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Review

A review of the knowledge base for the development of natural ingredients value chains for a sustainable biobased economy in Colombia

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Abstract
Natural ingredients (NIs) from plant biodiversity represent a value creation strategy in the transition to a sustainable biobased economy, especially in biodiversity rich countries. A necessary action to achieve this purpose is to orientate research and strengthen the knowledge base of NIs following a value chain (VC) approach. Although the promotion of NIVCs has gained increasing attention in the bioeconomy, a description of the scientific progress, research advances and gaps towards their development is necessary. This review aimed to scrutinize the existing literature on NIVCs to determine its state of progress. Firstly, we explored the global diffusion of research on natural plant ingredients. Secondly, we examined the research landscape in Colombia, focusing on the cooperation between countries, economic sectors impacted, and plant species reported. Lastly, we selected the most reported plant species as a promising NI source in Colombia to assess the literature that constitute the knowledge base of this plant in relation to the VC building blocks: biomass production, biomass processing, product development, and transversal aspects such as sustainability and governance. We show that research on NIs has risen worldwide, with notable scientific output from China, India, and the United States. In Colombia, the interest in NIs from plant biodiversity has also gained importance in the research agenda. Its progress is based on extensive collaboration between institutions, mainly from Spain, the United States, and Brazil. Its research prospects include diverse applications in the pharmaceutical and food sectors. We identify *Lippia origanoides* as the most reported native plant in scientific literature in Colombia. Using this plant as case study, we provide an overview of the knowledge base of *L. origanoides* in relation to the VC. Our results indicate that most publications focus on product development, suggesting a lack of comprehensive coverage of the VC and potentially neglected aspects. Based on this, we describe the current and desired scenario of *L. origanoides* VCs, as well as needs and opportunities for their sustainable implementation in Colombia. This contributes to build research and development roadmaps of sustainable NIVCs from plant diversity supported by multi-stakeholder collaboration.

Keywords Biobased value chain · Natural capital · Biodiversity · Bioeconomy · *Lippia origanoides* · Multi-disciplinary research · Sustainability · Governance

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1 Introduction

Biodiversity has intrinsically driven human well-being through the delivery of ecosystem services [1]. Its definition encompasses the variety and complexity among living organisms, including DNA, genes, the proteome, and the metabolome, and their interaction with ecological systems [2]. Biodiversity studies have always been associated with different areas of knowledge due to the plural values of biodiversity, and they have been the focus of the Bioeconomy (BE), particularly from a resource use perspective [3]. BE is a term that is booming globally and refers to all economic activities derived from biological resources, including related knowledge, science, technology, and innovation to provide information, products, processes, and services towards sustainable development [4]. The BE contributes to improving knowledge on biodiversity, conserving or restoring habitats, increasing social participation, and potentially helping to move towards a truly sustainable use of nature [5]. In highly biodiverse regions, the relationship between sustainable use of biodiversity and BE has become evident in research and policy agendas [6]. For example, the promotion of the BE using biodiversity resources for innovative natural products is one of the lines of action that receives increasing support in the Latin American and Caribbean regions [3].

Natural ingredients (NIs) provide a biodiversity-based BE opportunity. NIs, also called bio-ingredients or natural products, are any ingredient whose starting material originates from plants, minerals, microbes, or animals, as well as biological industry by-products [5, 7]. These have been used for food supplements, medicinal chemistry, pharmaceuticals, agrochemicals, fragrances, and cosmetics, and consequently have attracted growing interest in scientific communities that bridge research with industry [8]. The global market for NIs in natural cosmetics, phytotherapeutic products, and functional foods exceeds 43 billion dollars [9, 10]. The special attention paid to NIs has been triggered mainly by health and environmental issues [11]. In health, NIs exert functional properties in food products such as antidiabetic, anticancer, antiobesity, antioxidant, and antimicrobial properties [12]. For the environment, NIs based on renewable resources could contribute to close material and energy cycles and substitute minerals and chemicals [13]. NIs are also particularly interesting as a valorization strategy for biomass from novel plants, established crops, and residues by taking advantage of natural properties and extracting targeted constituents to produce specialty products [14].

Value chains (VCs) have the potential to promote bioproducts [15], such as NIs. A VC consists of actors' relations and a set of interlinked activities related to the primary production of biobased resources, the technological conversion to higher-value goods, commercialization, and use [16]. VCs rely on a knowledge base for their development and sustainable performance [17], where multiple social, cultural, environmental, economic, institutional and technological aspects converge [18]. The establishment of NIVCs encompasses bioprospecting, biofunctionality analysis, and product formulation, as well as production processes in the upstream and downstream (e.g., isolation, extraction, and separation) [7]. In addition, it includes the primary production of biomass, sustainability analysis, VC actors' relations, and governance [19, 20]. Studies from a VC perspective break with the paradigm of individual and isolated scientific fields that do not allow elucidating the preparedness and suitability of novel bioresources, such as NIs.

Colombia's BE mission focuses research efforts on bioprospecting and the development of NIVCs as strategies for the use of biodiversity from a material perspective [21, 22]. This mission is supported by national policies and programs such as the "Green Growth Policy" and the "Colombia BIO Program" [23]. Colombia has a comparative advantage over other countries as it is the second most biodiverse country in the world, which allows it to see biological resources as a key asset to change its productive matrix [24]. Colombia's rich biodiversity accounts for more than 28,900 reported plant species [25] (37,290 including non-vascular plants [26]) of which around 26% are reported to have human uses and socio-economic importance [25, 27]. Most of these plants, distributed across all bioregions and ecosystems of Colombia [28, 29] (Fig. 1), are locally marketed sources of food and medicine, such as Annatto (*Bixa orellana*) and Sauco (*Sambucus peruviana*) [30]. Strengthening competitiveness of NIVCs is among main goals of BE-oriented efforts between the government, academia, and the private sector in Colombia [31]. While NIVCs have recently gained interest in Colombia, there are few systematic efforts that critically document the state of the art of the research, thus limiting the identification of barriers, needs, and projections. Actions in Colombia could be implemented in another country rich in biodiversity with similar characteristics in terms of capacities and context conditions [29].

To move this field of study forward, we conducted a literature review to assess the knowledge base of NIs in Colombia for the development of VCs through a case study. The literature review was carried out in three steps, from the general to the particular. Firstly, the world literature reported in peer-reviewed journals on NIs was compiled and analyzed bibliometrically. Secondly, research on NIs associated with Colombia was characterized by international cooperation, impacted economic sectors, and informed plant species. Finally, the assessment of the literature of the most reported plant species as

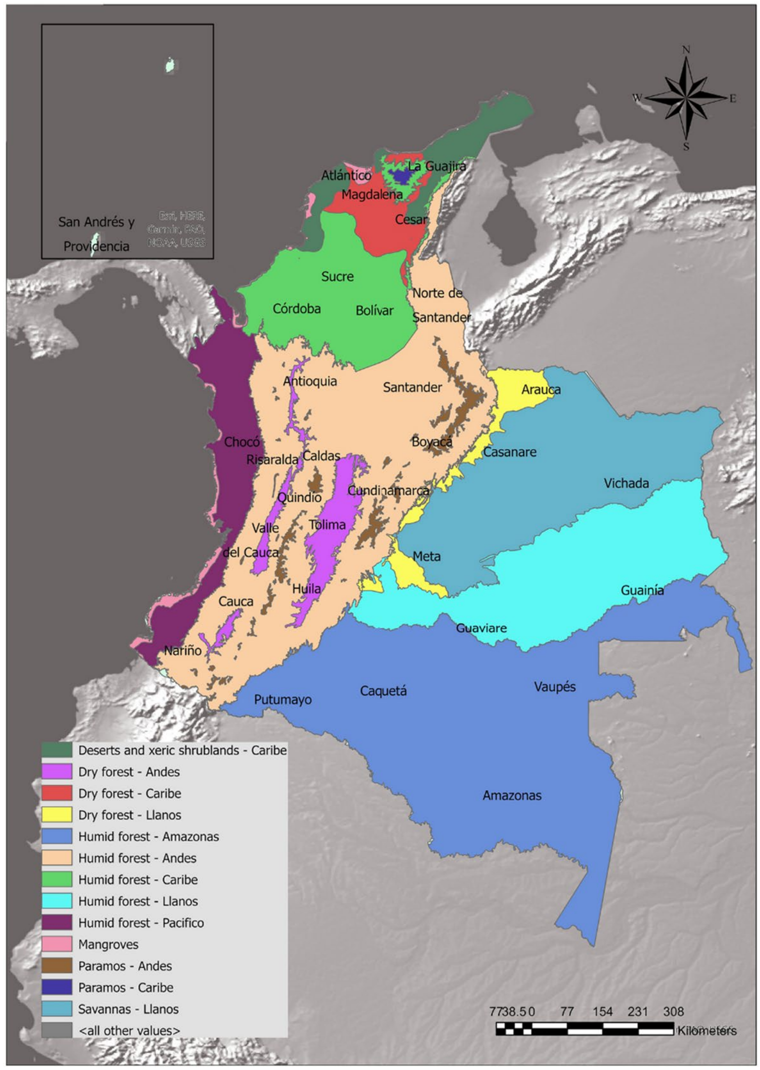

Fig. 1 Bioregions of Colombia (Gori et al. [28]) (CC BY 4.0)

novel sources of NIs was carried out by associating the findings of the publications to the VC's phases, from biomass production to end products, including sustainability and governance as transversal aspects. In that vein, insights were compiled, gaps were identified, and recommendations were proposed to provide an overview of its progress status and drive tangible actions. This work can be used as an interdisciplinary reference for BEs in countries rich in biodiversity and represents a call to promote the development of knowledge-based VCs for the sustainable production of NIs.

