: Esta revisión presenta los avances en la implementación de la secuenciación de alto rendimiento y su aplicación en el conocimiento de las plantas medicinales en Colombia. Realizamos una búsqueda bibliográfica de artículos publicados en las bases de datos de PubMed, Science Direct, Google Scholar, Scopus, and Web of Science y los resultados obtenidos los analizamos con el programa VOSviewer (version 1.6.19). Dado que las plantas medicinales son una fuente especializada de metabolitos con importantes propiedades farmacológicas y alto valor terapéutico, los investigadores de plantas alrededor del mundo tienen puesta su atención en ellas y han comenzado a estudiarse exhaustivamente. Los avances recientes en las tecnologías de secuenciación han reducido los costos y el tiempo de secuenciación, lo que ha acelerado la investigación en plantas medicinales. Estas investigaciones aprovechan la secuenciación de genoma completo, así como la secuenciación del ácido ribonucleico (ARN) y el análisis del transcriptoma para identificar marcadores moleculares de especies y genes funcionales que controlan rasgos biológicos clave, así como para comprender las rutas metabólicas de los metabolitos bioactivos y los mecanismos reguladores que tienen las plantas en respuesta al ambiente. Aunque las ómicas (transcriptómica, metabolómica, proteómica y genómica, entre otras) han sido aplicadas en el estudio de plantas medicinales, su uso en Colombia aún es poco y en algunas áreas completamente escaso.

Palabras clave: *Medicina tradicional, metabolómica, fitocompuestos, multiómicas y secuenciación de alto rendimiento*

INTRODUCTION

In recent decades, the field of plant research has undergone significant advancements in understanding the genetic relationships, chemical composition, and therapeutic potential of medicinal plants. Initially, the emergence of plant chemotaxonomy in the 1960s aimed to explore the genetic relationships and evolution of plants through the study of chemical compounds and traditional plant taxonomy. However, this approach had limitations as it focused primarily on certain plant groups and did not consider the pharmacological effects and variations among different populations (Zhang *et al*., 2015; Rao *et al*., 2019). The influence of genetic variations on drug metabolism, transport, and pharmacological responses, which can differ among individuals, further highlighted the need for a more comprehensive and integrated approach (Crettol *et al*., 2010; Hao *et al*., 2013a; Pandita *et al*., 2021; Yang *et al*., 2021).

Since the early 2000s, researchers have been combining chemotaxonomy with phytochemistry, pharmacology, molecular systematics, DNA studies, and omics technologies, leading to extensive investigations of various plant phytogroups with medicinal effects (Chunhong *et al*., 2013; Hao *et al*., 2017a; Gong *et al*., 2022). These advancements have allowed for the identification of pharmacological effects and therapeutic responses of natural products at the whole-genome level (Rao *et al*., 2019).

In recent years, the field of pharmacophylogenomics has emerged as a multidisciplinary approach that utilizes data obtained from the genomes of medicinal plants to reconstruct evolutionary relationships based on the similarity of their chemical profiles and healing effects (Hao & Xiao, 2015; Sahoo & Brijesh, 2019; Hao & Xiao, 2020; Gong *et al*., 2022). This integrative approach combines phylogenomics, pharmacogenomics, and phylotranscriptomics, analyzing the evolutionary history of plants with healing effects using sequencing technologies such as RAD-seq and GBS (Hao & Xiao, 2015; Hao & Xiao, 2020). Pharmacophylogenomics seeks to unravel the relationships between plants in terms of their phylogenetic and evolutionary connections, their chemical composition, and their preventive and healing effects. This holistic approach guides research, aids in the improvement of existing medicines, and facilitates the development of new therapeutic interventions (Hao & Yang, 2016; Hao *et al*., 2018; Gong *et al*., 2022). Furthermore, it enables the discovery of new plants, conservation efforts for endangered species, and the prediction of active compounds (Sun *et al*., 2022).

Currently, researchers have studied pharmacophylogenetic relationships of more than 24 plant groups. These studies have revealed that plants of the order Ranunculales contain a variety of compounds, including flavonoids, phenols, lignans, terpenoids, and saponins. In particular, the Berberidaceae and Menispermaceae families stand out for containing a high amount of BBI alkaloids (Bisbenzyl tetrahydroisoquinolines), chemical compounds with a wide range of biological and pharmacological properties, including anticancer/cytotoxic, antimicrobial, neuroprotective, and anti-inflammatory activity (Martinez, 2003; Chunhong *et al*., 2013; Hao *et al*., 2013b; Wang *et al*., 2013a; Hao *et al*., 2015; Hao *et al*., 2017b; Guzman & Molina, 2018; Martinez *et al*., 2018; Hao & Xiao, 2020; Leonti *et al*., 2020; Shan *et al*., 2021; Hao *et al*., 2022; Gong *et al*., 2022; Ma *et al*., 2022).

Other studies have focused on elucidating the therapeutic targets of the active biomolecules of some medicinal plants for the treatment of various pathologies. Researchers conducted a study on *Ricinus communis* L., *Solanum nigrum* L., and *Piper betle* L., plants using chemoinformatics and network pharmacology approaches. The study aimed to discover new molecular targets, predict compounds, and evaluate the pharmacological properties of these plants for combating lung cancer (Muthuramalingam *et al*., 2023). On the other hand, Wei *et al*. (2021), reported three curcuminoids (curcumin, CUR; demethoxycurcumin, DMC; bisdemethoxycurcumin, BDMC) in turmeric and demonstrated that they possess significant synergistic anticancer activities, using technologies such as glycoproteomics and proteomics. Similarly, in the investigation of turmeric for key genes involved in metabolite production, Jiang *et al*. (2021), employed co-expression networks to identify key genes involved in terpenoid biosynthesis (TBS), by combining transcriptome and metabolome analysis. The analysis identified 250 terpenoids in different plant tissues, along with a powerful genetic module containing 26 genes "characteristic" of pathways involved in TBS. This module included genes encoding various enzymes and 12 core transcription factors.

In Colombia, publications related to multiomic approaches are still scarce. Among them, the results obtained by Ballesteros-Vivas *et al*. (2020), stand out, who evaluated the changes in HT-29 colon cancer cells induced by an extract of *Passiflora mollissima* (Kunth) L. H. Bailey., seeds at the transcriptomic and metabolomic levels in combination with viability and cell cycle assays. The obtained results revealed that the extract notably affected the viability of HT-29 colon cancer cells after 48 and 72 hours, with minor effects on the viability of normal human colon fibroblast cells. Instead of solely focusing on the medicinal field, researchers in Colombia have also directed their attention toward investigating the origin, structure, and genetic diversity of medicinal plants. For instance, a study on *Lippia origanoides* Kunth, revealed the existence of three genetic lineages using genomics (SibColombia, 2023). Similarly, White *et al*., (2021), utilized the same technology to determine that the coca plants *Erythroxylum coca* Lam., and *Erythroxylum novogranatense* D. Morris., have undergone domestication two or three times from their wild ancestor *Erythroxylum gracilipes* Peyr.

Despite the significant advances in the whole genome approach and modern 'multi-omics' technologies, research on natural products in Colombia remains limited, hindering drug development and clinical trials. Therefore, the primary objective of this review is to present comprehensive and up-to-date information on the application of multiomics technologies in medicinal plant research. The review will highlight key findings related to the proteome, genome, transcriptome, and metabolome of medicinal plants, emphasizing important plants at the national level and their potential for drug production.

METHODOLOGY

We conducted a literature search using the following electronic databases: PubMed (https://pubmed.ncbi.nlm.nih.gov/), Science Direct (https://www.sciencedirect.com/), Google Scholar (https://scholar.google.com/), Scopus (https://www.scopus.com/), and Web of Science (https://www.webofscience.com/), between November 2022 and February 2023. The included studies consisted of reports on the use of techniques such as genomics, transcriptomics, proteomics, and metabolomics, to understand better the chemical profiles and evolutionary relationships of medicinal plants, as well as explore the pharmacological potential of some plant species, particularly in Colombia. We used the following combinations of keywords: "Plant name AND multiomics," "Plant name AND genome," "Plant name AND phytocompounds," "Multiomics," "Multiomics AND traditional medicine," "Plants AND High-throughput sequencing," "Multiomics AND Systems Pharmacology," "Array Express AND medicinal plants," "RNA-seq AND medicinal plants," "Comparative genomics AND medicinal plants," "Functional genomics AND medicinal plants “and” “Bioinformatics AND medicinal plants". Mendeley was the citation tool used to manage and organize all the references collected.

The studies included in the metanalysis were based on: (i) research articles, review articles, books, and experimental studies published in different languages; (ii) studies performed at the global and Colombia; (iii) studies that included author names, publication year, location, and medicinal plants used; and (iv) the availability of the full-text article. Eligible studies had the following characteristics: articles focused on the use of omics in the study of medicinal plants in Colombia and the world. We used the program VOSviewer version 1.6.19 (https://www.vosviewer.com/) to perform the meta-analysis and generate network graphics for each theme. Subsequently, we fused the individual graphics into a single graphic (Figure No. 1).

During the search process, we identified 722 studies. After eliminating duplicates, we left with 690 studies. After a formal review of the titles and abstracts, we selected 270 articles. Subsequently, we reviewed the full texts of these articles and further excluded 90 studies due to reasons such as repeated data and an unclear presentation of results. This selection process resulted in a final set of 180 eligible articles. We conducted the meta-analysis based on these 690 articles to select the keywords for the documents, namely traditional medicine, metabolomic, phytocompounds, multiomics, and High-throughput sequencing. Figure 1 illustrates the frequency of the most used words. We observed that Metabolomics (Bernal *et al*., 2017) was the most frequently mentioned, and we considered it relevant, as it is associated with multiomics. The second most common phrase was natural products (Muthuramalingam *et al*., 2023), which refers to phytocompounds. medicinal plants (Shan *et al*., 2021) and high-throughput sequencing (Hao *et al*., 2018).

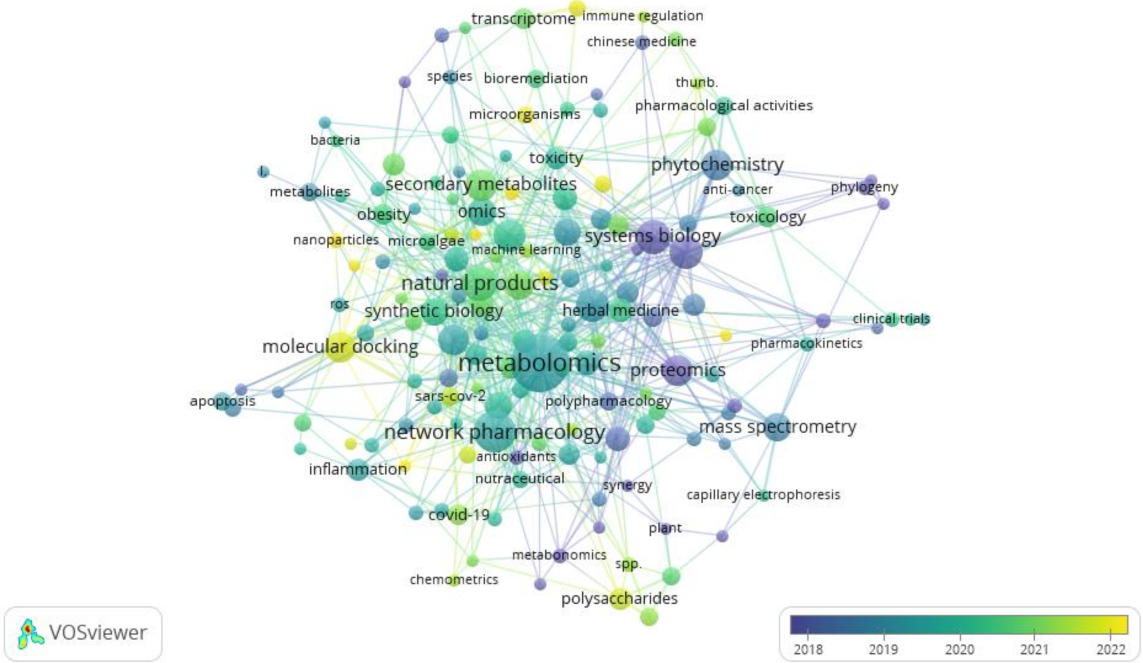

Figure No. 1
Network of keywords obtained from the meta-analysis of 690 articles that include traditional medicine, metabolomics, phytocompounds, multiomics, and high-throughput sequencing.

RESULTS

Status of medicinal plants in Colombia

In Colombia, approximately 29,769 plant species have been identified, and more than 7,000 of them are known to have some use for humans (Pajaro-Gonzalez *et al*., 2022; SiB Colombia, 2023). These species are primarily distributed across the different rainforests of the five geographic regions, with the Andes region showing the highest species richness (Bystriakova *et al*., 2021). However, it is important to consider the lack of information and documented knowledge from the Amazonia region. Around 50% of the production of medicinal plants in Colombia is dedicated to human consumption, 25% for cosmetics, 20% for the pharmaceutical industry, and 5% for other purposes (Cañigueral *et al*., 2003). Among these, researchers have identified 3,005 species with medicinal uses, of which 1,719 are native to Colombia, 558 are introduced, and 728 have uncertain origins (Castellanos *et al*., 2019). Among the mentioned species *Austroeupatorium inulifolium* Kunth. (Asteraceae), *Cymbopogon citratus* (DC.) Stapf (Poaceae), *Guazuma ulmifolia* Lam. (Malvaceae), *Jacaranda caucana* Pittier, *Solanum nudum* Humb. & Bonpl. ex Dunal (Solanaceae), *Xanthium strumarium* L. (Asteraceae), and *Hymenaea courbaril* L. (Leguminosae) are the most commonly used for treatment infections in general (Pajaro-Gonzalez *et al*., 2022).

Despite the rich traditional knowledge held by various rural communities, including Afro-descendant and indigenous groups, about the medicinal uses and properties of plants, there has been a lack of comprehensive scientific studies in this area. This information gap has created a disconnect between the ancestral knowledge of different plant species and the scientific evidence supporting their uses.

