

Current Research and Clinical Applications

Chinese Herbal Formula (PHY906) for Modulation of Chemotherapeutic Agents in Cancer Therapy

Ye Shen PhD
RMIT University

BACKGROUND

Cancer has been one of the leading causes of death for the past ten years in Australia.¹ Side-effects from the approved chemotherapeutics for treating cancer, including 5-fluorouracil (5-FU), capecitabine, CPT-11 (irinotecan), oxaliplatin, cetuximab and bevacizumab, not only prevent a patient from receiving the most effective therapeutic dose, but also significantly impact on the quality of a patient's life.

METHODS AND RESULTS

Using modern technologies, PhytoCeutica Inc. and a research team from Yale University developed a Chinese formula (PHY906) containing four traditional Chinese herbs: *Huangqin* (*Scutellaria baicalensis*), *Gancao* (*Glycyrrhiza uralensis*), *Dazao* (*Ziziphus jujube*) and *Shaoyao* (*Paeonia lactiflora*) in the ratio of 3:2:2:2.² The candidate herbs are traditionally used for the management of gastrointestinal ailments including diarrhoea, nausea and vomiting, which are common side-effects of chemotherapies. Their studies have been recently featured in a few major Australian newspapers.

The pre-clinical results demonstrated that in a mice cancer model, PHY906 increased the antitumor activity of the chemotherapy agents, as well as decreased weight loss of the animal. Based on evidence from the pharmacodynamic and pharmacokinetic studies, the research team elucidated that the potential mechanisms of actions of PHY906 may include (1) enhancement of cellular uptake of chemotherapeutic agent via inhibition

of multi-drug resistance mechanisms; (2) modulation of nuclear factor- κ B, cyclooxygenase-2 and inducible nitric oxide synthase activity; (3) inhibition of matrix metalloproteinase activity; and (4) inhibition of angiogenesis.³

With the compelling outcomes from the laboratory studies, PhytoCeutica is working closely with the US Food and Drug Administration through various clinical phases. Since the New Drug Application filed in 2001, two clinical trials (Phase I/II) in colorectal and primary liver cancers have been initiated.^{4,5} A phase I/IIA double-blind, randomised, placebo-controlled, cross-over, dose escalation clinical study of PHY906 as a modulator of irinotecan-based chemotherapy with advanced colorectal cancer has been carried out.⁶ Pharmacokinetic analysis indicated that PHY906 neither altered significantly the therapeutic effects of the CPT-11 nor its active SN-38 metabolite. In addition, the group receiving PHY and chemotherapies experienced significantly less diarrhoea and vomiting than those receiving chemotherapy alone. A second phase I/II clinical study evaluating the effect of PHY906 on the enhancement of the therapeutic efficacy of capecitabine chemotherapy in patients with advanced unresectable hepatocellular carcinoma was launched between 2003 and 2007. The outcomes suggest that PHY906 can increase the therapeutic index of capecitabine by reducing side-effects such as diarrhoea. In addition, four phase II trials are upcoming.

CONCLUSION

PHY906 not only meets the rigorous quality-control standards, but also has been shown in preclinical and clinical studies to have the dual effects of reducing the side-effects of chemotherapy as well as potentiating its antitumor actions. The company is actively pursuing FDA approval for PHY906 to become a botanical prescription medicine for treating serious, life-threatening diseases as an adjunct therapy.

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Cost Effectiveness of Complementary Medicines: Report by Access Economics for the National Institute of Complementary Medicine, August 2010

Johannah Shergis BAppSc
RMIT University

BACKGROUND

There is a growing body of scientific evidence supporting the efficacy and safety of complementary medicines. With Australians spending over \$3.5 billion each year on complementary medicines and therapies, evaluation of costs will assist in future directions for disease management and healthcare.

METHODS

The National Institute of Complementary Medicine (NICM) commissioned Access Economics to analyse the cost effectiveness of select complementary medicine interventions for some of the most common and costly chronic health concerns. Due to the varying heterogeneous modalities that the complementary medicine umbrella represents, the report focused on those interventions selected by a reference group 'where a reasonable body of evidence for safety and efficacy was available', reporting on five key areas:

1. Acupuncture for chronic low back pain;
2. St John's wort for depression;
3. Fish oils for prevention of heart disease among those who have experienced myocardial infarction;
4. Fish oils for rheumatoid arthritis; and
5. Phytodolor (a proprietary herbal anti-inflammatory and analgesic) for osteoarthritis.

Access Economics is one of Australia's leading economic forecasting consultancy firms. They presented a highly detailed report using a number of benchmarks to determine cost effectiveness of the selected complementary medicines. These included gross domestic product (GDP) per capita per quality adjusted life year (QALY) and disability adjusted life year (DALY), and reference points in

line with the Department of Health and Ageing and the Department of Finance and Deregulation.

The report included direct health costs only; indirect costs such as productivity losses were excluded. The literature was comprehensively reviewed to identify the effectiveness of complementary medicine therapies compared with usual treatment, best-practice standard care or placebo, with a preference for double-blind randomised controlled trials. To evaluate cost effectiveness, the economic analysis brought together relative expenditure (costs) with outcome measures (effects).

RESULTS

ACUPUNCTURE for chronic low back pain used as an adjunct therapy to standard care significantly increases pain outcomes and overall cost effectiveness of treatment when compared with standard care alone. In individuals with co-morbid depression, an even greater cost benefit would be seen. If indirect costs, e.g. absenteeism from work and reduced work effectiveness, were factored in, the true cost benefits from acupuncture could be up to double the estimated value.

ST JOHN'S WORT for mild to moderate depression, compared with standard treatment was shown to be cost effective. It could potentially save up to \$50 million per annum across the affected population in Australia.

FISH OILS were found to be highly cost effective for prevention of heart disease among those who have experienced a myocardial infarction, and as an intervention to prevent future cardiovascular mortality in Australia.

FISH OILS FOR RHEUMATOID ARTHRITIS as adjunctive therapy were compared with routine care alone. Studies indicated fish oils could reduce patient reliance on non steroidal anti-inflammatory drugs (NSAIDs) without deleterious change in the disease process. From the evidence, fish oils were not considered to be cost effective.

PHYTODOLOR (a proprietary herbal medicine) FOR OSTEOARTHRITIS was compared with Diclofenac (an NSAID). Limited quality evidence was available on the safety and efficacy of Phytodolor. Cost of product was therefore the major determinant of cost effectiveness. It was estimated that using Phytodolor could have a potential cost-saving of up to \$178 million per annum compared with Diclofenac; however, the report encourages more research in this area.

CONCLUSION

The report provides evidence of cost effectiveness in four out of the five evaluated interventions. Except fish oils for rheumatoid arthritis, the report highlights that complementary medicines could save millions in healthcare without compromising on patient outcomes, with added promise if indirect costs are added on.

The report fosters the idea of ongoing research and sets up discussion for complementary medicines in an integrated healthcare practice environment. This report will be an essential tool for assisting governments and researchers to further evaluate the role of complementary medicines in future clinical investigations.

<http://www.nicm.edu.au/content/view/159/276/>