2 Materials and methods

2.1 Global bibliometric analysis

A search of the publications on NIs reported between 2010 and 2020 was performed on May 20, 2021. The types of documents defined for the investigations included journal articles, books, book chapters, and conference articles. The Scopus index was selected as the data repository to search for documents because it provided a larger collection of this topic of scientific literature compared to the Web of Science. The search scope was "topic," which included the title, abstract, and keywords. Boolean operators (OR and AND), the truncation symbol (*), and the proximity operator ("") were used to facilitate and enable the selection of the investigations of interest. The terms used in the search strategy are proxies to the topic of study and were defined based on synonyms for NIs and biomass sources to focus the search particularly on vegetal biomass (dedicated crops—novel and conventional—, crop residues, non-domesticated plants) and applications

Table 1 Definition of the search equation applied in the Scopus database on NIs between 2010 to 2020

Parts of the search equation	Keywords and Boolean operators
Synonyms to NIs	("natural ingredient*" OR "plant extract*" OR "natural product*" OR "bioactiv*" OR "natural colorant*" OR "vegetable oil*" OR "plant metabolite*" OR "bioprosp*" OR "ethnobot*" OR "traditional use*" OR "essential oil*")
	AND
Sources of obtaining	("agr*" OR "forest*" OR "herb*" OR "biodivers*" OR "plant*") AND
Economic sectors impacted	("agr*" OR "cosmet*" OR "pharma*" OR "chemistr*" OR "food*" OR "medicin*" OR "fiber*" OR "fibre*" OR "therapeutic*" OR "bioeconom*" OR "biobased econom*" OR "bio-based econom*" OR "industr*" OR "nutraceut*") AND NOT
Topics excluded: renewable energy	("bio-ene*" OR "bioener*" OR "renewable ener*")

in economic sectors (Table 1). NIs represent a valorization strategy for biomass related to its material use. Therefore, renewable energy was excluded from the search with the aim of retrieving literature related to NIs and biobased products. The parameters provided by the Scopus database were: (i) number of publications per year; (ii) number of publications per country; (iii) number of publications per subject area in each year; and iv) number of publications per subject area in each country. The bibliometric analysis was performed using the results obtained from Scopus and the VOSviewer 1.6.14 software (University of Leiden, The Netherlands). The graphs were made using Prism 8 software (Graphpad, USA).

2.2 Data synthesis and analysis for Colombia

To study the literature related to Colombia, the publications were filtered both by country and by the keyword "colombia*", which was added to the search equation. A three-tiered and iterative classification process was developed for screening the retrieved publications. The first classification grouped publications into two categories: experimental and review or explorative articles. Explorative literature refers to ethnobotanical studies with valuable information for bioprospecting and key insights from traditional knowledge. As this work is oriented to assess the knowledge base in the context of NIVCs, only experimental publications that provide in-depth and technical data were selected for further analysis. A network analysis was carried out to identify the cooperation of countries with Colombia based on co-authorship. Using the VOSviewer 1.6.14 software package (University of Leiden, The Netherlands), the list of countries was filtered to a minimum of five publications. VOSviewer generated the network visualization map of country co-authorship, with countries clustered.

The second classification process was performed based on the plant species reported. The plant species were screened, listed, and characterized in their attribute of origin using the 'Catalogue of Plants and Lichens of Colombia' [32]. Non-reported plant species in this catalogue were further searched on the platform 'Global Biodiversity Information Facility' [33]. Plant species were classified as native, native and endemic, and native and cultivated to strengthen the focus on Colombian biodiversity. Those plants that were classified as naturalized, adventitious or non-native cultivated according to the consulted databases were excluded from further analysis. Consecutively, a ranking of the most investigated species was generated based on the frequency in the publication sample. Plants' applications to industrial sectors were assigned according to the information from the corresponding studies.

2.3 Value chain's knowledge base assessment of the most reported plant species

The plant species with the largest number of publications was selected as a case study for the assessment of the knowledge base of NIVCs in Colombia. A complementary search of publications reported up to the year 2020 in Scopus was carried out, using both the selected plant species and Colombia as keywords. Moreover, an exhaustive search of grey literature was carried out, including (i) government reports and other official documents; (ii) reports of national and international non-governmental organizations; and (iii) conference papers, technical notes, memories of seminars, and other scholarly publications that are not indexed in the peer-reviewed journals.

All the literature obtained was classified along four main building blocks or phases of biomass-based VCs: (i) biomass production, (ii) biomass processing, (iii) product development, and (iv) transversal aspects [20, 34–37]. Applied knowledge on biomass production embraces aspects related to germination, plant propagation, and agronomic management, supported by fundamental knowledge on species biology, phytochemistry, botanical aspects, plant ecology, and taxonomy. Knowledge on biomass processing covers the conversion into targeted intermediate or end products, including post-harvest and processing technologies. Knowledge of product development includes the identification of specific applications according to plant properties, quality, and product formulation. The transversal aspects include applied knowledge on sustainability performance as well as VC management, logistics, financing, actors, and governance. The classification was based on the publication's main focus by considering the actual content of the title, abstracts, and conclusions. In addition, a compilation of its content was described to analyze knowledge gaps, challenges, recommendations, and future research directions.

3 Results and discussion

3.1 Annual publications trend, documents by country, and subject areas

To study global trends in research on NIs, a bibliometric-based analysis of the publications reported between 2010 and 2020 around the world was performed. A database of 153,818 publications was obtained, which was mainly composed of research articles (85.8%) and review articles (9.1%). Overall, the publication trend was upward (Fig. 2-a), with an average annual increase of 6%. This indicates that research on NIs is receiving increasing attention. Various aspects promote interest in NIs. The global rise of the BE, for instance, in the political context has intensified efforts to expand knowledge in diversifying biobased products from biodiversity [38].

