



The Science of Complementary Medicines





Complementary medicines (CM) play a significant role in the health of our community. Increasingly, complementary medicines are being found to contribute to improved health outcomes, through increased effectiveness, safety and cost-effectiveness, and integration with conventional medical care. It has been estimated that 70 per cent of Australians use complementary medicines to support their health and wellbeing goals.

Australia's complementary medicines industry is backed by a risk-based regulatory regime that is regarded as one of the strongest in the world. The regulation of complementary medicines falls within the remit of the Therapeutic Goods Administration (TGA), an arm of the Department of Health, which also regulates over-the-counter, medical devices and prescription medicines. The TGA has responsibility for the oversight of product safety, quality, claims, listing, post-marketing monitoring and setting standards for manufacturing. Complementary medicines manufactured in Australia must be produced according to the code of Good Manufacturing Practice (GMP).

Whilst regulated by the TGA, complementary medicines do not place themselves in the same category as pharmaceutical interventions. They are regulated by a specialist branch, the Complementary & OTC Medicines Branch, and Australian consumers understand that complementary medicines are not a replacement for prescription medicines; rather complementary medicines are used to enhance overall wellbeing and for maintenance of health. The majority of complementary medicines are indicated for the relief of symptoms of minor, self-limiting conditions, maintaining health and wellbeing, or the promotion or enhancement of health.

As healthcare costs spiral, and as knowledge and attitudes evolve, greater numbers of people are interested in remaining healthy across their lifespan and desire active control over the decisions made in relation to their health. The wider community and health practitioners are steadily recognising the importance of moving towards a more preventive model of healthcare.

Due to the growing interest in this area of healthcare, and the inherent differences between complementary medicines and pharmaceuticals, this booklet has been produced to provide an introduction to the science behind the use and manufacture of complementary medicines in Australia.

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Executive Summary

- Complementary medicines (CM) play a significant role in the health of our community. Increasingly, complementary medicines are being found to contribute to improved health outcomes, through increased effectiveness, safety and cost-effectiveness, and integration with conventional medical care.
- The use of integrative medicine by biomedical practitioners, particularly GPs, as a part of routine clinical practice is becoming more common, both globally and in Australia. Integrative medicine is informed by evidence, and makes use of all appropriate therapeutic and lifestyle approaches to achieve optimal health.
- There is a commonly held belief that adequate nutrition is obtained from a well-balanced diet. However, studies have shown that malnutrition is common in the West, with most people not consuming a diet that is high in quality nutrients.
- In Australia, the evidence required to support indications and claims for complementary medicines must be based on a 'healthy' population, a population with no overt symptoms of disease. It takes a very long period of time, often decades, for a clinical trial to show the positive benefits of an intervention in a healthy population. In the case of a nutritional product, it is the equivalent of asking the question: How many days of eating an apple a day to keep the doctor away?
- Evidence-based medicine is shaping the future of healthcare, including complementary medicine. Developing scientific evidence in support of practices and the adoption of the latest evidence into clinical practice are an ongoing focus for every facet of healthcare.
- Randomised-controlled trials are seen as the 'gold standard' for testing a pharmaceutical, to ensure that the active agent is both able to effectively treat the majority of patients and that it is safe to use. While a pharmaceutical will typically have one active molecule, and is used to treat a specific disease or condition, a herbal medicine may contain 30 or more ingredients and a highly complex formulation that may be used to help with a variety of conditions. The complex formulations and variety of uses means that complementary medicines don't always lend themselves to being easily tested by random-controlled trials.
- Evaluation of singular tools of trade (e.g. one herb for one condition) is unlikely to be true to complementary medicine or natural therapies practice and will risk missing key clinical benefits. A thoughtful, rigorous and focused research strategy, based on the incorporation of epidemiological data, will better demonstrate the benefits of complementary medicines for contributing to the prevention and management of chronic illnesses and improving public health.

Role of Complementary Medicines

Many people interested in managing chronic disease, preventing the exacerbation of illness, or wishing to optimise wellbeing, choose complementary medicines and see complementary medicine practitioners to address their health issues and to live healthier lives. This is where complementary medicines fill an important role in the Australian healthcare landscape.

