Ethnopharmacological survey, fumigation efficiency, and pharmacovigilance of plant-based medicines for respiratory disease during COVID-19 in the Democratic Republic of Congo

Isaac E. Kaba
isaac_kaba@berkeley.edu
University of California, Berkeley https://orcid.org/0000-0003-0234-0626
Carmel G. Kandhe
University of South Carolina https://orcid.org/0009-0000-9839-1780
Messie M. Muipata
Nantes Université https://orcid.org/0000-0002-2462-3515
Blaise-Pascal I. Muntokole
University of Kinshasa https://orcid.org/0000-0001-6815-1866
Jonathan M. Mukanya
Rhodes University https://orcid.org/0000-0001-9966-8251
Dorcas L. Mukundi
Université de Liège https://orcid.org/0000-0001-5542-8803
Micheline A. Kingombe
Ministère de la Santé Publique, Hygiène et Prévoyance Sociale de la République Démocratique du Congo
Nadège K. Ngombe
University of Kinshasa https://orcid.org/0000-0002-2859-7238
Paulin K. Mutwale
paulin.mutwale@unikin.ac.cd
University of Kinshasa https://orcid.org/0000-0003-2946-4047

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Isaac Elaka Kaba[a,#,*], Carmel Gabha'bey Kandhe[b,#], Messie Muabilua Muipata[c,d,e], Blaise-Pascal Ilunga Muntokole[d,e], Jonathan Mpoyi Mukanya[d,e,f], Dorcas Lukusa Mukundi[d,e,g], Micheline Kingombe Abiba[h], Nadège Kabamba Ngombe[d,e], Paulin Kapepula Mutwale[d,e,*]

[a] *Department of Chemistry, College of Chemistry, University of California, Berkeley, CA 94720, United States*

[b] *Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC 29208, United States*

[c] *UFR des Sciences Pharmaceutiques et Biologiques, Nantes Université, BP 61112, 44035 Nantes Cedex, France*

[d] *Centre d'Études des Substances Naturelles d'Origine Végétale (CESNOV), Faculty of Pharmaceutical Sciences, University of Kinshasa, B.P. 212, Kinshasa XI, Democratic Republic of Congo*

[e] *Centre de Recherche en Nanotechnologies Appliquées aux Produits Naturels (CReNAPN), Faculty of Pharmaceutical Sciences, University of Kinshasa, B.P. 212, Kinshasa XI, Democratic Republic of Congo*

[f] *Center for Chemico and Bio-Medicinal Research (CCBR), Department of Chemistry, Faculty of Sciences, Rhodes University, PO Box 94, Grahamstown, Eastern Cape, South Africa*

[g] *Centre Interdisciplinaire de Recherche sur le Médicament (CIRM), Université de Liège, Liège, Belgique*

[h] *National Program for the Promotion of Traditional Medicine and Medicinal Plants, Ministry of Public Health, Kinshasa, Democratic Republic of Congo.*

#: Authors contributed equally

*** Corresponding authors:**

Isaac E. Kaba (isaac_kaba@berkeley.edu), Department of Chemistry, College of Chemistry, University of California, Berkeley, Berkeley, CA 94720, United States

Paulin K. Mutwale (paulin.mutwale@unikin.ac.cd), Centre d'Études des Substances Naturelles d'Origine Végétale (CESNOV) & Centre de Recherche en Nanotechnologies Appliquées aux Produits Naturels (CReNAPN), Faculty of Pharmaceutical Sciences, University of Kinshasa, B.P. 212, Kinshasa XI, Democratic Republic of the Congo

ABSTRACT

Background: With the onset of the COVID-19 pandemic, traditional plant-based medicines used for respiratory diseases experienced an extraordinary surge in use across the Democratic Republic of the Congo (DRC), where over 80% of the population relies on traditional medicine as its primary healthcare resource. Despite widespread public usage of herbal remedies for respiratory diseases during the pandemic, no prior study has reported community survey data on COVID-19-specific plant use from Kinshasa, the capital of DRC.

Objectives: We report results from a community survey documenting COVID-19 traditional plant use patterns in Kinshasa (n=500, June 2020), structured ethnobotanical interviews with traditional healers on fumigation and bath preparations, physicochemical analysis of the fumigation delivery efficiency of volatile phytochemicals, a pharmacovigilance assessment of a fatal adverse event linked to unregulated *Morinda morindoides* use, and an institutional analysis of the DRC Ministry of Scientific Research and Innovation Technology (MRSIT) regulatory response framework for traditional medicine candidates.

Methods: Mixed-methods study comprising: (i) cross-sectional online survey (n=500, June 2020) distributed via WhatsApp and email, assessing plant species use, preparation methods, and co-administration practices; (ii) structured face-to-face interviews with members of the Association of Traditional Practitioners of Congo (Utraco) on fumigation and bath plant preparations; (iii) physicochemical profiling of volatile constituents across fumigation species; (iv) qualitative thematic analysis of caregiver testimonials; and (v) documentary analysis of MRSIT Commission institutional records.

Results: Ten most cited plant species included *A. annua*, *Z. officinale*, *A. sativum*, *C. longa*, *E.* spp., and *M. morindoides*. Decoctions, fumigation, and herbal teas were the dominant preparations. Utraco healer interviews identified 18 fumigation and bath species, predominantly aromatic plants with documented anti-infective essential oil constituents. Physicochemical analysis confirmed that volatile phytochemicals in these species have vapor pressure and lipophilicity profiles consistent with efficient respiratory mucosal delivery by fumigation. A four-factor pharmacovigilance model for the *M. morindoides* fatal adverse event identifies multi-plant combination toxicology, pediatric pharmacokinetic vulnerability, purging formulation concentration, and social media-mediated adoption without safety guidance as converging risk factors.

Conclusions: Our study reports widespread, predominantly complementary use of traditional plant-based medicines for respiratory disease during COVID-19 in Kinshasa. The evaluation of fumigation efficiency of these plants may provide plausible respiratory delivery of bioactive compounds, supporting their scientific validation as inhalation-based formulations. While these practices remain an important healthcare resource for most of the population, stronger pharmacovigilance, safety monitoring, and evidence-based regulation of traditional medicines during public health emergencies are still needed in DRC.

Keywords: Respiratory diseases; Democratic Republic of Congo; traditional plant-based medicine; COVID-19; herbal remedies; pharmacovigilance; ethnopharmacology

1. INTRODUCTION

The Democratic Republic of the Congo (DRC) recorded its first COVID-19 case on 10 March 2020 and had accumulated 99,338 confirmed cases and 1,468 deaths by February 2024 **[1]**. Formal healthcare capacity was structurally limited well before the pandemic, and equitable access to approved COVID-19 antivirals and vaccines remained constrained throughout the emergency period **[2]**. Traditional plant medicine, the primary healthcare modality for more than 80% of the Congolese population **[3]**, underwent an extraordinary intensification during this period. Particularly, several medicinal and aromatic plant species became suddenly in high demand, and many traditional formulations and recipes for respiratory diseases circulated via WhatsApp and other social media platforms at a pace that outstripped any regulatory response **[4,5]**.

Africa is known for its rich biodiversity and extensive traditions of medicinal plant use, with thousands of species employed for nutrition **[6]** and the treatment of infectious, respiratory, and chronic diseases **[7]**. Over the past century, plants have been a major source of therapeutic agents, contributing directly or indirectly to the development of numerous modern medicines and continuing to provide essential healthcare resources for millions of people worldwide. To date, the scientific literature on African traditional medicines and COVID-19 has focused primarily on reviews of ethnobotanical candidates and *in silico* compound screening **[7,8,9]**. The Democratic Republic of the Congo (DRC), located in Central Africa and recognized as one of the continent's most biodiverse countries, possesses a particularly rich pharmacopeia of medicinal plants used by local communities and traditional healers **[10,11,49]**. Despite widespread public usage of herbal remedies for respiratory diseases during the pandemic, no prior study has reported community survey data on COVID-19-specific plant use from Kinshasa, the capital of DRC, to date. Specifically, there is a lack of primary quantitative data documenting patterns of traditional plant use, modes of preparation, and the potential health consequences associated with these practices during the COVID-19 pandemic. Here we provide a community-based survey of COVID-19-related medicinal plant use in Kinshasa, complemented by ethnobotanical documentation of traditional healer fumigation and bath preparations, as well as a structured analysis of the *M. morindoides* fatal adverse event, highlighting the need for stronger pharmacovigilance, safety monitoring, and evidence-based regulation of traditional medicines during public health emergencies.