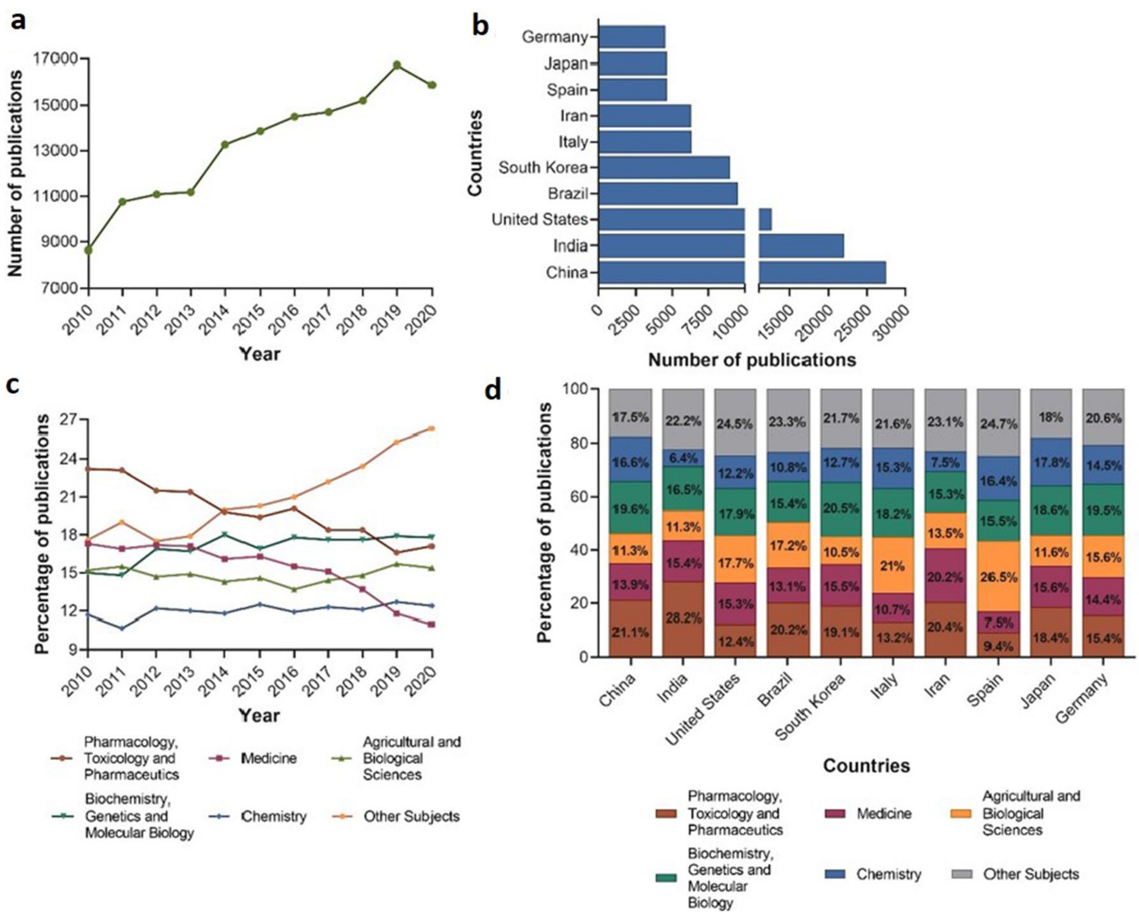

Fig. 2 Global overview of the dissemination of knowledge about NIs between 2010 and 2020. **a** Number of documents published each year. **b** Top 10 countries or territories with the most publications. **c** Annual percentage of publications by subject area. **d** Percentage of publications by thematic area in the top 10 countries

The bibliometric analysis showed the countries with the largest production of research publications in their respective subject areas. China leads the production of publications on NIs with 28,390 (Fig. 2b). India was ranked second with 22,670 documents, showing a considerable advantage over the United States (US), located in third place with 13,323 documents. Then, there were Brazil (10,003), South Korea (9206), Italy (6655), Iran (6561), Spain (4910), Japan (4768), and Germany (4761). This indicates that Asia led scientific production, followed by Europe and America. Asia has always been outstanding for its rich biodiversity and still has enormous potential to develop biobased products with NIs, mainly based on traditional medicine [39]. The prominence of Africa and Oceania is very scanty. Therefore, there is a need to develop research projects in these regions promoted by their governments and research institutions with a focus on the potential of biodiversity for a sustainable environment.

According to our study, the top five subject areas associated with NI research were: (i) biochemistry, genetics, and molecular biology; (ii) pharmacology, toxicology, and pharmacy; (iii) agriculture and biological sciences; (iv) chemistry; and (v) medicine (Fig. 2c). The category 'other subjects' consisted of more than five areas that presented percentages of publications much lower than the first five already mentioned. These areas were immunology and microbiology, nursing, earth and planetary sciences, mathematics, and multidisciplinary. Studies associated with environmental, social, and economic issues are possibly included in the multidisciplinary area, showing scarce prominence. Surprisingly, publication productivity showed contrasting trends across all subject areas. Both pharmacology, toxicology, pharmacy, and medicine were the only subject areas that showed a decrease over time (30%). The other three subject areas showed a similar number of publications each year.

The subject areas in the top ten countries with the largest documentary production were also analyzed (Figs. 1–d). South Korea is the country with the most research carried out in biochemistry, genetics, and molecular biology with 20.5%; India in pharmacology, toxicology, and pharmacy with 28.2%; Spain in agriculture and biological sciences with 26.5%; Japan in chemistry with 17.8%; and Iran in medicine with 20.2%. Finally, Spain was the country with the most research in the group of "other subjects," with 24.7%.

Research led by South Korea has been influential in the biological synthesis of phytochemicals, mainly silver nanoparticles, for the prevention and therapy of cancer, obesity, diabetes, and Alzheimer's. *Panax ginseng*, *Humulus japonicus*, *Scutellaria baicalensis*, *Cirsium setidens*, and *Schisandra chinensis* are the most studied plants [40–42]. India's focus is the application of novel drug delivery systems for herbal formulations such as *Curcuma longa*, *Withania somnifera*, *Bacopa monnieri*, *Aegle marmelos*, and *Ocimum sanctum*. Studies in cardiotoxicity, nephrotoxicity, Parkinson's disease, and atherosclerosis have been carried out [43–45].

In Spain, researchers work primarily on applications and new opportunities for bioactive compounds in the food industry. One of its most recent investigated approaches is the extraction of carotenoids, polyphenols, dietary fibers, vitamins, enzymes, and oils from fruit and vegetable waste [46–48]. Finally, Japan mainly leads the advancement of chemical extraction techniques used for botanical products in industrial uses and optimization strategies. For instance, the isolation of cellulose nanocrystals. Japan is also promoting modern plant metabolomics for natural product gene discovery [49, 50].

All the countries mentioned above that stand out in research on NIs have promoted BE strategies and policies, except Iran [51]. The US, Italy, Spain, Japan, and Germany have a dedicated BE strategy. China, India, Brazil, and South Korea have a BE-related strategy [52]. Although some of these countries differ in the scope of their BE actions, NIs do not represent a specific focus in any country. This does not mean that NIs are undervalued, but rather that these were included as a diversification strategy of plants' uses to increase their contribution to gross domestic product. In contrast, Costa Rica, France, Ireland, Malaysia, Norway, and Thailand have proposed specific efforts for NIs in their BE plans [53]. For instance, one of Malaysia's agricultural focuses is the production of high-value NI biobased fragrances, bioflavors, and functional foods [54]. Likewise, Costa Rica has promoted new rural agro-industries through NIVCs to enhance local resources [55].

3.2 Natural ingredients research in Colombia: an overview

We next sought to explore NI research in Colombia. In the database obtained, 689 documents (0.45% of publications worldwide) associated with Colombia between 2010 and 2020 were found. This set of scientific publications was classified by type of document into explorative and review (41.3%) and experimental studies (58.6%). For the following analysis steps, we focus on the experimental studies. The first feature that characterized the literature was the cooperation between countries, measured by the co-occurrence parameter based on co-authorship and authors' affiliations [56]. Cooperation in research can be analyzed using bibliometrics and is key to strengthening alliances and formulating future projects [57]. Colombia has conducted research on NIs with 11 countries. The most prominent are Spain, Brazil,

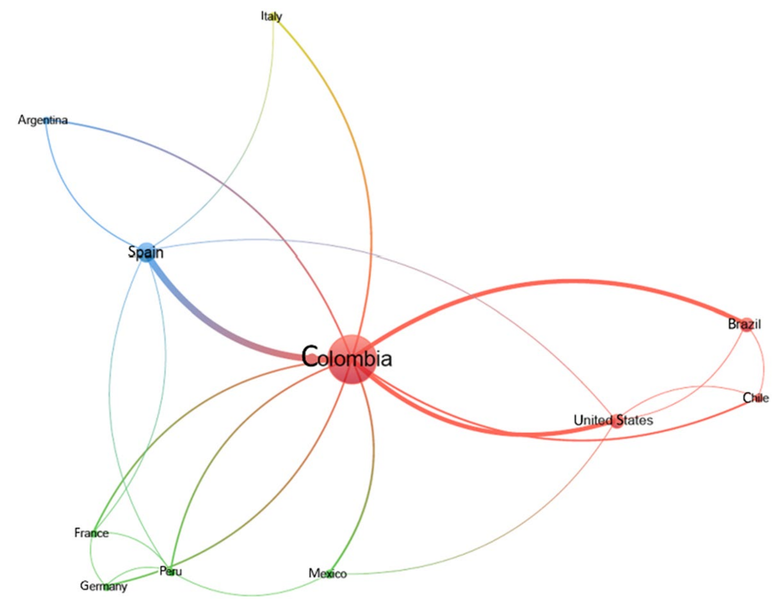

Fig. 3 Cooperation of countries with Colombia in research on NIs. The size of each node reflects the quantity of publications in co-authorship. The thickness of each link indicates the strength of the collaboration. Clusters are color-coded

and the United States (Fig. 3). The countries were distributed in four clusters, which were differentiated by colors. The first group included Brazil, Chile, the United States, and Colombia. The second is France, Germany, Mexico, and Peru. The third is Argentina and Spain, and the fourth is Italy. Cooperation with Spain has promoted work with various bioactive compounds from the asai fruit, cocoa extracts, and lettuce by-products [58–60]. Advances include a comprehensive database of carotenoid content in Ibero-American foods and the bioprospection of *Piperaceae* species in Choco (Colombia) to obtain essential oils (EO) [61, 62]. Collaboration with Brazil comprises studies on pharmacogenetics and ethnomedicine, herbal medicine, cardiovascular disorders, and psychiatric disorders [63, 64]. The synthesis, characterization, and application of biobased active food packaging have also been studied [65]. Additionally, the properties of *Baccharis trinervis*, *Lippia origanoides*, and *Echinacea* plants have been investigated [66–68]. Joint research with the United States has leveraged scientific advancement in mint, passion flowers, and African oil palm. Improvements of mint cultivars for