The World Health Organization (WHO) defines health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity. It is important to highlight that there are a number of dimensions to health across a wide spectrum, moving from illness, to average health and through to enhanced health. Under the biomedical model, health and well-being are defined by the absence of disease, yet absence of disease does not mean a patient is optimally healthy.

Complementary medicine and conventional medicine both have a common goal – to reduce human suffering and improve health outcomes; it is just their approach that differs.

Biomedical practitioners are predominantly focused on detecting and treating episodes of illness; moving people from ill-health to average health via treatment with drugs and surgery. The absence of symptomatic disease is often viewed as an ideal goal. Treatment guidelines often prescribe a standardised approach.

Complementary medicine practitioners focus on the area of prevention and moving people from average health to a state of enhanced health. They emphasise nutrition, lifestyle modifications, and the importance of taking personal responsibility for health as fundamental principles for improving quality of life. Complementary medicine practitioners offer multiple interventions, tailored to individual needs.

Integration of Care

Along with the popularity of complementary medicines among consumers, increasingly general practitioners (GPs) across the industrialised world are incorporating complementary medicines into their practice. The use of integrative medicine by biomedical practitioners, particularly GPs, as a part of routine clinical practice is also becoming more common in Australia. A survey indicated that about 30 per cent of GPs in Australia describe themselves as practising integrative medicine.ⁱ

Integrative medicine is the blending of conventional and evidenced based complementary medicines and/or therapies, along with lifestyle factors such as diet, exercise and reduction of stress. It also implies a greater emphasis on patient empowerment and choice, in addition to providing best-practice medical care. Integrative medicine requires patients to be active participants in the management of their health. Therapeutic options might include nutritional changes, exercise prescription, nutritional supplements, herbal remedies, psychological counselling, prescription medication, surgery and more.ⁱⁱ

The Academic Consortium for Integrative Medicine and Health shares the following definition for integrative medicine and health:

*Integrative medicine and health reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic and lifestyle approaches, healthcare professionals and disciplines to achieve optimal health and healing.*ⁱⁱⁱ

GPs who do not identify themselves as integrative medicine practitioners are also using complementary medicines, with 86 per cent having recommended and prescribed complementary medicines in the last 12 months. Glucosamine, calcium, fish oil, and vitamin D supplements are the most frequently prescribed or recommended complementary medicines by GPs^{iv}.

Evidence-Based Medicine

“The emergence of evidence-based medicine and, more recently, evidenced-based complementary medicine is challenging many previously held notions of best practice. As evidence emerges, many Western medical therapies are being confirmed as correct, or challenged as ineffective or harmful. Similarly, many complementary therapies are being confirmed as correct, while others are being found ineffective or harmful. Such is the inevitable evolution of healthcare.”

Professor Kerryn Phelps^v

Evidence-based medicine is a term coined in the 1990s and is a phenomenon that has resonated with all fields of healthcare. It was described by Sackett as the “the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients”.^{vi} Evidence-based medicine is shaping the future of healthcare, including complementary medicine.

There are many examples to demonstrate that complementary medicine and biomedicine can co-exist in a relationship that serves to maximise the health outcomes of the Australian population. This is not limited to, but includes the following:

- It is becoming common practice for GPs to recommend patients take probiotics in conjunction with a course of antibiotics. This use by GPs is based on numerous clinical studies supporting the benefit of taking probiotics for antibiotic associated diarrhoea. Some studies suggest that probiotics can decrease the relative risk of antibiotic-associated diarrhoea by 57% to 63%.^{vii viii}
- Acupuncture has been widely used for various conditions and particularly recognised as an effective treatment for chronic pain, including osteoarthritis, back pain, and various types of headaches. Many patients have acupuncture treatment alongside

medication such as anti-inflammatory drugs. There is strong established evidence supporting the effectiveness of acupuncture in reducing pain for certain conditions.^{ix}

- There is an increasing evidence base supporting the use of complementary medicines for women during pregnancy. Based on a number of positive studies, GPs are actively recommending the use of complementary medicines, particularly folic acid, vitamin D, and fish oil supplements for their pregnant patients.
- Several specific dietary supplements have been identified as being able to reduce the relative risk of experiencing a medical event associated with common conditions.^x These include:
 - magnesium and calcium/vitamin D combinations for osteoporosis;
 - folic acid/B6/B12 and omega-3 (fish or krill oils) for cardiovascular disease;
 - lutein & zeaxanthin for age-related macular degeneration; and
 - St John's Wort for depression.