Among the limited research conducted, some ethnobotanical studies have provided valuable information on the taxonomy, distribution, and traditional uses of medicinal plants. Notable works include 'Plantas útiles de Colombia' ('Useful plants of Colombia') by Perez Arbelaez (1978) and 'Flora medicinal de Colombia' ('Medicinal flora of Colombia') by García (1974). Efforts to delve into pharmacological research have led to the publication of the 'Vademecum colombiano de Plantas Medicinales' ('Handbook of colombian medicinal plants') by the Ministerio de Protección Social (Ministry of Social Protection), by resolution 2834 from 2008. This handbook not only covers the traditional uses of plants but also provides information on their main constituents, indications, contraindications, dosages, forms, and pharmacological activities. Consequently, it has contributed to the compilation of lists of potentially useful medicinal plant species registered by the INVIMA (National Institute for the Oversight of Medicines and Foods).

Recent endeavors to consolidate and make cultural knowledge and scientific research accessible have resulted in various publications. Notably, the books 'Pautas para el Conocimiento, Conservación y Uso Sostenible de las Plantas Medicinales Nativas en Colombia' ('Guidelines for the Knowledge, Conservation, and Sustainable Use of Native Medicinal Plants in Colombia') (Bernal, 2011) and a checklist of edible and medicinal plants of Colombia (Castellanos, 2019) have played a pivotal role in this effort. Additionally, Negrão *et al*. (2022), published a comprehensive catalog of medicinal plant usage. These recent efforts have marked significant progress in bridging the gap between traditional knowledge and scientific research, providing valuable insights into the medicinal potential of Colombia's native plant species.

Through the different research investigations performed in Colombia, around 200 families have been identified to contain medicinal potential, with the most representative being Fabaceae, Asteraceae, Lamiaceae, Rubiaceae, Solanaceae, and Piperaceae, among others (Bernal, 2011; Glecio *et al*., 2016; Perez & Matiz-Guerra, 2017; Castellanos, 2019) **(Figure No. 2)**. Of the different properties attributable to these plants that have been corroborated empirically, those that stand out include anti-inflammatory, antimicrobial, antifungal, antiviral, analgesic, antibiotic, and antiparasitic usages, among others. These properties have stemmed a great interest in the knowledge of these plants, which themselves contain and produce a large number of specialized metabolites that potentially have biotechnological uses (Xiao *et al*., 2013; Perez & Matiz-Guerra, 2017; Pajaro-Gonzalez *et al*., 2022).

Figure No. 2
Visual insight into four native medicinal plants of Colombia: A) *Lippia alba* (Mill.), B) *Petiveria alliacea* L., C) *Bidens pilosa* L., D) *Guadua angustifolia* Kunth, belonging to the Verbenaceae, Petiveriaceae, and Asteraceae and Poaceae families

These inherent compounds of medicinal plants have found extensive utilization in the production of natural products and medicines, addressing the direct or indirect effects of various illnesses at both local and global scales. This industry has been instrumental in promoting the bioeconomy within Colombia. Notably, during the pandemic caused by the SARS-CoV-2 virus, the use of different medicinal plants witnessed a surge, and traditional communal knowledge played a significant role in effectively treating various health and emotional effects (Bystriakova *et al*., 2021; Cordoba-Tovar *et al*., 2022). Another area where medicinal plants have been extensively explored is in the context of providing treatment support and pain relief for cancer patients. Research efforts have focused on studying different bioactive compounds derived from these plants, aiming to create more accessible phytomedicines that can serve as therapeutic alternatives. **Table No. 1** presents plant species that researchers have identified with potential biotechnological uses for medicinal purposes in Colombia. It lists their therapeutic applications, general locality, plant parts utilized, and secondary metabolites. This compilation incorporates data from various databases, including "Useful Plants of Colombia" (ColPlantA, 2023), the International Plant Names Index (IPNI, 2023), Common Names of Plants Used in Colombia (Bernal *et al*., 2017), the Catalogue of Plants and Lichens of Colombia (Bernal *et al*., 2019), and the IUCN Red List of Threatened Species (IUCN, 2023). For a more comprehensive understanding of each species, including taxonomic details (order, family, scientific name, common name, and synonyms), conservation status, origin, habitat, and genomic information, please refer to **S1**.

Table No. 1
Plant species with biotechnological potential to treat diseases as in Colombia

Plant species	Plant parts	Medicinal uses	References
***Ilex guayusa* Loes.**	Leaves	Narcotic, stimulant, hypnotic, diaphoretic, diuretic, anti-inflammatory, antifungal, antitumor-anticancer action, and anti-allergic.	(Miniterio de Protección Social, 2008; Sequeda-Castañeda *et al*., 2016; Bustillos & Cortez, 2021)
***Bidens pilosa* L.**	Leaves, flowers, seeds, and stem	Antifungal, antiseptic, diuretic, antidiabetic, gastrointestinal problems, antiviral, anti-inflammatory, antifungal, antitumor-anticancer action.	(Miniterio de Protección Social, 2008; Bartolome *et al*., 2013; Liu *et al*., 2013; Yang *et al*., 2014; Abasi *et al*., 2022)
Acmella ciliate (Kunth) cass.	Leaves	Analgesic, anti-inflammatory, antimalarial, antiplasmodial, and antioxidant.	(Kasper *et al*., 2010; Silveira *et al*., 2016; Shipa *et al*., 2022)
***Acmella oppositifolia* (Lam.) R.K.Jansen**	Flowers, root	Anti-inflammatory, antithrombotic, anesthetic, antiviral, antimicrobial, and analgesic.	(Miniterio de Protección Social, 2008; Elufioye *et al*., 2020; Abasi *et al*., 2022; ColPlantA,

			2023)
***Tillandsia usneoides* L.**	Whole plant	Hypoglycemic, antihyperglycemic, antifungal, anti-inflammatory, astringent, dermatological, anticancer, antiviral, and cytotoxic.	(Sequeda-Castañeda *et al*., 2016; Estrella-Parra *et al*., 2019; Miranda-Nuñez *et al*., 2021; Lasso *et al*., 2022)
***Tillandsia recurvata* L.**	Whole plant	Anti-inflammatory, antiviral, antispasmodic and antitumor activity.	(Lucena de Vasconcelos *et al*., 2013; Lowe *et al*., 2017)
***Guadua angustifolia* Kunth**	Stems, Leaves	Antioxidant, antiseptic, anti-inflammatory, antibiotic and antifungal, and antitumor potential	(Arboleda *et al*., 2012; Sequeda-Castañeda *et al*., 2016; Leal & Modesti, 2021; Cordoba-Tobar *et al*., 2022)
***Bursera tomentosa* (Jacq.) Triana & Planch**	Fruits, Leaves, Flowers, and Bark	Anti-inflammatory, antiviral, antibacterial, antimicrobial, cytotoxic, and hematoprotective.	(Camargo *et al*., 2010; Moreno *et al*., 2010; deCarlo *et al*., 2019)
***Tara spinosa* (Molina) Britton & Rose**	Leaves and stems	Anti-inflammatory, antiseptic, antibacterial, antiviral, antimicrobial, antitumor, and antioxidant.	(He *et al*., 2015, Prieto *et al*., 2019; Zhao *et al*., 2019; Gámez-Espinosa *et al*., 2021; Ballesteros-Ramirez *et al*., 2021)
***Passiflora ligularis* Juss.**	Leaves	Antioxidant, nephroprotective, antimicrobial, antifungal.	(Carraz *et al*., 2015; Carmona-Hernández *et al*., 2021; Castañeda *et al*., 2023)
***Passiflora mollissima* (Kunth) L.H.Bailey**	Leaves and seeds	Antiproliferative, antimicrobial, cytotoxic, antibacterial, antifungal, and antiproliferative.	(Calderon *et al*., 2019; Ballesteros-Vivas *et al*., 2020; Fonseca-Benitez *et al*., 2022)

***Passiflora quadrangularis* L.**	Leaves and stems	Antidiabetic, antioxidant, and cytotoxic.	(Rivas Mena *et al*., 2015)
***Acalypha macrostachya* Jacq.**	Leaves, stems, and roots	Antimicrobial.	(Seebaluck *et al*., 2015)
***Piper cumanense* Kunth**	Leaves and fruits	Antiparasitic, antifungal and cytotoxic, and antiproliferative.	(Velandia *et al*., 2018; Abasi *et al*., 2022; Prieto-Rodriguez *et al*., 2022)
***Piper aduncum* L.**	Leaves	Antiprotozoal, acaricidal, insecticidal, anthelmintic, antioxidant, cytotoxic, and anti-inflammatory.	(Monzote *et al*., 2017; Agüero-Hernandez *et al*., 2020; Abasi *et al*., 2022)
***Piper obliquum* Ruiz & Pav.**	Leaves	Anti-inflammatory, antiseptic, and antifungal	(Valdivia *et al*., 2008; Ruiz-Vasquez *et al*., 2022)
***Psychotria poeppigiana* Müll. Arg.**	Leaves	Anti-inflammatory, analgesic, antimicrobial, and antioxidant	(Leal & Modesti, 2021)
***Lippia alba* (Mill.) N. E. Br. ex Britton & P. Wilson**	Aerial parts and leaves	Antiseptic, anticarcinogenic, antimicrobial, antifungal, immunomodulatory, antioxidant, cytotoxic, antiviral, analgesic, and antibacterial	(Miniterio de Protección Social, 2008; Gomide *et al*., 2013; Santos *et al*., 2016; García *et al*., 2017;Leal & Modesti, 2021; Quintero *et al*., 2021)

The plants mentioned above have they have distinct life forms, from herbal, vines, trees, and shrubs, and are mostly native and naturalized cultivated plants. Their conservation statuses are Least Concern or Not Evaluated. On the other hand, different physiochemical studies have identified the principal constituents present in these species to be Caffeine, Theobromine, Theophylline, Steroids, Terpenoids, Phenolic acids, Flavonoids, Quinones, Glycosides, among others (Kasper *et al*., 2010; Yang, 2014; Sequeda-Castañeda *et al*., 2016); as well as more specific compounds according to the species such as Triterpenoids, Dioxacmelamide, Heliobuphthalmin, Cyclo-arthenone, C-glycosylated flavones, Limonene, α-humulene, β-Cadinene, Asebogenin, Cardamomin, Nerolidol, Methyllinderatin, Dillapiole (Lucena de Vasconcelos *et al*., 2013; Silveira *et al*., 2016; Jiang *et al*., 2021), among others. All of these confer these plants their distinct properties that have been utilized ancestrally and culturally.

It is important to note that the most common traditional uses of these plants involve the preparation of infusions from their leaves and flowers to treat digestive problems (Abasi *et al*., 2022). The next most common use is for treating respiratory problems (He *et al*., 2015; Prieto *et al*., 2019). In ointment form, plants have been utilized for the topical treatment of fungal, and microbial infections, and inflammation (Seebaluck *et al*., 2015). Culturally, several different uses of the listed plants have been registered, such as a diuretic, narcotic, sedative, analgesic, antiseptic, abortive, or for treating hemorrhoids, type I and II diabetes, hormonal disorders, cramps, and fertility problems (Elufioye *et al*., 2020; Leal & Modesti, 2021; Prieto-Rodriguez *et al*., 2022). As such, they have different reported pharmacological activities, including antioxidant, antihyperglycemic, antihypertensive, anti-inflammatory, cytotoxic, antidiabetic, antidiarrheal, antimicrobial, antifungal, antiparasitic, antiulcer, antiviral and anticancer (Bernal, 2011; Bartolome *et al*., 2013; Yang, 2014; Xuan & Khan, 2016).

Extensive studies have demonstrated the anticancer potential of these plants. Researchers have found that plants such as *Ilex guayusa* Loes., *Bidens pilosa* L., *Tillandsia usneoides* L., *Tillandsia recurvata* L., *Guadua angustifolia* Kunth., *Bursera tomentosa* Jacq., *Tara spinose* Molina., *Passiflora Mollissim* Kunth., *Piper cumanense* Kunt., *Piper aduncum* L., and *Lippia alba* Mill., contain different methanolic, hydroalcoholic, and ethanolic extracts that generate a cytotoxic effect promoting apoptosis in various cancerous cell lines. The most prominent effects have been observed in liver cancer (HepG-2), human epidermoid carcinoma (KB-3-1), human epithelial carcinoma (HeLa), human hepatocarcinoma (HepG2) carcinoma cells (Singh *et al*., 2017), breast cancer (MCF-7) and (4T1) (Lowe *et al*., 2017; Bustillos & Cortez, 2021; Lasso *et al*., 2022), lung carcinoma (A549) (Shen *et al*., 2018), chronic myelogenous leukemia cells (K562), and mouse colon carcinoma (CT26) (Gomide *et al*., 2013; Garcia *et al*., 2017).

In Colombia, the study of medicinal plants as an alternative or support in the treatment of different pathologies focused on their use, taxonomy, and ecology, mainly; recently has research started to generate knowledge on their genomics, evolution, and phylogeny with molecular techniques. For such studies, the most utilized areas are phytochemistry, phenotype, biology, and the metabolites of medicinal plants (Hao & Xiao, 2015). Researchers have primarily conducted whole genome sequencing on model plant species and important crop species. In the case of medicinal plants, genome sequencing has provided essential information on their origin, evolution, development, physiology, heritable traits, and epigenomic regulation, among other aspects (Boutanaev *et al*., 2015). Although there are limited reported genetic data for these species of interest, most genomic annotations pertain to the chloroplast, while the complete genome has only been published for the species *Cannabis sativa* L. subs. *indica* (ASM151000v1) (Clarke & Merlin, 2017), *Moringa oleifera* Lam. (ASM2139783v1) (Shyamli *et al*., 2021), *Passiflora edulis* Sims (ASM215610v1) (Araya *et al*., 2017), and *Artocarpus heterophyllus* Lam (ASM2540343v1) (Lin *et al*., 2022).

Omics Technologies and applications

The modern omics approaches (genomics, transcriptomics, proteomics, and metabolomics), are fields that utilize high-throughput sequencing data to identify and characterize gene networks, proteins, and metabolites with or without potential pharmacological and full genomes (Hao *et al*., 2017a) **Figure No. 2**. They also evaluate the response of human or animal cells to new drugs and play an important role in evaluating the large-scale production of plant-derived medicines (Hao *et al*., 2013a; Panossian *et al*., 2015; Jiang *et al*., 2021; Pandita *et al*., 2021). Additionally applying two or more “omics” methods at the same time (termed “multi-omics” or “integrated omics”) facilitates the knowledge of complex biological processes (Zhou *et al*., 2021).

