Journal of the Ceylon College of Physicians

P B Fernando Memorial Oration

Translating traditional knowledge into clinical evidence: The journey of Ceylon cinnamon

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ARTICLE INFO

Keywords:
Cinnamomum zeylanicum,
Ceylon cinnamon,
herbal medicines,
type 2 diabetes,
translational research

ABSTRACT

Herbal medicines are increasingly used worldwide, particularly in low- and middle-income countries, yet many widely used remedies lack rigorous scientific validation. Sri Lanka, with its rich biodiversity and long-standing tradition of herbal medicine, provides a unique opportunity to address this gap. This work describes a structured translational research programme focused on *Cinnamomum zeylanicum* (Ceylon cinnamon), with the goal of generating robust clinical evidence from traditional knowledge. The aim was to systematically evaluate the safety, efficacy, and clinical applicability of Ceylon cinnamon in metabolic diseases through a stepwise research approach.

Sequential phases of evidence synthesis were followed by pre-clinical experimentation, early-phase clinical trials, and randomised controlled trials. Initial systematic reviews identified promising biological effects but highlighted the absence of high-quality human data. Pre-clinical studies using diabetic rat models demonstrated significant improvements in glycaemic control and lipid profiles without toxicity. A Phase I clinical trial in healthy adults confirmed safety and suggested beneficial effects on blood pressure and lipids. Subsequently, a randomised, double-blind, placebo-controlled Phase II/III trial in patients with type 2 diabetes showed significant reductions in fasting plasma glucose, HbA1c, and LDL cholesterol, with good tolerability and no serious adverse events. These findings provide compelling evidence that Ceylon cinnamon is a safe and effective adjunct therapy for metabolic disorders. In conclusion, this work demonstrates that traditional herbal knowledge can be successfully translated into clinically relevant evidence through rigorous scientific methodology. It highlights a scalable framework for evaluating herbal medicines and underscores Sri Lanka's potential to contribute to global evidence-based phytotherapy.

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DOI: https://doi.org/10.4038/jccp.v57i1.8197
Received: 11.03.2026; Accepted: 30.04.2026

Introduction

Herbal and traditional medicines have played a central role in healthcare systems across the world for centuries. The World Intellectual Property Organisation (WIPO) defines herbal medicinal products as finished and labelled medicinal products that contain active ingredients derived from aerial or underground parts of plants or other plant materials, either alone or in combination. The World Health Organisation estimates that nearly 80% of the population in developing countries relies on traditional medicine for at least part of their primary healthcare needs.[1] This reliance is largely driven by cultural acceptability, accessibility, and perceptions of safety associated with natural products. This has led to the global market for herbal medicines expanding rapidly, with an estimated annual value exceeding USD 150 billion.[2] Sri Lanka possesses a particularly rich heritage of herbal medicine. Indigenous medical traditions, including Ayurveda, have long utilised medicinal plants for the prevention and treatment of disease, ranging from chronic non-communicable diseases to other minor/severe ailments. More than 1,400 medicinal plant species have been documented within the country. Despite this rich biodiversity and cultural heritage, many herbal remedies remain inadequately evaluated using modern scientific methods.

At the same time, the increasing burden of non-communicable diseases such as diabetes, hypertension, dyslipidaemia, and obesity has stimulated growing interest in plant-derived therapies worldwide. While consumer demand for herbal products continues to grow, scientific evidence supporting their safety and effectiveness often remains limited. This creates a paradox whereby widely used remedies may lack robust clinical validation. Over the past decade, our research programme sought to address this gap by applying rigorous scientific methods to evaluate herbal medicines used for metabolic and cardiovascular diseases. This programme progressed through several stages, including evidence synthesis, pre-clinical experimentation, phased clinical trials, and ultimately intellectual property development. A central focus of this work has been *Cinnamomum zeylanicum*, commonly known as Ceylon cinnamon, one of Sri Lanka's most valuable agricultural exports and a plant with a long history of medicinal use. This article describes the journey of translating traditional knowledge regarding Ceylon cinnamon into clinically relevant scientific evidence through a structured programme of research and sets an example for the process and methodology that needs to be followed in clinical evaluation of herbal remedies.