The scientific evidence to support the use of complementary medicines is increasingly being supported by credible, peer-reviewed research, with numerous complementary medicine specific databases having been established in the last decade. A significant amount of scientific research has been conducted looking at the direct health benefits of using complementary medicines. Numerous studies demonstrate that many of these medicines have a positive effect on reducing the risk of a secondary disease event.

Complementary Medicines Research

Developing scientific evidence in support of practices and the adoption of the latest evidence into clinical practice are an ongoing focus for every facet of healthcare.

Randomised-controlled trials are seen as the 'gold standard' for testing a pharmaceutical, to ensure that the active agent is both able to effectively treat the majority of patients and that it is safe to use. While a pharmaceutical will typically have one active molecule, and is used to treat a specific disease or condition, a herbal medicine may contain 30 or more ingredients and a highly complex formulation that may be used to help with a variety of conditions.

Based on pharmaceutical thinking, the usual approach to the clinical trial says that if you test a compound formula that has many ingredients and obtain a positive result, you cannot know which ingredient is providing the benefit, so you must test each ingredient individually.

Over the past 40 years, scientific research has enabled a better understanding of herbal medicines. In some cases, research has isolated and identified key active constituents and their mechanisms of action in a field of study called *phytochemistry*. Randomised controlled trials have been conducted and there is now a strong body of evidence (including Cochrane reviews) for the efficacy of certain standardised herbal extracts.^{xi} However, in the field of

phytochemistry, and in the fields of nutrition and natural therapies, the isolation of key ingredients as an approach doesn't always work.

“Evaluation of singular tools of trade (e.g. one herb for one condition) is unlikely to be true to complementary medicine or natural therapies practice and will risk missing key clinical benefits. Hence, consideration of the use of complementary medicines needs to take into account not only key tools of trade, but also whole multi-component systems of practice, with multiple study endpoints – including symptom relief, reducing disease severity, delaying disease progression, disease prevention, improving quality of life and patient satisfaction.”

Professor Alan Bensoussan^{xii}

Complementary medicines include vitamins, minerals and nutritional supplements, to Western herbal medicines, Ayurvedic and Traditional Chinese Medicine. Developing scientific evidence for some complementary medicines can be complicated, especially for Ayurveda and Traditional Chinese Medicine which hold foundational concepts that are not based on the biomedical model.

As complementary medicines don't always lend themselves to being easily tested by random-controlled trials some will never be supported by this 'pharmaceutical gold standard' level of study. This does not mean that they are invalid, but simply that evidence based medicine needs to be supported by common sense in clinical trial design and interpretation, and by clinical experience.^{xiii}

A large evidence base for complementary medicines has been established despite the limitations of standard drug trials to test the effectiveness and safety of complementary medicines and despite the lack of patent protection for products that use naturally-based ingredients.

A thoughtful, rigorous and focused research strategy, based on the incorporation of epidemiological data, will better demonstrate the benefits of complementary medicines for contributing to the prevention and management of chronic illnesses and improving public health.

Evidence in 'Healthy' Populations

In Australia, the evidence required to support indications and claims for complementary medicines must be based on a 'healthy' population, a population with no overt symptoms of disease.

The Therapeutic Goods Administration regulates complementary medicines as low-risk medicines because the majority have a safety profile more closely aligned to foods than to pharmaceuticals. This means that to scientifically evaluate complementary medicines, we would need to follow many more people for a much longer timeframe than for the evaluation of a drug in treating patients who are sick.

For the last 30 years, Harvard University has been running the Nurses' Health Study and the Male Physicians' Trial in around 180 000 people. In the randomised controlled Male Physicians Trial, taking a standard multivitamin did not show a clinical benefit until after 10 years, when there was a statistically significant 8 per cent reduction in common cancers. The 20 year data in men showed a 44 per cent reduction in cardiovascular disease by taking a good quality multivitamin each day.^{xiv}

A recent meta-analysis published in Mayo Clinic proceedings showed an 18 per cent reduction in cardiovascular events in people who consumed high-dose fish oil supplementation or regularly consumed fish over a long period of time.^{xv}

As demonstrated by the examples above, it takes a very long period of time, often decades, for a clinical trial to show the positive benefits of an intervention in a healthy population. In the case of a nutritional product, it is the equivalent of asking the question: How many days of eating an apple a day to keep the doctor away?