2. METHODS

2.1. Study design

Mixed-methods design integrating a cross-sectional community survey, structured professional healer interviews, qualitative caregiver testimonial analysis, and documentary analysis of institutional regulatory records. Ethics approval: University of Kinshasa School of Public Health Ethics Committee. All survey participants provided informed consent. Traditional healer interviews were conducted with written and verbal consent. All data were anonymized before analysis. Approval was obtained from the University of Kinshasa School of Public Health Ethics Committee (Approval No. ESP/CE/89B/2020) prior to any implementation of the research. To ensure confidentiality, data were collected online anonymously and were only available to study investigators using passwords. The study investigators are certified in ethical training as well as good clinical practices, and they are bound by professional secrecy with regard to all the information collected during this study. All participants provided e-consent or in-person written consent before submitting their responses.

2.2. Community survey (Survey 1)

An online French-language questionnaire was distributed between 1 and 30 June 2020 via: (a) direct email; and (b) WhatsApp snowball distribution. The questionnaire was developed by the researcher's group after an extensive review of literature related to similar studies. Inclusion criteria: DRC residence; age 18 years or older. The questionnaire covered five domains: demographics; COVID-19 awareness and prevention; general plant use history; COVID-19-specific plant use including species, preparation methods, and perceived effects; and information-seeking behavior. Data were collected in Google Forms and exported to Microsoft Excel. A target sample of 500 respondents was achieved.

2.3. Utraco traditional healer survey (Survey 2)

Structured face-to-face interviews with members of the Association of Traditional Practitioners of Congo (Utraco), a body registered under the DRC Ministry of Health. Practitioners were interviewed specifically on plants used in fumigation and therapeutic bath preparations for respiratory diseases. Data were collected by trained research team members representing multiple DRC ethnic groups. Plant identifications were verified against **[19]** and **[24]**, with nomenclature confirmed via The Plant List (www.theplantlist.org). Preparation descriptions, plant parts used, vernacular names, and documented biological activities are specified for all 18 species (**Table 2**).

2.4. Toxicological analysis

The *M. morindoides* adverse event (child deaths following ingestion of an unregulated M. morindoides-containing cocktail during the pandemic) was subjected to a structured pharmacovigilance analysis drawing on: the phytochemical literature on *M. morindoides* **[12,13,14]**; the published DRC medicinal plant nephrotoxicity review **[10]**; anthraquinone hepatotoxicity and nephrotoxicity data from the phytochemical safety literature; and pediatric pharmacokinetic principles. This analysis is not available in any prior publication.

2.5. MRSIT institutional analysis

Documentation from the MRSIT Scientific Commission, including Ministerial Decree No. 010/MIN.RSIT/CAB/JMK/2020, evaluation criteria, Phase IIB protocol design specifications, and candidate approval records were obtained from the University of Kinshasa research team's institutional archive and subjected to structured institutional assessment.

2.6. Data analysis

Data analyses were performed using SPSS v25 and NVivo software (Release 1.0, March 2020; QSR International Pty Ltd., Melbourne, Australia) and Python (version 3.x) with the SciPy (v1.x) and scikit-learn (v1.x) libraries.

3. RESULTS AND DISCUSSION

3.1. Community survey demographic profile

The results of demographic profiles of survey respondents are summarized in **Table 1**.

Table 1. Demographic characteristics of survey respondents (n=500, DRC, June 2020).

Variable	Category	n (%)
Gender	Male	238 (47.6%)
	Female	262 (52.4%)
Age group	18 to 25 years	148 (29.6%)
	26 to 35 years	171 (34.2%)
	36 to 45 years	112 (22.4%)
	46 years and above	69 (13.8%)
Education	Primary or secondary	143 (28.6%)
	University or tertiary	299 (59.8%)
	Not specified	58 (11.6%)
Province	Kinshasa	348 (69.6%)
	Other DRC provinces	152 (30.4%)
Survey platform	WhatsApp	301 (60.2%)
	Email	199 (39.8%)

Data are presented as n (%). Kinshasa over-representation (69.6%) reflects social media sampling methodology and is a stated limitation. DRC = Democratic Republic of the Congo.

3.2. Usage patterns of medicinal plants during COVID-19

Of 500 respondents, 45% (n=225) reported regular medicinal plant use prior to the COVID-19 pandemic. Since pandemic onset, 35% (n=175) specifically adopted traditional plant medicine for COVID-19 prevention or treatment: 22% used it alone, and 13% combined it with pharmaceutical treatment. Only 8% declined pharmaceutical treatment entirely, indicating that the dominant pattern was complementary rather than substitutive use. More than 50 species were cited. The ten most frequently cited in descending order were: *Artemisia annua* (68%), *Zingiber officinale* (64%), *Allium sativum* (61%), *Curcuma longa* (57%), *Eucalyptus* spp. (54%), *Morinda morindoides* (49%), *Citrus limon* (44%), *Ocimum gratissimum* (40%), *Mangifera indica* (37%), and *Lippia multiflora* (33%). Multiple responses were permitted. The pharmacological coherence of this list is striking: quercetin and flavonoids from *Artemisia* and *Allium* species are known to inhibit 3CLpro and PLpro *in vitro* **[15,16]**; curcumin from *Curcuma longa* has been reported to inhibit SARS-CoV-2 entry and replication **[17]**; and 1,8-cineole from *Eucalyptus* species has documented antiviral activity in respiratory pathogen models **[18]**. The convergence between community citation frequency and *in vitro* pharmacological evidence suggests empirical therapeutic knowledge encoding meaningful bioactive targets.

Preparation methods (multiple responses permitted): decoctions 72%; fumigation or steam inhalation 58%; herbal infusions and teas 51%; topical applications 28%; direct plant ingestion 22%; medicated baths 18%. The high frequency of fumigation, consistent across both the community survey and the Utraco healer data (**Section 3.3**), reflects the dominant traditional approach to respiratory disease management in the DRC. Fumigation delivers volatile phytochemicals directly to respiratory mucosa, a mechanistically sound route for respiratory pathogens **[18]**.

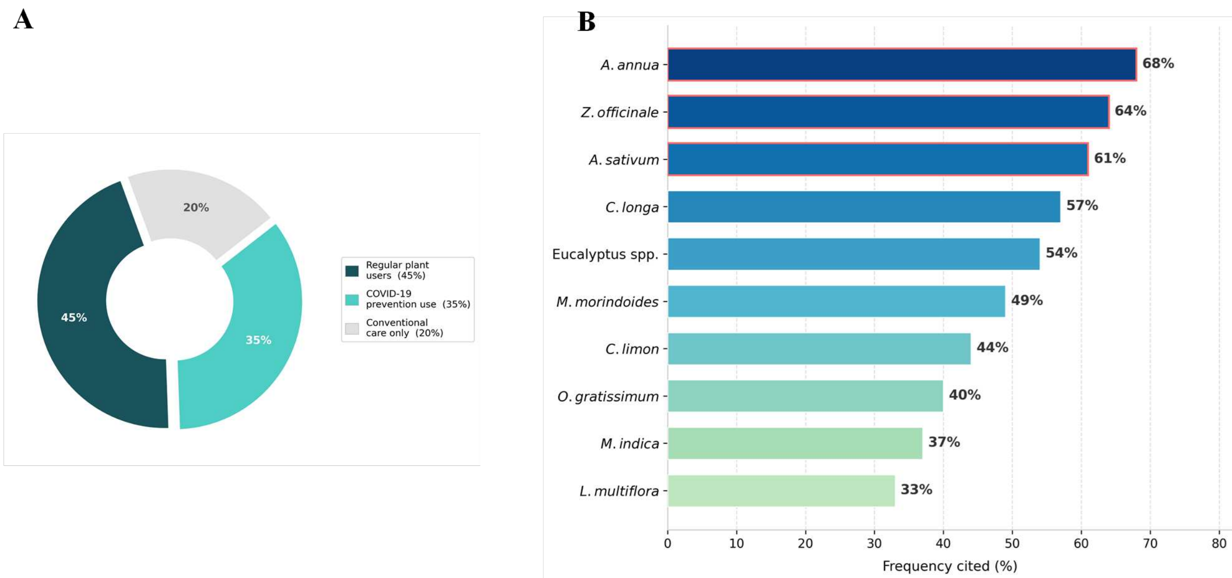

Fig. 1. Survey data on medicinal plant use among Congolese populations during COVID-19 (n=500). (**A**): Categorization of the purpose of frequent usage of medicinal plants. (**B**): Ten most frequently cited plants.