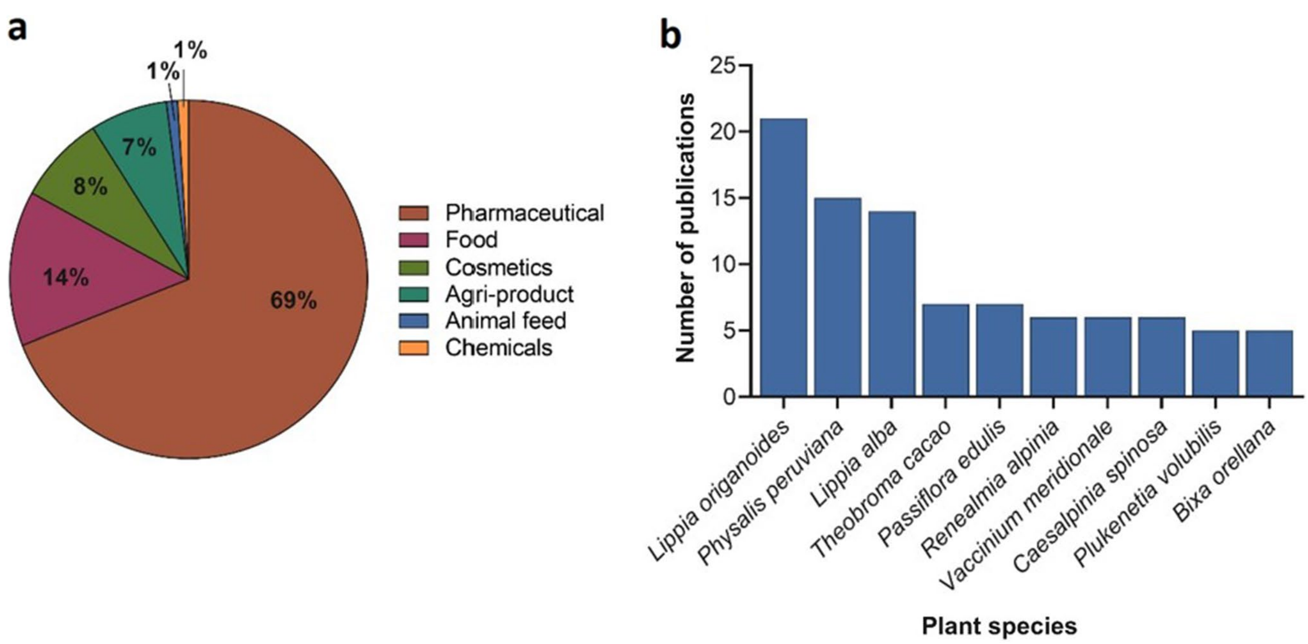

Fig. 4 Research overview on NIs in Colombia. **a** Percentage of applications in industrial sectors of NIs reported in publications. **b** Most reported plant species

germplasm banks and the modeling of influential factors of peppermint EO composition and yield have been documented [69, 70]. Evidence on the ability of polyphenol extracts from passion fruit to mitigate intestinal barrier dysfunction has been published [71]. Oil-palm-based biorefinery concepts and sustainability strategies for oil palm cultivation have been addressed [72, 73].

The second assessed feature aimed to elucidate the targeted industrial sectors and was based on those publications focused on plants from Colombian biodiversity (n=267) . We noted that the pharmaceutical sector is the most impacted, followed by the food sector (Fig. 4-a). These two sectors represented more than 80% of the studies. The cosmetics and agri-products sector accounted for 15%, and the remaining sectors reported were animal feed, chemicals, and energy. The orientation to the pharmaceutical sector is based on the bioprospecting of plants with attributes such as antifungal, neuroprotective, anti-toxoplasmic, and antiparasitic properties [74–76]. Plant derivatives against psychiatric disorders, snakebites, malaria, Chagas disease, and leishmaniasis are reported [77–79]. Furthermore, efforts in microencapsulation for the release of bioactives have spread, including bioactive compounds from cactus acid fruits and papaya [80, 81]. The food sector presented trends in antimicrobial food packaging systems, nanoemulsions, and functional foods [65, 82]. There has also been a growing interest in green cosmetics and the potential of agro-industrial by-products. Numerous plant species have been analyzed for properties such as UV-filtering, UV-absorbing, bleaching, skin-protecting, and antioxidant action to promote the cosmetic use of plant biodiversity [83]. The antioxidant capacity and bioactive compounds of coffee pulp, as well as natural pigments from the coffee exocarp, have been studied [84, 85]. The mango seed has been investigated for its high protein content with all the essential amino acids, lipids rich in unsaturated fatty acids, and high antioxidant capacity of seed extracts [86]. Further topics include the biological production of bee-pollen-based food [87, 88].

The third step was to determine the most studied plant species in the sample of literature. We found that *Lippia origanoides* is the most reported plant species associated with NIs in Colombia, with 21 publications (Fig. 4b). This observation supports the fact that *L. origanoides* has stood out for more than 20 years as one of the most studied

Table 2 Potential applications of *L. origanoides*, *P. peruviana*, and *L. alba* plants

Plant species	Potential uses	References
Lippia origanoides ('Oregano cimarrón')	Animal dietary supplement	[89]
	Antibacterial	[90]
	Anthelmintic	[91]
	Insecticidal	[92]
	Larvicidal	[93]
	Antiseptic, Antimicrobial antinociceptive activity Anti-inflammatory	[94]
Physalis peruviana (Goldenberry, 'Uchuva')	Anti-adipogenic	[95]
	Anti-inflammatory	[96]
	Anti-cancerigen	[97]
	Antioxidant	[98]
	Anti-hepatotoxic; Anti-inflammatory, Anti-hepatoma	[99]
Lippia alba (Bushy matgrass, 'Prontoalivio')	Insect repellent	[100]
	Deep anesthesia in fish	[101]
	Antiviral	[102]
	Antibacterial	[103]
	Anthelmintic	[104]
	Antifungal	[105]
	Anticonvulsant, sedative, analgesic, bronchodilator Antioxidant, anti-inflammatory	[94]
	Bactericide and fungicide	[106]
	Antibacterial and antifungal	[107]
	Antioxidant, antimicrobial insecticide, acaricide, Neurosedative, analgesic	[108]
	Therapeutic potential for treatment of non-communicable diseases (NCD) and cardiovascular conditions	[109]

plant species in Colombia [37]. *Physalis peruviana* and *Lippia alba* occupy the second and third places with 15 and 14 publications, respectively. *Theobroma cacao* and *Passiflora edulis* showed 7 publications, followed by a set of plant species with the lower number of publications. Potential applications of *L. origanoides*, *P. peruviana*, and *L. alba* plants include medicinal, cosmetic, and nutraceutical uses (Table 2). With the aim of assessing the knowledge base of NIVCs from plant biodiversity in Colombia, we selected *L. origanoides* as a case study because it was the most reported plant in our study, which indicates its potential for NIs.