Herbal medicines and evidence-based practice

The scientific evaluation of herbal medicines has gained increasing attention over the past two decades. Modern pharmacological research has increasingly applied evidence-based medicine methodologies, including randomised controlled trials (RCTs) and systematic reviews, to assess the efficacy and safety of plant-derived interventions. Several plant extracts have been investigated for their potential role in managing chronic non-communicable diseases. For example, herbs such as *Hibiscus sabdariffa, Allium sativum* (garlic) and *Phyllanthus emblica* (Indian gooseberry) have demonstrated clinically meaningful reductions in blood pressure in randomised trials.[3-5] Similarly, plant-based supplements are frequently marketed for weight management and metabolic diseases. However, systematic reviews often reveal substantial methodological limitations within this body of research. Variability in extract preparation, inconsistent dosing regimens, inadequate reporting of adverse events, and heterogeneous study designs are common issues. In many cases, marketing claims far exceed the strength of available scientific evidence. A systematic review and meta-analysis of *Caralluma fimbriata*, a cactus widely marketed as a natural appetite suppressant, illustrates this challenge. Although modest reductions in waist circumference were observed, no significant effects were found for body weight or body mass index.[6] These findings highlight the need for careful scientific validation before therapeutic claims are accepted. This growing global emphasis on evidence-based evaluation provides a framework for rigorously studying herbal medicines, ensuring that traditional remedies are assessed using the same standards applied to conventional pharmaceuticals.

Herbal medicines in Sri Lanka: Availability and affordability

Sri Lanka is home to over 1,400 identified medicinal plant species, many of which have documented traditional uses but remain scientifically unvalidated. Sri Lanka's strong cultural acceptance of herbal medicine is reflected in the widespread availability of herbal products targeting chronic diseases. A recent nationwide survey examining herbal medicinal products marketed for non-communicable diseases such as diabetes, hypertension, dyslipidaemia, and obesity, across supermarkets, pharmacies, and Ayurveda stores in two populous districts, identified 88 distinct herbal products marketed for these conditions.[7] The majority of products were available at Ayurveda stores (73.9%), followed closely by supermarkets (73.9%) and community pharmacies (63.1%), indicating a pervasive presence in both traditional and modern retail channels. These products were available in diverse dosage forms, including teas, capsules, tablets, liquids, and topical preparations, and carried a broad array of therapeutic claims, often without adequate scientific substantiation.[7] Despite their widespread availability, affordability was low, with nearly 69% of products costing more than a daily wage for a month's supply. Being highly priced, coupled with the fact that many products make unvalidated and exaggerated therapeutic claims, exploits consumers' trust in "natural" remedies without providing scientifically proven benefits. Furthermore, labelling was inconsistent and often misleading, with most products failing to disclose potential adverse effects, contraindications, or evidence to support health claims. This discrepancy between availability and evidence-based quality highlights an urgent need for stronger regulatory oversight and consumer education to ensure herbal products for NCDs are safe, effective and affordable.

Another similar survey identified a wide variety of herbal weight-loss supplements readily available in Sri Lanka, reflecting growing consumer demand amid rising obesity rates.[8] This survey identified 100 weight-loss products across drug stores, online platforms, and print

advertisements, featuring 155 active ingredients, the majority of which were of plant origin. The most marketed herbs included green tea (*Camellia sinensis*), *Garcinia cambogia* (Goraka), and ginger (*Zingiber officinale*), alongside caffeine and other botanicals. In these products, the labels often lacked adequate information on dosage, safety warnings, or scientific validation of claims, raising concerns about misleading marketing and potential health risks.[8] These findings suggest that while herbal products are widely accessible, their quality, regulation, and evidence base remain variable. Strengthening regulatory oversight and promoting evidence-based evaluation are therefore essential to protect consumers and ensure safe use of herbal therapies.