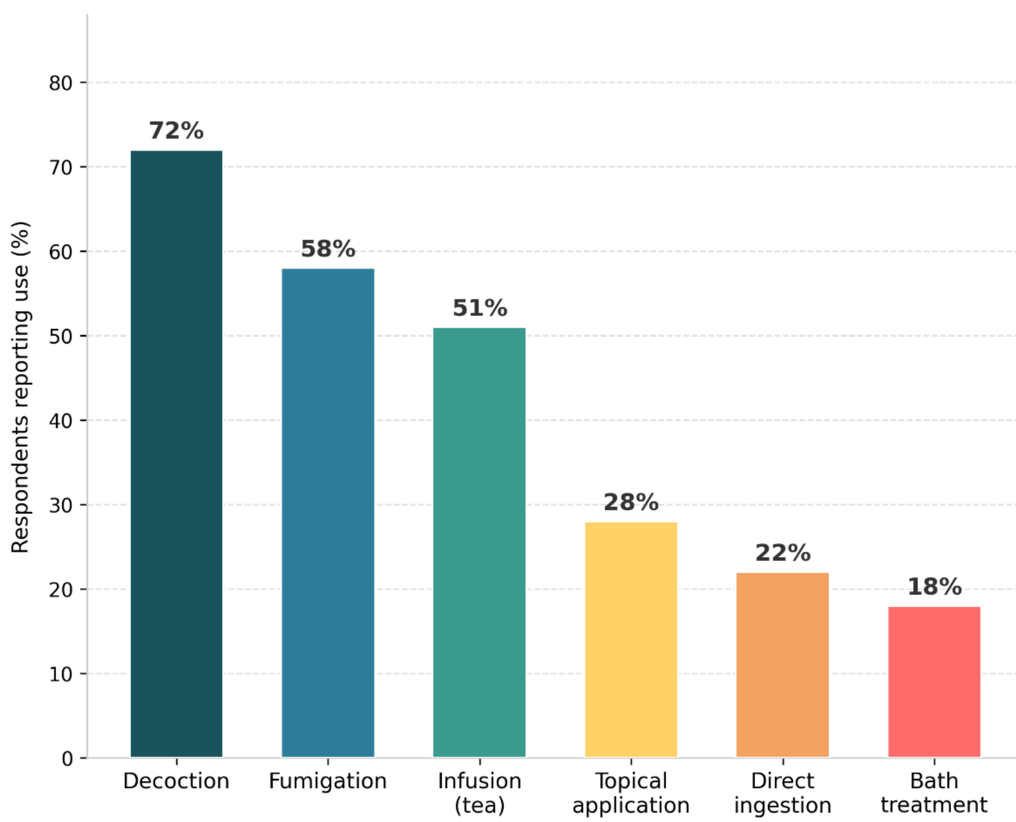

Fig. 2. Survey data on medicinal plant use among Congolese populations during COVID-19 (n=500). Frequencies of methods or modes of preparation of traditional plant-based medicines.

3.3. Utraco healer survey: fumigation and bath plants

Structured interviews with Utraco members yielded 18 verified plant species used in fumigation and bath preparations for respiratory disease management, reported here for the first time in peer-reviewed form (**Table 2**).

Table 2. Plants used in fumigation and bath preparations for respiratory disease management: Utraco healer survey (2020- 2021).

Plant species	Part used	Vernacular name(s)	Traditional use and documented activity	References
Aframomum alboviolaceum	Fruits	Ntundulu	Cough; anthelmintic	**[19]**
Aframomum melegueta	Seeds	Ndungu zi nzo; Mondongo	Cough; asthma; anti-inflammatory	**[20]**
Chenopodium ambrosioides	Whole plant	Nkasa kindongo	Cough; anthelmintic; antibacterial	**[21]**
Croton mubango	Stem bark	Mubangubangu	Respiratory infections; gastritis	**[22]**
Cymbopogon citratus	Leaves	Sinda dimputu	Cold; influenza; pneumonia; anti-inflammatory	**[23]**
Cyperus articulatus	Root bark	Munsaku nsaku	Asthma; fatigue; pain management	**[24]**
Dacryodes edulis	Leaves	Nsafu	Dysentery; antimicrobial	**[19]**
Eucalyptus spp.	Leaves	Not specified	Cold; influenza; antimicrobial	**[18]**
Lantana camara	Leaves	Landani; Kua	Cough; fever	**[24]**
Lantana montevidensis	Leaves	Kapokadisuta	Influenza; bronchitis; antioxidant	**[25]**
Lippia multiflora	Leaves	Bulukutu; Angasani	Cough; antiplasmodial; antioxidant	**[25]**
Morinda morindoides	Leaves	Meeso; Nkama	Colic; diabetes; antiplasmodial	**[12,13,14]**
Ocimum basilicum	Leaves	Mazula; Luenyi	Lung disease; antiviral; immunomodulatory	**[26]**
Ocimum canum	Leaves	Not specified	Insecticidal; antiplasmodial	**[27]**
Ocimum gratissimum	Leaves	Lumba lumba	Asthma; cough; antimicrobial; antidiabetic	**[28]**

Persea americana	Leaves	Divoka; Boboka	Anaemia; immunomodulatory	**[29]**
Tephrosia vogelii	Leaves and roots	Bwalu; Mbaka	Antibacterial; antifungal; insecticidal	**[30]**
Tetradenia riparia	Leaves	Mutuzo	Malaria; antimicrobial; antispasmodic	**[31,32]**

Of the 18 species, 13 are aromatic with documented essential oil content. Key volatile constituents with published antiviral or anti-infective activity include: 1,8-cineole (*Eucalyptus* spp.) [18], citral (*Cymbopogon citratus*) [**23**], eugenol and linalool (*Ocimum spp.*) **[26]**, thymol and its derivatives such as carvacrol, thymoquinone, thymohydroquinone, and thymol methyl ether (*Lantana species*) **[25]**. The traditional healer's selection of aromatic molecules (**Fig. 3**) for respiratory fumigation preparation is coherent with the antimicrobial properties of these volatile compounds, suggesting that empirically derived pharmacological knowledge may have a plausible mechanistic basis as medicines for the management of respiratory diseases, including SARS-CoV-2.

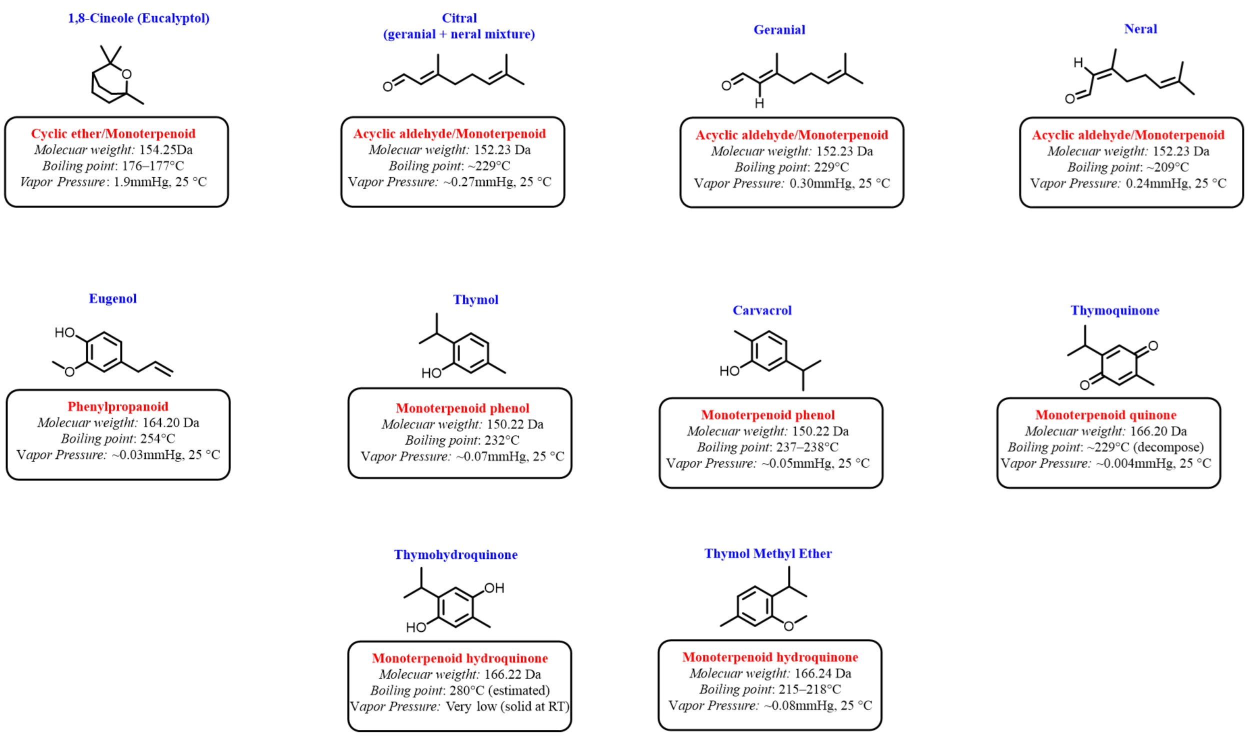

Fig. 3. Chemical structures, compound class, molecular weights, boiling point, and vapor pressure of the key volatile constituents identified in Utraco medicinal fumigation plants (Kinshasa, DRC) investigated in this study.