3.3 Knowledge base of VCs from *L. origanoides* in Colombia

The genus *Lippia* (Verbenaceae) includes around 200 species, mainly distributed in the Neotropics [110–112]. *Lippia origanoides* Kunth, first described in 1818 and popularly known as 'orégano cimarrón', 'orégano criollo," or 'orégano de cerro' in Colombia, is a native plant to the neotropics [113], distributed from Texas to Northern Argentina [114] (Fig. 5a). Most of *L. origanoides* is concentrated in semiarid areas of Mexico, Brazil, Venezuela, Trinidad and The Guianas [32, 115–118]. The use of *L. origanoides,* as for other plants from local biodiversity, contributes to satisfy human needs, diversify farming, promote natural products, and strengthen regional and national biodiversity-based bioeconomies in these countries [3, 5, 115, 117–119]. Efforts to consolidate the available information on the genetic variability of *L. origanoides* that enables the design of conservation strategies are being carried out recently [120]. Agricultural management of *L. origanoides* varies depending on cultural, socioeconomic, ecological, and technological factors in each country [121]. In Colombia, *L. origanoides* is highly abundant in large semiarid areas in seasonally dry tropical biomes of the biogeographic regions of the Andes, Llanura del Caribe, Valle del Cauca, and Valle del Magdalena [122, 123]. (Fig. 5-b). In particular, *L. origanoides* is widely and abundantly distributed along Chicamocha Canyon because of its ability to tolerate water stress and its phenotypic plasticity [124, 125]. It is naturally found at altitudes ranging from 500 to 800 m [126]. The morphology of *L. origanoides* is characterized by being a highly branched shrub up to 3.5 m tall with a strigose stem, elliptic and glandular leaves, and a flower with a tubular calyx. (Fig. 5c, d) [114, 127]. Given its natural abundance and potential for various applications, research on this species has increased in Colombia.

We identified 57 publications retrieved from Scopus and 9 reports as grey literature that represent the knowledge base of *L. origanoides* in Colombia. The approaches and objectives between the academic literature and the grey literature showed notable differences. While the academic literature displays in-depth species-specific knowledge, the grey literature mainly provides an overview of the species together with other prioritized species in specific regions of Colombia. As illustrated in Fig. 6, there is an unequal distribution of research across the four VC building blocks (i.e. biomass production, biomass processing, product development, and transversal aspects). The majority of published articles focus on the

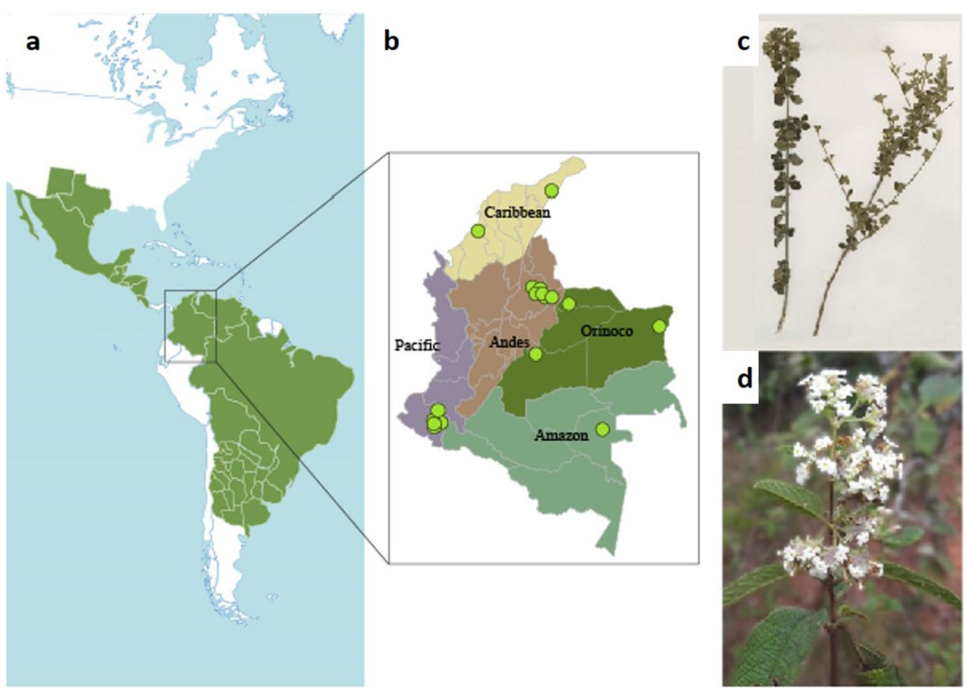

Fig. 5 Geographic distribution and phenotype of *Lippia origanoides*. Distribution in America (**a**) and in Colombia (**b**). Morphology of the stem and leaf (**c**), and the flower (**d**). Modified from: **a**, **b** ColPlantA (2023) [128], **c** © copyright of the Board of Trustees of the Royal Botanic Gardens, (d) KewInaturalist.lu/photos/32470319 CC BY-NC 4.0, ©Sam Flake

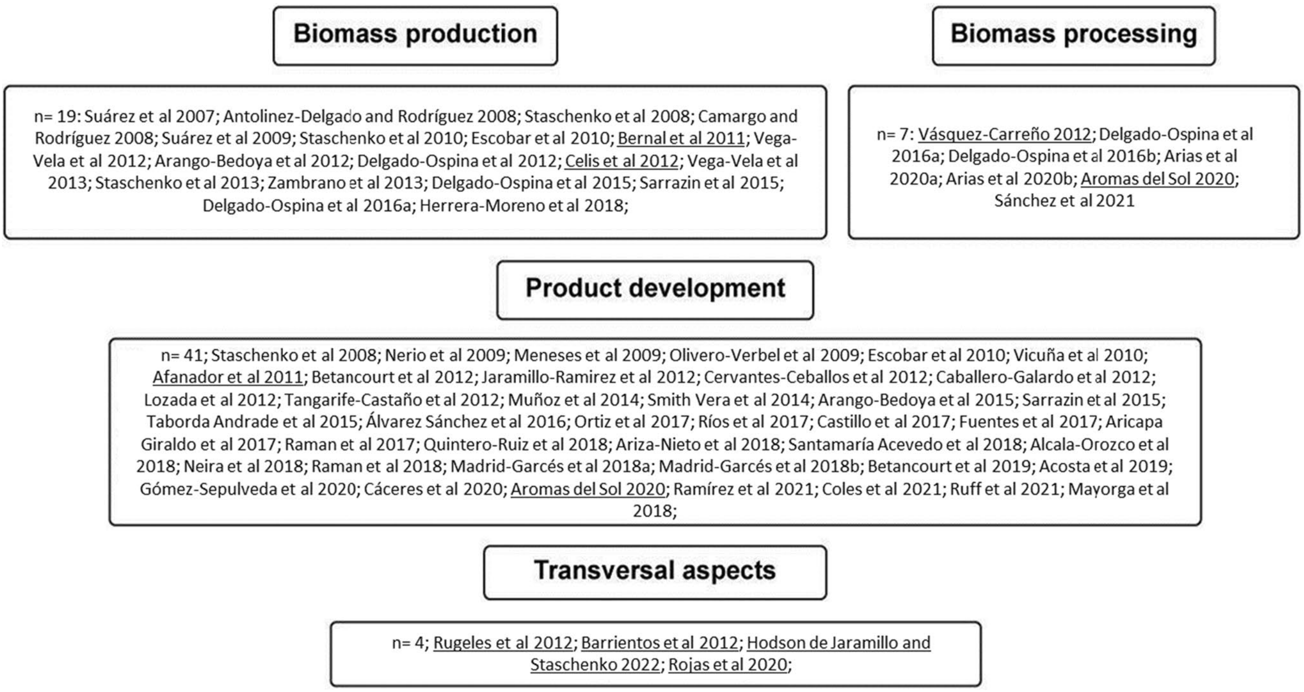

Fig. 6 Categorization of the knowledge base of *L. origanoides* in Colombia represented by the set of publications in each value chain building blocks or phases. The knowledge base includes peer-reviewed journal publications retrieved from Scopus (not underlined) and grey literature reports (underlined). Some studies cover more than one value chain building block

product development phase, with studies dealing with exploring plant properties and potential applications. Biomass production topics are reported to a lesser extent, while the biomass processing phase presents a smaller number of publications. Lastly, the least addressed phase corresponds to transversal aspects. These findings show that the study of potential plants' applications and products (the third VC building block) drives the introduction of novel plants in the BE. However, the absence of a VC approach to research that integrates biomass production, processing, products, use, and involved actors can limit the advance of production systems from promising plants for NIs such as *L. origanoides* [37]. For instance, research on the palm genus *Acrocomia* has shown a predominant focus on multiple applications in comparison to other VC phases [34]. In order to provide an in-depth overview of the *L. origanoides* literature, the results are presented and discussed below according to VC phases.

3.3.1 Biomass production

Fundamental knowledge on this species, especially at the biological and botanical levels, has been described through studies on genetic diversity, physiology, and phenotypic plasticity [124]. A close genetic relationship between *L. origanoides* and *L. graveolens* may indicate that they are synonyms [129]. The genetic structure of *L. origanoides* has been scarcely investigated in Colombia [123]. Existing studies focused on the Chicamocha River Canyon in the northeast of the country, revealing high levels of genetic variation within populations [123, 130, 131], contrary to the results from Suárez et al. [110].