High-throughput omics platforms are ideal tools for gathering large datasets. For example, transcriptomics is an efficient method for recovering information from numerous non-model therapeutic plants that lack reference genomes (Li *et al*., 2022) (Pandita *et al*., 2021). These data allow for the characterization of secondary metabolites to better understand the functioning of their therapeutic mechanisms at a cellular and molecular level (Hao *et al*., 2013; Panossian *et al*., 2015; Hao & Yang, 2016). RNA Sequencing (RNA-seq) allows for gene sequences to be obtained from plants even without a reference genome available, and for these sequences to be integrated into transcriptomic and metabolomic analyses (Tanuja, 2022). On the other hand, whole-transcriptome sequencing (WTS) makes it possible to probe the genes behind various processes of metabolite biosynthesis and the relation between the genes and the metabolites of genetically related or parent-offspring plants (Jiang *et al*., 2021). The metabolomic focus, together with the functional genomics of the gene products produced by ethnomedical plants, accelerates the discovery of new biosynthetic pathways of bioactive metabolites. This has improved the prospective discovery and generation of pharmaceutically important products (Jiang *et al*., 2021).

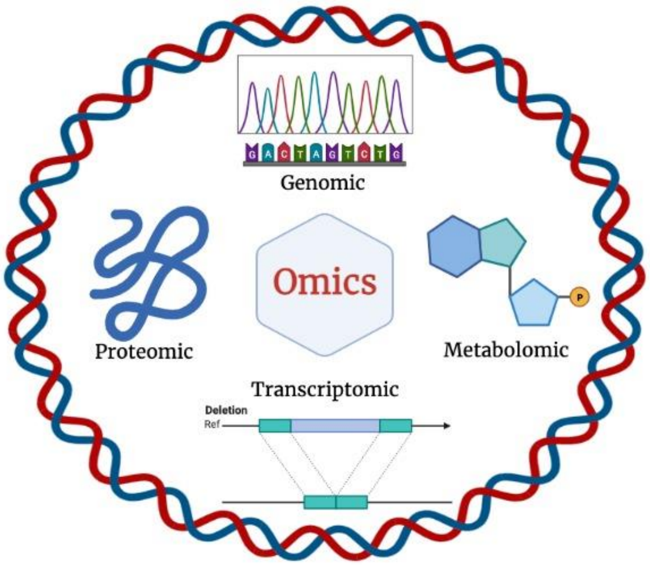

Figure No. 1
Omics in the study of medicinal plants, adapted from (Pandita *et al*., 2021)

Genomics

Thanks to the development of advanced automatic sequencing technologies such as Sanger, Next-Generation Sequencing (NGS), Nanopore, and efficient bioinformatic tools, it is now possible to elucidate a complete genome and study all genes at once, instead of analyzing them one by one (Rowe *et al*., 2011; Olivier *et al*., 2019). The field of science that encompasses this type of analysis is common to as "Genomics" and describes the development of genome-scale technologies, including mainly RNA transfection, microRNA (miRNA) transfection, real-time PCR analysis, and their applications (Li *et al*., 2022). It involves the study of the structure, function, and interactions of an individual's genome (Hao *et al*., 2013a). The results obtained from genomic studies include the generation of nucleotide sequences, expressed sequence tags (ESTs), full-length cDNAs, recombinant cDNAs, and gene arrays, within their respective chromosomes (Rai *et al*., 2016).

Currently, genomics can be studied functionally, where genomes/genes of the whole system, transcriptome expression, and the function of a living organism of interest are correlated, or comparatively, where phylogenetic analyses are performed to discover evolutionary genes (Rai *et al*., 2016). Thanks to these techniques, there are numerous reports of genomic sequences, both from eukaryotes and prokaryotes.

Regarding plant studies, DNA sequences from a genome provide vital information about the origin, development, and epigenomic regulation of a species (Pandita *et al*., 2021), representing a cornerstone for unraveling genomic and chemical diversity at unprecedented levels (Palazzotto & Weber, 2018). High-throughput sequencing of various pharmacologically potential plants has successfully elucidated biosynthetic pathways for obtaining molecules of interest and secondary metabolites, revolutionizing drug production and discovery (Boutanaev *et al*., 2015; Palazzotto & Weber, 2018).

From genomics, complete genomes of medicinal plants such as *Phalaenopsis equestris* (Schauer), *Brassica napus* L., *Capsicum annuum* L., *Momordica charantia* L., *Coffea canephora* Pierre ex A. Froehner, *Salvia miltiorrhiza* Bunge, *Ziziphus jujuba* Mill., *Glycyrrhiza uralensis* Fisch. Ex CC., *Dendrobium officinale* Kimura and Migo, *Azadirachta indica* A. Juss., *Catharanthus roseus* (L.), and *Salvia miltiorrhiza* Bunge (Danshen) have been obtained (Pandita *et al*., 2021). The presence of secondary metabolites such as Secolignans, Berberine, Ursolic acid, Periplocin, Cetuximab, and β-elemene has also been identified in plants like *Peperomia dindygulensis* Miq., *Coptis chinensis* Franch., *Prunella vulgaris* L., *Periploca sepium* Bunge, and *Curcuma longa* L., respectively. These metabolites show high therapeutic potential for treating gastrointestinal cancers by regulating apoptosis, cell proliferation, and metastasis (Li *et al*., 2022; Zhang *et al*., 2022). Other studies have allowed the identification of candidate genes related to the biosynthesis of steroidal alkaloids in medicinal plants of the genus *Fritallaria* (Hao *et al*., 2013a).

One of the benefits of sequencing genomes is that, based on this information, pre-existing drugs can be improved. For example, take the case of artemisinin, an antimalarial drug. By using the *Artemisia annua* L. plant and reproducing it with high-yield hybrids, researchers have been able to obtain more robust culture systems. Additionally, through the introduction of a redesigned microbial host into the plant, it was also possible to improve the artemisinin biosynthetic pathway (Pandita *et al*., 2021).

Another approach to study involves using genomic data to estimate the geographical origins and genetic diversity of medicinal plants. For example, White *et al*. (2021), found that coca plants *Erythroxylum coca* Lam., and *Erythroxylum novogranatense* (D. Morris) originated from *Erythroxylum gracilips* Peyr. On the other hand, Lin *et al*. (2022), discovered that Jackfruits from China originated independently in Southeast Asia and South Asia. These results provide insights into the domestication processes and evolutionary history of plants. For *Matricaria recutita* L., it was reported that its origin was due to artificial polyploidization from a limited set of genetic backgrounds (Otto *et al*., 2017).

Despite the numerous advantages of genomics, there are some technological limitations, such as the lack of a flawless method for whole-genome amplification and data interpretation (Zhou *et al*., 2021). Additionally, the process can be costly and demanding when the genome contains a large number of repetitive sequences, high levels of heterozygosity, and polyploidies (Palazzotto & Weber, 2018).

Transcriptomic

High-throughput sequencing has enabled not only the characterization of the genomes of plants with medicinal relevance but also their transcriptomes (Hao *et al*., 2015). In other words, it has become feasible to initiate the analysis of RNA molecules transcribed from DNA within a specific cell at a precise moment (Yang *et al*., 2014; Li *et al*., 2022). Transcriptomics involves high-throughput assays for compiling a comprehensive set of RNA transcripts (mRNA, rRNA, tRNA, and other non-coding RNAs produced within a cell), which serve as crucial intermediaries in gene expression, carrying the essential information for protein synthesis and performing various functions within the cell (Chakraborty *et al*., 2018; Pandita *et al*., 2021; Zhou *et al*., 2021). Moreover, transcriptomic studies facilitate the exploration of taxonomic and phylogenetic relationships among plants, as well as the comprehension of their genetic diversity (Hao *et al*., 2013c; Hao *et al*., 2015).

With their precision, sensitivity, high throughput, reproducibility, and specificity, techniques like RNA sequencing (RNA-seq), Roche 454 pyrosequencing, and Illumina high-throughput sequencing have been extensively employed to characterize essential traits linked to secondary metabolite formation and to investigate pertinent molecular mechanisms (Hao & Xiao, 2015; Hao *et al*., 2015; Li *et al*., 2022). Presently, the most widely used technique is RNA sequencing (RNA-seq), as it can detect the presence and abundance of RNA transcripts across the entire genome, encompassing non-coding regions such as intronic and intergenic regions (Chakraborty *et al*., 2018). Furthermore, it serves as a potent tool for assessing gene expression and identifying and characterizing molecular markers in non-model organisms (Hao & Xiao, 2015).

The transcriptomes of various medicinal plants, such as *Oenothera* L., *Rhodiola algida* (Ledeb.) Fisch. & C. A Mey., *Salvia sclarea* L., *Polygonum cuspidatum* Willd. ex Spreng., and *Taxus mairei* (Lemee & H. Lév.) S. Y. Hu., have been sequenced (Hao & Xiao, 2015). Researchers have also directed their efforts toward clarifying gene expression profiles, metabolic pathways, splice variants, and responses to stimuli or treatments. Through next-generation sequencing based on transcriptomic RNA-seq and proteomic quantitative-isobaric tags for relative and absolute quantification (iTRAQ), Lin *et al*. (2015), discovered that Tanshinone IIA (TIIA), isolated from *Salvia miltiorrhiza* Bunge., exerts antitumor effects on a gastric cancer cell line. Their extracts identified 16,603 unique transcripts and 102 proteins involved in regulating glucose metabolism within cancer cells. Other researchers, investigating the same plant but utilizing a combined metabolomics and transcriptomics approach, found that the biosynthesis of Tanshinones occurs in response to a stressful stimulus, hampering their production under artificial conditions (Hao *et al*., 2015).

In alignment with this research trajectory, Lan *et al*. (2021), in their analysis of Baicalin extract derived from *Scutellaria baicalensis* Georgi., identified 58 lncRNAs (long non-coding RNAs) and 31 miRNAs (microRNAs) implicated in the regulation of the circRNA MYH89/miR- 761 axis, connected to the extract's pharmacological potential in suppressing various types of osteosarcoma. Another study, conducted on a variety of poppies, unveiled the expression of 10 genes encoding five enzymes involved in noscapine HN1 production, a commercially produced antitumor alkaloid that induces apoptosis in dividing cells (Winzer *et al*., 2012). In the case of plants like *Andrographis alata* (Vahl) Nees, researchers sequenced the leaf transcriptome to identify genes contributing to the biosynthesis of neoandrographolide, a compound effective against viral infections like dengue, COVID-19, influenza, and chikungunya. Although *Andrographis paniculata* (Burm.f.) Wall., serves as the primary source for these compounds, but their availability is restricted. Therefore, *A. alata* stands as a promising alternative source, with neoandrographolide (NAG) being the principal antiviral compound within this species (Tanuja, 2022).

On the other hand, to assess the effectiveness of herbal treatments, Li *et al*. (2017), discovered that treating myocardial ischemia with a combination of six plants known as QSKL in pigs yielded effects that impact multiple genes and pharmacological targets. Researchers achieved these results using a transcriptome-based inference method with RNA-seq data.

Another significant aspect studied using transcriptomic data is the response of plants to attacks by various predators, such as deglycosylation, a precursor step to the formation of specialized metabolites involved in plant defense, mainly against herbivorous animals. Researchers have identified that plants like *Catharanthus roseus* (L.) G. Don., undergo an alternative splicing event in the SGD gene, leading to the creation of a shorter isoform of the enzyme (shSGD). SGD catalyzes the deglycosylation of strychosidine, forming a highly reactive aglycone involved in the synthesis of cytotoxic and aggressor protein-producing monoterpene indole alkaloids (MIAs) (Carqueijeiro *et al*., 2021).

Another approach in transcriptomic studies involves functionally validating products derived from medicinal plants through methods such as RNA interference (RNAi) analysis, including small interfering RNA (siRNA) and short hairpin RNA (shRNA). With this information, it becomes possible to decipher gene function and discover new targets in a specifically phenotypic manner (Zhang *et al*., 2021).

In contrast to genomic studies, RNA sequencing is more cost-effective and feasible for several reasons. These include lower RNA complexity, reduced repeatability and a focus on active regions, economic efficiency, and greater depth of coverage. This makes RNA sequencing a powerful tool in medicinal plant research. Additionally, genomic data can be obtained from numerous therapeutic plants categorized as non-model and lacking a reference genome (Yang *et al*., 2014; Hao *et al*., 2015; Zhou *et al*., 2021). However, it should be noted that insufficient reverse transcription and lack of amplification efficiency result from low RNA quantity. This, in turn, reduces the sensitivity and reliability of transcriptomic analyses. Furthermore, the volatility and degradation of RNA molecules decrease the number of transcripts, leading to elevated levels of technical noise and low capture efficiency (Zhou *et al*., 2021)**.**

Proteomics

Proteomics is a tool in the research of medicinal plants that involves the comprehensive analysis of all proteins encoded in an organism (Rai *et al*., 2016; Gonulalan *et al*., 2020). This omics approach allows us to gain crucial insights into the survival and adaptation of plants to biotic and abiotic stress conditions, as well as to understand the mode of action of drugs obtained from medicinal plants (Mishra *et al*., 2019; Pandita *et al*., 2021). Another significant application is evaluating changes in protein expression resulting from mutations or even transgenic processes. It also enables us to illustrate protein structures, understand protein functions and modifications, as well as protein-protein interactions occurring in both *in vitro* and *in vivo* conditions (Pedrete *et al*., 2019).

Through methodologies such as shotgun proteomic analysis, two-dimensional liquid chromatography-tandem mass spectrometry (2D-LC-MSMS), isobaric tags for relative and absolute quantification (iTRAQ), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS), and two-dimensional difference gel electrophoresis (2D-DIGE) (Tang *et al*., 2020; Li *et al*., 2022), the pharmacological potential of some plants in treating various diseases has been revealed (Olivier *et al*., 2019).

Notable examples of proteomics' application in medicinal plant research include the study of the antitumor potential of plants in various cancers, such as *Tripterygium wilfordii* Hook. F., which possesses an effective Diterpenoid Epoxide Triptolide for colon cancer treatment (Liu *et al*., 2011). *Andrographis paniculata* Burm. F., was the subject of a similar report, in which medicinal applications of diterpenoid compounds against various human disorders like cancer, hepatitis, and viral infections (Valdiani *et al*., 2012). Another metabolite identified through proteomic studies is periplocin, extracted from the bark and stems of *Periploca graeca* L., which can combat lung and colon cancers *in vivo* and *in vitro* via the beta-catenin/TCF signaling pathway, inducing apoptosis (Pandita *et al*., 2021). In *Aspongopus chinensis* Dallas, through shotgun proteomic analysis, Tan *et al*. (2919), discovered that the plant's cytochrome c could potentially be used for gastric cancer treatment.