3.4. Assessment of fumigation delivery efficiency of plant volatile molecules

Given that fumigation of aromatic plant material is conceived to work more effectively for respiratory diseases through direct volatile delivery to the airways **[33,34]**, we thought it worthwhile to analyze the fumigation suitability of ten aromatic volatile molecules identified across Utraco medicinal plants. We examined the vapor pressures and boiling points of these aromatics, which are the key physicochemical parameters governing the efficiency with which a chemical compound transitions from condensed plant material into the vapor phase and reaches the respiratory mucosa **[34]**. The physicochemical basis for the fumigation delivery efficiency of aromatic traditional plant-based preparations used by Utraco healers is illustrated in **Fig. 4**. We plotted vapor pressure against boiling point for the ten volatile constituents identified across the surveyed medicinal plants. Compounds residing within the optimal fumigation delivery zone, defined by a vapor pressure exceeding 0.1 mmHg at 25 °C and a boiling point between 150 and 240 °C, are those that are most readily volatilised during the heating of plant material and therefore most likely may reach the airway in higher concentrations during inhalation **[33]**. Among the compounds examined, 1,8-cineole (eucalyptol; BP 177 °C, VP 1.9 mmHg) occupied the most favourable position, consistent with its well-documented efficacy as an inhaled anti-inflammatory and mucolytic agent in respiratory conditions including asthma and chronic obstructive pulmonary disease **[35,36]**. The citral isomers (geranial and neral; BP 209–229 °C, VP 0.24–0.30 mmHg) and thymol methyl ether also fell within or proximal to this zone, corroborating the selection of *Cymbopogon citratus* and *Lantana* spp. by Utraco healers as fumigation species **[23]**. Thymol and carvacrol, while slightly below the vapor pressure threshold, retained decent volatility at fumigation temperatures, and their higher molecular lipophilicity may facilitate penetration of respiratory epithelial membranes upon deposition **[37]**. Conversely, thymohydroquinone (BP ~280

°C, VP 0.001 mmHg) and thymoquinone (VP 0.004 mmHg) exhibited markedly lower volatility, suggesting that their contribution to fumigation bioactivity is likely secondary to that of thymol and carvacrol, and may be more relevant in preparations involving direct plant-skin contact such as the medicated baths also recorded in this survey **[38,39]**. This analysis provides a chemical rationale for the empirical fumigation practices of Utraco traditional healers and demonstrates that aromatic plants most frequently selected for respiratory complaints possess aromatic and volatile phytochemicals well-suited to vapor-phase airway delivery.

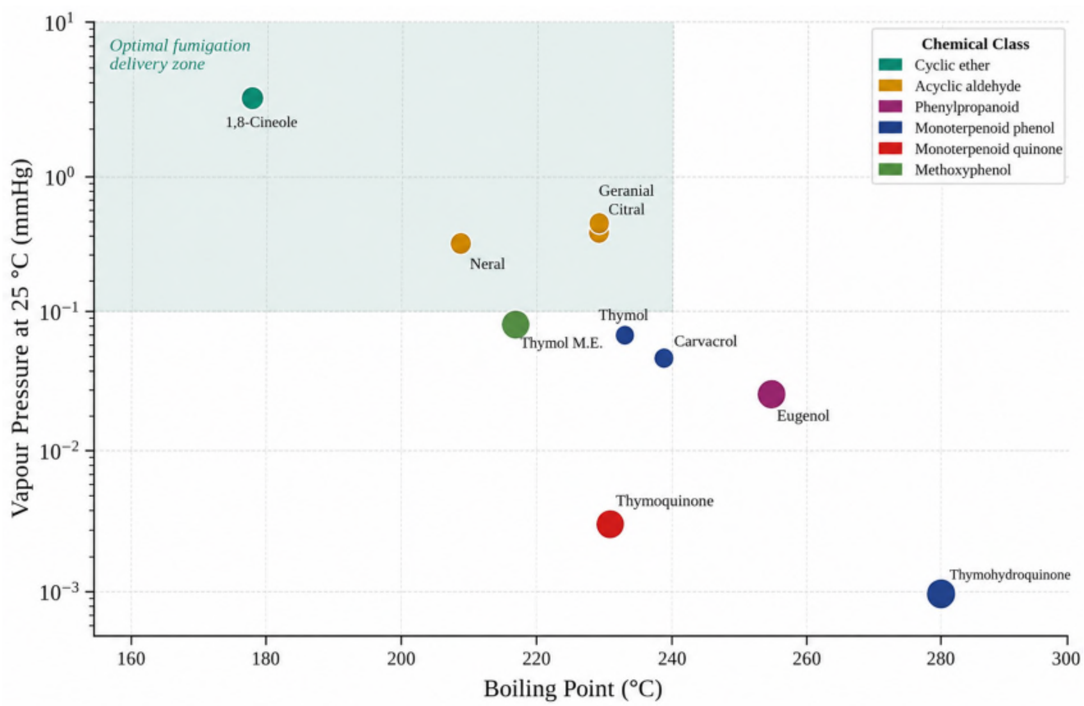

Fig. 4. Fumigation delivery efficiency of key volatile constituents identified in Utraco medicinal fumigation plants (Kinshasa, DRC). The vapor pressure at 25 °C (mmHg, log scale) is plotted against boiling point (°C) for ten compounds spanning five chemical classes. Bubble size is proportional to molecular weight. The shaded region denotes the optimal fumigation delivery zone, defined by a vapor pressure ≥ 0.1 mmHg and a boiling point between 150 and 240 °C.

3.5. Multi-target anti-inflammatory profiles and mechanisms

Inflammation is the hallmark of the host immune response to respiratory pathogens, and its dysregulation, particularly the cytokine storm phenomenon documented in several respiratory diseases and severe COVID-19. In most cases, inflammation could be driving disease progression from mild upper respiratory tract involvement to life-threatening pneumonitis and acute respiratory distress syndrome **[40,41,42]**. Thus, we thought it would be compelling to ask whether the volatile constituents collectively delivered through Utraco fumigation preparations were not merely coincidentally anti-inflammatory, but whether they in fact converged on the major signalling nodes known to drive long COVID and SARS-CoV-2-associated pulmonary injury.

Here, we mapped available pharmacological evidence onto six key inflammatory pathways for each compound identified across the surveyed plant species. The resulting heatmap, presented in **Fig. 5**, reveals a remarkably complementary multi-target profile in which no single constituent monopolises all pathways, yet as a whole, these volatile phytochemicals provide coverage across NF-κB inhibition, COX-1 and COX-2 inhibition, iNOS suppression, Nrf2 activation, and 5-LOX inhibition, the signalling axes most implicated in chronic-driven respiratory inflammation **[39,34]**. Eugenol is known as one of the most potent cyclooxygenase inhibitors targeting both COX-1 and COX-2. Eugenol is generally present in Ocimum basilicum and Ocimum gratissimum among the most cited Utraco fumigation plants for respiratory and febrile conditions **[26,43,44]**. Carvacrol and thymoquinone are reported in the literature as NF-κB suppressors and may be useful in limiting the oxidative tissue damage resulting from severe pulmonary inflammation **[38,45,50]**. Thymol, for its part, possesses the most balanced and broadly distributed activity signature of the monoterpenoid phenol subgroup and is known to block five of the six inflammatory pathways consolidating the pharmacological rationale for the high frequency with which Lantana camara, L.

montevidensis, and Lippia multiflora were nominated by Utraco healers for the management of COVID-19 symptoms **[25,37]**. Thymohydroquinone is reported to exhibit activity across several inflammatory pathways, comparable to that of its parent compound thymoquinone **[34,39]**. This heatmap highlights the polypharmacological synergy of these ten aromatic and volatile compounds and supports the growing evidence that the therapeutic value of complex herbal preparations derives from such multi-component complementarity rather than from any single dominant molecule **[46,47]**.