Phytochemical studies on the composition of essential oil (EO) have predominated. High genetic diversity and phenotypic plasticity of this species result in heterogeneity in the composition of its oils and extracts [123]. Characterization of EO has allowed the identification of three predominant chemotypes of *L. origanoides* in wild populations in Colombia: A—characterized by α- and β-phellandrenes, *p*-cymene and limonene, and low carvachol and thymol; B—carvachol-rich (32.3–42.7%); and C—thymol-rich (26–69.2%) (Table S1 in the supplementary material) [17, 68, 126, 132–137]. Concentration levels of thymol and carvacrol in EO up to 87.3% and 63.8% have been measured from different accessions [123, 138]. The thymol-rich chemotype is considered the most widespread in Colombia, particularly in the region of Alto Patía (south-west of Colombia) [123, 138, 139], an important aspect for the agroindustry [140]. Other observed chemotypes present *p*-cymene (16–20%), trans β-Caryophyllene (11.3%), and eucalyptol (21.9%) as major constituents (Table S1). Further constituents of EO as well as extract composition vary among chemotypes [133]. A large variety of flavonoids with high concentrations have been reported, such as quercetin, naringenin, luteolin, and pinocembrin [137]. Chemotypes with a low content of phenolic compounds (i.e., chemotype A) may reduce antioxidant activity [126].

As for *L. origanoides* cultivation, information about plant propagation and cropping techniques is scarce. Asexual propagation with stem cutting is used [141], although it has shown relatively poor performance [142]. The relationship between fertilization and yields has been studied. Nitrogen and phosphorus are influential for the biomass production of *L. origanoides*, particularly above ground [143]. The effect of nitrogen fertilization has been assessed in three accessions of *L. origanoides* (Patía, Típica, and Cítrica). Average biomass and oil yields vary from 2.6 to 4.7 tons of dry matter (DM) and 43.6 to 124.9 L of oil per hectare under different N application treatments (including both urea and organic fertilizer), as observed for the three accessions [144]. According to Delgado-Ospina (2015) [143], 55% of the total nutrient absorption occurs within the first four months, and these accumulate in the leaves, while the remaining localize in the stem and roots. Zambrano et al. (2013) [144] found that the highest essential oil concentration (4.0 ml/100 g) was obtained from the Pata accession treated with 100 kg of N (urea)/ha, while the Ctrica accession exhibited the highest biomass yield (5 t DM/ha) under the same treatment. The highest reported oil yield (150 L per ha) was observed for the Pata and Ctrica accessions when applying 50 and 100 kg of N (urea) per ha, respectively [144]. Other studies found oil yields ranging from 2.6% to 3.3% on a DM basis [138]. Considering a plant density of 20.000/ha in an open-air cultivation system and 3 harvests per year, a yield of 18 t/ha of *L. origanoides* (fresh biomass) and around 630 L of oil with a yield of 3.5% could be obtained [145]. The authors estimate that a yield of 24 t/ha of fresh biomass could be achieved through greenhouse farming with 4 harvests per year and 20.000 plants per hectare [145].

L. origanoides exhibits phenotypic plasticity with a high tolerance and specialization in habitats with low availability of water and poor soils [125]. An essay in Cauca (Colombia) found the influence of environmental factors in the biomass and composition of EOs, although the high variability can be inherent to the species ([146] cited in [113]) For instance, seasonal variation may influence the composition of EOs. Arango-Bedoya et al. (2012) [138] reported a higher content of thymol (80.3%) from leaves harvested in the Alto Patía region during the dry season in comparison to those collected in the rainy season (64.9% thymol). In contrast, EO from leaves collected in the rainy season in Mérida State (Venezuela) exhibited a higher concentration of thymol [147]. Oil yield and composition from three accessions in Colombia were not affected by seasonal variation or plant age [139, 140]. Similarly, oil yield, oil composition, and antimicrobial potential were not affected by seasonality, as found in samples from Santarém (Pará State, Brazil) [68, 140]. According to Hodson de Jaramillo and Stashenko [17], the cultivation of *L. origanoides* has been promoted through farmer training on good agricultural practices in some regions of Colombia [17].

3.3.2 Biomass processing

Some aspects and conditions have been assessed in the processing of *L. origanoides*. One condition evaluated is the biomass drying of fresh leaves (75% moisture content) under shading to 12% moisture content for a period ranging from 48 h to 10 days [138, 140, 148]. This pre-treatment can increase the concentration of less volatile compounds (i.e., thymol) and reduce the content of more volatile ones; therefore, depending on the targeted compound, drying can be a suitable strategy [140]. Chopping the biomass is recommended to increase the contact area during extraction [148]. Steam distillation, a common process for EO extraction, is used for *L. origanoides*. Yield values of 2,8% on a DM basis are reported, using not only leaves but also stems and flowers as raw materials [140, 145, 148, 149]. Other EO extraction methods based on hydrodistillation and supercritical fluids have been tested, with oil yields of 3% and up to 3,8% on a DM basis, respectively [148]. Extracts obtained through supercritical fluids under specific conditions (110 bar—60 °C) exhibited higher antioxidant activity [148].

Subsequent extraction as a valorization strategy using supercritical fluid techniques has been investigated to recover phenolic compounds such as flavonoids from residual biomass after steam distillation [150]. Approaches for processing suggest the possibility of integrating different technologies towards the development of biorefinery concepts from this plant and eventually from similar species. For instance, valorization of plant residues after oil extraction via steam distillation can be realized through supercritical CO_2 techniques to obtain medicinal flavonoids [151]. The energy use of *L. origanoides* bagasse after oil extraction has been investigated, indicating the possibility of stem combustion, eventually as a strategy to self-supply the energy demand for the extraction of high-value-added compounds [152]. A patent for the integral processing of *L. origanoides*—patent of invention WO2018122654A1: method for making full use of *Lippia origanoides*—is reported [17, 153]. Processing pilot units for the production of EO from *L. origanoides*, among other plants, have been implemented in some regions of Colombia [17].

3.3.3 Product development

L. origanoides EOs have a large potential in the poultry sector [139]. The use of EOs in broilers and laying hens represents a natural alternative to antibiotics [139, 154]. Antimicrobial and antiviral properties of EO have been reported to be effective against pathogenic bacteria (i.e., *E. coli and Salmonella*) in broilers and embryonated eggs [139, 155, 156]. An improvement in body weight and feed conversion ratio in broilers affected by coccidia (single-celled parasites) under supplementation with EO has been evidenced [157, 158] EOs from *L. origanoides* are able to promote the growth of broilers and generate gains in production, quality, and egg mass. These compounds can contribute to enhancing meat quality by improving its fatty acid profile and preventing lipid peroxidation [139, 159]. Broilers fed with EO from thymol-rich *L. origanoides* chemotypes presented enhanced growth in comparison to basal diets and were similar to feed regimes with growth-promoting antibiotics [139, 160]. EO contributed to the improvement of intestinal morphology in laying hens and broilers, thus improving digestive function and nutrient absorption [160, 161]. Additionally, these would not affect the abundance and diversity of microbiota in broilers [158]. Further positive effects of EO feed supplements include the oxidative stability of eggs [148, 162], as well as the increase in antioxidant response and mitigation of harmful effects caused by periods of stress (e.g., heat stress) in chickens [163]. Additives based on *L. origanoides* have also been tested in dairy cows, indicating a positive response in productivity and a reduction in methane emissions [164].

EO from *L. origanoides* is potentially applicable in the agricultural sector as a biocide for the integrated control of pests and phytopathogens. Antifungal action against *Phytophthora infestans*, *Alternaria solani*, *Botrytis cinerea*, *Moniliophthora roreri*, *Fusarium oxysporum*, *Trichophyton rubrum*, *T. mentagrophytes*, *Fusarium oxysporum, and Sitophilus zeamais* in crops such as potatoes, strawberries, cocoa, and corn has been reported [134, 165–169]. Likewise, insecticidal repellent and antiprotozoal activity against *Aedes aegypti*, *Ulomoides dermestoides*, *Tribolium castaneum*, *Sitophilus zeamais, and Trypanosoma cruzi* has been demonstrated [170–181]. This indicates the potential of EO against disease agents and vectors that affect human health. The impact of *L. origanoides* in the pharmaceutical industry includes its use for treating cutaneous leishmaniasis. dermatophytes infections and the potential of extracts from leaves, stems, and flowers against breast cancer cells [179–181]. The cytotoxic effects of EO from *L. origanoides* indicate its pharmacological potential, as observed in the brine shrimp (*Artemia franciscana)* lethality assay [137]. EOs also exhibit antibacterial properties against *Staphylococcus aureus* and *E. coli*, anti-biofilm, and anti-quorum sensing activities [68, 134, 172, 182–184]. Likewise, antigenotoxic activity against UV and against bleomycin-induced genotoxicity has been reported [185–187].