Proteomics has also confirmed the antiproliferative activity of curcumin, berberine, gambogic acid, and tanshinone IIA from *Curcuma longa* L., *Coptis chinensis* Franch, *Garcinia hanburyi* Hook. F., and *Salvia miltiorrhiza* Burge (Danshen), respectively, on various cancer cell lines (Pandita *et al*., 2021; Wei *et al*., 2021)**.** Regarding the treatment of other conditions, in the case of diabetes, Pedrete and colleagues (Pedrete *et al*., 2019). identified 131 proteins in *Chrysobalanus icaco* L., *Bauhinia forficate* Link., and *Bauhinia variegata* L. involved in glucose level control, cellular respiration, transport, metabolism, and photosynthesis.

Using this methodology, the identification of protein functions in organisms is also possible. For instance, the iTRAQ labeling technique identified 102 proteins related to the secondary metabolism of sesquiterpenes and triterpenes in wild varieties of *Panax ginseng* C. A. Meyer (Ma *et al*., 2023). In *Gloriosa superba* L., a tropical plant used to treat gout, rheumatism, and other ailments, researchers found proteins involved in the biosynthetic pathway of alkaloids and flavonoids were discovered (Gandra *et al*., 2022). Through the utilization of previously reported transcriptomic data, it is also possible to study medicinal plants. In *Artemisia annua* L., proteins known for their role in artemisinin biosynthesis were uncovered through enrichment based on genes from earlier studies (Bryant *et al*., 2016). Similar studies have reported the biosynthetic pathways of tanshinones for cardiovascular diseases and the anticancer agents Taxol and vinblastine (Zheng *et al*., 2022).

From proteomics, other lines of research have also seen the development, such as chemical proteomics, involving the monitoring of the specific interaction between a molecular probe (originally applied to a defined subset of an organism's protein complement, e.g., specific organelles) and its interaction with an active small molecule (Zhang *et al*., 2021). Methodologies like two-dimensional gel electrophoresis (2DE) and mass spectrometry (MS) have also been developed, enabling protein identification and quantification (Yang *et al*., 2014)**.**

Metabolomics

Given the above, an omics field emerges that utilizes nuclear magnetic resonance spectroscopy (NMR), mass spectrometry (MS), ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS), metabolic profiling (UPL-ESI-QTOFMS), spectroscopy (1H-NMR and GC-MS), combined with multivariate statistical analysis, to profile the production and/or alteration of metabolites in a cell, organ, or whole organism, known as metabolomics (Zhang *et al*., 2021; Li *et al*., 2022).

Metabolomics allows for the discovery of genes and biosynthetic pathways (Gonulalan *et al*., 2020); the detection of biomarkers; the isolation of metabolites and new chemical entities (NCE) for detection and drug development, as it aids in uncovering and profiling secondary metabolites in medicinal plants. Furthermore, it contributes to understanding drug response regulation and screening potential cytotoxic effects (Pandita *et al*., 2021). In the study of medicinal plants, metabolomics plays a dual role, as it serves to identify the spatial and temporal distribution of the target metabolite influenced by plant development or the environment. Additionally, it identifies related compounds, that researchers can consider as intermediate products of the biosynthesis of the metabolite under study (Summer *et al*., 2015)**.**

In this sense and using metabolomics researchers report that methylation of cytosine is involved in multiple aspects of plant development and diversification, including changes in gene expression, secondary metabolite biosynthesis, organogenesis, and stress response. For example, when cell cultures of *Vitis amurensis* Rupr. are exposed to high concentrations of salicylic acids, a change in metabolism occurs that decreases methylation occurs in the VaSTS2 and VaSSTS10 genes that results in a greater production of trans-resveratrol (Kiselev *et al*., 2015).

Other reports are based on the utilization of methodologies such as nuclear magnetic resonance and multivariate analysis to assess the metabolic profile and inhibitory effects of plants like *Aloe vera* L. Burm. f., where it has been found that this plant exerts an anticancer effect on the genome of hepatocellular carcinoma cells (Noorolahi *et al*., 2016). Similarly, in the metabolomic characterization of medicinal plants like *Panax ginseng* C. A. Mey., *Panax notoginseng (*Burkill) F. H. Chen, and *Panax japonicus* (T. Nees) C. A. Mey., the UPLC-QTOF-MS technique successfully identified secondary metabolites. Compounds such as chikusetsu IVa saponin and ginsenosides (Rb1, Rb2, Rc, Rg2, R0) were successfully identified, or *Persicaria minor* Opiz and *Polygonum minus* Huds. Where 48, 42, and 37 compounds were detected using GC×GCTOF MS, GC-MS, and GC-MS, respectively. Additionally, 85 flavonoids were successfully detected through LC-TOF analysis (Pandita *et al*., 2021).

Based on 1H-NMR spectroscopy, Gnocchi *et al*. (2021), discovered that the ethyl acetate extract of *Crithmum maritimum* L. could reverse the preferential use of glycolysis instead of oxidative phosphorylation for energy production by tumor cells by decreasing intracellular lactate. The ethyl acetate extract can also inhibit protein anabolism by reducing intracellular amino acid levels and altering membrane biosynthesis by decreasing choline and phosphocholine contents in these cells.

Another study reported that Salvia extracts analyzed by LC/DAD/ESI-MSn contained compounds such as phenolic acids (caffeic acid, RA), flavonoids (cirsimaritin, salvigenin, genkwanin), diterpenes (rosmadial, CL, CA, and methoxycarnosate), and triterpenes (oleanolic acid and ursolic acid) (Hao *et al*., 2017b).

Several studies have explored the therapeutic impact of plants on metabolism, as evidenced in the investigation conducted by Wang *et al*. (2013b). In this study, an examination of the constituents of Yinchenhao Tang (*Artemisia annua* L., *Gardenia jasminoids* Ellis, and *Rheum palmatum* L.) was undertaken. These botanicals are known for their primary active components: 6, 7-dimethyl esculetin (D), geniposide (G), and rhein (R), respectively. Yinchenhao Tang is an herbal compound formulation with proven clinical efficacy in treating hepatic injury syndrome. The investigation encompassed diverse approaches, including immunohistochemical, biochemical, metabolomic, and proteomic analyses. The findings demonstrated that each component lacks significant therapeutic potency on its own. However, when combined, these components exhibit a potent therapeutic effect.

Utilizing this "omics" approach, plants can also be compared based on their metabolic and proteomic profiles, as demonstrated in the case of *Valeriana officinalis* L., *Melissa officinalis* L., *Hypericum perforatum* L., and *Passiflora incarnata* L., which have traditionally been used as anxiolytics, sedatives, and hypnotics. Researchers conducted a metabolic profile analysis on these plants using GC-MS and LC-qTOF-MS systems, resulting in the identification of 94 metabolites related to the Krebs cycle. However, *H. perforatum* and *P. incarnata* exhibited higher activity than the rest (Gonulalan *et al*., 2020).

Multiomics

We know that under particular environmental conditions, the physiological and biochemical characteristics of plants change. A plant can produce diverse substances with distinct characteristics, which can help them confront the challenges of surviving in a specific environment. These characteristics may be the same or similar to those of other species that are closely related genetically (Hao & Xiao, 2015; Hao & Xiao, 2018; Hao & Xiao, 2020). Even if changes are slow/progressive or rapid/radical, they often result in the addition or alteration of chemical groups such as oxidation, methylation, ethylation, and benzylation, among others (Kiselev *et al*., 2015; Yang *et al*., 2018; Hao & Xiao, 2020; Ran *et al*., 2021).

The physiological and biochemical changes in plants may indicate the evolutionary pathway that has been or will be followed, as more complex chemical structures tend to have narrower phylogenetic distributions (Hao & Xiao, 2020). In alkaloids, we see that N-methylcytisine is abundant in the plant families Berberidaceae, Fabaceae, and Scrophulariaceae, despite these three families not sharing close genetic relationships. This suggests the parallel evolution of biosynthetic pathways to produce alkaloids (Rao *et al*., 2019; Hao & Xiao, 2020; Zhou *et al*., 2021). The distribution of phytocompounds in the plant kingdom shows diverse and complex situations, with similar or even identical constituents may appear in different taxonomic groups, within the same groups, we may find different types of chemical constituents.

To understand these changes and the complexity of biological processes, a single omics approach is not sufficient. Therefore, a multiomic approach is used nowadays, where data obtained from different databases (transcriptome, proteome, metabolome, and currently pharmacophylogenome) are analyzed to identify genetic variations, perform evolutionary reconstructions, and identify novel pharmacological targets **(Figure No. 3)** (Hao & Xiao, 2015; Sahoo & Brijesh, 2019; Hao & Xiao, 2020; Zhou *et al*., 2021; Gong *et al*., 2022). For instance, the integration of ionomics and metabolomics has become a valuable approach to explore the physiological response of *Camellia sinensis* (L.) Kuntze., to stress (Zhang *et al*., 2020). Following this line, but analyzing the genome, transcriptome, and metabolome of *Vitis vinifera* L., Suzuki *et al*. (2015), identified 238 genes and 2012 metabolites produced when cells are exposed to UV-C radiation. In *Papaver somniferum* L., genes P450 and STORR participating in the biosynthetic pathway of morphine were identified through genomics and transcriptomics (Sumner *et al*., 2015). In the same plant, (Guo *et al*. (2018), used high-throughput tools to discover phytochemicals such as carotenoids, flavonoids, lignans, and phenolic acids.

Exploring the metabolic pathways and networks of plants, multiomics approaches prove highly effective. For instance, in *Mahonia bealei* (Fortune) Carrière, proteomic and metabolomic analyses were conducted to demonstrate that the content of alkaloids and flavonoids in the leaves of this plant increased with the combined treatment of ultraviolet B rays and darkness (UV+D) (Zhu *et al*., 2021). A similar study, but on *Prunella vulgaris* L., using the same omics along with transcriptomic data and different developmental stages, revealed that terpenoids were primarily synthesized during the maturity stage. Furthermore, key enzymes and genes encoding downstream pathways were predominantly expressed during maturation (Zhang *et al*., 2022).

Considering that the pharmacological activity of plants doesn't stem from a single compound, but rather from the synergistic or antagonistic action of several, studies like that of Gonulalan *et al*. (2020), stand out. They employed integrated omics analyses to comprehend the impact of plant extracts, such as *Valeriana officinalis* L., *Melissa officinalis* L., *Hypericum perforatum* L., and *Passiflora incarnata* L., on the expression levels of brain-derived neurotrophic factor (BDNF) in the SH-SY5Y cell line. In their research, they discovered a group of metabolites related to the Krebs cycle that exhibited a positive correlation with BDNF activity.

The integrated use of various omics techniques also facilitates the enhancement of medicinal plants. This is evident in the case of artemisinin (an antimalarial drug), where this approach led to advancements in two key aspects. Firstly, researchers crossed *Artemisia annua* L., with high-performing hybrids to establish a robust cultivation system. Secondly, they engineered a microbial host by reconstructing the biosynthetic pathway of artemisinin, resulting in increased drug quantities (Pandita *et al*., 2021). Additionally, through the utilization of proteomics and metabolomics, scientists developed seeds to accumulate fewer abnormal fatty acids (Sumner *et al*., 2015).

Other studies have addressed the utilization of pharmacophylogenomics to comprehend processes like drug metabolism within the body. In this aspect, it's pivotal to comprehend that drug metabolism is divided into two phases: 1) Functionalization reactions, involving the action of enzymes from the cytochrome P450 superfamily (CYP450); and 2) Conjugative reactions, where transferases, including UDP-glucuronosyltransferases (UGT), sulfotransferases (SULT), glutathione S-transferases (GST), thiopurine S-methyltransferase (TPMT), and catechol O-methyltransferase (COMT), play significant roles (Crettol *et al*., 2010; Mazzari & Prieto; 2014; Hao & Yang, 2016; Rao *et al*., 2019). Both phases and enzyme complexes can transform lipophilic molecules into more polar forms. As outlined by Rao *et al*. (2019), these biotransformation processes determine the duration that drug molecules will remain within the body, thus influencing the extent of their pharmacological effect.

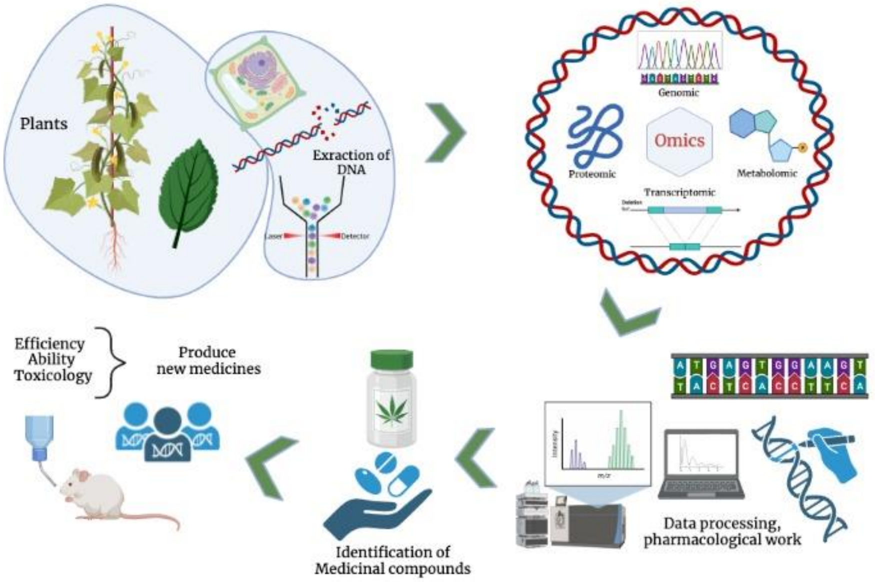

Figure No. 3
Multiomics in the medicinal plants, adapted to (Pandita *et al*., 2021)

As an example of the application of this approach, consider the analysis of RNA microarray data (transcriptomics) and protein expression (proteomics) to evaluate the combined effect of *Eleutherococcus* Maxim., *Schisandra* Michx., Fruit, and Rhizoma *Rhodiola* L., on human neuroglial cells (pharmacogenomics). At the end of the study, researchers determined that extracts from these plants do indeed affect certain genes (Panossian *et al*., 2015).