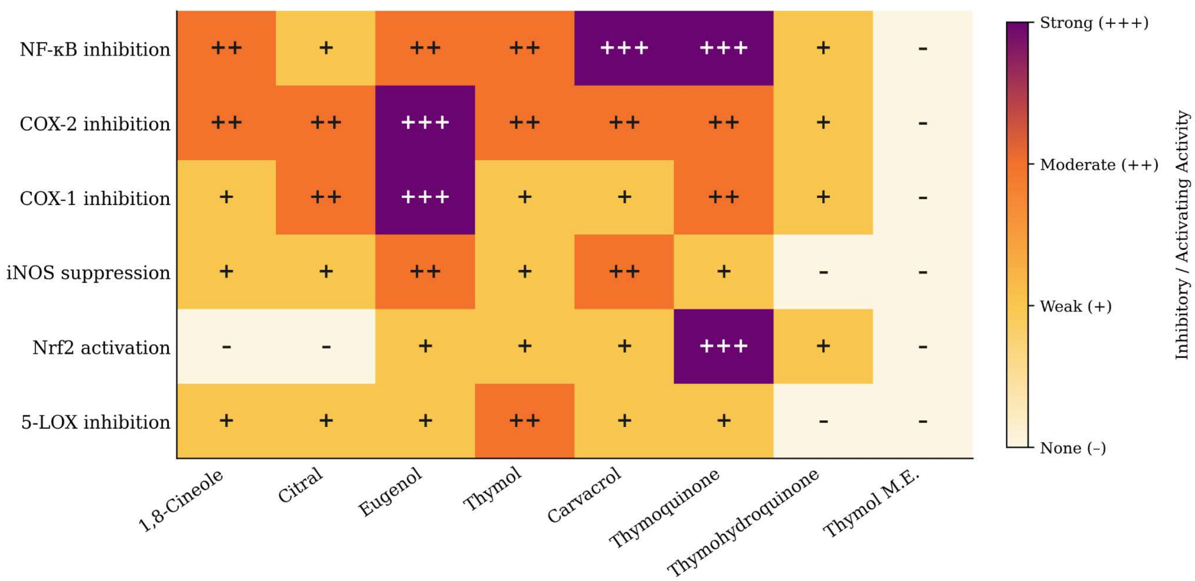

Fig. 5. Multi-target anti-inflammatory pathway inhibition profiles of volatile plant constituents identified in Utraco fumigation plant species.

3.6. Toxicological case analysis: a fatal adverse event

Morinda morindoides (Rubiaceae) experienced an extraordinary surge in demand at the onset of COVID-19 in Kinshasa, the capital of DRC, depleting urban supplies and requiring sourcing from provinces hundreds of kilometres away. The plant has well-documented antiplasmodial, antibacterial, antiamoebic, and spasmolytic activities, and contains anthraquinones, flavonoids, saponins, terpenes, and steroids **[12,13,14]**. During the pandemic, several children may have died following ingestion of an unregulated cocktail containing *M. morindoides* leaves, lemon juice, and additional unspecified plants, administered by their mothers as a protective purge. This event has been mentioned in grey literature and noted in passing in one prior publication **[10]** but has not been subjected to a structured pharmacovigilance analysis. We provide that analysis here through a four-factor convergence model.

Factor 1: Multi-plant combination toxicology. The cocktail combined *M. morindoides* with lemon juice and unspecified additional plants. Anthraquinone compounds (emodin, rhein, and related derivatives) present in *M. morindoides* are documented hepatotoxins and nephrotoxins at supraphysiological doses **[10]**. The addition of other plant species created pharmacological interactions unpredictable from individual plant toxicology profiles. The published DRC nephrotoxicity review **[10]** specifically identifies *Morinda* species as plants that could be associated with acute kidney injury in the DRC context.

Factor 2: Pediatric pharmacokinetic vulnerability. Children have reduced hepatic glucuronidation and conjugation capacity relative to adults, increasing the proportion of active anthraquinone metabolites at any given dose. Anthraquinone safety thresholds established for adults are not directly transferable to pediatric populations. No pediatric pharmacokinetic data exist for *M. morindoides* preparations.

Factor 3: Purging formulation concentration. The preparation was intended as a purgative, a delivery intent associated with higher plant-to-water ratios than standard therapeutic decoctions. Higher concentration increases the effective anthraquinone dose per ingestion event. Purging preparations of anthraquinone-containing plants carry well-documented risks of electrolyte disturbance, colitis, and renal damage at excessive doses.

Factor 4: Social media-mediated adoption without safety guidance. The preparation recipe circulated extensively via WhatsApp without dosage guidance, contraindications for pediatric use, or preparation concentration standards. The social media information ecosystem that drove rapid community adoption provided no pharmacovigilance infrastructure. The published DRC nephrotoxicity review **[10]** documented the absence of professional surveillance as an aggravating factor for plant-related kidney injury in the DRC context.

This four-factor model has direct clinical and policy implications. Factors 2, 3, and 4 are modifiable through targeted public health intervention: age-specific contraindication guidance, standardized preparation protocols, and rapid-response safety messaging on the same social media platforms through which recipes circulate. Factor 1, multi-plant combination toxicology, requires pre-clinical data and represents a specific gap in the evidence base. Any future clinical evaluation of *M. morindoides*-containing formulations must include: quantification of anthraquinone content by HPLC; dose-response toxicology in adult and pediatric animal models; and combination toxicology studies with the most commonly co-administered plants.

3.7. Caregiver testimonials: thematic analysis

Four themes were identified from caregiver interviews. Theme 1 (perceived symptomatic benefit): caregivers consistently described reduced cough and improved respiratory ease attributed to herbal fumigation combined with hydroxychloroquine-azithromycin or supportive care in mild-to-moderate presentations. Theme 2 (pragmatic substitution under pharmaceutical scarcity): multiple caregivers explicitly attributed traditional medicine use to pharmaceutical unavailability or unaffordability rather than to ideological preference, a finding relevant for herbal medicine practice in resource-limited settings. Theme 3 (attribution uncertainty): experienced caregivers acknowledged difficulty distinguishing treatment effect from natural disease resolution given COVID-19's high spontaneous recovery rate. Theme 4 (cultural and psychological benefit): traditional medicine use provided illness narrative coherence and psychological reassurance within Congolese cultural frameworks, which carries functional health implications independent of direct pharmacological effects. These themes suggest that future herbal medicine COVID-19 trials should incorporate patient-reported symptom outcome measures and quality-of-life endpoints alongside virological primary endpoints.

3.8. MRSIT regulatory framework

3.8.1. Three-axis evaluation framework

The MRSIT Scientific Commission (Ministerial Decree No. 010/MIN.RSIT/CAB/JMK/2020, 31 March 2020) adopted three mandatory evaluation axes before any candidate could proceed to patient exposure. Axis 1: scientific merit, assessed by an independent committee on methodological rigor, contribution significance, and scale-up potential. Axis 2: regulatory compliance, verified by the national drug regulatory authority against standardization and quality control requirements. Axis 3: ethics committee endorsement from a recognized institutional review board. The ethical basis for the pre-clinical data gate is explicitly stated in Commission documentation: it is impermissible to administer preparations to sick patients without prior safety data suggesting a reasonable probability of benefit, consistent with the Declaration of Helsinki and WHO Good Clinical Practice guidelines.

The three-axis framework distinguishes the DRC response from those of Madagascar, Guinea, and Burkina Faso, where marketing authorizations were granted without this pre-clinical gate. The *M. morindoides* adverse event documented in Section 4.4 illustrates the population-level consequence of inadequate pre-clinical safety evaluation: when plants are adopted at scale without evidence-based regulatory gatekeeping, pediatric deaths from combination toxicity become possible. The MRSIT framework prevents this at the clinical trial entry point. Extending this protection to community-level use requires the rapid-response safety communication infrastructure identified in Factor 4.

3.8.2. Phase IIB consolidated multi-arm design and approved candidates

The Commission adopted a consolidated multi-arm Phase IIB design evaluating all candidates in parallel arms within a single protocol. This reduces per-candidate sample size requirements, concentrates limited clinical trial expertise in a single study, and enables comparative evaluation across candidates within a shared regulatory and ethics framework. Primary endpoints include virological (nucleic acid test conversion timeline), immunological, hematological, radiological, and safety parameters (renal, hepatic, neurological, and cardiac function).

Table 3. Traditional medicine candidates approved by the MRSIT Commission for Phase IIB clinical trials (DRC, 2020).

