



BRIDGING THE GAP: CHALLENGES IN THE STANDARDIZATION AND CLINICAL TRANSLATION OF LEMONGRASS THERAPEUTICS

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Abstract

Lemongrass has been used for generations across tropical regions as a household remedy. The two species most often discussed in the scientific literature, *Cymbopogon citratus* and *C. flexuosus*, yield an essential oil whose dominant constituent is citral. Traditional healers prepare leaf infusions or steam the plant for digestive complaints, mild fevers, muscle aches and restlessness. Laboratory work published up to 2017 confirmed several of these folk uses and added new observations on antimicrobial and anti-inflammatory actions. Yet the step from promising extracts to a reproducible, clinically tested medicine has proved difficult. The reasons are both technical and practical, and they are examined here.

Key Words: *Cymbopogon citratus*, *Cymbopogon flexuosus*, Citral, Essential oil, Antimicrobial, Anti-inflammatory

1. Introduction

The genus *Cymbopogon* (Family: Poaceae) comprises volatile, aromatic grasses widely distributed across tropical and subtropical regions of Asia, Africa, and America. Among these, *Cymbopogon citratus* (DC.) Stapf (West Indian lemongrass) and *Cymbopogon flexuosus* (Nees ex Steud.) W.Watson (East Indian lemongrass) hold significant ethnomedicinal value. Preclinical evaluations validate their traditional use for conditions ranging from metabolic disorders and gastrointestinal distress to acute infections and chronic inflammation.

However, translating these empirical observations into validated, human-grade therapeutics presents substantial hurdles. The central bottlenecks involve:

- Unpredictable batch-to-batch phytochemical variability driven by environment and origin.
- Sub-therapeutic in vivo bioavailability and structural fragility of primary bioactives.
- A lack of standardized clinical trial frameworks tailored to multi-component botanical matrices.

2. Chemical composition and its inherent variability :

Steam distillation of fresh leaves typically recovers 0.4–1.2 percent oil. In most commercial samples the combined isomers of citral (geranial plus neral) account for 55–85 percent of the oil. The remaining fraction contains myrcene, limonene, linalool, geraniol and smaller amounts of sesquiterpenes. These proportions are not fixed. Plants grown in different soils, harvested at different times of day or distilled under slightly altered conditions produce oils that differ measurably in citral content and in the balance of secondary constituents. East-Indian types tend to be richer in citral; some West-Indian accessions contain more myrcene. Seasonal rainfall and altitude further shift the profile.

Aqueous and hydro-alcoholic extracts contain flavonoids and phenolic acids that contribute antioxidant capacity, but these polar compounds are rarely quantified with the same care given to the oil. The net result is that two laboratory samples labelled “lemongrass extract” can differ substantially in composition, making direct comparison of biological results unreliable.

3. Preclinical findings available by 2017 :

Antimicrobial activity is the property most frequently reported. Citral and the whole oil inhibit growth of *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans* and several filamentous fungi at concentrations that are achievable in topical formulations. Membrane disruption appears to be the principal mechanism. Anti-inflammatory effects have been shown in the classic carrageenan paw-edema and croton-oil ear-edema models; oral doses of the oil reduced swelling to a degree comparable with moderate doses of diclofenac in some experiments. Antioxidant assays (DPPH, FRAP) consistently demonstrate free-radical scavenging that correlates with both citral and the phenolic fraction.

Limited behavioural studies indicated that brief inhalation of the aroma reduced subjective anxiety scores in healthy volunteers subjected to the Stroop colour-word test. Analgesic activity was recorded in rodent models of inflammatory and visceral pain. A few reports also noted modest hypotensive and hypoglycaemic actions after oral administration of leaf decoctions. Collectively these data supplied a reasonable pharmacological rationale, yet almost every study used a different batch of oil whose exact composition was only partially described.

4. Obstacles to chemical standardization :

The first and most persistent difficulty is the natural variability already mentioned. Without defined cultivars grown under controlled agronomic conditions, a manufacturer cannot guarantee that successive batches will contain the same percentage of citral or the same spectrum of minor terpenes. Pharmacopoeial monographs available in 2017 usually specified only a minimum citral content and a few physical constants; they did not require a full chromatographic fingerprint or quantitative limits for the secondary constituents that may modulate activity or toxicity.