Omics in the study of medicinal plants: national context

One of the initial techniques employed to study the genetics of plants with potential medicinal uses in Colombia was the use of markers targeted with Polymerase Chain Reaction (PCR). Among these techniques, Inter-Simple Sequence Repeat microsatellites (ISSRs) were commonly utilized (Singh *et al*., 2014; Zhang *et al*., 2014; Castañeda-Cardona *et al*., 2021). For instance, in one study, researchers used 23 ISSR primers to evaluate the genetic diversity of native Chinese cultivars of *Cannabis sativa*. The results showed that the genetic distance found between the studied varieties was related to the geographic distance between them, and the observed regional hybridization might be a result of adaptations to the local environment through the exchange of germplasm. Other studies investigated *Guadua angustifolia* Kunth (Rugeles-Silva *et al*., 2012), *Passiflora alata* Curtis (Koehler-Santos *et al*., 2006), and *Lippia alba* Mill. (Manica-Cattani *et al*., 2009), and *Moringa oleifera* Lam. (Smit *et al*., 2013), employing markers such as RAMs (Randomly

Amplified Microsatellites) and RAPD (Random Amplified Polymorphic DNA) to identify DNA (deoxyribonucleic acid) variations between organisms

To evaluate genetic diversity are SSRs (Simple Sequence Repeats, or microsatellites). These serve as a functional code for regulating the eukaryotic genome, and researchers mostly use them as markers to map the relationships between different organisms. Microsatellite sequences play a direct role in the organization of the genome, recombination, genetic regulation, quantitative genetic variation, and gene evolution. Over the last few decades, researchers have identified specific microsatellite markers for many families and general medicinal plants. For example, these markers have been used to study the genetic variation within the bamboo species *Guadua angustifolia* Kunth (Marulanda *et al*., 2007; Muñoz-Florez *et al*., 2010). New SSR markers have been found within *Lippia alba* Mill. that may help elucidate their genetic diversity, which may be useful to breeding initiatives (Santos *et al*., 2012; Rocha *et al*., 2015). Also, fifteen microsatellites were identified in *Cannabis sativa* L. (Gilmore & Peakall, 2003), which have been useful in characterizing the genetic diversity of cultivated and naturalized populations.

In recent years, another type of genetic marker has emerged, SNPs (Single Nucleotide Polymorphisms), which are much more abundant than SSRs in the majority of species (Clevenger *et al*., 2015), including medicinal plants. SNPs are identifiers directly from genomic sequences of model plants; however, most medicinal plants lack genomic data. Thus, obtaining SNPs is limited to those obtained through transcriptome sequencing (Hao *et al*., 2012), as was done through the analysis of the non-coding RNA genome of *Cannabis sativa* L., allowing for the analysis of the complicated network of gene expression and regulation within this species (Wu *et al*., 2021).

Large quantities of SNPs can obtain through reduced-representation sequencing such as the RAD-seq technique (Restriction-Associated DNA Sequencing). This is a form of genotyping-by-sequencing that has been applied effectively in QTL analysis and mapping (Quantitative Trait Loci) across a wide range of organisms, including those highly heterogeneous and non-model species (Miller *et al*., 2007; Rowe *et al*., 2011; Eaton & Ree, 2013). This is one of the most informative techniques and is widely used in plants given that RAD-seq enables the reconstruction of the genome, which is effective for evaluating its heterozygosity and providing a basis for studying medicinal plants (Rubin *et al*., 2012). Another technique used is Genotyping-By-Sequencing (GBS), which sequences large genomes that are highly diverse (Elshire *et al*., 2011). Negi *et al*. (2022) used this technique to obtain 3,176 polymorphic SSRs, of which 2,015 were found to be hyper-polymorphic in black pepper (*Piper nigrum* L.).

Even though studies on the evolution and population genetics of medicinal plants are scarce, those that have been published have utilized different molecular tools, specifically the use of microsatellite markers, ITS (Internal Transcribed Spacers), and Next-Generation technology to study the therapeutic potential of plants to treat illnesses in different parts of the world (Hao & Xiao, 2015). Recently, some of the techniques and markers described above are starting to give way to the omics sciences.

In Colombia, publications with multiomic approaches are still scarce. Among them, the results obtained by Ballesteros-Vivas *et al*. (2020), stand out, who evaluated the changes in HT-29 colon cancer cells induced by an extract of *Passiflora mollissima* L.H.Bailey, seeds at the transcriptomic and metabolomic levels in combination with viability and cell cycle assays. The obtained results revealed that the extract notably affected the viability of HT-29 colon cancer cells after 48 and 72 hours, with minor effects on the viability of normal human colon fibroblast cells.

Instead of solely focusing on the medicinal field, researchers in Colombia have also directed their attention toward investigating the origin, structure, and genetic diversity of medicinal plants. For instance, a study on *Lippia origanoides* Kunth., revealed the existence of three genetic lineages using genomics (SiB Colombia, 2023). Similarly, White *et al*. (2021), utilized the same technology to determine that the coca plants *Erythroxylum coca* Lam., and *Erythroxylum novogranatense* D. Morris., have undergone domestication two or three times from their wild ancestor *Erythroxylum gracilipes* Peyr.

CONCLUSIONS

As the global population increases, there is a growing demand for medicinal compounds. In this context, comprehending the complete synthesis of specialized metabolites derived from plants becomes pivotal for identifying and developing reliable drugs in the future. However, due to the intricate network of biological regulation in medicinal plants, simple omics fields alone fall short of fully explaining specific biological phenomena. This has led to an upsurge in recent years in studies adopting multiomics approaches.

Investigations in functional genomics, transcriptional regulation networks, and protein-protein interactions will significantly contribute to unraveling the secondary metabolic pathways of drugs obtained from medicinal plants. Considering all the aspects discussed thus far, it is evident that comprehensive genome approaches integrating modern "omics" platforms and tools have displayed their efficacy and capacity to generate insights related to the proteome, genome, transcriptome, and metabolome of medicinal plants.

Furthermore, strides in pharmacogenetics and pharmacophylogenomics have progressively unveiled the genetic underpinnings of inter-individual variations in the pharmacological responses to different plants. Nevertheless, research on natural products still lags, and studies in Colombia remain limited despite the pressing need for drug development and clinical trials. **Table S1:** Taxonomy, traditional uses, pharmacological potential, antifungal, antitumor/anticancer activity, and genomic information of 18 medicinal plants used from Colombia. File format: .xls. Description of data: The attached table presents a list of medicinal plants with anticancer potential, a description of their taxonomy, traditional uses, pharmacological potential, antifungal, antitumor, or anticancer activity, and their current genomic information.

FUNDING

This work was supported by the Ministerio de Ciencia, Tecnología e Innovación (Colciencias), Ministerio de Educación Nacional, Ministerio de Industria, Comercio y Turismo e ICETEX (792–2017) 2a Convocatoria Ecosistema Científico - Colombia Científica para la Financiación de Proyectos de I + D + i), The World Bank, and Vicerrectoría de Investigaciones, Pontificia Universidad Javeriana, Bogotá, Colombia (contract no. FP44842-221-2018).

REFERENCES

Abasi F, Abdel-Massih RM, Aubert E, Aubouy A, Cabrera-Barraza J, Camara A, et al. Cerra-Dominguez J, Chan KWK, Chassagne F, Chen X, David B, De Canha MN, Deharo E, Dembetembe TT, Dénou A, Díaz-Castillo F, El Beyrouthy M, Fechter P, Gibango L, Graz B, Haddad M, Haidara M, Hajdari A, Houriet J, Kellogg JJ, Khalid N, Khan MF, Kritzinger Q, Lall N, Loggenberg SR, Marti G, Mashwani ZUR, Mustafa B, Oliveros-Diaz AF, Oosthuizen CB, Ortiz S, Pacheco R, Pajaro-Gonzalez Y, Peng J, Peng M, Phakeovilay C, Pitchon V, Quave CL, Raja NI, Sanogo R, Saroja SG, Seaman JL, Shabih S, Twilley D, Unnikrishnan R, Urumarudappa SKJ, Vansteelandt M, Vasudevan M, Vial T, Vonthron C, Wali R, Watanabe S, Wolfender JL. 2022. Medicinal plants as anti-infectives current knowledge and new perspectives. **Med Plant Anti-Infectives** **https://doi.org/10.1016/B978-0-323-90999-0.00021-5**

Araya S, Martins AM, Junqueira NTV, Costa AM, Faleiro FG. Ferreira ME. 2017. Microsatellite marker development by partial sequencing of the sour passion fruit genome (*Passiflora edulis* Sims). **BMC Genomics** 18: 549. **https://doi.org/10.1186/s12864-017-3881-5**

Arboleda C, Jaramillo F, Palacio H. 2012. Determinación del potencial antioxidante en extractos de vinagre *Guadua angustifolia* Kunth para aplicaciones alimenticias. **Rev Cuba Plantas Med** 17: 330 - 342.

Ballesteros-Ramírez R, Durán MI, Fiorentino S. 2021. Genotoxicity and mutagenicity assessment of a standardized extract (P2Et) obtained from *Caesalpinia spinosa*. **Toxicol Rep** 8: 258 - 263. **https://doi.org/10.1016/j.toxrep.2020.12.024**

Ballesteros-Vivas D, Alvarez-Rivera G, León C, Morantes SJ, Ibánez E, Parada-Alfonso F, Cifuentes A, Valdés A. 2020. Foodomics evaluation of the anti-proliferative potential of *Passiflora mollissima* seeds. **Food Res Int** 130: 108938. **https://doi.org/10.1016/j.foodres.2019.108938**

Bartolome AP, Villaseñor IM, Yang WC. 2013. *Bidens pilosa* L. (Asteraceae): Botanical properties, traditional uses, phytochemistry, and pharmacology. **Evid Based Complement Alternat Med** 2013: 51.

https://doi.org/10.1155/2013/340215

Bernal H. 2011. **Pautas para el conocimiento, conservación y uso sostenible de plantas medicinales nativas en Colombia**. Instituto de Investigación de Recursos Biológicos Alexander von Humboldt, Bogota, Colombia.

Bernal R, Galeano G, Rodríguez A, Sarmiento H, Gutiérrez M. 2017. Nombres comunes plantas de Colombia. **http://www.biovirtual.unal.edu.co/nombrescomunes**

Bernal R, Gradstein S, Celis M. 2019. Catálogo de plantas y líquenes de Colombia. Instituto de Ciencias Naturales. Universidad Nacional de Colombia. **http://catalogoplantasdecolombia.unal.edu.co**

Boutanaev AM, Moses T, Zi J, Nelson DR, Mugford ST, Peters RJ, Osbourn A. 2015. Investigation of terpene diversification across multiple sequenced plant genomes. **Proc Natl Acad Sci USA** 112: 81 - 88. **https://doi.org/10.1073/pnas.1419547112**

Bustillos A, Cortez JC. 2021. Anti-metastic and anti-proliferative activity of *Ilex guayusa*, *Uncaria tomentosa* and *Croton lechleri*, in the mcf7 cell line. **Invest Clin** 62: 86 - 94.

Bystriakova N, Tovar C, Monro A, Moat J, Hendrigo P, Carretero J, Torres-Morales G, Diazgranados M. 2021. Colombia's bioregions as a source of useful plants. **Plos One** 16: e0256457. **https://doi.org/10.1371/journal.pone.0256457**

Calderon A, Salas J, Dapello G, Gamboa E, Rosas J, Chávez J, Retuerto F, Mayta-Tovalino F. 2019. Assessment of antibacterial and antifungal properties and *in vivo* cytotoxicity of Peruvian *Passiflora mollisima*. **J Contemp Dent Pract** 20: 145 - 151.

Camargo JER, Alfonso ANT, Rojas-Rozo RA, de Castro C, de Murcia TR. 2010. *In vitro* cytotoxicity of extracts and fractions of *Bursera tomentosa* (Jacq.) Triana & Planch., Burseraceae, against human tumor cell. **Rev Bras Farmacogn** 20: 588 - 593.

Cañigueral S, Dellacassa E, Bandoni LA. 2003. Plantas medicinales y fitoterapia: ¿Indicadores de dependencia o factores de desarrollo? **Acta Farm Bonaer** 22: 78 - 265.

Carmona-Hernandez JC, Taborda-Ocampo G, González-Correa CH. 2021. Folin-Ciocalteu reaction alternatives for higher polyphenol quantitation in Colombian passion fruits. **Int J Food Sci** 2021: 1 - 10. **https://doi.org/10.1155/2021/8871301**

Carqueijeiro I, Koudounas K, de Bernonville TD, Sepúlveda LJ, Mosquera A, Bomzan DP, Oudin A, Lanoue A, Besseau S, Cruz PL, Kulagina N, Stander EA, Eymieux S, Burlaud-Gaillard J, Blanchard E, Clastre M, Atehortùa L, St-Pierre B, Giglioli-Guivarch N, Papon N, Nagegowda DA, O'Connor SE, Courdavault V. 2021. Alternative splicing creates a pseudo-strictosidine b-D-glucosidase modulating alkaloid synthesis in *Catharanthus roseus*. **Plant Physiol** 185: 836 - 856. **https://doi.org/10.1093/plphys/kiaa075**

Carraz M, Lavergne C, Jullian V, Wright M, Gairin JE, Gonzales de la Cruz M, Bourdy G. 2015. Antiproliferative activity and phenotypic modification induced by selected Peruvian medicinal plants on human hepatocellular carcinoma Hep3B cells. **J Ethnopharmacol** 166: 185 - 199. **https://doi.org/10.1016/j.jep.2015.02.028**

Castañeda-Cardona C, Portela R, Morillo Y. 2021. Caracterización molecular con marcadores ISSR de la colección de cítricos de la Universidad de los Llanos. **RIAA** 12

Castañeda R, Cáceres A, Cruz SM, Aceituno JA, Marroquín ES, Barrios Sosa AC, Strangman WK, Williamson RT. 2023. Nephroprotective plant species used in traditional Mayan Medicine for renal-associated diseases. **J Ethnopharmacol** 301: 115755. **https://doi.org/10.1016/j.jep.2022.115755**

Castellanos C, Valderrama N, Bernal Y, García N. 2019. **Plantas alimenticias y medicinales de Colombia**. Instituto de Investigación de Recursos Biológicos Alexander von Humboldt, Bogota, Colombia.