Product	Developer/source	Phytochemical profile	Regulatory status (DRC)	References
ManaCOVID	Bantangu; CRPL, Luozi, DRC	Quercetin, kaempferol, rhein, emodin, mangiferin, guaijaverin, saponins, steroids	Phase IIB approved (pre-clinical gate enforced)	**[7,10]**
Hemodrep	MRSIT-approved candidate	Undisclosed polyherbal extract	Phase IIB approved (pre-clinical gate)	**[10]**
Doubase C	MRSIT-approved candidate	Polyherbal vitamin C-enriched formulation	Phase IIB approved (pre-clinical gate)	**[10]**

Mathesia	MRSIT-approved candidate	Undisclosed phytomedicine	Phase IIB approved (pre-clinical gate)	**[10]**
Sickle Cell Solution	MRSIT candidate	Plant extract (undisclosed)	Conditional candidate status	**[10]**

Note : MRSIT = Ministère de la Recherche Scientifique et de l'Innovation Technologique; CRPL = Centre de Recherche Pharmaceutique de Luozi. As of 2020, all candidates were approved subject to provision of pre-clinical safety and efficacy data prior to trial initiation.

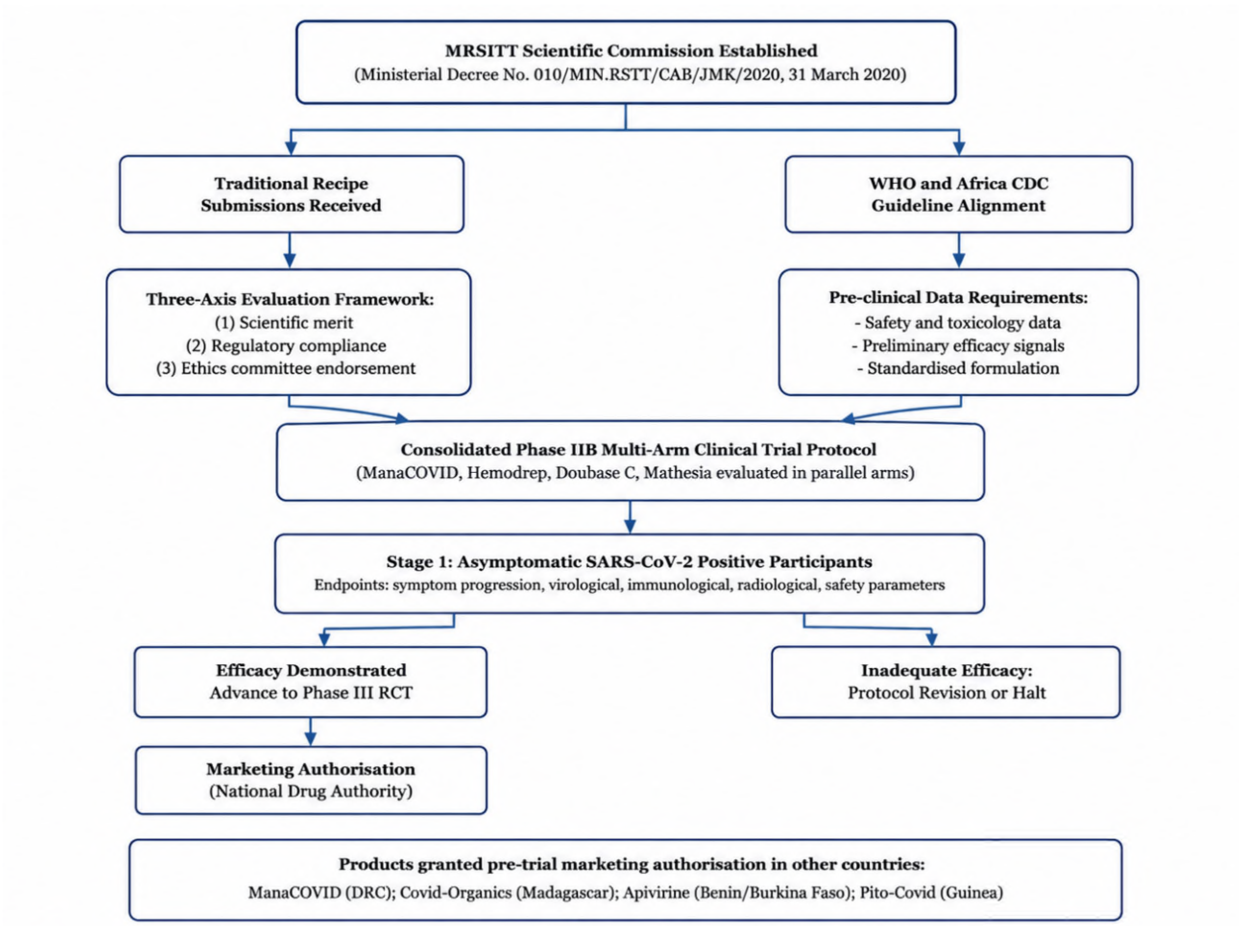

Fig. 6. Regulatory decision pathway established by the DRC MRSIT Scientific Commission for evaluating traditional medicine candidates against COVID-19. The mandatory pre-clinical data gate before patient exposure distinguishes the DRC approach from other African regulatory responses.

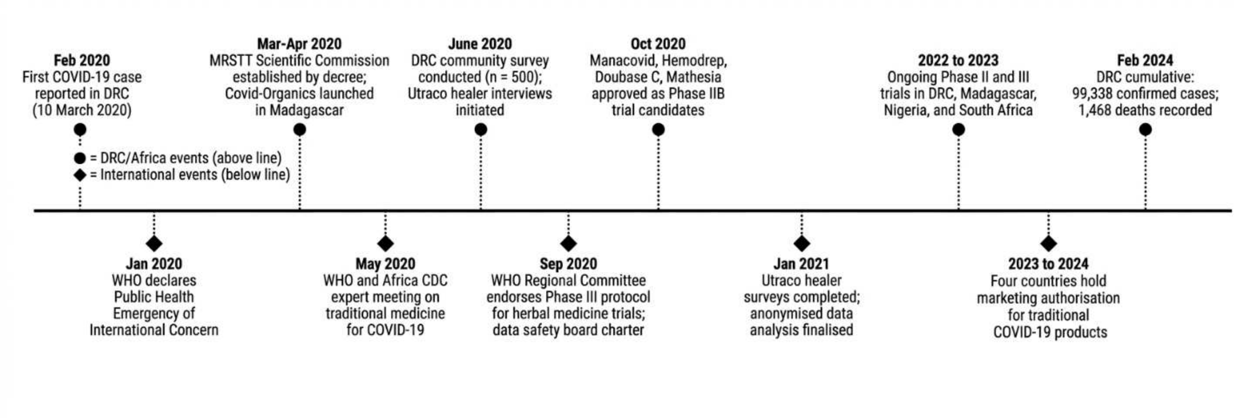

Fig. 7. Timeline of key events in the DRC and pan-African traditional medicine response to COVID-19 (2020 -2024). Circular markers: DRC-specific or African events. Diamond markers: international events.

3.9. What the survey data reveal

The 45% regular plant use and 35% COVID-19-specific adoption figures reported here are the first published quantification of these behaviors in Kinshasa during the pandemic period. The finding that 92% of traditional medicine users maintained or sought pharmaceutical treatment in parallel challenges the assumption that traditional medicine use is primarily a substitute for formal care. This has direct implications for herbal medicine practitioners and public health policy: integration of traditional medicine into COVID-19 management guidance would serve a large population already using both systems, not a population that must be separately engaged.

The most frequently cited species in this survey include plants whose active constituents (quercetin, allicin, curcumin, 1,8-cineole) have demonstrated activity against SARS-CoV-2 relevant molecular targets in cell-based assays **[15,16,17,18]**. This convergence between empirical community knowledge and experimental pharmacology is a pattern documented in other ethnopharmacological contexts **[48]** and suggests that systematic bioassay investigation of the top-cited DRC species is warranted. Fumigation delivers volatile essential oil constituents directly to respiratory mucosa via inhalation, bypassing the bioavailability limitations of oral decoctions. For a respiratory pathogen replicating primarily in upper airway epithelium, local delivery of antiviral volatile compounds represents a mechanistically superior route compared with systemic oral administration **[18]**. The aromatic species in the Utraco list, dominated by Eucalyptus, Cymbopogon, Ocimum, Lippia, and Lantana, contain volatile constituents with documented antimicrobial and antiviral activity at concentrations achievable by steam inhalation **[18,23,26,25]**. This traditional practice deserves formal clinical investigation as a low-cost, accessible respiratory intervention.

3.10. Limitations

Four limitations must be acknowledged. First, Survey 1 used convenience sampling via social media, producing over-representation of Kinshasa residents (69.6%) and tertiary-educated participants (59.8%); findings may not be generalized to rural populations or those with lower educational attainment. Second, Survey 2 healer interviews, while multi-ethnic, cannot claim national representation given geographic constraints on Utraco membership. Third, caregiver testimonials are subject to recall and attribution biases inherent in retrospective qualitative data. Fourth, the MRSIT institutional analysis is based on documentation held in the research team's archive; independent external audit of commission proceedings was not possible within the scope of this study.