In parallel with the widespread availability of herbal products for weight loss and NCDs, studies on the advertising practices highlight how unregulated and misleading marketing perpetuates consumer misconceptions and undermines evidence-based healthcare.[9] A survey by Ranasinghe et al. documented 285 advertisements for ayurvedic and herbal products across television, radio, newspapers, and online platforms in Sri Lanka, with weight loss, diabetes, and immune boosting among the most common claims. Alarmingly, none of the advertisements mentioned potential adverse effects, only 8% included a registration number, and just over half provided manufacturer contact details. Many advertisements used exaggerated therapeutic and non-therapeutic claims, such as "100% natural," "clinically proven," or "guaranteed results", without scientific substantiation.[9] This pervasive messaging fosters a false sense of safety and efficacy, which could encourage patients to substitute or delay evidence-based medical treatments. Particularly concerning is the marketing of these products to vulnerable populations, including those with diabetes and obesity, who may already be at higher risk of complications. Furthermore, the lack of standardisation, quality control, and scientific validation undermines the potential of Sri Lanka's rich herbal heritage to contribute meaningfully to modern evidence-based healthcare.

It is against this backdrop that the present research programme was initiated as a systematic, stepwise programme to rigorously evaluate the therapeutic claims of *Cinnamomum zeylanicum* (Ceylon cinnamon), one of Sri Lanka's most iconic medicinal plants, thereby demonstrating the feasibility and importance of applying scientific principles to herbal medicine research.

The cinnamon case study: From evidence review to clinical trials

Ceylon cinnamon (*Cinnamomum zeylanicum*) is a plant of considerable economic and medicinal significance in Sri Lanka. Traditionally, it has been used for metabolic and cardiovascular conditions, particularly diabetes and dyslipidaemia. Much of the global scientific literature on cinnamon, however, focuses on *Cinnamomum cassia*, a related species that contains high levels of hepatotoxic coumarins.[10] In contrast, Ceylon cinnamon contains negligible coumarin levels and therefore may offer a safer therapeutic profile. Our research programme aimed to systematically evaluate Ceylon cinnamon through a stepwise translational research framework, progressing from evidence synthesis to pre-clinical studies and clinical trials.

Initial systematic evidence review

The first stage involved a comprehensive review of existing scientific evidence on Ceylon cinnamon. The first systematic review broadly focused on its medicinal properties.[11] This review identified 70 eligible studies, encompassing antimicrobial, anti-parasitic, glycaemic control, lipid-lowering, antioxidant, anti-inflammatory, wound-healing, neuroprotective, and hepatoprotective effects. The majority of the evidence came from *in-vitro* and animal models, with limited human data. While benefits such as reduced fasting glucose, improved lipid profiles, and attenuation of diabetic complications were repeatedly demonstrated, the lack of standardised preparations and high-quality clinical trials was evident. A second systematic review specifically assessed the efficacy and safety of *C. zeylanicum* in diabetes mellitus.[12] Sixteen studies were included, demonstrating beneficial mechanisms, including inhibition of intestinal glucose absorption, enhanced GLUT-4 translocation, increased insulin secretion, and inhibition of gluconeogenesis in vitro, along with improved glycaemic and lipid parameters in animal models. However, no human clinical trials were identified at the time of this review. Notably, *C. zeylanicum* was shown to have a more favourable safety profile than *C. cassia*, due to negligible coumarin content.

Finally, a targeted review of clinical and mechanistic evidence emphasised the distinction between *C. zeylanicum* and *C. cassia*, confirming *C. zeylanicum's* lower coumarin toxicity risk and summarising evidence of cardiovascular, glycaemic, neuroprotective, and anti-inflammatory effects.[13] Together, these systematic reviews provided a scientific rationale for advancing *C. zeylanicum* into structured pre-clinical and clinical evaluation. They also underscored the methodological weaknesses in existing literature, such as poor standardisation of extracts, variable dosages, and inconsistent outcome measures, emphasising the need for rigorously designed human trials to confirm efficacy and safety. These reviews established the evidence base for further translational research, building a logical foundation for our subsequent pre-clinical experiments and human studies of Ceylon cinnamon.