Chakraborty S, Hosen MI, Ahmed M, Shekhar HU. 2018. Onco-multi-OMICS approach: A new frontier in cancer research. **Biomed Res Int** 2018: 9836256. **https://doi.org/10.1155/2018/9836256**

Chunhong H, Qian L, Jinhua L, Yongqing Z. 2013. Advances in the research of chemical constituents in Thalictrum **Plants** 54 - 58.

Clarke RC, Merlin MD. 2017. Critical reviews in plant sciences *Cannabis* domestication, breeding history, present-day genetic diversity, and future prospects. **Crit Rev Plant Sci** 35: 293 - 327. **https://doi.org/10.1080/07352689.2016.1267498**

Clevenger J, Chavarro C, Pearl SA, Ozias-Akins P, Jackson SA. 2015. Single nucleotide polymorphism identification in polyploids: A review, example, and recommendations. **Mol Plant** 8: 831 - 846. **https://doi.org/10.1016/j.molp.2015.02.002**

ColPlantA. 2023. Useful plants of Colombia. Facilitated by the Royal Botanic Gardens, Kew, UK. https://colplanta.org/cite-usCrettol S, Petrovic N, Murray M. 2010. Pharmacogenetics of Phase I and Phase II drug metabolism. **Curr Pharm Des** 16: 204 - 219. **https://doi.org/10.2174/138161210790112674**

Cordoba-Tovar L, Ríos-Geovo V, Largacha-Viveros MF, Salas-Moreno M, Marrugo-Negrete JL, Ramos PA, Mosquera Chaverra L, Jonathand MP. 2022. Cultural belief and medicinal plants in treating COVID 19 patients of Western Colombia. **Acta Ecol Sin** 42: 476 - 484. **https://doi.org/10.1016/j.chnaes.2021.10.011**

Crettol S, Petrovic N, Murray M. 2010. Pharmacogenetics of phase I and phase II drug metabolism. **Curr Pharmaceut Design** 16: 204 - 219. **https://doi.org/10.2174/138161210790112674**

DeCarlo A, Dosoky NS, Satyal P, Sorensen A, Setzer WN. 2019. **The essential oils of the Burseraceae.** In: Malik S. (Eds). Essential oil research. Springer, Cham. **https://doi.org/10.1007/978-3-030-16546-8_4**

Eaton DAR, Ree RH. 2013. Inferring phylogeny and introgression using RADseq data: an example from flowering plants (Pedicularis: Orobanchaceae). **Syst Biol** 62: 689 - 706. **https://doi.org/10.1093/sysbio/syt032**

Elshire RJ, Glaubitz JC, Sun Q, Poland JA, Kawamoto K, Buckler ES, Mitchell SE. 2011. A robust, simple genotyping-by-sequencing (GBS) approach for high diversity species. **Plos One** 6: e19379. **https://doi.or/10.1371/journal.pone.0019379**

Elufioye TO, Habtemariam S, Adejare A. 2020. Chemistry and pharmacology of alkylamides from natural origin. **Rev Bras Farmacogn** 30: 622 - 640. **https://doi.org/10.1007/s43450-020-00095-5**

Estrella-Parra E, Flores-Cruz M, Blancas-Flores G, Koch SD, Alarcón-Aguilar FJ. 2019. The *Tillandsia* genus: history, uses, chemistry, and biological activity. **Bol Latinoam Caribe Plant Med Aromat** 18: 239 - 264.

Fonseca-Benitez A, Morantes Medina SJ, Ballesteros-Vivas D, Parada-Alfonso F, Perdomo SJ. 2022. *Passiflora mollissima* seed extract induced antiproliferative and cytotoxic effects on CAL 27 spheroids. **Adv Pharmacol Pharm Sci** 2022: 4602413. **https://doi.org/10.1155/2022/4602413**

Gámez-Espinosa E, Deyá C, Cabello M, Bellotti N. 2021. Nanoparticles synthesised from *Caesalpinia spinosa*: assessment of the antifungal effects in protective systems. **Adv Nat Sci Nanosci Nanotechnol** 12: 015001. **https://doi.org/10.1088/2043-6254/abdfc1**

Gandra J, Kumar H, Kumar SA, Doma M, Deepthi Y. 2022. Metabolomic and proteomic signature of *Gloriosa superba* leaves treated with mercuric chloride and phenylalanine, a precursor of colchicine alkaloid. **Ind Crop Prod** 178: 114557. **https://doi.org/10.1016/j.indcrop.2022.114557**

García BH. 1974. **Flora medicinal de Colombia: Botánica médica**. Ed. Instituto de Ciencias Naturales, Universidad Nacional, Bogotá DC, Colombia.

García LT, Leal AF, Moreno EM, Stashenko EE, Arteaga HJ. 2017. Differential anti-proliferative effect on K562 leukemia cells of *Lippia alba* (Verbenaceae) essential oils produced under diverse growing, collection and extraction conditions. **Ind Crops Prod** 96: 140 - 148. **https://doi.org/10.1016/j.indcrop.2016.11.057**

Gilmore S, Peakall R. 2003. Isolation of microsatellite markers in Cannabis sativa L. (marijuana). **Mol Ecol Notes** 3: 105 - 107. **https://doi.org/10.1046/j.1471-8286.2003.00367.x**

Gnocchi D, Del Coco L, Girelli CR, Castellaneta F, Cesari G, Sabbà C, Fanizzi FP, Mazzocca A. 2021. H-NMR metabolomics reveals a multitarget action of *Crithmum maritimum* ethyl acetate extract in inhibiting hepatocellular carcinoma cell growth. **Sci Rep** 11: 1 - 13. **https://doi.org/10.1038/s41598-020-78867-1**

Gomide MS, Lemos FO, Lopes MTP, Alves TMA, Viccini LF, Coelho CM. 2013. The effect of the essential oils from five different *Lippia* species on the viability of tumor cell lines. **Rev Bras Farmacogn** 23: 895 - 902. **https://doi.org/10.1590/S0102-695X2013000600006**

Gong X, Yang M, He CN, Bi YQ, Zhang CH, Li MH, Xiao PG. 2022. Plant pharmacophylogeny: Review and future directions. **Chin J Integr Med** 28: 567 - 574. **https://doi.org/10.1007/s11655-020-3270-9**

Gonulalan EM, Nemutlu E, Bayazeid O, Koçak E, Yalçın FN. 2020. Metabolomics and proteomics profiles of some medicinal plants and correlation with BDNF activity. **Phytomedicine** 74: 152920. **https://doi.org/10.1016/j.phymed.2019.152920**

Guo L, Winzer T, Yang X, Li Y, Ning Z, He Z, Teodor R, Lu Y, Bowser TA, Graham IA, Ye K. 2018. The opium poppy genome and morphinan production. **Science** 362: 343 - 347.

https://doi.org/10.1126/science.aat4096

Guzman E, Molina J. 2018. The predictive utility of the plant phylogeny in identifying sources of cardiovascular drugs. **Pharm Biol** 56: 154 - 164. **https://doi.org/10.1080/13880209.2018.1444642**

Hao DC, Chen SL, Xiao PG, Liu M. 2012. Application of high-throughput sequencing in medicinal plant transcriptome studies. **Drug Dev Res** 73: 487 - 498.

Hao DC, Gu XJ, Xiao PG, Liang ZG, Xu LJ, Peng Y. 2013. Recent advance in chemical and biological studies on Cimicifugeae pharmaceutical resources. **Chin Herb Med** 5: 81 - 95. **https://doi.org/10.3969/j.issn.1674-6348.2013.02.001**

Hao DC, Gu XJ, Xiao PG, Peng Y. 2013a. Phytochemical and biological research of Fritillaria medicine resources. **Chin J Nat Med** 11: 330 - 344. **https://doi.org/10.1016/S1875-5364(13)60050-3**

Hao DC, Gu X, Xiao P, Liang Z, Xu L, Peng Y. 2013c. Research progress in the phytochemistry and biology of Ilex pharmaceutical resources. **Acta Pharm Sin B** 3: 8 - 19. **https://doi.org/10.1016/j.apsb.2012.12.008**

Hao DC, Xiao PG. 2015. Genomics and evolution in traditional medicinal plants: Road to a healthier life. **Evol Bioinforma** 11: 197 - 212. **https://doi.org/10.4137/EBO.S31326**

Hao DC, Gu XJ, Xiao PG. 2015. High-throughput sequencing in medicinal plant transcriptome studies. **Medicinal Plants** 2015: 49 - 96. **https://doi.org/10.1016/B978-0-08-100085-4.00002-5**

Hao DC, Yang L. 2016. Drug metabolism and disposition diversity of Ranunculales phytometabolites: a systems perspective. **Exp Opinion Drug Metab Toxicol** 12: 1047 - 1065. **https://doi.org/10.1080/17425255.2016.1201068**

Hao DC, Gu XJ, Xiao PG. 2017a. Anemone medicinal plants: Ethnopharmacology, phytochemistry and biology. **Acta Pharm Sin B** 7: 146 - 158. **https://doi.org/10.1016/j.apsb.2016.12.001**

Hao DC, Ge G, Xiao P. 2017b. Anticancer drug targets of Salvia phytometabolites: Chemistry, biology, and omics. **Curr Drug Targets** 19: 1 - 20. **https://doi.org/10.2174/1389450117666161207141020**

Hao DC, Ge GB, Xiao PG. 2018. Anticancer drug targets of Salvia phytometabolites: Chemistry, biology and omics. **Curr Drug Targets** 19: 1 - 20. **https://doi.org/10.2174/1389450117666161207141020**

Hao DC, Xiao PG. 2018. Deep in shadows: Epigenetic and epigenomic regulations of medicinal plants. **Chinese Herb Med** 10: 239 - 248. **https://doi.org/10.1016/j.chmed.2018.02.003**

Hao DC, Xiao P. 2020. Pharmaceutical resource discovery from traditional medicinal plants: Pharmacophylogeny and pharmacophylogenomics. **Chinese Herb Med** 12: 104 - 117. **https://doi.org/10.1016/j.chmed.2020.03.002**

Hao DC, Xu LJ, Zheng YW, Lyu HY, Xiao PG. 2022. Mining therapeutic efficacy from treasure chest of biodiversity and chemodiversity: Pharmacophylogeny of Ranunculales medicinal plants. **Chin J Integr Med** 28: 1111 - 1126.

He D, Li Y, Tang H, Ma R, Li X, Wang L. 2015. Six new cassane diterpenes from the twigs and leaves of Tara (*Caesalpinia spinosa* Kuntze). **Fitoterapia** 105: 273 - 277.

IPNI (International Plant Names Index). 2023. The Royal Botanic Gardens, Kew, Harvard University Herbaria & Libraries and Australian National Herbarium. **https://www.ipni.org/citeus**

IUCN. 2023. The IUCN Red List of threatened species. **https://www.iucnredlist.org**

Jiang C, Fei X, Pan X, Huang H, Qi Y, Wang X, Zhao Q, Li F, Zhang L, Shao Q, Li X, Wu Z. 2021. Tissue-specific transcriptome and metabolome analyses reveal a gene module regulating the terpenoid biosynthesis in *Curcuma wenyujin*. **Ind Crops Prod** 170: 113758. **https://doi.org/10.1016/j.indcrop.2021.113758**

Kasper J, Melzig M, Jenett-Siems K. 2010. New phenolic compounds of *Acmella ciliata*. **Planta Med** 76: 633 - 635. **https://doi.org/10.1055/s-0029-1240621**

Kiselev K V., Tyunin AP, Karetin YA. 2015. Salicylic acid induces alterations in the methylation pattern of the VaSTS1, VaSTS2, and VaSTS10 genes in *Vitis amurensis* Rupr. cell cultures. **Plant Cell Rep** 34: 311 - 320. **https://doi.org/10.1007/s00299-014-1708-2**

Koehler-Santos P, Lorenz-Lemke AP, Muschner VC, Bonatto SL, Salzano FM, Freitas LB. 2006. Molecular genetic variation in *Passiflora alata* (Passifloraceae), an invasive species in southern Brazil. **Biol J Linn Soc** 88: 611 - 630. **https://doi.org/10.1111/j.1095-8312.2006.00647.x**

Lan H, Wang H, Gao M, Luo G, Zhang J, Yi E, Liang C, Xiong X, Chen X, Wu Q, Chen R, Lin B, Qian D, Hong

W. 2021. Analysis and construction of a competitive endogenous RNA regulatory network of baicalin-induced apoptosis in human osteosarcoma cells. **Biomed Res Int** 2021: 9984112. **https://doi.org/10.1155/2021/9984112**

Lasso P, Rojas L, Arévalo C, Urueña C, Murillo N, Barreto A, Costa GM, Fiorentino S. 2022. *Tillandsia usneoides* extract decreases the primary tumor in a murine breast cancer model but not in melanoma. **Cancers** 14: 5383. **https://doi.org/10.3390/cancers14215383**

Leal DA, Modesti G. 2021. **Caracterización fitoquímica de especies vegetales en Colombia y evaluación de su actividad antifúngica contra *Candida albicans***. Tesis, Pontificia Universidad Javeriana; Bogotá, Colombia.