4. CONCLUSIONS

In this study, we report results of community survey data (n=500) documenting the prevalence, plant species profile, and preparation methods of COVID-19 traditional plant use in Kinshasa, which has revealed pharmacologically coherent community knowledge and predominantly complementary (not substitutive) use patterns. The Utraco healer interview data identify 18 fumigation and bath species with documented essential oil constituents and scientifically plausible respiratory anti-infective activity, representing a traditional pharmacopoeia worthy of further *in vitro* and *in vivo* investigations and systematic clinical evaluations. The four-factor pharmacovigilance model for the case analysis of *M. morindoides* fatal adverse event provides specific pre-clinical safety requirements for future clinical evaluation of *M. morindoides*, a widely used medicinal plant in DRC, and also highlights the need for pharmacovigilance and safety monitoring of combinations of traditional herbals during public health emergencies.

DECLARATIONS

Ethics approval

Ethics approval was granted by the University of Kinshasa School of Public Health Ethics Committee. All survey participants provided informed consent. Traditional healer interviews were conducted with written and verbal consent. Approval was obtained from the University of Kinshasa School of Public Health Ethics Committee (Approval No. ESP/CE/89B/2020). No patient-identifiable data are included. The case analysis of the *Morinda morindoides*-associated paediatric adverse event (Section 3.6) is based on secondary information from grey literature and a previously published report [10]; no primary data were collected from the affected children or their families, and no identifying information about them is presented in this manuscript.

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Data availability

Data (anonymized) will be made available upon request.

Competing interests

The authors declare no competing interests.

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CRediT authorship contribution statement

PKM, NKN: Conceptualization, Resources, Supervision, Writing – review & editing. IEK, CGK, MMM, JM, DL, MA: Investigation, Data curation, Formal Analysis, Methodology. PKM: Project administration. All authors: Writing – review & editing.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used Gemini and ChatGPT in order to generate images for visual illustrations of the graphical abstract. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

REFERENCES

[1] Worldometer, 2024. DR Congo COVID-19 statistics. https://www.worldometers.info/coronavirus/country/democratic-republic-of-the-congo/ (Accessed 11 February 2026).

[2] Yarlagadda, H., Patel, M.A., Gupta, V., Bansal, T., Upadhyay, S., Shaheen, N., et al., 2022. COVID-19 vaccine challenges in developing and developed countries. Cureus 14 (4), e23951. https://doi.org/10.7759/cureus.23951

[3] Dandara, C., Dzobo, K., Chirikure, S., 2021. COVID-19 pandemic and Africa: from the situation in Zimbabwe to a case for precision herbal medicine. OMICS 25 (4). https://doi.org/10.1089/omi.2020.0099

[4] Mutombo, P.N., Kasilo, O.M.J., James, P.B., Wardle, J., Kunle, O., Katerere, D., et al., 2023. Experiences and challenges of African traditional medicine: lessons from COVID-19 pandemic. BMJ Glob. Health 8 (8), e010813. https://doi.org/10.1136/bmjgh-2022-010813

[5] UNESCO, 2020. The place of African traditional medicine in response to COVID-19 and beyond. UNESCO News. https://unesdoc.unesco.org/ark:/48223/pf0000373722

[6] Kandhe, C.G., Enofo, D.E., Mbombo, M.N., Kaba, I.E., Kabeya, J.K., Mukanya, J.M., Ngombe, N.K., Mutwale, P.K., 2026. Kikanda, a Congolese traditional plant-based meat: microscopic features, phytochemical profile, and antioxidant activity. Direct Research Journal of Agriculture and Food Science 14 (2), 68–75. https://doi.org/10.26765/DRJAFS19050631

[7] Attah, A.F., Fagbemi, A.A., Olubiyi, O., Dada-Adegbola, H., Oluwadotun, A., Elujoba, A., et al., 2021. Therapeutic potentials of antiviral plants used in traditional African medicine with COVID-19 in focus. Front. Pharmacol. 12, 596855. https://doi.org/10.3389/fphar.2021.596855

[8] Akindele, A.J., Sowemimo, A., Agunbiade, F.O., Sofidiya, M.O., Awodele, O., Ade-Ademilua, O., et al., 2022. Bioprospecting for anti-COVID-19 interventions from African medicinal plants. Nat. Prod. Commun. 17. https://doi.org/10.1177/1934578X221096968

[9] Isamura, B.K., Patouossa, I., Kaba, I.E., Matondo, A., Mpiana, P.T., 2023. Computational study on the antioxidant activity of five plant food benzoic acid derivatives. S. Afr. J. Chem. 77, 111–118. https://doi.org/10.17159/0379-4350/2023/v77a13

[10] Falanga, M.C., Ndaba, M.M., Biye, T.N.J.-C., Masengo, A.C., Basosila, N., Iteku, B.J., et al., 2023. Use of medicinal plants in Africa: a case study from the Democratic Republic of Congo. Adv. Chronic Kidney Dis. 30 (1). https://doi.org/10.1053/j.ackd.2023.01.002

[11] Muipata, M.M., Mbwaka, S.N., Mbombo, P.M., Kaba, I.E., Mukanya, J.M., Lokole, P.B., et al., 2025. Phytochemical analysis, antioxidant and antibacterial capacities of a Congolese traditional recipe and medicinal plants commonly used in prostate diseases. J. Biosci. Med. 13, 382–399. https://doi.org/10.4236/jbm.2025.135030

[12] Cimanga, K., De Bruyne, T., Hu, J.P., Cos, P., Apers, S., Pieters, L., et al., 1999. Constituents from Morinda morindoides leaves as inhibitors of xanthine oxidase. Pharm. Pharmacol. Commun. 5 (6), 419–424. https://doi.org/10.1211/146080899128734911

[13] Cimanga, K., Kambu, K., Tona, L., Hermans, N., Apers, S., Totto, J., et al., 2006. Antiamoebic activity of iridoids from Morinda morindoides leaves. Planta Med. 72, 751–753. https://doi.org/10.1055/s-2006-946684

[14] Cimanga, R.K., Mukenyi, P.N.K., Kambu, O.K., Tona, G.L., Apers, S., Totte, J., et al., 2010. Spasmolytic activity of extracts from Morinda morindoides leaves. J. Ethnopharmacol. 127 (2), 215–220. https://doi.org/10.1016/j.jep.2009.10.021

[15] Jo, S., Kim, M.S., 2020. Inhibition of SARS-CoV 3CL protease by flavonoids. J. Enzyme Inhib. Med. Chem. 35 (1), 145–151. https://doi.org/10.1080/14756366.2019.1690480

[16] Shawky, E., Nada, A.A., Ibrahim, R.S., 2020. Potential role of medicinal plants and their constituents in the mitigation of SARS-CoV-2. RSC Adv. 10 (47), 27961–27983. https://doi.org/10.1039/D0RA05141A

[17] Soni, V.K., Mehta, A., Ratre, Y.K., Tiwari, A.K., Amit, A., Singh, R.P., et al., 2020. Curcumin, a traditional spice component, can hold the promise against COVID-19? Eur. J. Pharmacol. 886, 173551. https://doi.org/10.1016/j.ejphar.2020.173551

[18] Kanda, A., Ncube, F., Goronga, T.K., 2019. Trace elements in leaf extracts of Eucalyptus grandis traditionally used to treat common cold. J. Health Pollut. 9 (24), 191214. https://doi.org/10.5696/2156-9614-9.24.191214

[19] Latham, P., Konda ku Mbuta, A., 2014. Useful Plants of Bas-Congo Province, Democratic Republic of Congo, Vols. 1 and 2.

[20] Ilic, N.M., Dey, M., Poulev, A.A., Logendra, S., Kuhn, P.E., Raskin, I., 2014. Anti-inflammatory activity of grains of paradise (Aframomum melegueta Schum) extract. J. Agric. Food Chem. 62 (43), 10452–10457. https://doi.org/10.1021/jf5026086

[21] Ajaib, M., Hussain, T., Farooq, S., Ashiq, M., 2016. Analysis of antimicrobial and antioxidant activities of Chenopodium ambrosioides: an ethnomedicinal plant. J. Chem. 2016, 4827157. https://doi.org/10.1155/2016/4827157

[22] Rampa, K.M., Van De Venter, M., Koekemoer, T.C., Swanepoel, B., Venables, L., Hattingh, A.C., et al., 2022. Exploring four South African Croton species for potential anti-

inflammatory properties. J. Ethnopharmacol. 282, 114596. https://doi.org/10.1016/j.jep.2021.114596

[23] Tibenda, J.J., Yi, Q., Wang, X., Zhao, Q., 2022. Review of phytomedicine, phytochemistry, ethnopharmacology, toxicology, and pharmacological activities of Cymbopogon genus. Front. Pharmacol. 13, 997918. https://doi.org/10.3389/fphar.2022.997918

[24] Konda ku Mbuta, A., Mwima, K., Bitengeli, M., Itufa, Y., Mahuku, K., Mafuta, M., et al., 2012. Plantes medicinales de traditions: Province de l'Equateur, R.D. Congo. IRSS, Ouagadougou.