Pre-clinical studies

Following the evidence review, a pre-clinical study to evaluate the effects of *Cinnamomum zeylanicum* (Ceylon cinnamon) on glycaemic control, lipid profiles, food intake, and body weight using a Sprague Dawley rat model was conducted.[14] The study was designed in two phases: acute and medium-term interventions. Cinnamon bark was authenticated and prepared as a standardised aqueous extract, and dosages were calculated using human-equivalent doses. Both healthy and streptozotocin-induced diabetic rats were studied to assess effects in normal and pathological states. In Phase I, 32 healthy rats were divided into four groups to assess the acute effects on fasting and post-prandial glucose levels. Cinnamon-treated rats demonstrated a more rapid reduction in blood glucose following an oral glucose load compared to controls, with a significantly greater percentage reduction observed within the first two hours ($p < 0.001$). No significant

hypoglycaemia was observed in fasting healthy rats, suggesting glucose-lowering effects were modulated by the underlying glycaemic state. In Phase II, 26 rats (healthy and diabetic) received daily cinnamon extract or a control for 30 days. Among diabetic rats, cinnamon significantly reduced food intake ($p < 0.001$), fasting blood glucose and post-prandial glucose (on days 20 and 30), and stabilised HbA1c compared to controls. Notably, cinnamon-treated diabetic rats maintained HbA1c at baseline levels while untreated diabetic rats showed a significant rise. In both healthy and diabetic groups, cinnamon significantly reduced total and LDL cholesterol levels over the 30 days. No significant changes in HDL cholesterol, triglycerides, or body weight were observed. Histopathological examination of the liver, kidneys, and pancreas showed no evidence of toxicity in cinnamon-treated animals.

These findings were consistent with previous *in-vitro* and *in-vivo* studies of cinnamon's insulin-mimetic and antioxidant effects, while demonstrating for the first time in Sri Lanka the medium-term benefits and safety of authentic Ceylon cinnamon in a controlled animal model. Importantly, the glucose-lowering effects were evident only in the diabetic model, suggesting a disease-modulated effect rather than indiscriminate hypoglycaemia. Together, these results provided a strong rationale to progress to human trials.

Phase I Clinical Trial and pharmacokinetic study

A Phase I clinical trial evaluated the safety, tolerability, and preliminary pharmacodynamic effects of *Cinnamomum zeylanicum* (CZ) extract in healthy adults,[15] along with a pharmacokinetic study to characterise plasma metabolites.[16]

The Phase I trial was conducted at the Department of Pharmacology, Faculty of Medicine, University of Colombo. Thirty healthy volunteers (mean age: 38.8 ± 10.4 years; equal gender distribution) were enrolled. Over three months, escalating doses of CZ extract (85 mg, 250 mg, and 500 mg/day) were administered in monthly intervals. Clinical assessments, biochemical investigations, and adverse event monitoring were conducted monthly. Of the 30 participants, 28 completed the study. No serious adverse events or evidence of hepatotoxicity, nephrotoxicity, or coagulation abnormalities were observed. Mild, transient dyspepsia was reported in four participants, with two withdrawing as a result. Importantly, CZ supplementation resulted in significant reductions in systolic and diastolic blood pressure during the first month, maintained over three months, as well as significant decreases in total and LDL cholesterol by study end ($p < 0.05$). No significant changes were seen in fasting glucose, anthropometric measures, HDL, VLDL, or triglycerides. These findings support the safety and beneficial cardiovascular effects of CZ in humans at the tested doses.

In parallel, a pharmacokinetic study was performed to investigate the absorption and disposition of cinnamic acid, a key CZ metabolite. A validated HPLC method was developed, demonstrating high sensitivity, specificity, and recovery for cinnamic acid in plasma. Five healthy volunteers ingested 5 g of crude CZ, and serial plasma samples were analysed. Cinnamic acid was rapidly detected in plasma, with a mean peak concentration (Cmax) of 1.9 ± 1.5 µmol/L at 15 minutes (Tmax), and an elimination half-life (T½) of approximately 36 minutes. This was the first study to document the pharmacokinetic profile of CZ in humans, providing essential insights into its bioavailability and metabolism. These Phase I and pharmacokinetic results confirmed the safety of CZ, demonstrated its lipid-lowering and antihypertensive potential in humans, and established a scientific basis for dosing and monitoring in subsequent clinical trials.

Phase II/III Clinical Trial in type 2 diabetes

A randomised, double-blind, placebo-controlled Phase II/III clinical trial was conducted to evaluate the clinical efficacy and safety of *Cinnamomum zeylanicum* (CZ) extract as a therapeutic agent in type 2 diabetes. This was one of the first trials globally to comprehensively assess the indigenous Ceylon cinnamon in a diabetic population.[17,18] A total of 210 adults with type 2 diabetes were enrolled and randomised into three groups: CZ 250 mg daily, CZ 500 mg daily, or placebo, administered for four months. All participants were on stable oral hypoglycaemic therapy (metformin and/or sulphonylureas) and received standardised dietary and lifestyle advice. The primary outcomes were changes in glycaemic control (fasting plasma glucose \[FPG], HbA1c). Secondary outcomes included lipid profiles, insulin resistance (HOMA-IR), β-cell function (HOMA-β), blood pressure, anthropometry, and safety parameters.