Leonti M, Casu L, de Oliveira Martins DT, Rodrigues E, Benítez G. 2020. Ecological theories and major hypotheses in ethnobotany: Their relevance for ethnopharmacology and pharmacognosy in the context of historical data. **Rev Bras Farmacogn** 30: 451 - 466. **https://doi.org/10.1007/s43450-020-00074-w**

Li P, Chen J, Zhang W, Fu B, Wang W. 2017. Transcriptome inference and systems approaches to polypharmacology and drug discovery in herbal medicine. **J Ethnopharmacol** 195: 127 - 136. **https://doi.org/10.1016/j.jep.2016.10.020**

Li SY, Wang WJ, Li QY, Yang PH, Li XL, Yan Y, Yuan Y, Feng YB, Hong M. 2022. Using omics approaches to dissect the therapeutic effects of Chinese herbal medicines on gastrointestinal cancers. **Front Pharmacol** 13: 884822. **https://doi.org/10.3389/fphar.2022.884822**

Lin LL, Hsia CR, Hsu CL, Huang HC, Juan HF. 2015. Integrating transcriptomics and proteomics to show that tanshinone IIA suppresses cell growth by blocking glucose metabolism in gastric cancer cells. **BMC Genomics** 16: 1 - 17. **https://doi.org/10.1186/s12864-015-1230-0**

Lin X, Feng C, Lin T, Harris A, Li Y, Kang M. 2022. Jackfruit genome and population genomics provide insights into fruit evolution and domestication history in. **Hortic Res** 9: 1 - 13. **https://doi.org/10.1093/hr/uhac173**

Liu Z, Ma L, Zhou GB. 2011. The main anticancer bullets of the Chinese medicinal herb, thunder god vine. **Molecules** 16: 5283 - 5297. **https://doi.org/10.3390/molecules16065283**

Liu X, Wu WY, Jiang BH, Yang M, Guo DA. 2013. Pharmacological tools for the development of traditional Chinese medicine. **Trends Pharmacol Sci** 34: 620 - 628. **https://doi.org/10.1016/j.tips.2013.09.004**

Lowe HIC, Toyang NJ, Watson CT, Ayeah KN, Bryant J. 2017. HLBT-100: A highly potent anti-cancer flavanone from *Tillandsia recurvata* (L.) L. **Cancer Cell Int** 17: 38. **https://doi.org/10.1186/s12935-017-0404-z**

Lucena de Vasconcelos A, Lucena de Vasconcelos A, Azevedo Ximenes E, Perrelli Randau K. 2013. *Tillandsia recurvata* L. (Bromeliaceae): aspectos farmacognósticos. **Rev Cienc Farm Basicas Apl** 34: 151 - 159.

Ma J, Huang J, Hua S, Zhang Y, Zhang Y, Li T, Dong L, Gao Q, Fu X. 2019. The ethnopharmacology, phytochemistry and pharmacology of *Angelica biserrata* – A review. **J Ethnopharmacol** 231: 152 - 169. **https://doi.org/10.1016/j.jep.2018.10.040**

Ma R, Yang P, Jing C, Fu B, Teng X, Zhao D. 2023. Comparison of the metabolomic and proteomic profiles associated with triterpene and phytosterol accumulation between wild and cultivated ginseng. **Plant Physiol Biochem** 195: 288 - 299. **https://doi.org/10.1016/j.plaphy.2023.01.020**

Manica-Cattani MF, Zacaria J, Pauletti G, Atti-Serafini L, Echeverrigaray S. 2009. Genetic variation among South Brazilian accessions of *Lippia alba* Mill. (Verbenaceae) detected by ISSR and RAPD markers. **Brazilian J Biol** 69: 375 - 380. **https://doi.org/10.1590/S1519-69842009000200020**

Martínez JL. 2003. Alcaloides bisbencilisoquinolinicos como antagonista de calcio de origen natural: comparación de actividades (artículo de revisión). **Rev Asoc Colomb Cienc Biol** 15: 11 – 32.

Martínez JL, Benites J, Gomez H, Vargas-Rueda S, Vinet R, Jaimes L, Laurido C. 2018. Effects of two bisbenzylisoquinoline alkaloids, antioquine and tetrandrine, compared to verapamil in rat thoracic aorta. **Ann Braz Acad Sci** 90: 1459 - 1463. **https://doi.org/10.1590/0001-3765201820170608**

Marulanda ML, López AM, Claroz JL. 2007. Analyzing the genetic diversity of *Guadua* spp. in Colombia using rice and sugarcane microsatellites. **Crop Breed Appl Biotechnol** 7: 43 - 51. **https://doi.org/10.12702/1984-7033.v07n01a07**

Mazzari ALDA, Prieto JM. 2014. Herbal medicines in Brazil: Pharmacokinetic profile and potential herb-drug interactions. **Front Pharmacol** 5: 1 - 12. **https://doi.org/10.3389/fphar.2014.00162**

Miller MR, Dunham JP, Amores A, Cresko WA, Johnson EA. 2007. Rapid and cost-effective polymorphism identification and genotyping using restriction site associated DNA (RAD) markers. **Genome Res** 17: 240 - 248. **https://doi.org/10.1101/gr.5681207**

Ministerio de Protección Social. 2008. **Vademécum Colombiano de plantas medicinales**. Bogotá, Colombia.

Miranda-Nuñez JE, Zamilpa-Alvarez A, Fortis-Barrera A, Alarcon-Aguilar FJ, Loza-Rodriguez H, Gomez-Quiroz LE, Salas-Silva S, Flores-Cruz M, Zavala-Sanchez MA, Blancas-Flores G. 2021. GLUT4 translocation in C2C12 myoblasts and primary mouse hepatocytes by an antihyperglycemic flavone from *Tillandsia usneoides*. **Phytomedicine** 89: 153622. **https://doi.org/10.1016/j.phymed.2021.153622**

Mishra A, Medhi K, Malaviya P, Thakur IS. 2019. Omics approaches for microalgal applications: Prospects and challenges. **Bioresour Technol** 291: 121890. **https://doi.org/10.1016/j.biortech.2019.121890**

Monzote L, Scull R, Cos P, Setzer WN. 2017. Essential oil from *Piper aduncum*: Chemical analysis, antimicrobial assessment, and literature review. **Medicines** 4: 49. **https://doi.org/10.3390/medicines4030049**

Moreno J, Aparicio R, Velasco J, Rojas LB, Usubillaga A, Lue-Merú M. 2010. Chemical composition and antibacterial activity of the essential oil from fruits of *Bursera tomentosa*. **Nat Prod Commun** 5: 311 - 313.

Muñoz Florez JE, Londoño X, Rugeles P, Posso AM, Vallejo FA. 2010. Diversidad y estructura genética de Guadua angustifolia en la Ecorregión Cafetera colombiana. **Recursos Naturales y Ambiente** 62: 45 - 52.

Muthuramalingam P, Akassh S, Rithiga SB, Prithika S, Gunasekaran R, Shin H, Kumar R, Baskar V, Kim J. 2023. Integrated omics profiling and network pharmacology uncovers the prognostic genes and multi-targeted therapeutic bioactives to combat lung cancer. **Eur J Pharmacol** 940: 175479. **https://doi.org/10.1016/j.ejphar.2022.175479**

Negi A, Singh K, Jaiswal S, Kokkat JG, Angadi UB, Iquebal MA, Umadevi P, Rai A, Kumar D. 2022. Rapid genome-wide location-specific polymorphic SSR marker discovery in black pepper by GBS approach. **Front Plant Sci** 13: 1445. **https://doi.org/10.3389/fpls.2022.846937**

Negrão R, Monro AK, Castellanos-Castro C, Diazgranados M. 2022. **Catalogue of useful plants of Colombia**. Royal Botanic Gardens Kew, Bogota, Colombia.

Noorolahi SM, Sadeghi S, Mohammadi M, Azadi M, Rahimi NA, Vahabi F, Arjmand M, Hosseini H, Mosallatpur S, Zamani Z. 2016. Metabolomic profiling of cancer cells to Aloe vera extract by 1HNMR spectroscopy. **J Metabolomics** 2: 1 - 7. **https://doi.org/10.7243/2059-0008-2-1**

Olivier M, Asmis R, Hawkins GA, Howard TD, Cox LA. 2019. The need for multi-omics biomarker signatures in precision medicine. **Int J Mol Sci** 20: 1 - 13. **https://doi.org/10.3390/ijms20194781**

Otto LG, Mondal P, Brassac J, Preiss S, Degenhardt J, He S, Reif JC, Sharbel TF. 2017. Use of genotyping-by-sequencing to determine the genetic structure in the medicinal plant chamomille, and to identify flowering time and alpha-bisabolol associated SNP-loci by genome-wide association mapping. **BMC Genomics** 18: 1 - 18. **https://doi.org/10.1186/s12864-017-3991-0**

Pájaro-González Y, Oliveros-Díaz AF, Cabrera-Barraza J, Fernández-Daza E, Reyes N, Montes-Guevara OA, Caro-Fuentes D, Franco-Ospina L, Quiñones-Fletcher W, Quave CL, Díaz-Castillo F. 2022. Mammea B/BA isolated from the seeds of *Mammea americana* L. (Calophyllaceae) is a potent inhibitor of methicillin-resistant *Staphylococcus aureus*. **Front Pharmacol** 13: 1 - 13. **https://doi.org/10.3389/fphar.2022.826404**

Pájaro-González Y, Oliveros-Díaz A, Cabrera-Barraza J, Cerra-Dominguez J, Díaz-Castillo F. 2022. A review of medicinal plants used as antimicrobials in Colombia. **Med Plants Anti-Infectives** 2022: 3 - 57. **https://doi.org/10.1016/B978-0-323-90999-0.00006-7**

Palazzotto E, Weber T. 2018. Omics and multi-omics approaches to study the biosynthesis of secondary metabolites in microorganisms. **Curr Opin Microbiol** 45: 109 - 116. **https://doi.org/10.1016/j.mib.2018.03.004**

Pandita D, Pandita A, Wani SH, Abdelmohsen SAM, Alyousef HA, Abdelbacki AMM, Al-Yafrasi MA, Al-Mana FA, Elansary HO. 2021. Crosstalk of multi-omics platforms with plants of therapeutic importance. **Cells** 10: 1296. **https://doi.org/10.3390/cells10061296**

Panossian A, Seo EJ, Wikman G, Efferth T. 2015. Synergy assessment of fixed combinations of *Herba andrographidis* and *Radix eleutherococci* extracts by transcriptome-wide microarray profiling. **Phytomedicine** 22: 981 - 992. **https://doi.org/10.1016/j.phymed.2015.08.004**

Pedrete TA, Hauser-Davis RA, Moreira JC. 2019. Proteomic characterization of medicinal plants used in the treatment of diabetes. **Int J Biol Macromol** 140: 294 - 302. **https://doi.org/10.1016/j.ijbiomac.2019.08.035**

Pérez D, Matiz-Guerra LC. 2017. Uso de las plantas por comunidades campesinas en la ruralidad de Bogotá D.C., Colombia. **Caldasia** 39: 68.

Pérez Arbeláez E. 1978. **Plantas útiles de Colombia**. Ed. 4 DAMA Fondo FEN Jardín Botánico de Bogotá José Celestino Mutis, Bogotá DC, Colombia.

Prieto K, Cao Y, Mohamed E, Trillo-Tinoco J, Sierra RA, Ureña C, Sandoval TA, Fiorentino S, Rodriguez PC, Barreto A. 2019. Polyphenol-rich extract induces apoptosis with immunogenic markers in melanoma cells through the ER stress-associated kinase PERK. **Cell Death Discov** 5: 134. **https://doi.org/10.1038/s41420-019-0214-2**

Prieto-Rodríguez JA, Lévuok-Mena KP, Cardozo-Muñoz JC, Parra-Amin JE, Lopez-Vallejo F, Cuca-Suárez LE, Patiño-Ladino OJ. 2022. *In vitro* and *in silico* study of the α-glucosidase and lipase inhibitory activities of chemical constituents from *Piper cumanense* (Piperaceae) and synthetic analogs. **Plants** 11: 2188. **https://doi.org/10.3390/plants11172188**

Quintero WL, Moreno EM, Pinto SML, Sanabria SM, Stashenko E, García LT. 2021. Immunomodulatory, trypanocide, and antioxidant properties of essential oil fractions of *Lippia alba* (Verbenaceae). **BMC Complement Med Ther** 21. **https://doi.org/10.1186/s12906-021-03347-6**

Rai V, Karthikaichamy A, Das D, Noronha S, Wangikar PP, Srivastava S. 2016. Techniques and progress to explore biofuels in the postgenomics world. **J Integ Biol** 20: 387 - 399. **https://doi.org/10.1089/omi.2016.0065**

Ran D, Hong W, Yan W, Mengdie W. 2021. Properties and molecular mechanisms underlying geniposide-mediated therapeutic effects in chronic inflammatory diseases. **J Ethnopharmacol** 273: 113958. **https://doi.org/10.1016/j.jep.2021.113958**

Rao T, Tan Z, Peng J, Guo Y, Chen Y, Zhou H, Ouyang D. 2019. The pharmacogenetics of natural products: A pharmacokinetic and pharmacodynamic perspective. **Pharmacol Res** 146: 104283. **https://doi.org/10.1016/j.phrs.2019.104283**

Rivas Mena KE, Muñoz DL, Pino Benítez CN, Balcázar Morales N. 2015. Antioxidant activity, total phenolic content and cytotoxicity of polar extracts from colombian antidiabetic plants. **Rev Cuba Plant Med** 20: 277 - 289.

Rocha D, Santos C, Bajay M, Campos J, Blank A, Pinheiro J, Zucchi MI. 2015. Development of a novel set of microsatellite markers for *Lippia alba* (Verbenaceae). **Genet Mol Res** 14: 971 - 974. **https://doi.org/10.4238/2015.February.3.4**

Rowe HC, Renaut S, Guggisberg A. 2011. RAD in the realm of next-generation sequencing technologies. **Mol Ecol** 20: 3499 - 3502. **https://doi.org/10.1111/j.1365-294x.2011.05197.x**

Rubin BER, Ree RH, Moreau CS. 2012. Inferring phylogenies from RAD sequence data. **Plos One** 7: e33394. **https://doi.org/10.1371/journal.pone.0033394**

Rugeles-Silva PA, Posso-Terranova AM, Londoño X, Marín NB, Muñoz-Flórez JE. 2012. Caracterización molecular de *Guadua angustifolia* Kunth mediante marcadores moleculares RAMs. **Acta Agronómica** 61: 325 - 330.