[25] Kapepula, P.M., Mungitshi, P.M., Franck, T., Ngoyi, D.M., Kalenda, P.D.T., Ngombe, N.K., et al., 2017. Antioxidant potentiality of three herbal teas consumed in Bandundu rural areas of Congo. Nat. Prod. Res. 31 (16), 1940–1943. https://doi.org/10.1080/14786419.2016.1269102

[26] Kamelnia, E., Mohebbati, R., Kamelnia, R., El-Seedi, H.R., Boskabady, M.H., 2023. Anti-inflammatory, immunomodulatory and anti-oxidant effects of Ocimum basilicum and its main constituents. Iran. J. Basic Med. Sci. 26 (6), 617–627. https://doi.org/10.22038/IJBMS.2023.68417.14923

[27] Ntonga, A.P., Baldovini, N., Mouray, E., Mambu, M., Belong, P., Grellier, P., 2014. Activity of Ocimum basilicum, Ocimum canum and Cymbopogon citratus essential oils against Plasmodium falciparum. Parasite 21, 33. https://doi.org/10.1051/parasite/2014033

[28] Ugbogu, O.C., Emmanuel, O., Agi, G.O., Ibe, C., Ekweogu, C.N., Ude, V.C., et al., 2021. A review on Ocimum gratissimum L. Heliyon 7 (11), e08404. https://doi.org/10.1016/j.heliyon.2021.e08404

[29] Waly, D.A., Zeid, A.H.A., Attia, H.N., Ahmed, K.A., El-Kashoury, E.A., El Halawany, A.M., et al., 2023. Comprehensive phytochemical characterization of Persea americana fruit. Inflammopharmacology 31 (6), 3243–3262. https://doi.org/10.1007/s10787-023-01362-x

[30] Zhang, P., Qin, D., Chen, J., Zhang, Z., 2020. Plants in the genus Tephrosia: valuable resources for botanical insecticides. Insects 11 (10), 1–18. https://doi.org/10.3390/insects11100721

[31] Panda, S.K., Gazim, Z.C., Swain, S.S., Bento, M.C.V.A., Sena, J.D.S., Mukazayire, M.J., et al., 2022. Ethnomedicinal, phytochemical and pharmacological investigations of Tetradenia riparia. Front. Pharmacol. 13, 896078. https://doi.org/10.3389/fphar.2022.896078

[32] Elaka, I.K., Kapepula, P.M., Ngombe, N.K., Mpoyi, J.M., Lukusa, D.M., Muabilwa, M.M., et al., 2020. Microscopic features, antioxidant and antibacterial capacities of plants of the Congolese cosmetopoeia, raw materials of cosmeceuticals. J. Biosci. Med. 8, 149–166. https://doi.org/10.4236/jbm.2020.89013

[33] Kohlert, C., van Rensen, I., März, R., Schindler, G., Graefe, E.U., Veit, M., 2000. Bioavailability and pharmacokinetics of natural volatile terpenes in animals and humans. Planta Med. 66 (6), 495–505. https://doi.org/10.1055/s-2000-8616

[34] Tisserand, R., Young, R., 2014. Essential Oil Safety: A Guide for Health Care Professionals, 2nd ed. Churchill Livingstone/Elsevier, Edinburgh.

[35] Juergens, U.R., Dethlefsen, U., Steinkamp, G., Gillissen, A., Repges, R., Vetter, H., 2003. Anti-inflammatory activity of 1.8-cineol (eucalyptol) in bronchial asthma: a double-blind placebo-controlled trial. Respir. Med. 97 (3), 250–256. https://doi.org/10.1053/rmed.2003.1432

[36] Worth, H., Schacher, C., Dethlefsen, U., 2009. Concomitant therapy with cineole (eucalyptole) reduces exacerbations in COPD: a placebo-controlled double-blind trial. Respir. Res. 10, 69. https://doi.org/10.1186/1465-9921-10-69

[37] Marchese, A., Orhan, I.E., Daglia, M., Barbieri, R., Di Lorenzo, A., Nabavi, S.F., Gortzi, O., Izadi, M., Nabavi, S.M., 2016. Antibacterial and antifungal activities of thymol: a brief review of the literature. Food Chemistry 210, 402–414. https://doi.org/10.1016/j.foodchem.2016.04.111

[38] Koshak, A.E., Koshak, E.A., 2020. Nigella sativa L. as a potential phytotherapy for coronavirus disease 2019: a mini review of in silico studies. Curr. Ther. Res. Clin. Exp. 93, 100602. https://doi.org/10.1016/j.curtheres.2020.100602

[39] Darakhshan, S., Bidmeshki Pour, A., Hosseinzadeh Colagar, A., Sisakhtnezhad, S., 2015. Thymoquinone and its therapeutic potentials. Pharmacol. Res. 95–96, 138–158. https://doi.org/10.1016/j.phrs.2015.03.011

[40] Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J., Cao, B., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet 395, 497–506. https://doi.org/10.1016/S0140-6736(20)30183-5

[41] Mehta, P., McAuley, D.F., Brown, M., Sanchez, E., Tattersall, R.S., Manson, J.J., 2020. COVID-19: consider cytokine storm syndromes and immunosuppression. The Lancet 395, 1033–1034. https://doi.org/10.1016/S0140-6736(20)30628-0

[42] Tay, M.Z., Poh, C.M., Rénia, L., MacAry, P.A., Ng, L.F.P., 2020. The trinity of COVID-19: immunity, inflammation and intervention. Nature Reviews Immunology 20, 363–374. https://doi.org/10.1038/s41577-020-0311-8

[43] Marchese, A., Barbieri, R., Coppo, E., Orhan, I.E., Daglia, M., Nabavi, S.F., Izadi, M., Abdollahi, M., Nabavi, S.M., Ajami, M., 2017. Antimicrobial activity of eugenol and

essential oils containing eugenol: a mechanistic viewpoint. Critical Reviews in Microbiology 43, 668–689. https://doi.org/10.1080/1040841X.2017.1295225

[44] Tragoolpua, Y., Jatisatienr, A., 2007. Anti-herpes simplex virus activities of Eugenia caryophyllus (Spreng.) Bullock & S.G. Harrison and essential oil, eugenol. Phytotherapy Research 21, 1153–1158. https://doi.org/10.1002/ptr.2226

[45] Hotta, M., Nakata, R., Katsukawa, M., Hori, K., Takahashi, S., Inoue, H., 2010. Carvacrol, a component of thyme oil, activates PPARα and γ and suppresses COX-2 expression. J. Lipid Res. 51 (1), 132–139. https://doi.org/10.1194/jlr.M900255-JLR200

[46] Wagner, H., Ulrich-Merzenich, G., 2009. Synergy research: approaching a new generation of phytopharmaceuticals. Phytomedicine 16, 97–110. https://doi.org/10.1016/j.phymed.2008.12.018

[47] Williamson, E.M., 2001. Synergy and other interactions in phytomedicines. Phytomedicine 8, 401–409. https://doi.org/10.1078/0944-7113-00060

[48] Heinrich, M., Appendino, G., Efferth, T., Furst, R., Izzo, A.A., Kayser, O., et al., 2020. Best practice in research: overcoming common challenges in phytopharmacological research. J. Ethnopharmacol. 246, 112230. https://doi.org/10.1016/j.jep.2019.112230

[49] Poungam, E., Muipata, M., Kaba, I., Kandhe, C., Moke, B., Mukanya, J., Mutwale, P., Ngombe, N., 2026. Phytochemical profiling, antioxidant and anti-inflammatory activities of four West African spices incorporated as bioactive ingredients for dermatological formulations. Preprint. Research Square. https://doi.org/10.21203/rs.3.rs-9964544/v1

[50] Gholamnezhad, Z., Keyhanmanesh, R., Boskabady, M.H., 2016. Preclinical and clinical effects of Nigella sativa and its constituent, thymoquinone: a review. J. Ethnopharmacol. 190, 372–386. https://doi.org/10.1016/j.jep.2016.06.061