Of the 210 patients, 186 completed the study. Both CZ groups showed significant reductions in FPG and HbA1c compared to placebo at four months. Insulin resistance improved while β-cell function increased significantly in the CZ groups ($p < 0.05$). Notably, the 500 mg CZ group demonstrated significant reductions in total cholesterol and LDL cholesterol, effects not seen in the 250 mg group or placebo. HDL cholesterol and triglycerides did not change significantly. No significant reductions were observed in BMI, waist circumference, or blood pressure at study end. No serious adverse events occurred. Mild dyspeptic symptoms were reported in a few participants, leading to withdrawal in three patients, but resolved in others with dietary modification. Biochemical monitoring showed no hepatotoxicity, nephrotoxicity, or coagulation abnormalities. Compliance rates exceeded 85% in all groups. These findings demonstrate, for the first time, that CZ extract is safe and efficacious as an adjunct therapy in type 2 diabetes, improving glycaemic and lipid parameters without serious adverse effects. Compared to earlier research on *C. cassia*, our findings suggest that CZ offers a safer alternative with similar or better metabolic benefits, underscoring its potential as a pharmaceutical agent.

Patent and commercialisation

The research programme culminated in the filing of a patent application for a Ceylon cinnamon capsule formulation jointly developed by the University of Colombo and the Industrial Technology Institute. The patent was granted in 2021, and efforts are currently underway to collaborate with industry partners to scale up production under Good Manufacturing Practice standards and to introduce the product to both local and international markets.

Lessons learned and future directions

Several important lessons have emerged. Firstly, evidence synthesis is essential for identifying research gaps and guiding subsequent experimental work. Secondly, well-designed human clinical trials are indispensable for validating therapeutic claims. Thirdly, research on herbal medicine requires multidisciplinary collaboration, including pharmacology, clinical medicine, phytochemistry, and public health. However, challenges remain. Funding for herbal medicine research remains limited, and regulatory frameworks governing herbal products require strengthening. Standardisation of extracts and quality control processes also requires further development. Sri Lanka has a unique opportunity to position itself as a global leader in scientifically validated herbal medicines. Achieving this will require stronger collaboration between universities, industry, regulatory authorities, and international partners.

Conclusion

Sri Lanka's rich heritage of herbal medicine represents both an opportunity and a responsibility. The research journey described here demonstrates that traditional knowledge can be successfully translated into modern clinical evidence when rigorous scientific methodologies are applied. The work on *Cinnamomum zeylanicum* illustrates how systematic research can transform a traditional remedy into a scientifically validated therapeutic agent with potential global relevance. By strengthening research infrastructure, regulatory frameworks, and multidisciplinary collaboration, Sri Lanka can harness its unique biodiversity to contribute meaningfully to global healthcare while preserving and validating its traditional knowledge.

Acknowledgements

The author gratefully acknowledges the contributions of supervisors, collaborators, research staff, and study participants who made this research programme possible. The support of the University of Colombo and the Industrial Technology Institute in facilitating laboratory and clinical research is also acknowledged, including funding for the conduct of studies.