3.3.4 Transversal aspects

The economic viability of *L. origanoides* EOS has been projected for open-air cultivation systems, indicating a positive profitability performance, whereas the economic profitability of greenhouse farming can be increased through a plant density higher than 20.000 plants per ha [145]. The authors estimated that 90% of the extraction costs are represented by biomass. High projected costs for the cultivation of *L. origanoides*, especially for greenhouse farming, can be a barrier for smallholder farmers [145]. On the other hand, the cultivation of *L. origanoides* could be a source of new jobs [145]. A market differentiation strategy towards high-added-value products can increase the economic viability and competitiveness of *L. origanoides* [145]. Ensuring a biomass supply is key to the production of EO. Barrientos et al. (2012) [145] estimated that around 300 tons of biomass are required annually (between 7 and 16 ha) to operate an extraction plant with a capacity of 1200 kg/day. This can represent opportunities for smallholder farmer associations (horizontal integration) and vertical cooperation schemes with established EO agroindustries closely located [37, 145]. In fact, according to Hodson de Jaramillo and Stashenko (2022) [17], more than 200 family farmers are involved in the cultivation and production of EO from aromatic plants in Colombia. Farmers could also benefit from using food supplements based on EO from *L. origanoides*. Although the use of EO as feed supplements in poultry, laying hens, and dairy cows could increase feeding costs, compensation through gains in productivity is expected [139, 164].

The actors currently involved in the production and use of *L. origanoides* include local communities through traditional and commercial use, research institutions, and processing companies. Main research institutions are the National Research Center for the Agro-industrialization of Aromatic Plant Species and Tropical Medicines (CENIVAM, Universidad Industrial de Santander) and the Plants Medicine Research Group of the Universidad Nacional de Colombia [37]. There are three companies dedicated to the production and supply of products from *L. origanoides*: Naturpiel, Aromas del Sol, and Magia Chicamocha, a CENIVAM spin-off. The products correspond to EOs, described as final goods for the cosmetic, personal care, and cleaning sectors [24, 149, 188].

3.4 Challenges and future directions for *L. origanoides* VCs

The present review confirms the potential of *L. origanoides* as a novel resource for the development of NIVCs from biodiversity in Colombia, as pointed out in earlier reviews and prospective studies [17, Cluster Development 2020 cited in 24, 37, 145]. Aspects such as positive market prospects and favourability with regard to its degree of domestication (currently from wild plants and orchards), abundance, natural distribution, usability, knowledge about bioactive compounds, and species-specific production capacity indicate the potentiality of *L. origanoides* [24]. The potential of *L. origanoides* as a source of natural antibiotics and its possibility to diversify farming while contributing to ecosystem services constitute sustainability advantages. However, in order to foster the development of NIVCs, it is necessary to assess the knowledge base, integrate it along the VC and intensify its use to advance the preparedness of *L. origanoides*, from biomass production to high-added-value products [17, 34, 35, 189]. This review contributes to this endeavour adding a new and applied perspective—the value chain—and provides a diagnostic of the knowledge status and needs towards the development of NIVCs, building upon previous reports and results from diverse research studies (Fig. 7). For novel resources like *L. origanoides*, ensuring biomass supply is key [145]. In this regard, advances in plant material and biomass production are necessary for the cultivation of specific chemotypes of *L. origanoides* that fit site-specific ecophysiological conditions and applications. Biomass production is partially addressed in the retrieved literature. There is reported knowledge on species-specific biology, phytochemistry, botanical aspects, plant ecology, and the taxonomy of *L. origanoides*. However, there is limited documented knowledge on germination, plant propagation, the development of planting material, and the agro-ecological zoning of suitable cultivation areas. Genetic studies to understand the relationship between EO

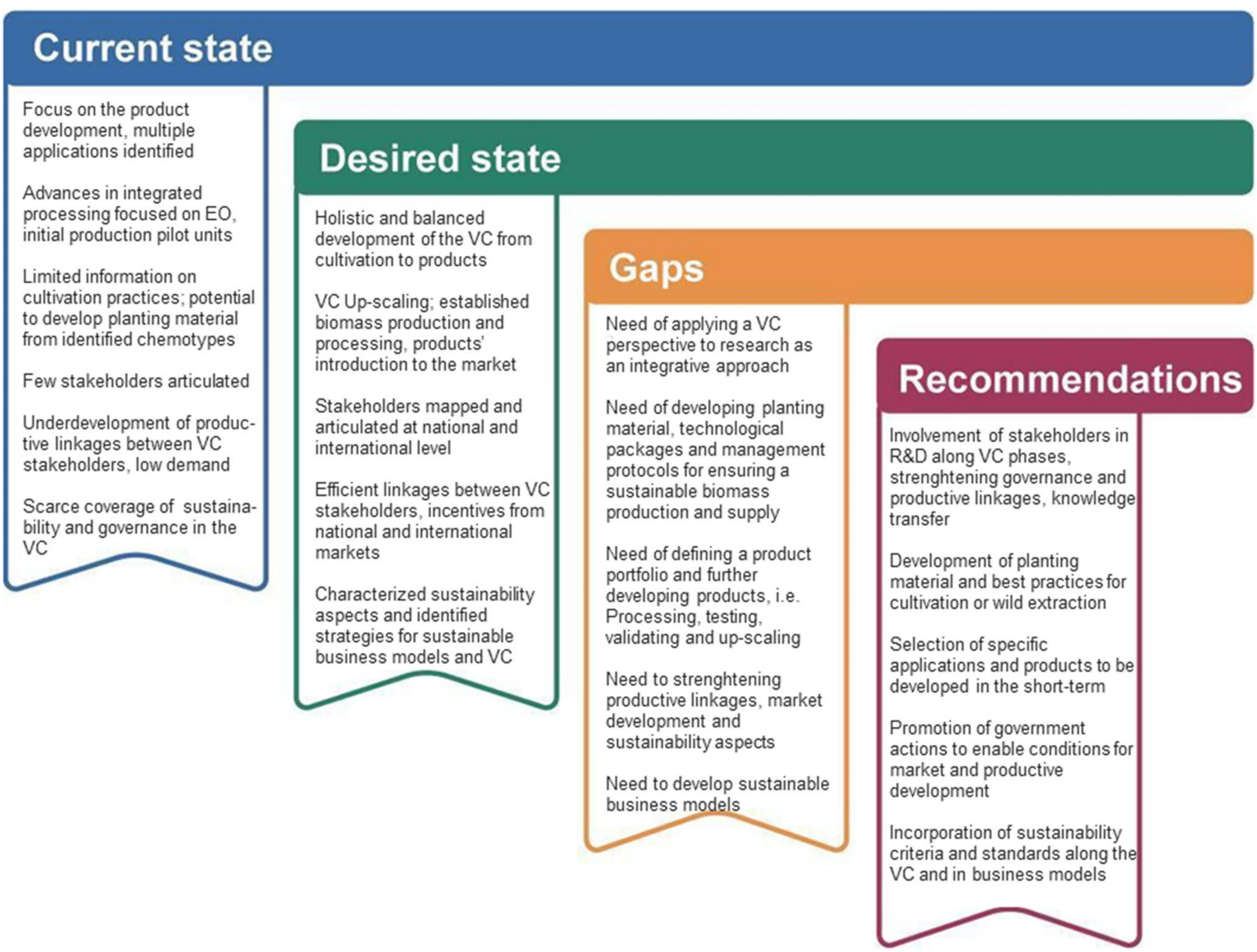

Fig. 7 Current panorama and prospects of *L. origanoides* value chains in Colombia based on the reported literature. Adapted from [197]

composition and genetic variation are needed to guide plant breeding strategies [123, 131]. Use and management protocols and cultivation technology packages are necessary for this species, including agronomic practices, plant density, harvesting, yield stability, and plantation (re)establishment [24, 145]. Nevertheless, farmer training on cultivation and the initial production of *L. origanoides* in Colombia are reported [17]. Sourcing *L. origanoides* from natural stands (i.e., wild collection) can represent an alternative or complementary biomass supply strategy. In this regard, recent advances for the sustainable use of biodiversity include the Act 690 (2021), which regulates the use of wild plants [190, 191].