The global collection of scientific data supporting the use of complementary medicines is typically from studies in diseased populations so that the potential benefits can become apparent in a timelier manner.

Traditional Evidence

Over the centuries, empirical knowledge has amassed to form a body of evidence commonly referred to as traditional evidence. This form of evidence is not simply 'anecdotal' as it is the accumulation of observations by generations of practitioners and is based on the basic tenets of good clinical practice: careful observation of people, their environment and the diseases they acquire.^{xvi xvii}

In 1985, it was noted by Professor Norman Farnsworth that of the 119 drugs of known structure that had been derived from plants, 75 per cent had the same use in conventional biomedicine as they did in traditional medicine.^{xviii}

Evidence-based medicine benefits when it is acknowledged that there are multiple dimensions of evidence, including expert evidence and also a patient's own experience of complementary medicines, their level of satisfaction with the care received and perception of its effectiveness.

Complementary medicine practice operates as a whole-of-system approach, where a range of interventions are used together to create an outcome, such as diet and lifestyle, herbal medicines, nutritional supplements, yoga, massage and stress reduction. The combination of recommendations is more likely to have greater impact upon the patient's health than any component offered in isolation.^{xix}

Focus on Nutrition

“There is a commonly held belief that adequate nutrition is obtained from a well-balanced diet. However, studies such as the US department of agriculture survey of micronutrient intake have revealed that malnutrition is common in the West.” - Dr Paul Clayton^{xx}

A healthy diet and lifestyle are prerequisites for the prevention of many chronic diseases. Unfortunately, Australians are not consuming a diet that is high in quality nutrients. The latest report from the Australian Bureau of Statistics (ABS) indicated that just 7 per cent of adults met the recommended intake of vegetables and just under half, at 49.8 per cent, met the recommendation for serves of fruit.^{xxi}

The impact of a poor diet is being highlighted by research such as that which was published in the journal *Diabetic Medicine* in 2016, illuminating that scurvy has been detected in a number of patients at Sydney’s Westmead Hospital.^{xxii}

The authors found that several patients with long-running unhealed wounds were cured by a simple course of vitamin C, and therefore stressed the importance of a diet rich in fresh fruit and vegetables. A lack of vitamin C in the diet results in the defective formation of collagen and connective tissues, which can lead to bruising, bleeding gums, loose teeth, joint pain and impaired wound healing.

Research in Australia

The high level of use by Australians is resulting in complementary medicines becoming an important subject amongst primary health care professionals and policy makers.

Australia has world class academic and research bodies, including two five-star Australian Research Council recognised institutions, the National Institute of Complementary Medicines and the Australian Research Centre in Complementary and Integrative Medicine. Australia also boasts exceptional research centres outside of the university sector, such as Endeavour College of Natural Health and Blackmores Institute.

There is a long history of engagement between philanthropic organisations, industry and universities in medical discovery and knowledge building. In fact, a recent study from the USA’s John Hopkins University found that drug companies and device makers contribute six times more to clinical research than the US National Institutes of Health.

Partnerships between private organisations and universities are a longstanding and necessary part of research – Australian taxpayers cannot and should not be required to fund all research.

As noted in the Australian 2013 McKeon *Strategic Review of Health and Medical Research*, private research funding from industry and philanthropic sources has always been an important contributor to health and medical research. Effective health and medical research depends upon industry and philanthropic funding, with most medical research institutes accounting for 30 per cent or more of their funding sources from private funding.

A recent study by the National Institute of Complementary Medicine (NICM) showed that Australia has 160 lead investigators working on 295 complementary medicine research projects, and over \$30 million is being invested in research. Despite these figures, NICM also found that while Australia's use of complementary medicines is increasing, investment in complementary medicines research has been decreasing. Less than one per cent of National Health and Medical Research Council (NHMRC) funds have been allocated to complementary medicine research over the last decade. In this context, there is a need to encourage industry support of the research effort in Australia.

CM Manufacturing in Australia

In Australia, complementary medicines must be manufactured under pharmaceutical-standard Good Manufacturing Practice (GMP) in TGA approved and licensed facilities.