Analytical methods themselves were adequate in principle. Gas chromatography coupled to mass spectrometry could identify and quantify the major volatiles, and HPLC methods existed for selected phenolics. In practice many published papers still reported only total oil yield or an incomplete list of peaks. Validated, multi-marker assays suitable for routine quality control of finished products remained uncommon. Stability presented a further problem. Citral oxidises and isomerises on exposure to light and air; after a few months of ordinary storage the measured content can fall by 10–20 percent unless the oil is protected by antioxidants or micro-encapsulation. Encapsulation techniques were being explored but had not yet entered commercial medicinal products.

Authentication of the plant material itself was another weak point. Morphological characters alone do not always distinguish closely related *Cymbopogon* species, and the risk of substitution or dilution with lower-grade oils was real. DNA-based methods were only beginning to be tested on the genus and were not part of routine quality systems.

5. Gaps that hinder clinical translation :

Human data published by 2017 were few and methodologically limited. Short trials of diluted lemongrass-oil mouthwashes showed reductions in plaque and gingival indices roughly comparable to chlorhexidine over periods of two to four weeks. One randomised comparison of 10 percent lemongrass oil against clotrimazole cream for tinea corporis found similar cure rates. Small aromatherapy studies suggested mild calming effects after inhalation. A single investigation of lemongrass tea recorded a transient lowering of blood pressure in healthy subjects. Sample sizes were almost always under one hundred participants, treatment periods were short, and the test materials were rarely standardised to a defined citral content. Safety monitoring was rudimentary.

Pharmacokinetic information was equally sparse. Citral is rapidly metabolised; after oral administration systemic exposure is low because of extensive first-pass conjugation. Topical and inhalational routes achieve higher local concentrations, yet quantitative human data on absorption, distribution and elimination were virtually absent. Without such data it is difficult to choose rational doses or to predict interactions with conventional drugs.

Toxicological knowledge was incomplete. Acute oral toxicity in rodents is relatively low, but high doses of citral have produced reproductive findings in animal studies. Contact dermatitis and sensitisation are documented with topical use. Long-term safety, effects in pregnancy, and possible enzyme-inducing properties of the terpene fraction had not been examined systematically.

Formulation presented practical difficulties. The oil is poorly soluble in water and loses potency in simple aqueous vehicles. Emulsions, gels and solid dispersions that keep citral stable and deliver it in a controlled manner were still at the laboratory stage. Taste and odour also limited the acceptability of oral preparations intended for systemic use.

Regulatory pathways added another layer of complexity. In many countries lemongrass preparations could be sold as traditional or food products with minimal efficacy requirements. In jurisdictions that treat herbal medicines as pharmaceuticals, a full dossier of standardised composition, pharmacokinetics and controlled trials was required. The cost of generating such data for a multi-component natural product whose intellectual-property protection is weak discouraged large investment.

6. Possible routes forward suggested by work up to 2017 :

Several practical steps were already visible. Selection and vegetative propagation of high-citral clones under defined cultivation protocols can reduce compositional scatter. Adoption of quantitative GC and HPLC assays for a small set of marker compounds (citral isomers plus two or three characteristic phenolics) would allow meaningful batch release specifications. Micro-encapsulation and related technologies improve shelf-life and may enhance local bioavailability. Clinical development is most realistic if it begins with local applications—oral rinses, topical antifungals or anti-inflammatory creams—where systemic exposure is limited and traditional use supplies a baseline of safety.

Parallel pharmacokinetic studies using sensitive analytical methods are essential even for these indications. Larger, multi-centre trials with clearly defined, standardised extracts and clinically relevant endpoints would then become feasible. Harmonisation of quality standards across national pharmacopoeias would further ease collaborative research.

7. Concluding remarks:

By the end of 2017 the preclinical literature on lemongrass had established a coherent picture of antimicrobial, anti-inflammatory and mild anxiolytic activity linked chiefly to citral.

The same literature, however, revealed persistent weaknesses in chemical standardisation, pharmacokinetic characterisation and clinical evidence. These weaknesses are not unique to lemongrass; they are shared by many aromatic plants that contain labile, multi-component oils. Closing the gap requires coordinated attention to agronomy, analytical chemistry, formulation science and carefully designed human studies. Only then can the traditional reputation of the plant be converted into medicines whose composition, efficacy and safety are known with confidence.

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