Knowledge transfer to farmers, appropriate business models, and linkages with processors are elemental aspects for advancing the VC. Moreover, labor availability in a context of rural migration must be ensured to promote the cultivation of *L. origanoides* [192]. VC governance processes and productive linkages related to *L. origanoides* are currently weak [24, 134]. The involvement of community-based organizations could foster the development of VCs. However, these types of actors are lacking in the case of *L. origanoides* in Colombia [24]. Economic viability for *L. origanoides* cultivation determines farmers' decision-making to adopt a new crop over conventional farming activities [37]. Therefore, inclusive arrangements are required between primary producers (i.e. farmers) and processors of *L. origanoides* to create and distribute value, thus providing incentives to participate in the VC [37].

Standardization of biomass processing is key to responding with high quality standards to the national and international markets [24]. Process development and up-scaling at commercial level of (pre-) processing technologies requires the screening and evaluation of technological pathways (i.e., oil extraction methods and by-product valorisation), piloting, and process validation to obtain targeted plant extracts, as well as process optimization [193]. Adapting available processing technologies used for EO extraction, such as steam distillation, offers a possibility for processing *L. origanoides*. Implemented pilot units for EO production in Santander, Arauca and Cundinamarca can contribute to this purpose [17]. The application of biorefining principles can result in *L. origanoides* value webs by using all biomass fractions and integrating different plants, processes, and products [194–196].

Accumulated knowledge about the properties and applications of *L. origanoides* extracts serves to consolidate a product portfolio, enabling further product development steps [17, 36]. Efforts on product development, formulation, product functionality and safety testing, and intellectual property protection are needed [17, 139, 191]. Accomplishing the regulatory framework is key for the production and commercialization of NIs [191]. In addition, market introduction of novel NIs requires marketing efforts and knowledge dissemination to stimulate demand, which is low at the moment for *L. origanoides* products [145, 191]. One possibility for *L. origanoides* EOs is to enter existing markets for known chemotypes such as thymol [145]. The market for NIs from *L. origanoides* indicates positive prospects for natural products (cosmetics, pharma, and food sectors) based on a growing demand nationally and internationally and the possibility to participate in other markets such as the animal nutrition sector [Cluster Development 2020 cited in 24;37). For instance, the poultry industry is among the main agricultural activities in Colombia, thus representing a great potential for feed supplements based on *L. origanoides* [139]. Although already established, the EO sector in Colombia is integrated by few small companies, partly due to the lack of knowledge on extraction and refining technologies, the low supply of raw materials, and market uncertainty [198]. Many aromatic plants are marketed traditionally in Colombia with a low level of transformation and value added [145, 192]. It has been estimated that 90% of NIs in Colombia are imported [199]. Imports of EO for the food and personal care sectors in Colombia indicate the potential for local substitutes [24, 198]. Therefore, if the production and supply of NIs from plants like *L. origanoides* are encouraged, imports could be reduced and exports increased.

The current research on *L. origanoides* in Colombia does not substantially account for transversal aspects such as sustainability dimensions (mainly in terms of environmental and social aspects), VC governance, business models, and VC management. This pattern can be common for novel crops and VCs in the early stages of development [34]. The consideration of sustainability along the NIVC is key and requires the integration of criteria related to the environmental, social, economic and their interplay with technical and regulatory dimensions for guiding the design of VCs [24, 35, 37, 199]. Related aspects of relevance for biobased business models around NI from native plants such as *L. origanoides* include sustainable practices for plant production, supply and processing implementing low-input systems and environmental-friendly processes, natural resource and biodiversity conservation strategies and social responsibility measures [24, 35, 37, 199, 200]. Corporate and VC strategies towards value creation and fair distribution of benefits, product functionality, quality and safety, social inclusion and acceptance and the accomplishment of regulatory frameworks are suggested specially in NI sectors [24, 35, 37, 199, 200]. In fact, the increasing focus on sustainable VC rises the need for emerging businesses in NI sectors to deliver products that fulfil sustainability criteria as prerequisite to participate in markets through e.g. certifications and standards [24, 37, 199].

A holistic characterization and analysis of *L. origanoides* VCs can contribute to promoting linkages between stakeholders and facilitating VC-integral actions for biomass production, processing, product and market development [198]. For this, NIVC structures applied in Rugeles et al. (2012) [37], Gómez (2017) [199], Murcia-López et al. (2021) [189], and Rojas et al. (2022) [201] can serve as references. Mapping current and potential stakeholders (i.e., farmers, processors, NI industrial producers, national and international marketers, the public sector, research institutions, and consumers) can contribute to their involvement in the early stages of VC development by facilitating the identification of upgrade and innovation strategies, requirements, and knowledge transfer. Available guidelines for developing NIVCs in Colombia, such as the guide published by Rojas et al. (2021) [191], can contribute to accomplishing regulations and requirements for the production and commercialization of NIs.

Strategic partnerships and multi-stakeholder approaches to R&D are necessary to address both technical and non-technical challenges, co-create solutions, finance, and up-scale VCs [35, 191]. It is thus key to develop robust science, technology, and innovation instruments that articulate the VC based on the experience of research projects on aromatic plants led by public entities and research centers. These have contributed to the accumulation and transfer of knowledge on cultivation, post-harvesting, and EO production [17]. Building partnerships between farmers, processors, and NIs companies with a high technological level and the implementation of inclusive VC models can contribute to both product differentiation and organizational innovation of VCs from *L. origanoides* [37].

Advancing *L. origanoides* VCs is favored by an enabling environment promoted by the National Plan of Green Businesses, the Green Growth Policy, and the National Bioeconomy Mission [24, 199, 201]. International cooperation programs and projects such as the 'Useful Plants and Mushrooms from Colombia' project (Kew Royal Botanic Gardens and the Institute Alexander von Humboldt) and the 'Colombia más competitiva" program contribute to generating applied knowledge and tools for fostering the NIs sector [24]. The use of native plants as a promising source of new products can also offer possibilities for ecosystem restoration, thus making them multi-purpose plants [32, 34]. For instance, *L. origanoides* grows mainly in tropical dry forests [122, 189, 202], one of the most degraded ecosystems in the country. Thus, the sustainable use of this plant can contribute to the productive restoration of this ecosystem [189]. These benefits can be the source of new incentives in business models for ecosystem restoration. All aspects critically analyzed and consolidated represent the first review of NICVs in Colombia.

4 Conclusions

The global interest in the research and development of NIs is continuously growing. Leading countries in scientific production in terms of publications on NIs have implemented either BE-related or BE-dedicated strategies in the last decade, becoming a driver for increasing research on biomass applications. Areas such as biochemistry and biopharmacy are among the most prominent, which can be explained by the promotion of research and development in line with the priorities of BE strategies in countries with robust R&D capacities and a focus on knowledge- and technology-intensive BE transformation paths.

In Colombia, NIs from plant biodiversity have gained importance in the policy and research agenda as a strategy for adding value to biomass and pursuing contributions to industrialization, rural development, and economic development. International cooperation with leading countries in research on NIs contributes to expanding the knowledge base for developing VCs. While cooperation with rich biodiverse countries and leaders in NI R&D such as Brazil can strengthen capacities for biomass production and processing, collaboration with countries such as Spain and the United States can contribute to product and market development. Increasing research activities have resulted in a large portfolio of plants that are promising sources of NIs in Colombia. Nevertheless, for the evolution into VCs and sustainable performance, advancing biomass production, processing methods, product development, business models, and governance arrangements is key.

Understanding the prospects of VCs from *L. origanoides*, a prioritized plant species for NIs in Colombia, can serve as a blueprint for novel resources from local biodiversity to guide R&D for VCs. The current knowledge base of *L. origanoides*, represented by the set of reported publications, does not fully cover the VC. There is an imbalance in the amount of literature between the phases of the VC. The publications are concentrated on the identification of product potential related to the product development phase. In contrast, biomass production, a key enabler of VCs, is partially covered in the literature. The most commonly identified challenge is the need to promote an integrative VC approach in R&D. Particular issues are caused by the limited evidence on (i) plant propagation, agronomic management, and harvest practices; (ii) process optimization for specific NIs; (iii) advanced product development prioritizing specific applications; (iv)

VC actors' relations, governance, and business models; and (v) environmental, social, and economic performance. Joint R&D and multi-stakeholder endeavors are needed for consolidating and advancing the knowledge base, while offering both technical and non-technical enabling conditions at the territorial level for developing sustainable VCs from plants such as *L. origanoides*. Regional NIs clusters integrated by active research institutions and networks, farmers, processors such as the EO industry, and market sectors can foster the upgrade of VCs from *L. origanoides*. This can facilitate the integration of interventions in each VC phase, reducing uncertainty, attracting investments, transferring knowledge, and guiding the development of novel NI value webs from plant biodiversity in the territories.

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