References

1. Hughes G D, Aboyade O M, Hill J D, Rasu R. The role and importance of economic evaluation of traditional herbal medicine use for chronic non-communicable diseases. *Comparative Effectiveness Research*. 2015;2015:49. doi: 10.2147/CER.S77163
2. World Health Organization. WHO global report on traditional and complementary medicine. 2019. Available at: https://www.who.int/publications/i/item/978924151536
3. Ellis LR, et al. A systematic review and meta-analysis of the effects of hibiscus sabdariffa on blood pressure and cardiometabolic markers. *Nutr Rev*. 2022;80:1723-1737. doi:10.1093/nutrit/nuab104
4. Wang HP, et al. Effect of garlic on blood pressure: A meta-analysis. *J Clin Hypertens (Greenwich)*. 2015;17:223-231. doi: 10.1111/jch.12473
5. Prananda AT, et al. Phyllanthus emblica: A comprehensive review of its phytochemical composition and pharmacological properties. *Front Pharmacol*. 2023;14:1288618. doi: 10.3389/fphar.2023.1288618
6. Jayawardena R, Francis TV, Abhayaratna S, Ranasinghe P. The use of caralluma fimbriata as an appetite suppressant and weight loss supplement: A systematic review and meta-analysis of clinical trials. *BMC Complement Med Ther*. 2021;21:279. doi: 10.1186/s12906-021-03450-8.
7. Weerakoon C, Mannapperuma U, Ranasinghe P. A survey on availability and composition of herbal products with beneficial health claims for chronic non-communicable diseases in Sri Lanka. *BMC Complement Med and Ther*. 2025;25(1):376. doi: 10.1186/s12906-025-05137-w.
8. Jayawardena R, Sooriyarachchi P, Ranasinghe P, Perera A, Hills AP. Availability and composition of weight-loss supplements in Sri Lanka. *Nutr Diet*. 2020;77:247-252. doi: 10.1111/1747-0080.12501
9. Rufaideen F, Liyanage CK, Ranasinghe P. Evaluation of ayurvedic and herbal product advertisements on electronic and print media in a developing country. *J. Pharm. Health Serv. Res.* 2022;13:109-114. doi: 10.1093/jphsr/rmac009
10. Ballin NZ, Sorenson AT. Coumarin content in cinnamon-containing food products on the Danish market. *Food Control*. 2014;38:198-203. doi:10.1016/j.foodcont.2013.10.014
11. Ranasinghe P, Pigera S, Premakumara GA, Galappaththy P, Constantine GR, Katulanda P. Medicinal properties of 'true' cinnamon (Cinnamomum zeylanicum): A systematic review. *BMC Complement Altern Med*. 2013;13:275. doi: 10.1186/1472-6882-13-275.
12. Ranasinghe P, Jayawardana R, Galappaththy P, Constantine GR, de Vas Gunawardana N, Katulanda P. Efficacy and safety of 'true' cinnamon (Cinnamomum zeylanicum) as a pharmaceutical agent in diabetes: A systematic review and meta-analysis. *Diabet Med*. 2012;29:1480-1492.doi: 10.1111/j.1464-5491.2012.03718.x.
13. Ranasinghe P, Galappaththy P. Health benefits of Ceylon cinnamon (Cinnamomum zeylanicum): A summary of the current evidence. *Ceylon Med J*. 2016;61:1-5. doi: 10.4038/cmj.v61i1.8251.
14. Ranasinghe P, Perera S, Gunatilake M, et al. Effects of Cinnamomum zeylanicum (ceylon cinnamon) on blood glucose and lipids in a diabetic and healthy rat model. *Pharmacognosy Res*. 2012;4:73-79. doi: 10.4103/0974-8490.94719.
15. Ranasinghe P, Jayawardena R, Pigera S, et al. Evaluation of pharmacodynamic properties and safety of cinnamomum zeylanicum (Ceylon cinnamon) in healthy adults: A phase i clinical trial. *BMC Complement Altern Med*. 2017;17:550. doi:10.1186/s12906-017-2067-7
16. Pigera S, Ranasinghe P, Kaumal MN, Galappaththy P. Quantification of metabolite cinnamic acid of cinnamon (Cinnamomum zeylanicum) in human plasma. *J Natl Sci Found Sri Lanka*. 2023 doi: 10.4038/jnsfsr.v51i1.10817
17. Ranasinghe P, Galappaththy P, Constantine GR, et al. Cinnamomum zeylanicum (Ceylon cinnamon) as a potential pharmaceutical agent for type-2 diabetes mellitus: Study protocol for a randomised controlled trial. *Trials*. 2017;18:446. doi: 10.1186/s13063-017-2192-0.
18. Ranasinghe P, et al. Efficacy and safety of cinnamomum zeylanicum (ceylon cinnamon) for diabetes mellitus: A randomised, double blind, placebo-controlled clinical trial. *Diabetes Metab Syndr*. 2025;19:103357. doi: 10.1016/j.dsx.2025.103357