Our industry operates within one of the most tightly regulated systems in the world, where products are manufactured to a pharmaceutical standard under Good Manufacturing Practice (GMP), and strict safety and quality regulations are enforced. In fact, the Australian regulatory regime for complementary medicines is such that it is viewed by most countries as the consumer protection benchmark.

Before they are marketed in Australia listed complementary medicines must:

- only include low risk ingredients which have been evaluated for safety and quality;
- only carry low level indications for therapeutic use that are limited to self-limiting, non-serious conditions;
- have all active ingredients in the product tested and verified as raw materials before the product is manufactured;
- have every batch of final product tested to ensure that what is in the product is what is on the label;
- have ongoing stability trials so that the finished product is tested to demonstrate that it remains potent and safe for the entire shelf life of the product;
- have a product quality review conducted – this tracks the quality of the product over time and allows sponsors to identify and act on any issues arising over time; and
- have any serious adverse events monitored by the TGA so that any trends emerging with the use of specific complementary medicines can be identified and action taken quickly.

The manufacture of complementary medicines under a pharmaceutical standard raises unique challenges. As discussed above, because a complementary medicine may contain 30 or more ingredients in a complex formulation, it means that the evidence is best generated using the

raw materials rather than the finished product. The development and validation of testing techniques for chemically complex herbal medicines can also be very difficult.

In comparable countries, such as the UK, USA and NZ, the manufacturing standards for similar products are considerably lower, with many treated as supplemented food and manufactured accordingly. With the cost burden of pharmaceutical standards, scientific trials and regulatory fees, it is not surprising that one of the biggest risks to the Australian industry competitiveness is our level of over-regulation.

IP Protection

For many complementary medicines, their individual ingredients have traditional medicinal uses and are already in the public domain. This means that one of the major barriers for business to invest in clinical trials as there is a lack of data protection and/or market exclusivity.

As a result, sponsors who undertake research to support their products are currently not provided with any form of protection. A competitor may be able to make similar claims about their product without incurring the expense of research. This has led to sponsors typically relying on research conducted elsewhere, or a history of traditional use, in the sale and distribution of complementary medicines in Australia. This has also resulted in very little Australian innovation in this area, despite extensive potential and opportunities for new product development.

The 2015 Expert Panel's *Report on the Regulatory Frameworks for Complementary Medicines and Advertising of Therapeutic Goods* recommended that the Australian Government gives consideration to improving the competitiveness of the Australian complementary medicines industry by providing incentives for innovation, noting the cross government responsibility for innovation policy. Whilst this aligns with the National Innovation and Science Agenda, the Panel did not propose specific recommendations in favour of any particular mechanism to protect innovation.

Implementing formal IP protection mechanisms to incentivise innovation within the regulatory framework is likely to provide the greatest reward for investment in research and development. CMA would like to acknowledge the work that is being conducted by the TGA to provide greater regulatory incentives for greater investment in clinical investigations by the complementary medicines sector.

“I see orthodox medicine like a high-performance motorcar. You get from A to B very quickly but with the potential of crashing and killing yourself if you are not careful, whereas, complementary medicine in my view is like a bicycle. It will get you from A to B much slower but you also get some exercise along the way. Clearly the rules for the high-performance motor have to be completely different than the rules for the bicycle.”

Cardiologist Dr Ross Walker^{xxiii}

Complementary Medicines Australia

Complementary Medicines Australia (CMA) is the peak industry body for the complementary medicines industry, representing members across the supply chain, including manufacturers, importers, exporters, raw material suppliers, wholesalers, distributors and retailers. CMA promotes appropriate industry regulation and advancement to ensure consumers have access to complementary medicines of the highest quality.

Regulated in Australia as medicines under the Therapeutic Goods Act 1989, complementary medicines include vitamins, mineral and nutritional supplements, homeopathic, aromatherapy products and herbal medicines (unless specifically exempt). The term ‘complementary medicines’ also comprises traditional medicines, including traditional Chinese medicines, Ayurvedic, Australian Indigenous and Western herbal medicines. Traditional and long-term use is taken into account in establishing safety as a medicine. Other natural healthcare products may be regulated as foods, such as functional foods and special purpose foods, or as cosmetics, such as natural cosmetics that use herbals and botanicals.

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