Ruiz-Vásquez L, Ruiz Mesia L, Caballero Ceferino HD, Ruiz Mesia W, Andrés MF, Díaz CE, Gonzalez-Coloma A. 2022. Antifungal and herbicidal potential of *Piper* essential oils from the Peruvian Amazonia. **Plants** 11: 1793. **https://doi.org/10.3390/plants11141793**

Sahoo S, Brijesh S. 2019. Pharmacogenomic assessment of herbal drugs in affective disorders. **Biomed Pharmacother** 109: 1148 - 1162. **https://doi.org/10.1016/j.biopha.2018.10.135**

Santos FRC, Lima PF, Priolli RHG, Siqueira WJ, Colombo CA. 2012. Isolation and characteristics of eight novel polymorphic microsatellite loci in *Lippia alba* (Verbenaceae). **Am J Bot** 99: e301-3.

https://doi.org/10.3732/ajb.1100578

Santos NO, Pascon RC, Vallim MA, Figueiredo CR, Soares MG, Lago JHG, Sartorelli P. 2016. Cytotoxic and antimicrobial constituents from the essential oil of *Lippia alba* (Verbenaceae). **Medicines** 3: 22. **https://doi.org/10.3390/medicines3030022**

Seebaluck R, Gurib-Fakim A, Mahomoodally F. 2015. Medicinal plants from the genus *Acalypha* (Euphorbiaceae)– A review of their ethnopharmacology and phytochemistry. **J Ethnopharmacol** 159: 137 - 157. **https://doi.org/10.1016/j.jep.2014.10.040**

Sequeda-Castañeda L, Modesti-Costa G, Celis C, Gamboa F, Gutiérrez S, Luengas P. 2016. *Ilex guayusa* (Aquifoliaceae): Amazon and andean native plant. **Pharmacologyonline** 2016: 193 - 202.

Shan Y, Wang F, Wei Z, Lu Y. 2021. Synthetic lethality theory approaches to effective substance discovery and functional mechanisms elucidation of anti-cancer phytomedicine. **Phytomedicine** 91: 153718. **https://doi.org/10.1016/j.phymed.2021.153718**

Shen Y, Sun Z, Shi P, Wang G, Wu Y, Li S, Zheng Y, Huang L, Lin L, Lin X, Yao H. 2018. Anticancer effect of petroleum ether extract from *Bidens pilosa* L and its constituent's analysis by GC-MS. **J Ethnopharmacol** 217: 126 - 133. **https://doi.org/10.1016/j.jep.2018.02.019**

Shipa SJ, Khandokar L, Bari MS, Qais N, Rashid MA, Haque MA, Mohamed IN. 2022. An insight into the anti-ulcerogenic potentials of medicinal herbs and their bioactive metabolites. **J Ethnopharmacol** 293: 115245. **https://doi.org/10.1016/j.jep.2022.115245**

Shyamli PS, Pradhan S, Panda M, Parida A. 2021. De novo whole-genome assembly of *Moringa oleifera* helps identify genes regulating drought stress tolerance. **Front Plant Sci** 12: 1 - 14. **https://doi.org/10.3389/fpls.2021.766999**

SiB Colombia (Sistema de Información sobre Biodiversidad de Colombia). 2023. **https://cifras.biodiversidad.co**

Silveira N, Saar J, Santos ADC, Barison A, Sandjo LP, Kaiser M, Schmidt TJ, Biavatti MW. 2016. A new alkamide with an endoperoxide structure from *Acmella ciliata* (Asteraceae) and its *in vitro* antiplasmodial activity. **Molecules** 21. **https://doi.org/10.3390/molecules21060765**

Singh PK, Sharma H, Srivastava N, Bhagyawant SS, Singh PK, Sharma H. 2014. Analysis of genetic diversity among wild and cultivated chickpea genotypes employing ISSR and RAPD markers. **Am J Plant Sci** 5: 676 - 682. **https://doi.org/10.4236/ajps.2014.55082**

Singh G, Passsari AK, Singh P, Leo VV, Subbarayan S, Kumar B, Singh BP, Lalhlenmawia H, Kumar NS. 2017. Pharmacological potential of *Bidens pilosa* L. and determination of bioactive compounds using UHPLC-QqQLIT-MS/MS and GC/MS. **BMC Complement Altern Med** 17. **https://doi.org/10.1186/s12906-017-2000-0**

Smit R, Du Toit ES, Vorster BJ. 2013. RAPD and SSR genetic diversity analysis of *Moringa oleifera*. **South Afric J Bot** 86: 182. **https://doi.org/10.1016/j.sajb.2013.02.162**

Sumner LW, Lei Z, Nikolau BJ, Saito K. 2015. Modern plant metabolomics: advanced natural product gene discoveries, improved technologies, and future prospects. **Nat Prod Rep** 32: 212 - 229. **https://doi.org/10.1039/c4np00072b**

Sun Q, Gong T, Liu M, Ren S, Yang H, Zeng S, Zhao H, Chen L, Ming T, Meng X, Xu H. 2022. Shikonin, a naphthalene ingredient: Therapeutic actions, pharmacokinetics, toxicology, clinical trials and pharmaceutical researches. **Phytomedicine** 94: 153805. **https://doi.org/10.1016/j.phymed.2021.153805**

Suzuki M, Nakabayashi R, Ogata Y, Sakurai N, Tokimatsu T, Goto S, Suzuki M, Jasinski M, Martinoia E, Otagaki S, Matsumoto S, Saito K, Shiratake K. 2015. Multiomics in grape berry skin revealed specific induction of the stilbene synthetic pathway by ultraviolet-C irradiation. **Plant Physiol** 168: 47 - 59. **https://doi.org/10.1104/pp.114.254375**

Tan J, Tian Y, Cai R, Yi T, Jin D, Guo J. 2019. Antiproliferative and proapoptotic effects of a protein component purified from *Aspongopus chinensis* Dallas on cancer cells *in vitro* and *in vivo*. **Evid Based Complement Alternat Med** 2019: 8934794. **https://doi.org/10.1155/2019/8934794**

Tang XM, Guo JL, Chen L, Ho PCL. 2020. Application for proteomics analysis technology in studying animal-derived traditional Chinese medicine: A review. **J Pharm Biomed Anal** 191: 113609. **https://doi.org/10.1016/j.jpba.2020.113609**

Tanuja, Parani M. 2022. Whole transcriptome analysis identifies full-length genes for neoandrographolide biosynthesis from *Andrographis alata*, an alternate source for antiviral compounds. **Gene** 851: 146981. **https://doi.org/10.1016/j.gene.2022.146981**

Valdiani A, Abdul M, Soon K, Tan G. 2012. Nain-e Havandi *Andrographis paniculata* present yesterday, absent today: a plenary review on underutilized herb of Irans pharmaceutical plants. **Mol Biol Rep** 39: 5409 - 5424. **https://doi.org/10.1007/s11033-011-1341-x**

Valdivia C, Marquez N, Eriksson J, Vilaseca A, Muñoz E, Sterner O. 2008. Bioactive alkenylphenols from *Piper obliquum*. **Bioorg Med Chem** 16: 4120 - 4126. **https://doi.org/10.1016/j.bmc.2008.01.018**

Velandia SA, Quintero E, Stashenko EE, Ocazionez RE. 2018. Actividad antiproliferativa de aceites esenciales de plantas cultivadas en Colombia. **Acta Biol Colomb** 23: 189 - 198. **https://doi.org/10.15446/abc.v23n2.67394**

Wang X, Zhang A, Wang P, Sun H, Wu G, Sun W, et al. Lv H, Jiao G, Xu H, Yuan Y, Liu L, Zou D, Wu Z, Han Y, Yan G, Dong W, Wu F, Dong T, Yu Y, Zhang S, Wu X, Tong X, Meng X. 2013. Metabolomics coupled with proteomics advancing drug discovery toward more agile development of targeted combination therapies. **Mol Cell Proteomics** 12: 1226 - 1238. **https://doi.org/10.1074/mcp.M112.021683**

Wang XJ, Yan GL, Zhang AH, Sun H, Piao CY, Li WY, Sun C, Wu XH, Li XH, Chen Y. 2013. Metabolomics and proteomics approaches to characterize and assess proteins of bear bile powder for hepatitis C virus. **Chin J Nat Med** 11: 653 - 665. **https://doi.org/10.1016/S1875-5364(13)60076-X**

Wei MM, Zhao SJ, Dong XM, Wang YJ, Fang C, Wu P, Song GQ, Gao JN, Huang ZH, Xie T, Zhou JL. 2021. A combination index and glycoproteomics-based approach revealed synergistic anticancer effects of curcuminoids of turmeric against prostate cancer PC3 cells. **J Ethnopharmacol** 267: 113467. **https://doi.org/10.1016/j.jep.2020.113467**

White DM, Huang JP, Jara-Muñoz OA, Madriñán, Ree RH, Mason-Gamer RJ. 2021. The origins of Coca: Museum genomics reveals multiple independent domestications from progenitor *Erythroxylum gracilipes*. **Syst Biol** 70: 1 - 13. **https://doi.org/10.1093/sysbio/syaa074**

Winzer T, Winzer T, Gazda V, He Z, Kaminski F, Kern M, Larson TR, Li Y, Meade F, Teodor R, Vaistij FE, Walker C, Bowser TA, Graham IA. 2012. *Papaver somniferum* 10-gene cluster for synthesis of the anticancer alkaloid noscapine. **Science** 336: 1704 - 1708. **https://doi.org/10.1126/science.1220757**

Wu B, Li Y, Li J, Xie Z, Luan M, Gao C, Shi Y, Chen S. 2021. Genome-wide analysis of alternative splicing and non-coding RNAs reveal complicated transcriptional regulation in *Cannabis sativa* L. **Int J Mol Sci** 22: 11989. **https://doi.org/10.3390/ijms222111989**

Xiao M, Zhang Y, Chen X, Lee EJ, Barber CJS, Chakrabarty R, Desgagné-Penix I, Haslam TM, Kim YB, Liu E, MacNevin G, Masada-Atsumi S, Reed DW, Stout JM, Zerbe P, Zhang Y, Bohlmann J, Covello PS, De Luca V, Page JE, Ro DK, Martin VJJ, Facchini PJ, Sensen CW. 2013. Transcriptome analysis based on next-generation sequencing of non-model plants producing specialized metabolites of biotechnological interest. **J Biotechnol** 166: 122 - 134. **https://doi.org/10.1016/j.jbiotec.2013.04.004**

Xuan TD, Khan TD. 2016. Chemistry and pharmacology of *Bidens pilosa*: an overview. **J Pharm Investig** 46: 91 - 132. **https://doi.org/10.1007/s40005-016-0231-6**

Yang D, Du X, Yang Z, Liang Z, Guo Z, Liu Y. 2014. Transcriptomics, proteomics, and metabolomics to reveal mechanisms underlying plant secondary metabolism. **Eng Life Sci** 14: 456 - 466.

Yang WC. 2014. Botanical, pharmacological, phytochemical, and toxicological aspects of the antidiabetic plant *Bidens pilosa* L. **Evid Based Complement Alternat Med** 2014: Article 698617. **https://doi.org/10.1155/2014/698617**

Yang L, Xu L, Zhou Y, Liu M, Wang L, Kijas JW, Zhang H, Li L, Liu GE. 2018. Diversity of copy number variation in a worldwide population of sheep. **Genomics** 110: 143 - 148. **https://doi.org/10.1016/j.ygeno.2017.09.005**

Yang S, He Y, Chen X, Kalim U, Wang Y, Yang S, Qi H, Cheng HZ, Lu X, Wang X, Shen Q, Zhang W. 2021. Viral metagenomics reveals diverse viruses in the feces samples of raccoon dogs. **Front Vet Sci** 8: 1 - 12. **https://doi.org/10.3389/fvets.2021.693564**

Zhang C, Yin A, Li H, Wang R, Wu G, Shen J, Zhang M, Wang L, Hou Y, Ouyang H, Zhang Y, Zheng Y, Wang J, Lv X, Wang Y, Zhang F, Zeng B, Li W, Yan F, Zhao Y, Pang X, Zhang X, Fu H, Chen F, Zhao N, Hamaker BR, Bridgewater LC, Weinkove D, Clement K, Dore J, Holmes E, Xiao H, Zhao G, Yang S, Bork P, Nicholson JK, Wei H, Tang H, Zhang X, Zhao L. 2015. Dietary modulation of gut microbiota contributes to alleviation of both genetic and simple obesity in children. **EBioMedicine** 2: 968 - 984. **https://doi.org/10.1016/j.ebiom.2015.07.007**

Zhang C, Wang M, Gao X, Zhou F, Shen C, Liu Z. 2020. Multi-omics research in albino tea plants: Past, present, and future. **Sci Hortic** 261: 108943. **https://doi.org/10.1016/j.scienta.2019.108943**

Zhang HW, Lv C, Zhang LJ, Guo X, Shen YW, Nagle DG, Zhou YD, Liu SH, Zhang WD, Luan X. 2021. Application of omics- and multi-omics-based techniques for natural product target discovery. **Biomed Pharmacother** 141: 111833. **https://doi.org/10.1016/j.biopha.2021.111833**

Zhang LG, Chang Y, Zhang XF, Guan FZ, Yuan HM, Yu Y, Zhao LJ. 2014. Analysis of the genetic diversity of Chinese native *Cannabis sativa* cultivars by using ISSR and chromosome markers. **Genet Mol Res** 13: 10490 - 10500. **https://doi.org/10.4238/2014.December.12.10**

Zhang Z, Su Q, Xia B, Li Y, Qin X, Luo H, Lin Y, Xie J, Wu P, Lin L, Liao D. 2022. Fitoterapia Integrative transcriptomic, proteomic and metabolomic analysis reveals the dynamic regulation of secondary metabolism upon development of Prunella. **Fitoterapia** 163: 105334. **https://doi.org/10.1016/j.fitote.2022.105334**

Zhao J, Fang Z, Zha Z, Sun Q, Wang H, Sun M, Qiao B. 2019. Quercetin inhibits cell viability, migration and invasion by regulating miR-16/HOXA10 axis in oral cancer. **Eur J Pharmacol** 847: 11 - 18. **https://doi.org/10.1016/j.ejphar.2019.01.006**

Zheng H, Fu X, Shao J, Tang Y, Yu M, Li L, Huang L, Tang K. 2022. Transcriptional regulatory network of high-value active ingredients in medicinal plants. **Trends Plant Sci** 28: 429 - 446. **https://doi.org/10.1016/j.tplants.2022.12.007**

Zhou M, Varol A, Efferth T. 2021. Multi-omics approaches to improve malaria therapy. **Pharmacol Res** 167: 105570**.** **https://doi.org/10.1016/j.phrs.2021.105570**

Zhu W, Han H, Liu A, Guan Q, Kang J, David L. 2021. Combined ultraviolet and darkness regulation of medicinal metabolites in *Mahonia bealei* revealed by proteomics and metabolomics. **J Proteomics** 233: 104081. **https://doi.org/10.1016/j.jprot.2020.104081**